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EDITORIAL

This abstract supplement unites *SLEEP* and the science of the SLEEP 2009 23rd Annual Meeting of the Associated Professional Sleep Societies, LLC (APSS) in a convenient format. All abstracts presented at SLEEP 2009 held June 6-11, 2009, in Seattle, Washington are included in this special issue.

The abstract supplement provides all Sleep Research Society and American Academy of Sleep Medicine members, including those unable to attend the meeting, a glimpse into the new ideas and latest research taking place in the field of sleep.

This year, there was a 12 percent increase in the number of abstracts submitted for SLEEP 2009; a record number – 1,307 – abstracts will be presented at the meeting. 148 will be presented in an oral presentation format, and the remainder will be presented in a poster format. Similar to prior meetings, the Program Committee elected to:

1) Group posters into thematic groups.
2) Display each poster on one of the three scheduled poster days (June 8, 9 and 10).

The poster sessions will continue to be two hours in length to allow attendees greater opportunity to view posters and interact with presenters. Each poster has a unique four-digit number and is assigned to one of the 19 categories listed below to facilitate identification and location.

Category A – Neuroscience
Category B – Physiology/Phylogeny/Ontogeny
Category C – Pharmacology
Category D – Circadian Rhythms
Category E – Pediatrics
Category F – Aging
Category G – Sleep Deprivation
Category H – Sleep Disorders – Breathing
Category I – Sleep Disorders – Narcolepsy/Hypersomnia
Category J – Sleep Disorders – Insomnia
Category K – Sleep Disorders – Parasomnias
Category L – Sleep Disorders – Movement Disorders
Category M – Sleep Disorders – Neurologic Disorders
Category N – Sleep in Medical Disorders
Category O – Sleep in Psychiatric Disorders
Category P – Instrumentation & Methodology
Category Q – Healthcare Services, Research & Education
Category R – Molecular Biology & Genetics
Category S – Behavior, Cognition & Dreams

SLEEP 2009 fosters an environment in which members and attendees obtain education on the latest basic science, clinical science and technologies, which will further promote the continued growth of the field through the dissemination of new knowledge. We look forward to sharing in the success of this pivotal event.

David F. Dinges, PhD
Editor-in-Chief

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0001

THE SEDATING ANTIDEPRESSANT TRAZODONE IMPAIRS SLEEP-DEPENDENT CORTICAL PLASTICITY

Aton S, Seibt J, Dumoulin M, Coleman T, Shiraishi M, Frank MG
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Introduction: The effects of hypnotics on synaptic mechanisms underlying sleep-dependent learning and memory consolidation are largely unknown. We assessed the effects of commonly-prescribed medications for the treatment of insomnia in a canonical model of sleep-dependent, in vivo synaptic plasticity in the primary visual cortex (V1) known as ocular dominance plasticity.
Methods: After a 6-h baseline period of sleep/wake polysomnographic recording, cats underwent 6 h of continuous waking combined with monocular deprivation (MD) to trigger synaptic remodeling. Cats subsequently received an i.p. injection of either vehicle, trazodone (10 mg/kg), zaleplon (10 mg/kg), or eszopiclone (1-10 mg/kg), and were allowed an 8-h period of post-MD sleep before ocular dominance plasticity was assessed.
Results: We found that while zaleplon and eszopiclone had profound effects on sleeping cortical electroencephalographic (EEG) activity, only trazodone (which did not alter EEG activity) significantly impaired sleep-dependent consolidation of ocular dominance plasticity. This was associated with deficits in both the normal depression of V1 neuronal responses to deprived-eye stimulation, and potentiation of responses to non-deprived eye stimulation, which accompany ocular dominance plasticity.
Conclusion: Taken together, our data suggest that the monoamine receptors targeted by trazodone play an important role in sleep-dependent consolidation of synaptic plasticity. They also demonstrate that changes in sleep architecture are not necessarily reliable predictors of how hypnotics affect sleep-dependent neural functions.
Support (optional): This work was supported by the University of Pennsylvania, Sepracor Pharmaceuticals, Pickwick postdoctoral fellowships from the National Sleep Foundation (to S.J.A. and J.S.), and a National Research Service Award from the National Eye Institute (to S.J.A.).

0002

BLOCKADE OF OREXIN-1 RECEPTORS ATTENUATES OREXIN-2 RECEPTOR ANTAGONISM INDUCED SLEEP PROMOTION IN THE RAT

Dugovic C, Shelton J, Aluisio L, Fraser I, Sutton S, Pascal B, Yun S, Li X, Dvorak C, Lovenberg T
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Introduction: Orexins are peptides produced by lateral hypothalamic neurons that exert a prominent role in the maintenance of wakefulness by activating orexin-1 (OX1R) and orexin-2 (OX2R) receptors located in wake-active structures. Pharmacological blockade of both receptors by the dual OX1/2R antagonist almorexant has been shown to promote sleep in animals and humans during their active period. However, the distinct distribution of OX1R and OX2R in neurotransmitter systems may result in a differential impact of these receptors in sleep-wake modulation. The respective role of OX1R and OX2R on sleep in correlation with monoamine release was evaluated in rats treated with selective antagonists alone or in combination.
Methods: Sleep experiments were performed in rats implanted with telemetric devices for recording of EEG/EMG signals, locomotor activity and body temperature. Microdialysis studies were conducted in freely moving rats implanted with a guide cannula either in the lateral hypothalamus for histamine levels (LC/MS/MS) or the prefrontal cortex for dopamine, 5-HT and NE levels (HPLC-ECD) measurements. Separate groups of animals received selective antagonists at OX1R (SB-408124, 30 mg/kg) or OX2R (JNJ-10397049, 0.3-30 mg/kg), or the dual OX1/2R antagonist almorexant (30 mg/kg) sc either at two hours into the light phase or at dark onset.
Results: When administered in either phase of the light-dark cycle, the OX2R antagonist JNJ-10397049 decreased the latency for persistent sleep and increased NREM and REM sleep time. Almorexant produced less hypnotic activity whereas the OX1R antagonist SB-405124 had no effect. Microdialysis studies showed that JNJ-10397049 and almorexant decreased extracellular histamine concentration in the lateral hypothalamus whereas both almorexant and SB-405124 increased dopamine release in the prefrontal cortex. Finally, administration of SB-405124 in combination with JNJ-10397049 greatly attenuated the sleep- promoting effects of the selective OX2R antagonist.
Conclusion: These results indicate that blockade of OX2R is sufficient to initiate and prolong sleep, consistent with the hypothesis of a deactivation of the histaminergic system. In addition, it is suggested that simultaneous inhibition of OX1R attenuates the sleep-promoting effects mediated by selective OX2R blockade, possibly correlated with dopaminergic neurotransmission.

0003

MODULATION OF FMRI ASSESSED BRAIN RESPONSES TO BLUE AND GREEN LIGHT BY SLEEP HOMEOSTASIS, CIRCADIAN PHASE AND PER3 POLYMORPHISM

Vandewalle G[1], Archer SN[2], Wuillaume C[1], Balteau E[1], Degueldre C[1], Luxen A[1], Dijk D[2], Maquet P[1]
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Introduction: Light elicits numerous physiological and behavioural non-visual responses, such as acute effects on attention and arousal, and long term regulation of sleep/wake cycles. These responses are mediated by the recently discovered melanopsin-dependent and the classical photoreception systems. We have previously investigated non-visual effects of light on various brain functions as assessed by fMRI and PET and identified some of the areas and pathways mediating these effects during either the day or night. Recent data in nocturnal rodents suggest that the non-visual effects of light on sleep propensity are modulated by both circadian phase and homeostatic sleep pressure. We used a genetic marker (VNTR polymorphism in PER3) for inter-individual differences in the build up of homeostatic sleep pressure and the negative effects of sleep loss on performance and brain activity to further investigate these interactions in humans.
Methods: Fifteen PER3 4/4 (7F; 24.13 ± 0.95 y.o.) and 12 PER3 5/5 (5F; 24.17 ± 1.17 y.o.) healthy individuals were recruited solely on the basis of their PER3 genotype. Brain responses to an auditory 3-back working memory task were recorded in 4 fMRI sessions during 2 separate visits. In each visit, they were recorded in the evening and the following morning. In one visit subjects slept in the laboratory between both sessions, while in the other, they remained awake (25.5h sleep deprivation). Sleep deprivation (SD) and sleep visits were counterbalanced within and between genotypes. In each session, participants were exposed to alternating 60s blue (473nm) and green (527nm) monochromatic light exposures. Irradiance levels of half of the illuminations were set at 7x10^12 ph/cm^2/s, the other half at 3x10^13 ph/cm^2/s. Orders of irradiances and wavelengths were counter-balanced.
Results: In PER3 4/4 individuals, non-visual (i.e. blue > green light) modulation of brain activity by light in the morning declined from after sleep to after SD in the bilateral parietal cortex, and in two right prefrontal cortex areas involved in contextual and episodic control of behavior. This decline was already detected in the right parietal cortex in the evening before SD. In PER3 5/5 no significant changes in non-visual modulation of brain activity by light was detected.
Conclusion: The data suggest that non-visual responses to light are modulated by sleep homeostasis, circadian phase and PER3 polymorphism.
Support (optional): FNRS, FMRE, ULg, Wellcome Trust, BBSRC.

0004

SELECTIVE REM SLEEP DEPRIVATION OF THE NORTHERN FUR SEAL ON LAND

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Introduction: Fur seals display two patterns of sleep: bilaterally symmetrical slow wave sleep (SWS) with episodes of rapid eye movement (REM) sleep lasting up to 15 min when on land (as in terrestrial mammals) and SWS with striking interhemispheric EEG asymmetry and a very low amount of REM sleep while in water (as in cetaceans). In this study we deprived fur seals of REM sleep while on land and examined the effects of REM sleep deprivation on the pattern of SWS.
Methods: Four northern fur seals (*Callorhinus ursinus*) kept on land were sleep deprived (SD) of REM sleep for 3 consecutive days, followed by two recovery days. SWS and REM sleep were scored visually and EEG asymmetry was evaluated by the difference in slow wave power (1.2-4.0 Hz) between the two hemispheres.
Results: SD significantly reduced the percentage of REM sleep (one way ANOVA, $p<0.001$; on average from $3.2\pm0.8\%$ of 24-h during baseline to $0.5\pm0.1\%$ during SD; n=4; 18% of baseline) while the percentage of SWS did not change ($18.5\pm3.8\%$ and $18.4\pm3.4\%$, respectively). In all seals the number of REM sleep interruptions on SD day 3 was greater (on average 64 ± 9) than on day 1 (39 ± 7). In two of the four seals this number rose progressively across 3 consecutive days. In all 4 seals REM sleep increased on the first recovery day on average to $4.9\pm1.0\%$ of 24-h (159% of baseline). The amount of recovered REM sleep did not correlate with the amount of REM sleep lost during SD. The percentage of asymmetrical SWS during baseline, SD and recovery varied between 22 and 86% of SWS in different seals ($p=0.2$).
Conclusion: Although seals display a greatly reduced amount of REM sleep when in water for several weeks, they do show a drive for REM sleep and rebound when deprived while sleeping on land.
Support (optional): The research was supported by NSF, The VA Medical Service and by Utrish Dolphinarium Ltd.

0005

GABAB-MEDIATED INHIBITION PLAYS A CRITICAL ROLE IN MEDIATING REM SLEEP ATONIA

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Introduction: Skeletal muscle tone is potently suppressed during REM sleep. We recently found that REM sleep atonia could not be prevented in masseter muscles by blockade of glycine and GABAA receptors at the trigeminal motor pool. REM atonia persisted even when glycine- and GABAA-mediated inhibition was blocked and high doses of AMPA were simultaneously applied. Accordingly, we concluded that REM atonia is triggered by an unidentified inhibitory mechanism(s). Although GABAB receptors are present on somatic motoneurons and postsynaptically inhibit them, the role of these receptors in mediating REM atonia is unknown. The aim of this study was to determine if GABAB receptors play a role in suppressing muscle tone during REM sleep.
Methods: Rats (n=6) were implanted with microdialysis probes in the trigeminal motor pool for application of candidate drugs across the sleep-wake cycle. GABAB receptors were antagonized on trigeminal motoneurons (via CGP52432) and the resulting effects on masseter EMG tone were determined.
Results: We found that GABAB receptor blockade at the trigeminal motor pool increased masseter tone during waking and NREM sleep, but had no effect on REM atonia. However, when GABAB receptors as well as both GABAA and glycine receptors were simultaneously blocked (via 0.2mM CGP52432, 0.1mM bicuculline, and 0.1mM strychnine), this not only increased masseter muscle tone during waking and NREM sleep ($p<0.001$ for both states), it also triggered a robust increase in basal muscle tone during REM sleep ($p=0.024$).
Conclusion: We show for the first time that an endogenous GABAB drive inhibits motoneurons and suppresses masseter tone during both waking and sleep. While GABAB-mediated inhibition itself does not trigger REM sleep atonia, blockade of GABAB as well as GABAA and glycine receptors is capable overriding REM atonia, indicating that GABAB receptors play a critical role in mediating this motor phenomenon.

0006

UNIQUE NEURONAL PRODUCTION OF INDUCIBLE NITRIC OXIDE SYNTHASE AND NITRIC OXIDE IN THE BASAL FOREBRAIN AS A MECHANISM OF HOMEOSTATIC SLEEP CONTROL

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Introduction: Sleep deprivation (SD)-induced increase in nitric oxide (NO) production in the basal forebrain (BF) is essential for recovery sleep (Kalinchuk et al., J Neurochem., 2006). SD-induced NO increase is, at least partially, mediated by inducible nitric oxide synthase (iNOS) (Kalinchuk et al., Eur J Neurosci., 2006). Our next goal was to elucidate the cellular source of SD-induced iNOS/NO production. Towards that, we developed a new method, which allows detection of in vivo NO production using the fluorescent indicator 4,5-diaminofluorescein diacetate (DAF-2/DA). iNOS production was detected immunohistochemically.
Methods: Male Wistar rats were chronically implanted with ICV microdialysis cannulae and electrodes for EEG/EMG recording. SD group animals were sleep-deprived for 6h. To decrease basal NO level, selective neuronal NOS (nNOS) inhibitor (N-omega-propyl-L-arginine, L-NPA) was infused during SD. Before the end of SD, rats were infused with DAF-2/DA and then euthanized together with undisturbed controls who also received L-NPA and DAF-2/DA. Brains were collected for immunihistochemistry and double-/triple-labeling with antibody markers specific for neurons (neuron-specific nuclear protein, NeuN), astrocytes (glial fibrillary acidic protein, GFAP), cholinergic neurons (acetylcholinetransferase, ChAT) and iNOS.
Results: SD induced abundant DAF+ staining in the BF area with an intensity 4-fold higher than in control group. SD-induced DAF+ staining was co-localized with NeuN but not with GFAP. The majority of DAF+ cells in SD group were iNOS+. The SD group had dramatic increases in both the number of iNOS+ cells and the intensity of iNOS+ staining in the BF (4- and 5-fold respectively). SD-induced iNOS production was observed in 93% of the BF cholinergic neurons and some non-cholinergic neurons. Finally, the increase in intensity of iNOS+ staining during SD positively correlated with an increase in EEG theta power, a marker of sleep propensity during wake ($r=0.963$, $p<0.001$).
Conclusion: Our data show that SD-induced iNOS production followed by NO release is a unique mechanism of homeostatic sleep control which is triggered by SD in the BF cholinergic and probably other wake-active neurons.
Support (optional): VA Merit Award (RB), NIMH Grant MH 39683

0007

USE-DEPENDENT PLASTICITY IN DROSOPHILA CLOCK NEURONS REGULATES SLEEP NEED

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Introduction: Sleep is important for memory consolidation and is responsive to waking experience. Unfortunately the underlying mechanisms are unknown. The circadian clock regulates sleep and influences memory. Thus, clock circuitry is uniquely positioned to coordinate interactions between processes underlying memory and sleep-need. Here we examine whether plasticity in core circadian clock circuitry is involved in the consolidation of long-term memory and in regulation of sleep after social experience.
Methods: Flies were housed in socially isolated (n=1) or socially enriched (n=35-45) enclosures for five days and subsequent sleep was measured using Drosophila Activity Monitors. Long-term memory was examined using a courtship conditioning assay.
Results: Flies mutant for the adenylyl cyclase rutabaga (rut), the clock gene period (per), and the Drosophila homologue of Serum Response Factor, blistered (bs), are deficient for experience-dependent increases in sleep. Rescue of each of these genes within the Pigment Dispersing Factor (pdf)-expressing ventral lateral neurons (LNVs) restores increased sleep following social enrichment. Rescue of wild-type bs or per within the LNVs restores long-term memory after Courtship Conditioning. Social experiences that induce increased sleep are associated with an increase in the number of synaptic terminals in the LNV projections into the medulla. Moreover, the number of synaptic terminals is reduced during sleep and this decline is prevented by sleep deprivation.
Conclusion: These results are consistent with the hypothesis that the function of sleep is for synaptic down-scaling and demonstrates that the clock plays a fundamental role in plasticity and sleep.

0008

LOCAL CORTICAL ADMINISTRATION OF A GHRH ANTAGONIST SURPRESSES EEG DELTA WAVE POWER DURING NREMS

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Introduction: Growth hormone releasing hormone (GHRH) is a sleep regulatory substance involved in the regulation of non-rapid eye movement sleep (NREMS). The hypothalamus is a well-characterized sleep-promoting site of action for GHRH. However, GHRH also plays a role in the cortex; application of GHRH to the surface of the cortex changes electroencephalogram (EEG) delta power, a measure of the NREMS intensity. GHRH and the GHRH receptor (GHRHR) and their mRNAs are detectable in the rat cortex and the expression of cortical GHRHR is activity-dependent. Here we microinject a GHRH antagonist unilaterally onto the surface of somatosensory cortex of the rat brain. We posited that if GHRH normally influenced EEG delta power during NREMS, then the antagonist would alter this sleep phenotype.
Methods: Rats (Sprague Dawley; 300-330 gm kept at 24oC on a 12:12 h L/D cycle) were provided two cortical EEG electrodes over the somatosensory cortex on each side of the brain and one EMG electrode in neck muscle. Two guide cannulae for injections were implanted with their tips positioned under the EEG electrodes between the surface of the somatosensory cortex and the dura. One side of the brain received an injection of 5 nmol GHRH antagonist (Bachem; H-4884.0500) and the other side received an injection of vehicle as control. After injections EEG and EMG were recorded for 23 hours; records were scored for sleep by standard criteria.
Results: Unilateral application of the GHRH antagonist decreased EEG delta wave power during NREMS ($p<0.01$), but not during wakefulness, during the initial 40 min after injection. Insufficient REMS epochs occurred during this 40 min period to allow power analyses during REMS.
Conclusion: The results suggest that endogenous cortical GHRH has a role in the regulation of state-dependent localized EEG delta power.
Support (optional): NIH NS27250

0009

REPORTED SLEEP DURATION AND HIPPOCAMPAL GREY MATTER VOLUME IN HEALTHY WOMEN

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Introduction: Experimental studies have shown that sleep affects brain structure and function. In a recent observational study, Riemann and colleagues (Riemann et al., 2007; Sleep, 30:955-8) reported that, compared to good sleeper controls, patients with chronic insomnia showed bilateral reductions in MRI-measured hippocampal volume. In the present study, we hypothesized that short sleep duration in healthy adults without insomnia would similarly be associated with decreased hippocampal grey matter volume.
Methods: Study participants were 50 post-menopausal women enrolled in the Healthy Women's Study (mean age = 68 + 1) (Matthews et al., 1989; N Engl J Med, 321, 641-6). Eligibility criteria for the imaging protocol required that participants were all in good health (e.g., no history of cerebrovascular disease, diabetes, cancer, neurological or psychiatric disorders or use of anti-hypertensive, psychotropic or glucoregulatory medication), without contraindications for MRI. Participants completed a daily sleep diary (Monk et al., 1994; J Sleep Res; 3: 111-120) over the 7-day period immediately preceding the MRI. These data were used to derive estimates of habitual sleep duration. Brain volumetric measures included total grey matter and semiquantitative visual ratings of diffuse brain abnormalities (white matter hyperintensities, ventricular enlargement and subcortical brain infarcts).
Results: A two-step hierarchical regression model was used to evaluate cross-sectional relationships among sleep duration and hippocampal volume after adjusting for selected covariates known to affects sleep and/or brain structure. In Step 1 of the model, HRT status, smoking, alcohol consumption, white matter hyperintensities and total grey matter volume explained 46% of the variance in hippocampal volume, with total grey matter volume being a significant predictor (beta=0.61, $p<.0001$). In Step 2, sleep duration explained an additional 8.5% of the variance in hippocampal volume (beta=0.33, $p=.012$).
Conclusion: Results extend previous work on sleep loss, insomnia and the brain by demonstrating that short sleep duration is associated with smaller hippocampal volume in healthy post-menopausal women after adjusting for other factors important to brain structure.
Support (optional): These data were collected and analyzed with support from the Pittsburgh Mind-Body Center (HL076852) and the Neuroscience-Clinical and Translational Research Center (RR024153).

0010

IS OROFACIAL PAIN PRESENT IN ANIMAL MODEL OF PERIODONTAL DISEASE?

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Introduction: Periodontal disease (PD) is a common chronic inflammatory condition. Periodontitis is characterized by the interaction between

the immune system and pain in the trigeminal nuclei, with several outcomes such as sleep disturbances. Objective: The present study examined the effects of an animal model of PD on sleep architecture.
Methods: Male Wistar rats were implanted electrodes that enabled the recording of their electrocorticogram (ECoG) and electromyogram (EMG). Male rats were assigned randomly in two groups: control (n=8, non-ligated sites) and PD (n=8). In PD group, both mandibular first molars of each animal received cotton ligatures in the dental-gingival area to induce experimental periodontitis. Control group were submitted to a sham procedure. After these procedures, sleep recordings were monitored for 28 days. The electrophysiological signals were collected by a digital polygraph, and the recorded sleep stages were classified as wake, non-REM sleep, and REM sleep.
Results: Subsequent to the ligature-induced PD, the rats presented a significant reduction in sleep efficiency and in total non-REM sleep time as well as an increase in the number of arousal events from day 7 to 28 in comparison to the control group during the light phase (period that rats sleep most). In the dark period, rats also had lower sleep efficiency (day 7 to 28). REM sleep was only affected at the end of the experimental period (day 21-28).
Conclusion: Our results suggest that PD resulted in marked sleep disruption, especially in non-REM sleep, probably due to the development of orofacial pain.
Support (optional): This work was supported by grants from AFIP, CNPq and FAPESP (07/56620-6 and CEPID #98/14303-3).

0011

GABA LEVELS IN CAT PONTINE RETICULAR FORMATION (PRF) ARE LOWER DURING RAPID EYE MOVEMENT (REM) SLEEP AND THE NEOSTIGMINE-INDUCED REM SLEEP-LIKE STATE (REM-NEO) THAN DURING WAKEFULNESS

Vanini G, Wathen BL, Lydic R, Baghdoyan HA
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Introduction: Many lines of evidence support the conclusion that an increase in PRF GABAergic transmission promotes wakefulness whereas a reduction in PRF GABA decreases wakefulness and increases REM sleep (J Neurophysiol 82:2015, 1999; ibid 90:938, 2003; Sleep 31:453, 2008). Based on predictions from these data, the present study tested the hypothesis that endogenous GABA levels in cat PRF are greatest during wakefulness, intermediate during non-REM (NREM) sleep, and lowest during REM sleep.
Methods: Adult male cats (n=6) implanted with electrodes for scoring sleep/wake states were conditioned to sleep in a head-restrained position. A microdialysis probe stereotaxically aimed for the PRF was continuously perfused with Ringer's. Dialysis samples were collected during wakefulness, NREM sleep, REM sleep, and REM-Neo induced by pontine microinjection of neostigmine (6µg/0.25µl). At the end of each microdialysis experiment, fluorescent microspheres were injected into the dialysis site for histological localization. Measures of GABA levels in the PRF (pmol/10µl) across states of arousal were quantified by HPLC-ECD as previously described (Anesthesiology 109:978, 2008).
Results: PRF GABA levels varied significantly ($p<0.0001$) as a function of arousal state. GABA levels during wakefulness (n=195 dialysis samples) were significantly ($p=0.0002$) greater than during REM sleep (n=34) and REM-Neo (n=47). Relative to NREM sleep (n=120), GABA levels were significantly ($p=0.002$) lower during REM and REM-Neo. There was no difference in GABA levels between REM sleep and REM-Neo.
Conclusion: These direct measures of PRF GABA support the hypothesis that endogenous PRF GABA modulates states of wakefulness and REM sleep.
Support (optional): National Institutes of Health grants MH45361, HL40881, and the Department of Anesthesiology.

0012

HYPOCRETIN INDUCES EITHER ACTIVE (REM) SLEEP OR WAKEFULNESS DEPENDING ON THE STATE OF THE ANIMAL AT THE TIME OF ADMINISTRATION

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Introduction: We recently reported that the microinjection of hypoctretin-1 into the nucleus pontis oralis (NPO) induces a behavioral state that is comparable to naturally-occurring active sleep. However, other laboratories have found that comparable injections of hypocretin into the NPO result in extended periods of wakefulness. We hypothesized that these discrepant data might be due to the fact that hypocretin was administered during different behavioral states. Accordingly, we compared the behavioral responses of chronic, unanesthetized cats following the injection of hypoctretin-1 either during sleep or wakefulness.
Methods: Adult cats were prepared for monitoring behavioral states and for the administration of hypocretin into the NPO. Injections of hypocretin-1 (0.25 µl, 500 µM in saline) or control solutions of saline (0.25 µl) were carried out while the animals were either awake or during quiet (NREM) sleep. States of sleep and wakefulness were scored during the first hour following the administration of hypocretin or saline.
Results: When the animals were in a state of quiet sleep, the injection of hypocretin-1 into the NPO induced active sleep with a short latency. In addition, the percentage of time spent in active sleep significantly increased (60.2%). However, when the animals were awake, the administration of hypocretin-1 did not induce active sleep; instead, there was a significant increase in wakefulness (114.6%) and a significant decrease in active sleep (49.8%) and quiet sleep (75.8%).
Conclusion: These data support our hypothesis that hypocretin not only acts to promote ongoing states of wakefulness and their accompanying patterns of somatomotor activation, but that hypocretin is also responsible for producing active sleep and somatomotor inhibition that occurs during this state. Thus, the present results resolve previous "apparently" paradoxical findings by demonstrating that the state of the animal at the time of the injection of hypocretin determines whether active sleep or wakefulness is induced.
Support (optional): Research supported by USPHS grants MH43362.

0013

SLEEP DEPRIVATION AND SLEEP DISTURBANCE AGGRAVATE FOCAL CEREBRAL ISCHEMIA IN THE RAT

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Introduction: Sleep-wake disturbances are frequently observed in stroke patients and are linked with poorer function outcomes. Human and experimental data suggest a physiological role of sleep in neuronal recovery and neuroplasticity. The effect of sleep deprivation (SD) and sleep disturbance (SDis) on focal brain ischemia is unknown.
Methods: Focal cerebral ischemia was induced by coagulating the distal middle cerebral artery (MCA) in Sprague Dawley rats (n=44). 12 h after the ischemia surgery, sleep deprivation (SD) was carried out for 12 hours by gentle handling. In the SD experiment, 12h-SD was carried out once and in the SDis experiment for 3 consecutive days (n=6 for each groups). EEG was registered to evaluate vigilance states, infarct volumetry and TUNEL-positive cells were determined to assess brain damage, and the Taqman® PCR assay was for expression of several neuroplasticity-related genes, such as growth-promoting genes c-jun, gap43 and the growth-inhibiting gene neurocan. The plasma corticosterone level was determined by Radio Immuno Assay.
Results: Both SD and SDis significantly increased the infarct volume and number of tunnel-positive cells. Compared to the paired control groups, the infarct volume was increased by 41% in the SD (94.1±16.9 vs.66.5±18.2mm3, $p=0.022$) and 88% in the SDis group (74.6±40.9

vs.39.7±43.4mm3, p=0.023) respectively, and the number of TUNEL-positive cells was increased by 137% in the SD (46.8±15 vs.19.7±7.7/mm2, p<0.001) and 219% in the SDis group (32.9±13.2 vs.10.3±2.5/mm2, p=0.002), respectively. SDis also significantly increased by 134% the expression of neurocan (14.3±0.4 vs.6.2±0.1, p<0.001), an axonal extension inhibitory molecule, in the ipsilateral hemisphere to ischemia. Neither in the SD nor in the SDis experiment was the corticosterone level increased significantly.
Conclusion: Both SD and SDis aggravate ischemia-induced brain injury and SDis also alters expression of neuroplaticity-related genes. The impact of these changes on function recovery needs to be further investigated.

0014

ELECTROENCEPHALOGRAM (EEG) POWER DURING WAKEFULNESS AND RAPID EYE MOVEMENT (REM) SLEEP IS INCREASED BY MICROINJECTION OF THE $GABA_A$ RECEPTOR AGONIST MUSCIMOL INTO THE PONTINE RETICULAR NUCLEUS, ORAL PART (PNO) OF C57BL/6J (B6) MOUSE

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Introduction: The PnO plays an important role in generating the cortical EEG activation characterizing wakefulness and REM sleep (Anesthesiology 109:978, 2008). Microinjection of muscimol into B6 mouse PnO increases wakefulness (Soc Neuroscience Abst 631.5, 2007), but the effects of PnO muscimol on EEG power have not been quantified. The present study is testing the hypothesis that microinjection of muscimol into the PnO of B6 mouse alters EEG power during wakefulness.
Methods: Adult male B6 mice (n = 4) were each implanted with a microinjection guide tube stereotaxically aimed for the PnO, and with electrodes for recording EEG and electromyogram. Every mouse received randomized microinjections (50 nL) of muscimol (5.71 and 57.1 ng; 1 and 10 mM) and saline (vehicle control) followed by a 4 h recording. States of wakefulness, non-REM (NREM) sleep, and REM sleep were analyzed manually in 10 s bins. Fast Fourier Transform (FFT) analysis was used to identify dominant EEG waveform frequencies as previously described (Neuroscience 144:375, 2007). The data were evaluated by repeated measures two-way analysis of variance and post-hoc comparison of treatment at each frequency.
Results: Microinjection sites were histologically localized to the PnO. During wakefulness, muscimol (57.1 ng) significantly increased EEG power between 0.5-1.5 Hz and 2.5-4.5 Hz. During REM sleep, muscimol (5.71 ng) significantly increased EEG power between 7.5-9.5 Hz. There was no effect of muscimol on EEG power during NREM sleep.
Conclusion: Some clinically used GABAergic drugs can cause a dissociation between mental and behavioral states, and data from B6 mouse demonstrated that intraperitoneal (i.p.) muscimol administration increased EEG delta power during wakefulness (Neuroscience 147:833, 2007). The present findings show for the first time that the increase in EEG delta power caused by i.p. muscimol is mediated, at least in part, by $GABA_A$ receptors in the PnO.
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0015

ARMODAFINIL IMPROVES BRAIN ACTIVITY RELATED TO SENSORY MEMORY AND PRE-ATTENTIVE NOVELTY DETECTION IN PATIENTS WITH SHIFT WORK DISORDER

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Introduction: Although excessive sleepiness associated with shift work disorder (SWD) is improved by armodafinil the mechanisms of this enhanced alertness remain ill defined. This study evaluated the effect of armodafinil on specific brain regions involved in memory and attentional processes measured by event-related brain potentials (ERPs) in night shift workers with and without excessive sleepiness (i.e. SWD).
Methods: Otherwise healthy SWD patients (n=5) and matched control shift workers (n=6) were screened for other sleep disorders. For SWD patients, armodafinil (150 mg) or placebo was administered (2300) in a double-blind, cross-over design. ERP measures of sensory memory (MMN) and pre-attentive novelty detection (N1 and P3a) processes were collected during nocturnal completion of an oddball mismatch paradigm (2400-0100) and compared to shift worker controls with placebo administration only.
Results: Polysomnograms collected during habitual bed time (0900±1h to1500±1h), Epworth sleepiness scale, and insomnia severity index showed that SWD patients had more sleep wake signs and symptoms than controls. ERP MMN amplitude was lower over front-central brain regions in patients compared to controls (-0.5μV vs. -1.9μV at FCz; P<0.05). Following armodafinil administration the MMN amplitude in SWD patients increased from -0.5μV to -1.2μV (P<0.05) and was comparable to that seen in controls. Brain activity related to novelty detection evaluated by N1 also showed amplitude recovery following armodafinil administration (-0.1μV vs. -0.9μV P<0.06) among SWD subjects relative to controls (-0.8μV at Cz). The P3a ERP component did not show amplitude differences between placebo and armodafinil conditions in SWD patients or between SWD and controls.
Conclusion: This ongoing study shows a beneficial effect of armodafinil in SWD patients on specific brain regions involved in sensory memory and attentional processes related to frontal lobe functions. Improvements in these functions resulted in a return to control values in these functions.
Support (optional): Cephalon, Inc (USA)

0016

DEVELOPMENTAL CHANGES OF THE SLEEP EEG IN POST-PUBERTAL ADOLESCENTS

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Introduction: One of the most striking features of adolescent cortical development in humans is a marked decline in grey matter volume and cerebral blood glucose metabolism. These changes are thought to be due to synaptic pruning that occurs in the healthy adolescent cortex. Synchronous synaptic activity is reflected in the amplitude of the EEG signal. Several sleep EEG studies have shown a significant decline in sleep EEG power during early adolescence; however, no longitudinal

data exist on developmental changes in the sleep EEG during later adolescence.
Methods: Longitudinal sleep EEG data were recorded from twelve healthy participants (8 girls). Standard sleep recordings were run in lab for two consecutive nights when the participants were 15- or 16-years-old and again 2-3 years later (mean interval = 2.5, SD = 0.14). Time in bed at the recording sessions and the amount of sleep for one week prior to the in-lab was the same on both occasions (9 hr). EEG was recorded from C3/A2, C4/A1, O1/A2 and O2/A1. Sleep stages were visually scored in 30-second epochs using standard criteria (Rechtschaffen & Kales, 1968), and power spectra were calculated on each epoch using a Fourier transform.
Results: Adolescents at time 2 had an average of 14 percent more stage 2 sleep and 31 percent less slow wave sleep (stages 3 and 4). Both effects were statistically significant at $p < .01$. Moreover, amplitude of the EEG signal decreased from the initial recording session to the follow-up session for NREM and REM sleep. This effect was statistically significant across electrodes and frequencies (0.6 to 16 Hz).
Conclusion: The state nonspecific decline in sleep EEG amplitude over this span may indicate that the synaptic pruning process initiated in late childhood continues into later adolescence.
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0017

MICRODIALYSIS DELIVERY OF MORPHINE DECREASES ADENOSINE LEVELS IN RAT BASAL FOREBRAIN AND COADMINISTRATION OF AN ADENOSINE DEAMINASE INHIBITOR REVERSES THE MORPHINE-INDUCED DECREASE

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Introduction: Opioids are widely used for pain management but have the unwanted side effect of sleep disruption (Sleep and Pain ed by G. Lavigne et al. IASP Press 2007). Sleep deprivation heightens the perception of pain (Semin Neurol 25:106, 2005) and diminishes quality of life (Sleep 29:145, 2006). Adenosine is a sleep-promoting molecule (Science 276:1265, 1997) and opioids significantly decrease adenosine levels in the pontine reticular formation (FASEB J 22:945.11 2008). Therefore, decreasing adenosine in sleep-related brain regions may be one mechanism by which opioids disrupt sleep. This study is testing the hypothesis that microdialysis delivery of morphine to the substantia innominata (SI) of rat basal forebrain decreases adenosine levels and that coadministration of the adenosine deaminase inhibitor erythro-9-(2-hydroxy-3-nonyl)adenine (EHNA) prevents the morphine-induced decrease in SI adenosine.
Methods: Sprague Dawley adult male rats (n=8) were anesthetized with isoflurane. A dialysis probe was aimed for the SI and samples (30 μL) were collected every 15 min during dialysis with Ringer's (control) followed by Ringer's containing either morphine sulfate (100 μM) or morphine plus EHNA (100 μM). HPLC with UV detection was used to quantify adenosine (nM) in each microdialysis sample.
Results: Histological analysis confirmed that all dialysis sites were localized to the SI. Morphine caused a significant (p=0.004) decrease (-27.8%) in SI adenosine levels. Coadministration of EHNA and morphine prevented the morphine-induced decrease in SI adenosine.
Conclusion: Adenosine antagonists increase wakefulness, and the increase in adenosine levels that occurs during prolonged wakefulness promotes the transition into sleep. The present results support the conclusion that decreasing adenosine in the SI may be one mechanism by which opioids disrupt sleep. The finding that EHNA prevents the morphine-induced decrease in adenosine encourages ongoing efforts to develop adjunctive therapies that diminish pain without disrupting sleep.
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0018

HYPOCRETIN-1 MICROINJECTED INTO THE PONTINE RETICULAR NUCELUS, ORAL PART (PNO) OF SPRAGUE DAWLEY RAT CAUSES A CONCENTRATION DEPENDENT INCREASE IN WAKEFULNESS AND DECREASE IN SLEEP

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Introduction: Hypocretins are important for maintaining wakefulness (Front Neuroendocrinol 29:70, 2007), and hypocretin receptor antagonists show promise for the treatment of insomnia (Expert Opin Investig Drugs 16:1785, 2007). The PnO is a component of the ascending reticular activating system and contributes to the cortical activation of wakefulness and REM sleep. Microinjection of hypocretin-1 into rat PnO increases wakefulness and decreases sleep (Sleep 31:453, 2008). To determine whether the effects of hypocretin-1 on sleep and wakefulness are receptor mediated, the present study is testing the hypothesis that microinjection of hypocretin-1 into rat PnO causes a concentration dependent increase in wakefulness and decrease in sleep.
Methods: Adult male rats (n=9) were anesthetized with isoflurane and implanted with electrodes for recording the cortical electroencephalogram and neck electromyogram, and with a guide cannula aimed for the PnO. Two hour sleep recordings began after microinjection (100 nl) of Ringer's, 1, 10, 100, and 1000 μM hypocretin-1 (0, 0.35, 3.56, 35.6, 356 ng, respectively). Data were scored manually in 10 s bins as wakefulness, NREM sleep, or REM sleep using Icelus software (Physiol Behav 63:67, 1998).
Results: During the first hour post injection, hypocretin-1 caused a concentration dependent increase in the amount of wakefulness (p=0.049), decrease in the amount of NREM sleep (p=0.05), and decrease in the average duration of NREM sleep (p=0.05). All dependent measures of sleep and wakefulness returned to control levels during the second hour post injection.
Conclusion: The present results demonstrate that PnO administration of hypocretin-1 causes a concentration dependent increase in wakefulness and decrease in NREM sleep. These results, and previous data showing that the hypocretin-1-induced increase in wakefulness is blocked by the hypocretin receptor-1 antagonist SB-334867 (Soc Neurosci Abstr 285.14, 2008), support the conclusion that hypocretin receptors in the PnO contribute to the regulation of wakefulness.
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0019

FUNCTIONAL ROLE OF BRAIN MAST CELL-DERIVED HISTAMINE OF MICE IN SLEEP-WAKE REGULATION

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Introduction: Histamine has been known as the wake-active amine. There are two major sources of histamine in the brain. One is the histaminergic neurons, and the other is brain mast cells. The role of neuron-derived histamine in sleep-wake regulation has been investigated, while the role of mast cell-derived histamine remains unknown. We have therefore examined the role of brain mast cell-derived histamine for sleep-wake regulation using mast cell deficient mice (W/Wv mice).
Methods: Male W/Wv mice (n = 10) and their wildtype littermates (n = 10) were used in these experiments. All mice were chronically implanted with electroencephalogram (EEG) and electromyogram (EMG) electrodes for polysomnographic recordings. Recordings were scored in 10-sec epochs as wake, REM, or slow wave sleep. Two sets of experiments were carried out: (1) systematic sleep evaluation (baseline and homeostatic [i.e. 6h sleep deprivation] aspects of sleep phenotype) (2) pharmacological manipulations; histamine H1 antagonists (mepyramine

0.25, 1, 4 mg/kg, diphenhydramine 2.5, 10 mg/kg, chlorpheniramine 2.5, 10 mg/kg, and cyproheptadine 2.5, 10 mg/kg at ZT14), H3 antagonist (thioperamide 1.25, 5, 10 mg/kg at ZT2) and histidine decarboxylase (HDC) inhibitor (alpha-FMH 50, 100 mg/kg at just before ZT12) were administered intraperitoneally and their effects on sleep parameters were evaluated.
Results: Results We found that sleep patterns of mast cell deficient mice are identical with those of their wildtype littermates in baseline and after 6h sleep deprivation. Cyproheptadine 2.5 mg/kg and mepyramine 1 mg/kg increased slow wave sleep in both types of mice but were significantly less effective in mast cell deficient mice. Thioperamide increased and alpha-FMH decreased the amount of wake with no significant difference between the EEG patterns of mast cell deficient mice and those of wildtype animals.
Conclusion: Our results suggest that neuron-derived histamine (and histamine neurons) is sufficient to maintain normal sleep/wake patterns, forced wakefulness, and sleep rebound. Mast cells may play a role for the pharmacological regulation of sleep, since sleep induction by H1 antagonist was attenuated in the mast cell deficient mice. The mechanisms underlying this phenomenon need to be studied. Mast cells also contain cytokines, 5HT, somatostatin, endorphin, prostaglandin D2, classes of neurotransmitters/modulators involved in sleep-wake regulation, and functional roles of these mast cell-derived substances also need to be examined.
Support (optional): The research supported by NIH Grants (R01MH072525 and R03MH079258).

0020

TRAIT-LIKE CHARACTERISTICS IN THE SLEEP EEG DURING EARLY ADOLESCENCE: PRELIMINARY RESULTS

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Introduction: Waking and sleep EEG studies in adults show high heritability of trait-like characteristics in EEG spectra. This phenomenon has not been examined in children and adolescents in whom brain development may affect the sleep EEG (e.g., change in spindle frequency). The present study examines whether a stable trait-like sleep EEG pattern is detected across early adolescent development.
Methods: Two consecutive nights of standard sleep recordings were performed in ten healthy children (3 girls) aged 9 or 10 (time 1) and again 2-3 years later (time 2; mean = 2.32 years, SD =0.28). EEG signals (C3/A2) were Fourier transformed (Hanning window, average of six 5-s epochs) and artifacts rejected using a semi-automated procedure; data were then averaged across the night independent of the vigilance states. Spectra were normalized by dividing the power in each frequency bin by the mean power in the 0.6 to 16 Hz range. Log-transformed average spectra were considered as a 77-dimensional vector (0.6-16 Hz; 0.2 Hz bins) for each night of recording, resulting in four such vectors per subject. Data were classified by hierarchical cluster analysis.
Results: Analysis for two nights at each time resulted in correct pairing of each participant's nights into the same cluster. With all 40 nights in the analysis, all four nights from a single participant were correctly classified except for one participant, for whom the two nights at time 1 and time 2 were paired but not all 4 nights, possibly due to a 0.4 Hz increase in the spindle frequency peak at time 2.
Conclusion: Successful clustering based on sleep EEG in 90% of this preliminary sample indicates that--in spite of neuro-developmental changes--trait-like characteristics are largely preserved in early adolescence. Future analyses will include a larger sample size and examine NREM and REM sleep separately.
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0021

CRF1 BUT NOT CRF2 RECEPTORS IN THE CENTRAL NUCLEUS OF THE AMYGDALA (CNA) REGULATE RAPID EYE MOVEMENT SLEEP (REM) IN RATS

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Introduction: The CNA is involved in the control of sleep and arousal, in particular REM, as well as in stress responses. CRF receptors located in the CNA are known to have neuroregulatory and neuromodulatory actions. Microinjection of low, but not higher, dosages of CRF into CNA reduces REM. However, little is known about the potential role CRF receptors within CNA play in regulating sleep and arousal. Here, we examined the effects on sleep of microinjections into CNA of the CRF1 agonist, stressin I (STR), and the CRF2 agonist, urocortin III (UCN).
Methods: Wistar rats (n=12) were implanted with electrodes for recording sleep and with cannulae aimed bilaterally into CNA. After recovery from surgery, the animals underwent baseline sleep recording, habituation to the injection procedure over two days, and were randomly assigned to two groups (STR, n=6 and UCN, n = 6). Animals in both groups received three 0.2µL microinjections (3.3nM, 10nM and distilled H20 (vehicle) during the 4th hour of the light period, each separated by 7 days. Sleep was recorded for 20 h post-injection (8h light, 12h dark) and scored for NREM, REM, and wakefulness.
Results: Injections of 10nM STR were followed by significant increases in REM during the 2nd 4h of light compared to vehicle (p=0.02). This increase in REM just missed significance for the entire 8h light period (p=0.054). Injections of UCN at either dose did not change levels of REM. Moreover, no changes were observed for NREM or total sleep following injections of either drug at both doses compared to vehicle.
Conclusion: Activation of CRF1 receptors within the CNA during the light period was followed by a delayed increase in REM. Conversely, activation of CRF2 receptors did not significantly alter subsequent sleep. The results suggest a differential role for CRF1 and CRF2 receptors in CNA in the regulation of REM.
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0022

CONTROLLABLE AND UNCONTROLLABLE STRESS PRODUCE DIRECTIONALLY DIFFERENT EFFECTS ON SLEEP IN MICE

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Introduction: Training with inescapable shock (IS, an uncontrollable stressor) and presentation of IS-associated fearful cues and contexts produce prominent reductions in rapid eye movement sleep (REM). In this study, we compared sleep in animals trained with IS to that in animals trained in an escapable shock (ES, a controllable stressor) paradigm in which animals always received shock but could terminate it by their actions
Methods: Male BALB/cJ mice were implanted with telemetry transmitters (DataSciences ETA10-F20) for recording EEG and activity. After recovery from surgery, uninterrupted baseline sleep recordings were obtained for 2 days. The mice were then randomly assigned to ES (n=9) and IS (n=9) conditions. Mice in the ES condition could learn to escape a footshock (20 trials; 0.5 mA; 5.0 sec maximum duration; 1.0 min in-

tervals) by moving to the non-occupied chamber in a shuttlebox. This terminated shock delivery to both ES mice and yoked-control IS mice receiving shock in a separate shuttlebox and insured that both animals received identical amounts of footshock. The mice received two days of shock training (ST1; ST2) and also were re-exposed to the shuttlebox without the presentation of footshock (context alone). On each day, the mice were returned to their home cages and EEG and activity were collected for 20 h.
Results: Compared to baseline recordings, ES mice showed significantly increased REM and IS mice showed significantly decreased REM after ST1, ST2 and context alone. Total REM during ST2 (20.44±3.16) was significantly greater than during ST1 (15.78±2.26) during the second 4 h of recording, $t(8)=2.67$, $p < .03$. Changes in NREM were variable, but total NREM was decreased after shock training in IS mice.
Conclusion: ES and IS produced directionally opposite changes in REM suggesting that this paradigm may be a good model for examining the role(s) stressor controllability and sleep may play in successful coping with stress.
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0023

EFFECTS OF CORTICOTROPIN RELEASING FACTOR (CRF) ON SLEEP FOLLOWING CONTROLLABLE STRESS IN MICE

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Introduction: CRF plays a major role in central nervous system responses to stressors and it has been implicated in stress-induced alterations in sleep. Controllability is an important determinant of the effects of stress on behavior and on post-stress arousal and sleep. Uncontrollable stress such as contextual fear associated with inescapable shock (IS) produces significant decreases in REM that are exacerbated by CRF and attenuated by antagonizing CRF. Training with escapable shock (ES), a controllable stressor, enhances REM. We examined the influence of CRF and astressin (AST), a non-specific CRF antagonist, on sleep after ES training to determine whether CRF would block enhanced REM after ES.
Methods: Eight male BALB/cJ mice were implanted for recording sleep via telemetry and with a guide cannula aimed into a lateral ventricle. After recovery, sleep was recorded following exposure to a novel chamber as a handling control. On experimental day 1, the mice received ES training (20 trials, 0.5 mA, up to 0.5 s duration, 1.0 min interstimulus interval). On days 7 & 14, the mice received ICV microinjections (counterbalanced) of either saline (SAL, 0.2µL) or CRF (0.2µg) prior to ES. On days 21 & 28, the mice received ICV microinjections (counterbalanced) of either SAL or AST (0.4µg) prior to ES. On each experimental day following ES, sleep was recorded for 20 hours (8h light and 12h dark).
Results: REM after SAL+ES was increased compared to the novel chamber, a mild stressor that also enhances REM. Compared to SAL+ES, CRF+ES significantly decreased REM duration ($p<0.001$) as well as REM% ($p<0.001$) over the entire 20h of recorded sleep. In contrast, AST+ES did not significantly alter REM compared to SAL+ES. No significant alterations were found in NREM or total sleep.
Conclusion: Together with findings from studies involving uncontrollable stress (IS), these data demonstrate CRF activation is an important regulator of stress-induced changes in REM.
Support (optional): Supported by NIH research grants MH61716 and MH64827.

0024

GROUP II METABOTROPIC GLUTAMATE (MGLU) RECEPTORS IN THE BASAL AMYGDALA (BA) REGULATE RAPID EYE MOVEMENT SLEEP (REM)

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Introduction: Systemic administration of the Group II mGlu receptor agonist, LY379268, has been reported to decrease REM sleep and to depress theta and high-frequency power in the EEG during wakefulness and non-REM (NREM). To our knowledge, the specific brain area(s) involved have not been identified. Group II mGlu receptors are highly expressed in the amygdala, a brain region involved in the regulation of sleep and arousal as well as EEG spectra. Therefore, we examined the effects of LY379268 on sleep after microinjection into BA.
Methods: Six Wistar rats were implanted with electrodes for recording sleep and with bilateral cannulae aimed into BA for drug administration. After recovery from surgery, the rats were habituated to the injection procedure over two consecutive days. Each rat then received 4 bilateral microinjections of LY379268 (0.6µg/µl, 1.0µg/µl and 2.0µg/µl) or vehicle alone (distilled water; 0.5 µl) administered in a counterbalanced order at 5-day intervals. Following each injection, the animals were returned to their home cages for 20h sleep recording (8h light, 12h dark). NREM, REM and wakefulness were scored in 10 sec epochs.
Results: Compared to vehicle, microinjections into BA of LY379268 significantly reduced REM during the first 14 h of sleep recording. All three drug dosages induced similar reductions in REM and there were no significant differences between dosages. In contrast, there were no significant effects observed in amounts of NREM or total sleep.
Conclusion: These are the first data demonstrating that BA may be able to selectively impact REM without significant alterations in wakefulness or NREM. This suggests that group II mGlu receptors may influence specific cells in BA that control descending output (via the central nucleus of the amygdala or bed nucleus of the stria terminalis) that in turn regulates REM generator regions in the pons.
Support (optional): Supported by NIH grants MH64827 and MH61716.

0025

FEAR-INDUCED ACTIVATION OF STRESS AND AROUSAL REGIONS IS MEDIATED BY CORTICOTROPIN RELEASING FACTOR (CRF) 1 RECEPTORS IN THE CENTRAL NUCLEUS OF THE AMYGDALA (CNA)

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Introduction: Contextual fear is followed by significant reductions in rapid eye movement sleep (REM) and/or non-REM. CNA is critical for behavioral and physiological signs of contextual fear including fear-induced alterations in sleep. The neuropeptide CRF plays a major role in regulating central aspects of the stress response as well the regulation of arousal. CRF in CNA has been implicated in stress-related behavior. Previously, we demonstrated that microinjecting the CRF1 antagonist, antalarmin (ANT) into CNA attenuated fear-induced reductions in REM. In this study, we also examined c-Fos, a marker of neuronal activity, to evaluate fear-induced activation in regions implicated in the stress response and control of REM (hypothalamic paraventricular nucleus (PVN), dorsal raphe nucleus (DRN) and locus coeruleus (LC)).
Methods: Wistar rats were implanted with electrodes for recording EEG and EMG and with cannulae aimed into CNA for administration of drug. On separate days, the rats were subjected to handling control (HC) and two shock training sessions (ST1 and ST2) with 20 footshocks (0.5 s, 0.8 mA) at 1 min intervals. Afterwards, the rats received microinjections (0.2 µl) of ANT (4.8 mM; n=8) or vehicle alone (VEH; n=7) prior to

exposure to the fearful context alone. Sleep was recorded for 2 h in each condition. The rats were then sacrificed to assess c-Fos expression.
Results: Compared to HC, S1 and S2 significantly reduced REM in the 2nd hour of recording. VEH rats exposed to the fearful context also showed reduced REM. By comparison, ANT rats exposed to the fearful context showed levels of REM that did not differ from HC. Fos expression was decreased in PVN, LC and DRN after ANT compared to VEH.
Conclusion: Antagonizing CRF1 receptors in CNA attenuates fear-induced reductions in REM and reduces neural activation (as indicated by c-Fos) in stress and REM regulatory regions.
Support (optional): Supported by NIH grants MH64827 and MH61716.

0026

ADAPTIVE PATTERN OF CHANGES IN CINGULATE CORTEX BETA-ADRENERGIC RECEPTOR MRNA LEVEL DURING CHRONIC SLEEP RESTRICTION IN RATS

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Introduction: Recent rodent studies revealed that the sleep responses to chronic sleep restriction (CSR) are fundamentally different from those to short-term total sleep deprivation. Specifically, when CSR continues for several consecutive days, animals fail to express compensatory responses in total sleep time and sleep intensity as measured by NREM EEG delta power. Norepinephrine may play a key role in modulating NREM delta power by promoting cortical long-term potentiation induction via beta-adrenergic receptors (AR). Here we investigated the changes in adrenergic receptor mRNA level in response to CSR using a rat model.
Methods: After a baseline sleep day, rats underwent 18-h sleep deprivation followed by 6-h sleep opportunity (SO) given during the first 6h of the light period. This sleep restriction (SR) protocol was repeated for 5 consecutive days, followed by 3 days of unrestricted recovery sleep. EEG activity of rats was continuously monitored during all 9 experimental days. A separate group of rats went through the same experimental procedure without EEG surgery. Their brains were collected at the light onset (i.e. immediately following 18-h SD on SR days). The mRNA levels of alpha 1, alpha 2, and beta-AR were measured in several brain areas using RT-PCR technique.
Results: NREM delta power during the 6-h SO was significantly increased by +49.5% on SR day 1, but returned to the baseline level on days 2 to 5. The total sleep time data showed a similar adaptive pattern. Alpha 1 and alpha 2-AR mRNA levels in the anterior cingulate cortex were not changed significantly throughout 9 experimental days. In contrast, beta-AR mRNA levels were decreased significantly by -33.9% on SR1, but gradually returned to the baseline level from SR3.
Conclusion: The time pattern of changes in the cingulate cortex beta-AR mRNA level matches the pattern of the adaptive responses of sleep time/intensity observed during CSR. Therefore, changes in the cortical beta-AR may mediate the adaptive responses of CSR.
Support (optional): the Department of Veteran Affairs and MH039683

0027

AROUSAL THRESHOLD TO AUDITORY STIMULI IN RATS

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Introduction: In order to understand the relationship between stimulus intensity, evoked response amplitude, and arousal threshold during sleep, we measured the arousal threshold to auditory stimuli and the corresponding size and shape of evoked response potentials. We previously demonstrated that individual cortical columns exhibit sleep-like and wake-like states with evoked response potentials of large and small amplitudes correspondingly. We hypothesized that deeper sleep states will require more intense stimuli to wake an animal, and that the field evoked response potential will be smaller (wake-like state) when animals wake to a stimulus compared to when they stay asleep.
Methods: We fitted ECoG electrodes over the auditory cortex of rats, and recorded EEG and EMG signals while auditory stimuli were given in random intervals of 6-12s for 24 hours. The stimulus intensity varied in each recording between 50 and 75dB. We divided recordings two second epochs and determined the sleep/wake state for each epoch. After identifying whether the animal stayed asleep or woke from each stimulus, we measured the evoked response amplitude.
Results: In agreement with other studies, we found that an animal is more likely to wake from either light sleep or REM compared to a deep sleep. Additionally, we observed that the evoked response amplitude was larger when an animal stayed asleep.
Conclusion: Different arousal thresholds exist for different sleep states; Being more difficult to arouse an animal from deeper sleep. Since the evoked response was smaller when a stimulus woke an animal for any sleep states, the underlying state of the cortical tissue may modulate arousal threshold.
Support (optional): WM. Keck Foundation, NIMH 71830

0028

PONTINE RETICULAR FORMATION (PRF) ADMINISTRATION OF DIAZEPAM AND ZOLPIDEM, BUT NOT ESZOPICLONE INCREASES ELECTROENCEPHALOGRAM (EEG) DELTA POWER IN SPRAGUE-DAWLEY RAT

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Introduction: Insomnia is the most common sleep disorder and significantly decreases quality of life (J Clin Sleep Med 3:63, 2007). Benzodiazepine receptor agonists are widely used for the treatment of insomnia but their mechanisms of action remain poorly understood. Acetylcholine (ACh) release in the PRF is increased during rapid eye movement sleep (J Neurosci 17:774, 1997) and PRF ACh release is increased by microdialysis delivery of zolpidem and eszopiclone to the PRF (Soc Neuroscience Abstract 285.16, 2008). EEG activity varies as a function of PRF ACh release, and the present study is testing the hypothesis that EEG delta power is altered by microdialysis delivery of diazepam, zolpidem, and eszopiclone to the PRF.
Methods: Adult male Sprague-Dawley rats were anesthetized with isoflurane. A CMA/11 microdialysis probe was placed in the PRF and cortical EEG electrodes were implanted. EEG was recorded while PRF ACh release was measured during dialysis with Ringer's (control) followed by Ringer's containing 100 μM diazepam, zolpidem, or eszopiclone. EEG delta power (0.5 to 4 Hz) was analyzed in 0.5 Hz intervals. Data were evaluated by repeated measures two-way ANOVA and post-hoc tests for comparison of treatment at each frequency.
Results: Microdialysis sites were histologically localized to the PRF. Diazepam (n=3 rats) caused a significant increase in EEG power between 1 and 1.5 Hz. Zolpidem (n=3) significantly increased EEG power between 0.5 and 1.5 Hz. To date no changes in EEG power during dialysis delivery of eszopiclone (n=2) have been observed.
Conclusion: The results demonstrate the feasibility of specifying brain regions and neurotransmitter systems through which sedative/hypnotic molecules differentially alter the EEG. The finding that some sedative/hypnotics increase EEG delta power is of interest relative to recent evidence that isoflurane, which also binds at $GABA_A$ receptors, increased EEG delta power (Anesthesiology 109: 978, 2008).
Support (optional): Sepracor, Inc., National Institutes of Health grants HL40881 and MH45361, and the Department of Anesthesiology.

0029

IMPROVED RAT PSYCHOMOTOR VIGILANCE TEST WITH FAST RESPONSE TIMES

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Introduction: In order to investigate physiological mechanisms in the control of sleep, we require an animal model of the psychomotor vigilance test (PVT) with fast response times. For rats, whisker stimulation produces a rapid and robust evoked response. A fast lick response can be obtained using water as a reward. Our prior experiments used deprivation-based approaches to maximize operant conditioned responses. Recent evidence suggests that deprivation states can dramatically alter brain function and therefore, the present study was designed to identify alternative methods to maintain operant responding. Licking behavior was used to obtain a cognitive operant response and test reaction times as short as 100ms.
Methods: We conditioned rats for immobilization and head restraint, then trained them to lick in response to whisker twitching. Two whiskers were twitched in a random order with one designated as the reward whisker and the other a control whisker. A sucrose solution reinforced correct responses when the animal licked to the reward whisker. A high density 64 channel electrode array was chronically implanted to measure whisker barrel evoked response potentials (ERPs) during whisker stimulation.
Results: After one to two months of immobilization training, animals remained calm for up to an hour while restrained. After 15 sessions of lick training, the animals produced approximately 50% correct responses to the twitch stimulus. The 64 channel electrode array created high spatial and temporal resolution electrical maps of the cortical surface, allowing visualization of the cortical column responses.
Conclusion: Approximately 30 more training sessions will be needed to reach the desired criterion of 80% correct responses to the stimulus. Additionally, reward and punishment protocols may also be needed. This conditioned learning paradigm will aid in the study of localized sleep-like functional states that may occur in the cortical columns.
Support (optional): W.M Keck Foundation, NIMH 71830

0030

NEUROANATOMICAL INVESTIGATION OF BRAINSTEM PROJECTIONS TO THE MEDIAL MAMMILLARY BODY: POSSIBLE IMPLICATIONS FOR THE MODULATION OF THETA RHYTHM

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Introduction: Theta is a 4-12 Hz, nearly sinusoidal EEG rhythm that is prominent during movement, attention, and mnemonic processing in waking and also during REM sleep. Two pathways control theta, one of which involves glutamatergic neurons of the medial mammillary body (MMB), which may drive theta via projections in the Papez circuit to the anterior ventral thalamus. Since electrical stimulation of the brainstem is a potent trigger for theta rhythm generation, we investigated the prominent brainstem projections to MMB, employing retrograde tracer injections, combined with immunohistochemical identification of afferent neuronal phenotypes.
Methods: The retrograde tracer tetramethylrhodamine detxran amine was pressure injected into MMB of GAD67-GFP knock-in mice. After a recovery period of 5 days, brains were removed, sectioned, and stained for choline acetyltransferase (anti-ChAT antibodies; cholinergic neurons) or tryptophan hydroxylase (anti-TrypH antibodies; serotonin neurons). GABAergic neurons were identified by their intrinsic GFP fluorescence. Single- and double-labeled neurons were schematically plotted using Neurolucida, and illustrated with photomicrographs.
Results: Many neurons in the ventral tegmental nucleus of Gudden (VTg) were retrogradely labeled following MMB injections, and a large proportion was GABAergic. Dorsal and median raphe nuclei were also retrogradely labeled, of which a small proportion were serotonergic. A small number of retrogradely labeled neurons were evident in the tegmental nuclei, of which a few were ChAT-positive.
Conclusion: We describe here ascending brainstem projections to MMB that may be involved in theta rhythm activation, including a strong GABAergic projection from VTg to MMB. Reciprocal connections between these two nuclei are likely to be important in generating theta in the Papez circuit, since VTg neurons have also been shown to fire bursts of action potentials synchronized with theta. Our recent in vitro electrophysiological studies suggest cholinergic brainstem input may promote theta rhythmicity, while serotonergic projections from the raphe nuclei may inhibit theta bursting in MMB neurons.
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0031

THE CSF AND CIRCULATORY SYSTEM TRANSPORT HYPOCRETIN FROM THE CNS TO PERIPHERAL ORGANS

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Introduction: Hypocretins (orexins) are neuropeptides that are expressed by a group of neurons located exclusively in the lateral hypothalamus. The intracerebroventricular administration of hypocretin-1 promotes centrally-mediated behaviors such as arousal, locomotion, and food consumption, and also induces peripheral effects that support these behaviors, such as changes in the secretion of insulin by the pancreas. However, it is unknown how centrally-generated hypocretin is able to activate hypocretinergic receptors in peripheral organs, such as the pancreas. One possible route is via the CSF; accordingly, we were interested in determining whether the CSF serves as a functional transport system for the conveyance of hypocretin from the brain to a peripheral organ.
Methods: Hypocretin-1, which was conjugated with superparamagnetic iron oxide nanoparticles, was injected into the lateral ventricle of guinea pigs. After 10 hours, the animals were perfused transcardially with a fixative. The brain and pancreas were removed and processed in order to carry out a Prussian blue reaction to determine the location of the hypocretin-conjugated nanoparticles. Immunohistochemical reactions were performed to identify the location of hypocretin-1 receptors. The sections were then examined under light microscopy.
Results: Hypocretin-conjugated nanoparticles, which were indentified by precipitates of the Prussian blue reaction, were located in the endocrine (islets of Langerhans) and exocrine portions of the pancreas. In these regions, the hypocretin-conjugated nanoparticles were found to be juxtaposed to cells that exhibited hypocretin receptor-1 immunoreactivity.
Conclusion: The present results demonstrate that the CSF transports hypocretin from the CNS to the circulatory system and that blood-borne hypocretin is capable of activating its cognizant receptors, which are expressed by both endocrine and exocrine cells of the pancreas. Therefore, we suggest that the hypocretinergic system not only controls CNS sites, but also has direct effects on peripheral organs through volume transmission that is mediated by the CSF.
Support (optional): The Brain Sciences Foundation, the Epilepsy Foundation of America and the Stein-Oppenheimer Award (UCLA School of Medicine). Patents PCT/US06/10334, EU06739214.2.

0032

LONG-LASTING PLATEAU POTENTIALS AND CARBACHOL SUPPRESSION OF OREXIN EXCITATION IN GABAERGIC VENTRAL TEGMENTAL NUCLEUS OF GUDDEN NEURONS: IMPLICATIONS FOR THETA BURST FIRING

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Introduction: The theta rhythm synchronizes brain regions involved in spatial navigation and memory formation, including those in the Papez circuit. One part of this circuit, the medial mammillary body (MM), is reciprocally connected with GABAergic ventral tegmental nucleus of Gudden (VTg) neurons. In vivo single-unit recording studies showed that VTg neurons fire long-lasting fire bursts of action potentials at theta rhythms. The mechanisms underlying this rhythmic firing are unknown.
Methods: We performed whole-cell patch-clamp recordings from identified GABAergic neurons in the VTg in brain slices prepared from juvenile (8-16d) GAD67-GFP knock-in mice.
Results: GFP-positive (GABAergic) VTg neurons exhibited striking intrinsic membrane properties including a strong H-current and large, calcium-dependent, long-lasting plateau potentials (PP) following hyperpolarizing current steps. Pharmacological analysis suggested that PP were due to activation of a low-threshold calcium current followed by a calcium-activated mixed cation current. Orexins (500 nM) caused a large depolarization (12 mV) of VTg neurons in the presence of tetrodotoxin (TTX). In contrast, application of the cholinergic agonist carbachol (CARB, 10 μM) caused a small hyperpolarization (4 mV) and CARB applied at the peak of the orexin depolarization completely reversed the orexin excitation. Application of the glutamatergic agonist NMDA (30 μM) in the presence of CARB caused rhythmic membrane potential oscillations and burst firing at theta frequencies (3-5 Hz).
Conclusion: During states when theta rhythm is observed acetylcholine suppresses the depolarizing effect of orexins on VTg neurons and maintains them in a hyperpolarized state. Glutamatergic inputs to VTg neurons (from MM) activate NMDA receptors and cause depolarization. This triggers PP and a long-lasting burst of action potentials. The burst causes release of GABA from VTg neurons onto MM neurons, triggering bursts in these neurons. Through its connections with other parts of the Papez circuit, the MM may act as a pacemaker for theta.
Support (optional): Dept. of Veterans Affairs (Merit award to RWM), NIH HL060292, MH039683, and MH062522.

0033

HOW SLOW CAN YOU GO? UNIQUE FMRI CORRELATIONS WITH EEG ACTIVITY BELOW 0.1 HZ DURING SLEEP

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Introduction: It has been suggested that EEG frequency bands below 1.0 Hz during sleep may participate in restorative processes and the cortical plasticity associated with sleep-dependent learning. Assessment of the fMRI correlates of spectral power in these bands may provide information regarding the mechanisms by which these frequencies are generated as well as their functional significance. We examined the unique fMRI correlates of activity in two bands below 1.0 Hz (0.05-0.099 and 0.66-0.99) as differentiated from each other and activity in the 1.0-3.9 band.
Methods: Simultaneous EEG-fMRI (BOLD) measures were employed. Sessions were included if the EEG was artifact free and contained stage 3 or 4 sleep. Spectral analysis was performed and each of the three bands were modeled separately. The three sets of EEG-fMRI correlations were subjected to a conjunction analysis. The relative uniqueness of all three bands was assessed by comparing the number of voxels classified into the conjunction category where there was a significant correlation for the band in question and a non-significant correlation for the other two bands.
Results: The category for the 0.05-0.099 band contained the largest number of uniquely correlated voxels. The significant positive correlations for unique activity in the 0.05-0.099 band were mostly in subcortical areas (medial thalamus, hypothalamus, hippocampus) while negative correlations were mostly in neocortical areas (medial prefrontal, precuneus/posterior cingulate).
Conclusion: These data suggest that EEG activity below 0.1 Hz plays a prominent role in sleep-dependent processes relative to other "slow" bands. Correlations with thalamic activity may relate to the thalamic generation of this EEG band. Correlations with hippocampal and neocortical activity (which included nodes in the default-mode network) may reflect a process of hippocampically-directed cortical plasticity. The present subcortical-positive and neocortical-negative pattern of correlations is also consistent with findings from studies where fMRI activity was correlated with 8.0-11.9 Hz EEG activity.

0034

PHARMACODYNAMICS OF D2/D3 AGONIST-INDUCED SLEEP

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Introduction: Dopamine (DA) D2/D3 receptor agonists such as pramipexole and ropinirole are known to induce sleepiness and sleep attacks in patients with Parkinson's Disease. In rat experiments, a low dose of D2/D3 agonist (quinpirole: 30μg/kg i.p.) acutely induces sleep, whereas a high dose (1000μg/kg) induces wakefulness (APSS 2008). In this study, we monitored sleep parameters over 24-hrs following quinpirole administration to examine if dynamics of sleep changes may explain the drug-induced sleepiness. Change in the extracellular DA levels after the drug administration was also measured in the prefrontal cortex.
Methods: Male Sprague-Dawley rats underwent surgery for EEG and EMG electrodes. Vehicle was injected (i.p.) at 5 minutes before the beginning of lights-off period (ZT12) on day 1, and sleep was recorded for 24-hrs. On day 2, quinpirole (30μg or 1000μg/kg) was injected. Amounts of each sleep parameters (SWS, REM sleep, and wakefulness) for the 24-hrs following the quinpirole administration were compared to those following vehicle injections.
Results: The high dose of quinpirole increases wake for 3-4 hrs followed by a large increase in the amount of sleep that lasted until the end of the active period. This increase in sleep was much larger than the amount of sleep loss in the initial hours. The amount of sleep enhancement was also much larger than amount of sleep rebound seen after the total sleep deprivation of 4-hrs (ZT12-16). Therefore, the high dose of quinpirole may actively promote sleep after the initial phase of wake-promotion.
Conclusion: D2/D3 agonists reduce dopamine release by acting on presynaptic D2/D3 autoreceptors, while high doses predominantly activate postsynaptic D2 receptors. A low dose of quinpirole reduced DA release immediately by 60% and gradually returned to the baseline level over 7-hours. A high dose of quinpirole produced much longer reduction in DA release and the effect lasted for 12-hrs. Interestingly, the recovery of DA release started to occur at 4 hours after the high dose injection, and the slope of the recovery after 4 hours is identical to that occurred after the low quinpirole dose administration (which accompanied by sleep induction). These results suggest that a shift from postsynaptic (excit-

atory) to presynaptic (inhibitory) action may occur 4 hrs after the administration of high dose of quinpirole, and this may paradoxically induce sleep. This mechanism may partially explain the D2/D3 agonist-induced excessive sleepiness seen in human patients.
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0035

BRAIN HISTAMINE RELEASE IN FREELY MOVING NARCOLEPTIC AND WILD TYPE MICE

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Introduction: Histamine is one of the wake-active amines. Histamine release is correlated with amount of wakefulness and is high during active period and low during resting period. Recent animal and human studies had suggested that central histamine levels are decreased in hypocretin/orexin receptor mutated narcoleptic dogs (in the brain) and hypocretin ligand deficient human narcolepsy (in the CSF). However, the pattern of histamine release across the day or night in narcoleptic subjects is not known. In the current study, we have measured histamine release in the brain in hypocretin deficient narcoleptic mice over 3 days with simultaneous sleep recordings. The histamine release in narcoleptic mice was compared with those in wild type mice.
Methods: EEG/EMG electrodes and one microdialysis probe (Bregma -0.26, L =0.5, D=-5) were implanted in three orexin-ataxin-3 transgenic [TG] mice and their littermate wild type (WT) mice. After 3 days of accommodation period in the recording cage, microdialysis perfusate was collected in a 30-miniute sampling bin while sleep was continuously monitored over 72 hours in the automated floor rotating cage (Osaka-micro, Suita, Osaka). Histamine contents in each microdialys perfusate were measured by HPLC. Sleep was scored for the same 30 minutes bin.
Results: We found that histamine exhibit a clear diurnal fluctuation pattern, and levels were high during dark (active) periods and low during light (resting) periods in both WT and TG mice. Histamine contents were positively correlated with amount of wakefulness in both TG and WT mice. We however, found that the mean histamine levels in the microdialysis perfusate in TG was much lower compared to WT (about 50%) throughout the recoding period.
Conclusion: Our results in mice confirm the reduced histamine neurotransmission in hypocretin deficient narcolepsy. Altered histamine levels are unlikely to be secondary to the sleep changes in narcoleptic mice considering the fact that low histamine levels were consistently observed in TG mice during the light period when both TG and WT mice spent a similar amount of time in sleep. Altered histamine levels may thus be actively involved in the phenotype expression of the narcoleptic mice.
Support (optional): The research supported by NIH Grants (R01MH072525 and R03MH079258).

0036

REM HEART RATE CHANGES IN WISTAR-KYOTO (WKY) VERSUS WISTAR (WIS) RATS SUGGEST NOREPINEPHRINE (NE) SURGES AS A POSSIBLE CAUSE OF REM FRAGMENTATION

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Introduction: DaSilva et al. have reported greater REM fragmentation in WKY compared to WIS following fear conditioning. This fragmentation could be associated with increased NE activity. We examined heart rate (HR) changes as a possible marker for NE activity in WKY versus WIS, postulating a greater change in WKY HR from baseline.
Methods: Animals habituated to a recording chamber had baseline 4 hrs sleep recorded in light and were fear-conditioned the next day to ten presentations (30s ISI) of a tone co-terminating with a foot shock (1.0 mA, 0.5s). The following day (Day 1) and 14 days later, three tones were presented every 30s, without shock, and sleep was recorded for 4 hrs. We analyzed HR (beats/sec) recorded in the neck muscle EMG during REM atonia, with artifacts excluded.
Results: A significant day x strain interaction for HR was found [p= .03]. WKY had an average HR increase from 4.77 ± .09 at baseline to 5.09 ± .10 on Day 1 [p=.02] and to 5.11 ± .04 on Day 14 [p=.01]. There were no significant changes in HR observed within WIS on either test day. Between strains there was a difference in baseline HR (WIS: 5.47 ± .37; WKY: 4.77 ± .09; [p=.05]) and a difference in HR at Day 14 (WIS: 5.32 ± .31; WKY: 5.11 ± .04; [p=.005]).
Conclusion: Compared to WIS, HR increase in WKY at Day 14 demonstrated a physiological difference following fear conditioning. Morilak et al. reported heightened NE release in WKY compared to a control strain after repeated stress exposure. Fear conditioning stresses WIS and WKY, but our results indicate that a tone reminder was more stressful in WKY at Day 14. HR rise in WKY on Days 1 and 14 may mark surges in NE activity associated with REM fragmentation.
Support (optional): Research funded by USPHS Grants MH072897 to A.R.M. and AA 015921 to S.T-B.

0037

OLANZAPINE, AN ATYPICAL ANTIPSYCHOTIC, DELIVERED TO THE PREFRONTAL CORTEX (PFC) DIFFERENTIALLY INCREASES PFC ACETYLCHOLINE (ACH) RELEASE IN C57BL/6J (B6) AND B6.V-LEP^{OB}/J (OBESE) MOUSE BUT DOES NOT ALTER CORTICAL ELECTROENCEPHALOGRAPHIC (EEG) POWER OR BEHAVIORAL AROUSAL

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Introduction: The mechanisms by which olanzapine exerts its desired antipsychotic effects and unwanted side effects of EEG slowing and excessive weight gain are unknown. Olanzapine antagonizes the actions of several neurotransmitters and blocks muscarinic receptors (Prog Neuropsychopharmacol Biol Psychiatry 27:1125, 2003). Compared to the congenic B6 line, obese mice demonstrate altered sleep responses to activating muscarinic receptors in the pontine reticular formation (J Appl Physiol 98:918, 2005). The present study tested the hypothesis that dialysis administration of olanzapine to the PFC of B6 and obese mouse alters PFC ACh release, EEG power, and anesthesia recovery time as a function of mouse line and olanzapine concentration.
Methods: Adult male B6 (n=24) and obese (n=24) mice were anesthetized with isoflurane. A microdialysis probe was aimed for the PFC and

samples were collected during dialysis with Ringer's (control) followed by Ringer's containing olanzapine (0, 0.1, 0.3, 1, 3, 10, 30, or 100 μM). EEG was recorded during dialysis sample collection and ACh release was quantified by HPLC. Anesthesia was discontinued and the time to resumption of righting (min) was measured.
Results: Two-way ANOVA revealed a significant mouse line by concentration interaction ($P<0.0007$) and effect of olanzapine concentration on PFC ACh release ($P<0.0001$). Olanzapine was more potent in obese mice, but caused a greater ACh increase in B6 mice. Olanzapine did not change EEG power or anesthesia recovery time. Histological analyses confirmed that all dialysis sites were localized to the PFC.
Conclusion: The finding that olanzapine caused a concentration dependent increase in PFC ACh release indicates mediation by muscarinic autoreceptors. Differences in olanzapine potency between B6 and obese mice suggest a role for leptin in the ACh response to olanzapine. The lack of an olanzapine effect on EEG power and anesthesia recovery time is consistent with antagonism of postsynaptic muscarinic receptors.
Support (optional): National Institutes of Health grants MH45361, HL40881, HL65272, and the Department of Anesthesiology.

0038

GREATER MEMORY INTERFERENCE BY NEGATIVE EMOTIONAL DISTRACTERS FOLLOWING SLEEP DEPRIVATION: BLAME YOUR AMYGDALA

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Introduction: Sleep deprivation (SD) results in declines in attention and working memory. SD has been observed to cause heightened amygdala responses to aversive emotional stimuli. Given these observations, we hypothesized that SD would increase the distraction evoked by negative emotional stimuli, compounding their adverse impact on working memory.
Methods: 24 volunteers (14 females, mean age = 22.3 years, std = 1.34 years) underwent fMRI in two sessions, following a night of normal sleep (rested wakefulness; RW) and after 24 h of SD. Subjects performed a delayed-response working memory task involving three faces. Two distracters were presented during the maintenance phase and these differed in content: highly-arousing, negative emotional scenes, low-arousing, neutral scenes, and digitally-scrambled versions of the pictures. 120 trials were presented in each state. No stimulus was repeated across states.
Results: Consistent with previous findings, at RW, emotional distracters had the greatest impact on lowering working memory accuracy (74.9%), relative to the neutral (73.7%) and scrambled (72.1%) conditions. The effect of SD was most pronounced for emotional distracters (66.4%, $p = .01$) compared to neutral (70.4%, $p = .15$) and scrambled (70.4%, $p = .05$) distracters. Emotional distraction was associated with decreased activity during the maintenance phase in dorsolateral PFC (dlPFC), and increased activity in ventrolateral PFC (vlPFC), fusiform gyrus, and amygdala. Across the group, SD resulted in reduction of maintenance-related vlPFC and amygdala activity. However, although SD did not elicit a systematic reduction in maintenance-related dlPFC activity during emotional distraction, there were individuals who showed heightened activity in these regions when sleep deprived. The extent to which activity was increased following SD was positively correlated with SD-related increase in emotional distractibility.
Conclusion: Individual variation in distractability by negative emotional pictures when sleep deprived can be related to SD-related increases in amygdala and vlPFC activation.
Support (optional): This work was supported by Defense Science and Technology Agency, Singapore (POD0713897) and a STaR award to Dr. Chee.

0039

DIFFERENCES IN HOW THE BRAIN PROCESSES AND RETRIEVES EMOTIONAL PICTURES ENCODED DURING SLEEP DEPRIVATION AND AFTER A NORMAL NIGHT'S SLEEP

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Introduction: Information encoded in the setting of sleep deprivation (SD) is less well remembered. Emotional stimuli are better retrieved than neutral stimuli after normal sleep and this advantage has been shown to extend to SD when tested a few days after encoding (Sterpenich et al,. 2007). Here, we investigated if different neural substrates are engaged during the successful recognition of negative-emotional scenes encoded during SD and after a normal night of sleep (RW) when individuals are tested a month after initial encoding.
Methods: 21 volunteers (11F, mean age=22.5 years, SD=1.33) were exposed to negative-emotional and neutral pictures in two test sessions: at RW and after 24h of SD. The order of sessions was counterbalanced across individuals and conducted a week apart. 80 pictures from each condition (emotional, neutral) were presented during each session. One month following their last session, participants underwent fMRI while performing an incidental delayed-recognition task. There were 640 stimuli, with equal numbers of targets and foils for both conditions.
Results: Behavior was indexed using corrected recognition (Hits-FA). We observed two main effects without interaction: Emotional stimuli were better recognized a month later relative to neutral pictures. Recognition was poorer for both emotional and neutral stimuli encoded during SD. For stimuli encoded at RW, successful recognition for emotional vs. neutral scenes elicited relatively lower activity in the caudate nucleus and medial prefrontal cortex and higher activity in the fusiform gyrus. For stimuli encoded at SD, successfully-recognized emotional scenes elicited greater activity, relative to neutral, in the inferior frontal gyrus and amygdala. A direct comparison between the two conditions showed that the retrieval of emotional stimuli encoded during SD engages the right amygdala to a greater extent.
Conclusion: The present observations extend previous findings that emotional stimuli are processed in a manner that facilitates better recognition relative to neutral stimuli - even after a month. How brain areas are engaged during successful retrieval of such emotional stimuli is influenced by sleep deprivation and the amygdala may be an important structure in this regard.
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0040

SPONTANEOUS SLEEP-RELATED CORTICAL AROUSALS IN HEALTHY POPULATION: WHAT ARE THE NORMS?

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Introduction: Arousal index (AI), the number of cortical arousal per hour of sleep, represents the degree of sleep fragmentation. It usually includes arousals secondary to respiratory events, limb movements and spontaneous arousals. No systematic studies are done in healthy subjects to determine the norms for spontaneous AI.
Methods: 350 polysomnograms of subjects ≥ 18 y.o. with no sleep disorders (AHI <5, periodic limbs movement index (PLMI) <10, periodic limbs movement arousal index (PLMAI) <5, no upper airway resistance syndrome) or oxygen desaturation (minimum saturation > 90%) and

no comorbid health problems were reviewed. Scoring based on 2007 AASM scoring criteria.
Results: Descriptive data: sleep efficiency 80.1± 9 %, sleep latency 20.8±19.5 min, REM latency 113.7± 59.2 min, stage N1 9.5± 6.2%, stage N2 62.4±8.8%, stage N3 7.4±7.2%, and REM 20.6±5.2%. AI significantly correlated with age (r = 0.7, p<0.01), sleep efficiency (r= -0.16, p<0.01), sleep latency (r = 0.14, p<0.05), REM latency (r = 0.12, p<0.05), stage N1 (r = 0.15, p<0.01), stage N2 (r = 0.12, p<0.05), stage N3 (r = -0.27, p<0.01), AHI (r = 0.24, p<0.01), PLMI (r = 0.18, p<0.01), PLMAI (r = 0.25, p<0.01) and nadir oxygen saturation (r = -0.17, p<0.01). A significant correlation was noted between age and sleep efficiency (r=-0.19, p<0.01), REM latency (r=0.13, p <0.05), stage N1 (r=0.16, p<0.01), stage N2 (r=0.21, p<0.01), stage N3 (r=-0.39, p<0.01), AHI (r=0.13, p<0.05), PLMAI (r=0.12, p<0.05), and nadir oxygen saturation (r=-0.16, p<0.01). Logistic regression model and multivariate analysis showed, after adjustment for co-variates, a strong linear relationship exists between AI with age (r=0.70, p<0.01). The prediction equation for the arousal index in healthy adults is: AI = 0.3*age (yr)-2.77.
Conclusion: A linear correlation exists between age and AI after controlling for factors that influence AI. The age-adjusted normal arousal index in healthy adults can be calculated by the given formula.

0041

MEDIAN PREOPTIC NUCLEUS AND SLEEP HOMEOSTASIS: EFFECTS OF THE NUCLEUS LESIONS

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Introduction: Recent studies, which employed immunostaining for c-Fos protein, provided evidence that activation of subsets of Median Preoptic nucleus (MnPN) neurons is correlated with the level of sleep need/pressure, and defined a role for MnPN GABAergic neurons in the homeostatic aspects of sleep regulation. In the present sudy, we examined the effects of MnPN electrolytic lesions on the regulation of sleep homeostasis in rats.
Methods: Adult male rats (n=12) were implanted with cortical EEG and dorsal neck EMG electrodes for assessment of sleep-wakefulness states in the condition of chronic experiment, and with bipolar electrodes for MnPN lesions. Animals were allowed a 5-day recovery period following surgery. On the 6th -10th days following surgery, animals were adapted to the recording environment and to a sleep deprivation (SD) procedure. On the 11th day post-surgery, rats were EEG/EMG recorded for 24 hours to determine baseline diurnal organization of sleep and waking. After that, a group of rats (n=6) was subjected to the MnPN lesion and then divided into two subgroups; rats that were assigned to 24-h sleep-waking recordings on the third, seventh and fourteenth days following the lesion and, rats subjected to 2-hours SD protocol on the third day following the lesion. The same schedule of experiments was applied to control rats (n=6). The tracks of the lesion electrodes were identified histologically.
Results: MnPN-lesined rats exhibited a fragmented pattern of sleep-waking cycle and revealed less prominent homeostatic responses to the SD, compared to control animals. Within the first week following the lesion, the MnPN-lesioned rats demonstrated a significant decrease (by %50, p<0.01) in total sleep time, compared to the control condtion.
Conclusion: Findings of the present study define potential roles for MnPN GABAergic neurons in homeostatic aspects of sleep regulation.
Support (optional): Georgian National Science Foundation, GNSF/ST07/6-219, supported this study.

0042

EEG SPECTRUM AND MOTOR CORTICAL PLASTICITY AFTER FOCAL BRAIN ISCHEMIA IN THE RAT

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Introduction: Sleep is believed to facilitate neuroplasticity under physiological conditions. Its role in modulation of neuronal reorganization and function outcomes in neurological diseases, such as ischemic stroke, is subject of research. In this study we used a rat ischemia model to investigate forelimb movement and electrical activity over motor cortex (M1), the representation of the forelimb, in different vigilance states during stroke recovery.
Methods: Eight male Sprague-Dawley rats were subjected to focal cerebral ischemia by occlusion of the distal middle cerebral artery (MCAo), damaging the somatosensory cortex, but sparing M1. Eight sham-operated rats served as controls. The forelimb movement was assessed by single pellet reaching and EEG was recorded over M1 in both hemispheres. Both pellet reaching and EEG were registered during a 30-day recovery period. EEG power spectra were calculated for slow wave sleep (SWS), paradoxical sleep (PS) and wakefulness (W). Brain sections were stained with cresyl violet to examine brain damage.
Results: Performance in pellet reaching dropped after ischemia and returned to baseline during the recovery period (p=0.008). Similarly, EEG power over M1 ipsilateral to the ischemia showed an immediate reduction in the 16-25 Hz beta frequency band and a slow return. This change was most prominent during PS (p<0.001). Seven out of 8 MCAo-rats showed a positive correlation between pellet reaching performance and beta power density in the affected hemisphere during PS (r=0.4; p=0.04 when grouped together). Histology confirmed the MCAo-induced damage in the ipsilateral somatosensory cortex with the lesion size 9.6 ± 3.3 % of the contralateral hemisphere.
Conclusion: The EEG beta band over motor cortex exhibits plasticity during stroke recovery and its correlation with motor function suggests that the transient power change during PS may serve as a relevant indicator of functional recovery.

0043

DECIPHERING THE ROLE OF THE GABA-A ALPHA4-SUBTYPE IN SLEEP

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Introduction: GABA, the predominant inhibitory transmitter in the brain, and its GABA-A receptors play an important role in sleep regulation. A vast repertoire of GABA-A receptor subtypes has been identified, underlying the complexity of GABA-A-mediated transmission. The GABA-A alpha4-subtype shows a very discrete expression in the brain. Notably, it is highly expressed in the thalamic relay nuclei which play a key-role in generating patterns of electrical activity characteristic of vigilance states. These receptors show specific electrophysiological properties (i.e., tonic inhibition) and pharmacological profile. We made use of GABA-A alpha4 subunit-knockout (KO) mice to study the role of this receptor subtype in sleep and sleep regulation.
Methods: We performed continuous electroencephalogram (EEG) recordings (parietal and frontal derivation) under baseline conditions (24 h), followed by 6 h sleep deprivation and 18 h recovery (GABA-A alpha4-KO mice, n=9 versus wild-type littermate controls, n=8). Sleep deprivation by gentle procedures is a well-established method to enhance sleep pressure and thereby uncover differences in sleep regulation which may not be evident under baseline conditions.
Results: Preliminary analyses of the EEG recordings showed no difference in time spent in waking, non-rapid eye movement (NREM) sleep

and REM sleep. Spectral analysis of the baseline EEG showed a decrease in EEG power spectrum in NREM sleep in alpha4-KO mice, specifically in the frontal derivation, in frequencies between 9-15 Hz encompassing the spindle frequency band. In contrast, the waking and REM sleep EEG power spectra showed no differences between the genotypes. Further analyses are ongoing to evaluate the response of alpha4-KO mice to sleep deprivation.
Conclusion: The specific decrease in EEG power density observed during NREM sleep in alpha4-KO mice suggests a role of the alpha4-subtype, and thereby tonic inhibition, in generating brain oscillations associated with NREM sleep.
Support (optional): Forschungskredit from the University of Zurich (to RWS); EU Marie Curie grant MCRTN-CT-2004-512362 (to IT).

0044

FEASIBILITY OF SELECTIVE MUSCLE FIBER DENSITY EXAMINATION IN THE GENIOGLOSSUS

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Introduction: It is well accepted that the multiunit electromyographic signal is increased in the genioglossus in OSA versus controls during wakefulness (Mezzanotte et al 1992). Interestingly, it has recently been shown that this may be in part due to peripheral changes in the motor unit, without global increases in single motor units discharge frequencies (Saboisky et al 2007). We employed EMG techniques to assist in clarifying the extent of peripheral remodelling of the genioglossus in OSA patients. Fiber density is a method to assess the local arrangement of muscle fibers within one motor unit. Following axon loss, surviving motor units have higher fiber density due to collateral sprouting (fiber grouping). In contrast, it would be anticipated that increased central drive without neurogenic changes would result in normal fiber density and the recruitment of additional motor units with higher discharge frequencies in the population.
Methods: Fiber density measurements were recorded in awake healthy subjects (n=3, to date) and OSA patients (n=2). Fiber density was recorded with 26g Single Fiber Needles with a recording area of 25μm. The needle was positioned, after ultrasound measures that determined the depth of the musculature, to record and trigger the action potential of a single muscle fiber. The number of synchronous action potentials indicates the number of fibers in close proximity that are innervated by the same motor unit. The number of potentials was counted from 20 individual sites and the mean presented as the fiber density.
Results: Genioglossus fiber density in controls: i) 1.25. ii) 1.45. iii) 1.5 and in OSA i) 1.25. ii) 1.4.
Conclusion: These preliminary data illustrate the feasibility of fiber density recordings in the genioglossus. Mezzanotte et al 1992 J Clin Invest 89:1571-9 Saboisky et al 2007 J Physiol 585:135-46

0045

GENDER DIFFERENCES IN STRESS-INDUCED CHANGES IN SLEEP ARCHITECTURE AND SLEEP EEG

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Introduction: Clinical studies and sleep surveys have shown pronounced gender differences in the occurrence of insomnia and other sleep pathologies. Gender differences in sleep, while subtle under baseline conditions, may increase in magnitude under biological or environmental challenges. Here we applied an animal model to examine gender differences in sleep after stressors of different modalities.
Methods: The experiments were performed with adult male and female Wistar rats. The female rats were ovariectomized and received low dose of estradiol replacement to maintain normal physiology. The rats were exposed to a 1h stress session at the beginning of their resting phase, i.e., a physical stressor (footshock) or an emotional stressor (reexposure to the shockbox). EEG/EMG was recorded and visually scored for wakefulness, NREM sleep and REM sleep. As a control procedure, animals were subjected to 1h sleep deprivation by mild stimulation without major stress.
Results: The data show a clear effect of stress on sleep that was not visible after short sleep deprivation by mild stimulation. Female rats displayed an increase in NREM sleep slow wave activity (SWA) especially following the physical footshock stressor. After the emotional stressor, the increase in SWA was less profound but there was a tendency for an increase in the time spent in NREM sleep. Males generally showed less profound changes in sleep.
Conclusion: These data support the notion of gender differences in sleep, particularly under conditions of stress. Also, the increases in NREM sleep time or slow-wave activity may suggest that sleep is important for recovery from the consequences of stress.

0046

DEEP BRAIN SLEEP RECORDINGS IN HUMANS: DIFFERENTIAL ACTIVITY RECORDED FROM THALAMIC, HYPOTHALAMIC, SUBTHALAMIC AND PALLIDAL SITES DURING REM SLEEP

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Introduction: Models of REM sleep and dreaming have proposed a role of several structures of the midbrain, especially the basal ganglia, in the diffusion and modulation of REM sleep phenomena. We sought to identify and characterize slow and fast synchronized oscillations recorded through Deep Brain Stimulation (DBS) electrodes implanted for therapeutic purposes in different subcortical structures during sleep in humans.
Methods: DBS functional neurosurgery was conducted to alleviate severely disabled patients with different chronic pathologies. Neurophysiologic monitoring, magnetic resonance neuroimaging and clinical outcome revealed a positive therapeutic localization of the DBS-electrode's contacts within the target structures: thalamic, hypothalamic, subthalamic, and pallidal nuclei. Local field potentials (LFPs) from bilateral or unilateral DBS-electrodes and polysomnography (PSG) were simultaneously recorded. LFPs and PSG derivations were analyzed in terms of amplitude, time and frequency domains, and submitted to statistical analyses. Visual scoring of sleep stages was performed blind from DBS-electrode traces according to standard criteria.
Results: During REM sleep, a bilateral pattern of phasic and enhanced fast oscillations was recorded as LFPs showing polarity reversal in the human subthalamic nucleus (STN); these activities were time-related to the occurrence of rapid eye movements (REMs) and EMG atonia. In contrast, pallidal and hypothalamic sites showed non-polarity reversed phasic field potentials that were not associated with enhanced fast oscillations. The thalamic Vim nucleus showed a pattern of rhythmic delta waves of irregular high amplitude and no significant fast oscillations. At motor cortex level (M1) enhanced fast oscillations were found to be associated with the bursts of REMs.

Conclusion: Our results confirm the implication of the STN in an ascending activating network involved in the modulation of EEG activation, REMs and muscular atonia in humans during REM sleep. This project, based on human pathological models, helps to elucidate about human normal sleep.

0047

STATE SPACE MAPPING OF SLEEP AND WAKEFULNESS IN PARKINSON PATIENTS AND HEALTHY CONTROLS

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Introduction: Sleep is commonly scored in stages, but the succession of behavioral states is only poorly understood. For a better description of sleep-wake dynamics, we have adapted state space analysis (as previously reported in rodents) to analyze sleep in patients with Parkinson's disease (PD) and healthy controls.
Methods: We obtained polysomnographic recordings from 7 PD patients and 7 age-matched healthy controls. 30-s epochs were scored visually. EEG data were Fourier-transformed to obtain the power spectral density for each epoch. Thereafter, we calculated 3 ratios of frequency bands. While these ratios aim at capturing specific spectral features, their final nature is heuristic. After data processing via principal component analysis, smoothed time series were plotted as clusters and trajectories in a three-dimensional state space. The congruence between visual scoring and the classification based on EEG spectra was quantified with discriminant analysis (DA). We assessed ratios for optimal cluster discrimination (optimized for maximal surface of the triangle spanned between the centroids of the DA) and congruence.
Results: Power spectra revealed only minor differences between PD patients and controls. Optimal power ratios focus on alpha peaks and spindle frequency ranges. Congruent scoring was obtained for a median of 90% of epochs in PD patients, and 93% in controls. The median surface of the triangle between centroids was 49 for PD patients and 180 for controls. In all subjects, trajectory velocity within clusters was low for NREM4 and REM sleep, indicating high stability of these behavioral states. Highest velocities were found for NREM1 and wakefulness. The same pattern of velocities appeared for epochs adjacent to state transitions.
Conclusion: State space analysis can be applied to sleep EEG recordings of both healthy controls and PD patients. Embedding of further polysomnographic parameters may improve discriminatory power.

0048

SATURATION THRESHOLDS OF NEUROVASCULAR COUPLING UNDER HIGH INTENSITY AUDITORY STIMULATION

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Introduction: Stimulation of the auditory cortex results in an electrical evoked response (ERP) which requires energy, drawing oxygen and glucose from the blood. As a result, local blood vessels temporarily dilate increasing the availability of blood to the region. Both the ERP and blood volume increase with higher stimulus intensities, following a psychometric function. Due to the physical limits of blood vessel dilation and electrical responsiveness, we expect both of these parameters to saturate at high stimulus intensities. Since the evoked blood volume response may depend on prior use, and is modulated by sleep, we hypothesize that evoked blood volume response may reach saturation before the ERP saturates.
Methods: Four adult female Spague-Dawley rats were implanted with a LED emitting 660 nm light and a photodiode that collected changes in light absorption from the somatosensory cortex. One EEG screw electrode was implanted to measure the ERP. Auditory stimulation was provided using single speaker clicks delivered at random intervals between 2 and 13 seconds at 0.2 ms pulse width, 47-88 dB in intensity.
Results: ERP amplitude followed a psychometric function with increasing stimulus intensity and continued to increase even with the highest stimulus intensity. However, the blood volume response appeared to reach saturation as it approached the 88 dB stimulus intensity.
Conclusion: Due to the limits of blood vessel dilation, there is a finite volume of blood that can be delivered to an activated region of the brain. This concept is illustrated in the saturation of the blood volume response while the electrical response continued to increase. When the activated brain region has used up its blood supply, it may require sleep to restore the vascular ability to deliver metabolites. Mechanisms to enable vascular restoration may exist within localized brain regions, and require further investigation.
Support (optional): This worked was supported by the WM Keck Foundation and the National Institute of Health, MH71830.

0049

DIFFERENTIAL EFFECTS OF OREXIN AND DYNORPHIN ON CORTICALLY-PROJECTING NEURONS OF THE BASAL FOREBRAIN: AN IN VITRO STUDY

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Introduction: The basal forebrain (BF) is an important component of the ascending arousal system and may be a key site though which the orexin neurons promote arousal. BF neurons activate the prefrontal cortex (PFC), and people with narcolepsy have impaired performance on PFC-dependent tasks and reduced activation of the PFC. It is known that orexin neurons also contain the inhibitory peptide dynorphin, and orexin and dynorphin are probably co-released. Here we study the effects of orexin and dynorphin on neurons of the substantia innominata (SI) that directly project to the medial PFC (mPFC).
Methods: We performed patch-clamp recordings on SI cortically-projecting neurons using in vitro slices of mice. SI neurons were labeled in vivo, by combining injections of fluorescent latex beads (green) into the mPFC and i.c.v injections of Cy3-p75-IgG (red). Fluorescent beads retrogradely labeled neurons projecting to the mPFC and Cy3-p75-IgG immunolabeled neurons that expressed p75 receptors, which in the BF are only the cholinergic population. In the slices, cholinergic neurons projecting to mPFC were recognized by the presence of both green beads and Cy3-p75-IgG. Non-cholinergic, cortically-projecting neurons contained green beads but lack red Cy3-p75-IgG.
Results: We found that SI cholinergic neurons were directly excited by orexin but did not respond to dynorphin. In addition, orexin increased the glutamatergic input to cholinergic SI neurons. We found two populations of non-cholinergic SI neurons that project to the mPFC: in one cell type, orexin was excitatory whereas dynorphin inhibited the excitatory input. In the other population showed no response to orexin but was directly inhibited by dynorphin.
Conclusion: Orexin and dynorphin have specific effects on different classes of BF neurons. These responses may provide a synergistic mechanism by which the co-release of orexin and dynorphin can promote wakefulness and improve cognitive performance.
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0050

COMPARISON OF THE EFFECT OF ESZOPICLONE AND OTHER GABAA RECEPTOR MODULATORS ON HIPPOCAMPAL THETA OSCILLATIONS

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Introduction: Cortical interneurons show high diversity and neuron type-specific functional relationship to cortical oscillations. GABAA

receptors composed of different subunits have characteristic cellular and subcellular distributions and are associated with different types of interneurons. This study tested whether the effect of various GABAA modulators on cortical oscillations depends on their profile of subunit selectivity.

Methods: Eleven rats were implanted with EEG and EMG electrodes for chronic recordings of sleep wake states and hippocampal field potentials. The total power in the delta and theta bands of the hippocampal EEG was calculated and the characteristics of theta oscillations were studied selectively for 4s windows in which this rhythm was dominant, i.e. when theta power exceeded delta power by at least 4 times. The rats were recorded daily for 8-10 hours undisturbed, except when the injection occurred at the beginning of the fifth hour of recording. Drugs: eszopiclone (3, 6, and 10 mg/kg b.w.), diazepam (1 and 3 mg/kg), zolpidem (2.5, 5 and 7.5 mg/kg), etomidate (5 mg/kg); vehicle controls: saline, cyclodextrin, and DMSO.

Results: Total theta power showed similar alterations for all GABAA modulators according to their known effects on behavioral states. The characteristics of theta rhythm, however, markedly differed after eszopiclone vs. the other GABAA modulators. A shift of the theta peak to lower frequencies, characteristic for all these compounds, was accompanied by a significant dose-dependent increase in peak power after eszopiclone and by either a decrease or no change after zolpidem, diazepam, and etomidate.

Conclusion: Interneurons are critical for rhythmic synchronization in the cortex and hippocampus and these data demonstrate that enhancement of GABAA mediated inhibition can lead to increased synchronization in the hippocampus. The ability of different GABAA modulators on theta synchrony most likely depend on the subunit composition of the receptors associated with different classes of interneurons.

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0051

EFFECTS OF LESIONING THE GLOBUS PALLIDUS ON RAT SLEEP

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Introduction: Adenosine, an inhibitory nucleoside, is believed to be involved in sleep/wake regulation. Administering an adenosine agonist at the A_1 or A_{2A} adenosine receptors has been found to increase high voltage sleep in rats. There are high levels of the A_{2A} receptor within the basal ganglia. The present study sought to determine if the globus pallidus influences sleep and wake states.

Methods: Ten male Sprague-Dawley rats, weighing approximately 300g, received unilateral ibotenic acid lesions in the globus pallidus. Nine rats served as lesion controls. Sleep was recorded and analyzed 12 days following surgery. Immediately after recording sleep, rats were transcardially perfused for fixation. Sections were stained with neutral red and NeuN. Stained sections were examined with light microscopy to determine the extent of the lesion.

Results: A 2 x 2 x 3 repeated measures ANOVA found lesioned rats had a significant increase in waking and a significant decrease in high-voltage sleep during the light cycle ($F = 3095.73, p < .001$). No change in paradoxical sleep was found. Also, no significant differences were found for type of lesion or vigilance state (Wake, High Voltage, and Paradoxical) during the dark cycle.

Conclusion: These results suggest that the globus pallidus is involved in sleep regulation due to the change in sleep/wake architecture found in lesioned versus control rats.

0052

NORADRENERGIC MODULATION OF MUSCLE TONE DURING CATAPLEXY IN HYPOCRETIN/OREXIN KNOCKOUT MICE

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Introduction: Cataplexy is a primary symptom of narcolepsy and is characterized by involuntary loss of postural muscle tone during waking. Cells in the locus coeruleus cease firing during cataplectic attacks in narcoleptic dogs indicating that reduced noradrenergic excitation of motoneurons may trigger cataplexy. Although monoaminergic reuptake inhibitors improve cataplexy, it is unknown if such effects are mediated by increasing noradrenaline levels within somatic motor pools. The aim of this study was to determine whether restoring noradrenergic drive to the trigeminal motor pool would reverse loss of masseter muscle tone during cataplexy in hypocretin knockout (KO) mice.

Methods: We used reverse microdialysis to apply phenylephrine (an α1-noradrenergic receptor agonist) onto trigeminal motoneurons during cataplectic episodes in freely-behaving hypocretin KO mice. We quantified levels of masseter muscle tone during cataplexy (and across the sleep-wake cycle) before and during noradrenergic excitation of trigeminal motoneurons. Cataplexy and sleep-wake state were determined using EEG, EMG (neck and left/right masseters) and videography.

Results: We quantified 14 episodes of cataplexy while applying either aCSF (n=7) or 1mM phenylephrine (n=7) at the trigeminal motor pool in 4 hypocretin KO mice. We showed that masseter muscle tone was potently suppressed below waking levels during individual cataplectic attacks ($p=0.003$). Importantly, we found that increasing noradrenergic drive by activating α1-noradrenergic receptors at the trigeminal motor pool significantly increased masseter tone during cataplexy ($p=0.004$); however, such activation did not restore masseter tone to waking levels ($p=0.008$).

Conclusion: We conclude that reduced noradrenergic drive onto somatic motoneurons contributes, at least in part, to the loss of muscle tone during cataplexy. However, changes in release profiles of other neurotransmitters must also be involved in triggering loss of muscle tone during cataplexy.

0053

TRIHEXYPHENYDIL AS AN ANALOG OF PHENCYCLIDINE, WHICH ANTAGONIZES NMDA RECEPTORS PHENCYCLIDINE SITES, DISRUPTS INTEGRITY OF REM SLEEP

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Introduction: It is already known that "REM-on" neurons are not only cholinergic, glutamatergic neurons may also be of "REM-on" type. We have therefore got interested what would happen with REM sleep in case when NMDA glutamate receptors function is modulated by blocking of their phencyclidines' site. For this aim we studied the effects of phencyclidine analog, trihexyphenydil, on the EEG and vegetative patterns of REM sleep.

Methods: On cats (n=5) metallic electrodes were implanted under overall anesthesia (by sodium ethaminal 35-40 mg/kg). Continuous EEG registration lasting 12 hr daily started after animals' recovery. Trihexyphenydil was administered intraperitoneally (2 mg/kg -5 mg/kg). Statistical processing was made by Students' t test.

Results: It appeared that modulation of NMDA receptors function by antagonizing their phencyclidine sites resulted increase of REM sleep latency and decrease of its frequency and total time. This indicates that the NMDA glutamate receptors must be involved in REM sleep modulating mechanisms and that performance of this function is possible only when

the NMDA receptors phencyclidine sites are not blocked. Trihexyphenydil disrupted REM sleep integrity and resulted dissociated triggering of REM sleep patterns. There occurred sharp dissociation between EEG and vegetative parameters of this phase, namely rapid eye movements and ponto-geniculo-occipital waves appeared during behavioral active waking state. As soon as animal closed eyes the synchronization degree increased and both parameters were completely suppressed. Therefore on the background of behavioral active waking, according to electrical activity of the visual cortex and rapid eye movements, electrographic patterns of REM sleep were recorded.
Conclusion: The normal functioning of the NMDA glutamate receptors' phencyclidine sites is considered as a mechanism which inhibits and/or hinders development of hallucinations. Among exciting amino acid receptors only NMDA glutamate receptors, possessing a phencyclidine site, have REM sleep modulating effect.

0054

OREXIN 1 AND 2 RECEPTOR ANTAGONIST, ALMOREXANT, ATTENUATES ACTIVATION OF HYPOGLOSSAL (XII) MOTONEURONS ELICITED BY BICUCULLINE FROM THE POSTERIOR LATERAL HYPOTHALAMUS

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Introduction: In anesthetized rats, injections of the $GABA_A$ receptor antagonist, bicuculline, into the perifornical region of the posterior hypothalamus (PF) locally activate many cells, including the wake-promoting orexin neurons, elicit cortical and hippocampal activation, increase XII nerve activity and respiratory rhythm. XII motoneuron activation from the wake-promoting PF region may play an important role in upper airway control in patients with obstructive sleep apnea syndrome. To date, we determined that neither systemic antagonism of orexin 1 receptors with SB334867 nor combined antagonism of α1-adrenerdic and serotonergic receptors located in the XII nucleus region can abolish the activation of XII motoneurons from the PF region (Lu *et al.*, J. Physiol., 2007; Fenik *et al.*, APSS Meeting-2008). We now assessed whether antagonism of both type 1 and 2 orexin receptors can attenuate this activation.
Methods: In 15 urethane-anesthetized, paralyzed, vagotomized and artificially ventilated rats, we recorded XII nerve, cortical and hippocampal activity. In 7 rats, Almorexant injections (100 mg/kg, i.p.) were followed at 30 and 120 min with two successive PF microinjections of 1 mM bicuculline (20 nl). In 8 control rats, bicuculline injections were made with the same timing after vehicle administration (H_2O).
Results: The baseline levels of XII nerve activity, basal central respiratory rates and bicuculline-induced respiratory rate increases were not different between the first and second bicuculline injections within and between the two groups of animals. In Almorexant-treated rats, increase of XII nerve activity following the first PF bicuculline injection was about twice larger than that after the second bicuculline injection made when Almorexant approached its peak level in the brain (increases by 106±25(SE)% and 57±14% of the pre-bicuculline levels, respectively, $p<0.035$). In the vehicle group, the activating effects of the two successive bicuculline injections were similar (124±32% vs. 120±25%). Both bicuculline injections induced similar changes in cortical and hippocampal power spectra in both groups.
Conclusion: A significant portion of the excitatory effect of PF bicuculline on XII motoneurons is mediated by orexin, probably orexin-2, receptors.
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0055

ULTRASONIC VOCALIZATIONS PREDICT CATAPLEXY IN HYPOCRETIN/OREXIN KNOCKOUT MICE

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Introduction: Cataplexy, the sudden loss of postural muscle tone during waking, is a symptom of the sleep disorder narcolepsy. In human narcoleptics cataplexy is often preceded by laughter or strong positive emotions. In hypocretin knockout mice cataplexy is associated with rewarding experiences such as wheel running and presentation of palatable food. Ultrasonic vocalizations in rats and mice are associated with positive experiences, including social interaction. This study identifies a link between ultrasonic vocalizations and cataplexy in a murine model of narcolepsy.
Methods: We studied female hypocretin knockout mice and wild type littermates (C57Black/6) in a social reunion paradigm. Two cage mates were separated for 7 hours, followed by reunion. Ultrasonic vocalizations and video were recorded for 20 minutes post-reunion, with cataplexy scoring by blind, experienced observers.
Results: Hypocretin knockout mice vocalize in response to social reunion, just as wild type mice do. We found that increased vocalizations were correlated with time spent in cataplexy ($R2=0.52$; $p=0.001$); pairs that vocalized more in response to social reunion had increased amounts of cataplexy. We also observed a temporal relationship between ultrasonic vocalizations and cataplexy onset; on average animals vocalized more in the minute preceding cataplexy then at any other time during the recording period and 30% of cataplectic episodes were immediately preceded (within 9 ± 4s) by ultrasonic vocalizations.
Conclusion: This study supports a link between ultrasonic vocalizations and cataplexy in a murine model of narcolepsy, indicating that cataplexy may be elicited by positive emotions in mice as it is in humans.

0056

LIGHT-REARING ALTERS RETINAL INPUT AND IMMEDIATE EARLY GENE RESPONSES TO LIGHT IN THE VENTRAL HYPOTHALAMUS OF THE ALBINO RAT

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Introduction: Data from our lab have demonstrated that the early lighting environment affects sleep-wakefulness behaviors; specifically, dark-reared rats show enhanced sleep responses to acute light changes, whereas light-reared rats show diminished acute responses to light (Prichard et al., 2004). In order to investigate possible mechanisms underlying the blunted sleep responses to light in light-reared rats, we evaluated differences in retinofugal projections and c-Fos responses to light in retinorecipient nuclei of light-reared (LL) and light-dark-reared (LD) rats. Furthermore, to determine whether these potential changes are reversible, we compared rats that were switched from a constant light environment to a light-dark environment (LLLD), or vice versa (LDLL) at 3 months, to rats that were maintained in the LL or LD environments for a full 5-6 months.
Methods: We quantified Fos expression in all regions of the subcortical visual system in LD, LL, LDLL and LLLD rats (n=6 per condition) that were exposed to 1 hour of light following 18 hours of darkness. To determine whether rearing condition altered retinofugal projections, we injected the anterograde tracer cholera-toxin β (CTβ) into the vitreous humor of a separate group of rats (n = 5-6 per condition), and quantified the density and distribution of CTβ-stained fibers throughout the subcortical visual system.

Results: We found that LL-rearing was associated with pronounced alterations in the ventral hypothalamic region. In LL-reared rats, there was an increase in retinal input to and a significant reduction in light-induced Fos-expression in the ventral hypothalamus. These differences were reduced, but not eliminated, by a switch to LD environment at 3 months.
Conclusion: These data provide novel information about the influence of light on the postnatal development of subcortical visual nuclei, and support a mechanism whereby the effects of light-rearing on the timing of sleep/wakefulness might be explained.

0057

PUBERTAL MATURATION, REWARD-RELATED BRAIN FUNCTION, AND SLEEP IN ADOLESCENTS

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Introduction: Puberty is a time of dramatic changes, including changes in sleep. The onset of adolescence is also a period of new health concerns related to increases in risk-taking, sensation-seeking, depression, substance use, and accidents. The larger study examined puberty-specific changes in adolescents' reward-related behavior and included functional neuroimaging of reward as well as objective and subjective measures of sleep. This presentation will focus on the relationship between sleep and reward.
Methods: 58 participants age 11-13 completed four-days of home actigraphy and self-reported sleep ratings and a functional magnetic resonance imaging scan using a guessing task with monetary rewards that separated reward anticipation from reward outcome. Sleep variables included in the analyses were mean weekend minutes asleep and self-reported sleep quality.
Results: During reward anticipation, both fewer minutes asleep ($t=2.67$, $p<.01$, 23 voxels at 0, 1, 18) and lower sleep quality ($t=2.44$, $p<.01$, 13 voxels at -4, 2, 11) were associated with less activation in the caudate. During reward outcome lower sleep quality was associated with less activation in the caudate ($t=2.86$, $p<.005$, 214 voxels at -6, 6, 11).
Conclusion: Our results support the hypothesis that sleep patterns in adolescence are associated with altered patterns of activation in reward circuitry in ways that could have important health implications. One set of hypotheses about response to reward in adolescents is that adolescents' low reactivity in reward-related brain areas could lead to compensatory increases in reward-driven behavior. These findings suggest that sleep characteristics could also contribute to such behavior. Because decreased sleep has been associated with risky behavior and negative mood, these findings raise concerns about a negative spiral of effects whereby maturational effects of puberty and sleep deprivation may have synergistic effects on reward processing, contributing to adolescent behavioral and emotional health problems.

0058

GABAA RECEPTORS IMPLICATED IN REM SLEEP CONTROL

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Introduction: The sublaterodorsal nucleus (SLD) is one brain area identified in the rat as a REM sleep induction zone. Local application of GABAA receptor antagonists to the SLD can induce REM sleep. This finding is consistent with local GABAA receptors exerting negative-control over REM sleep. Here we sought to determine the GABAergic innervation and subunit composition of the GABAA receptors implicated in REM sleep control. Two GABAergic afferents were studied, that from the caudal, ventrolateral periaquiductal grey (vlPAG) and nucleus pontis oralis (PnO).
Methods: Long-Evans Hooded rats were unilaterally injected in the vlPAG or PnO with a solution of biotinylated dextran amine (BDA, 10k MW) and sacrificed 10 days later. Coronal sections were studied through the SLD after multiple labeling of orthogradely transported BDA, the vesicular GABA transporter (VGAT) to visualize GABAergic terminals, and an antibody to one of the GABAA receptor subunit proteins. Colocalization of immunoreactivity was visualized with fluorescence, laser scanning, confocal microscopy. The experimental strategy sought to find triple-labeled varicosities in SLD that would identify the source of GABA terminals and post synaptically apposed receptor subunits.
Results: We found GABAergic terminals (BDA/VGAT labeled varicosities) in SLD that have their source in neurons located in the PnO and vlPAG. Many of these terminals have a somatic location where they can provide a potent inhibitory effect. Conclusive evidence for the co-localization of a receptor subunit is still being sought with a variety of antibodies.
Conclusion: Based on studies of c-Fos expression, PnO and SLD contain GABAergic neurons with a REM-off pattern of activity. The withdrawal of GABA release by these neurons in the SLD may be an important mechanism in control of REM sleep. Identification of the GABAergic receptor subtype(s) mediating these effects in SLD could provide a novel target for therapeutic pharmacological agents.
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0059

EFFECTS OF CIRCADIAN PERIOD AND SLEEP PRESSURE ON HYPOCRETIN-MEDIATED SLEEP-TO-WAKE TRANSITIONS

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Introduction: The Hypocretins (Hcrts, also called Orexins) are two neuropeptides expressed in the lateral hypothalamus that play a crucial role in boundary state control. Previously, our laboratory demonstrated that in vivo photostimulation of Hcrt neurons genetically targeted with ChR2, a light-activated cation channel, is sufficient to increase the probability of an awakening event during both slow wave sleep (SWS) and rapid eye movement (REM) sleep. In the current study, we ask whether Hcrt-mediated sleep-to-wake transitions are affected by circadian period and sleep pressure.
Methods: We stimulated Hcrt neurons in mice during either SWS or REM sleep and then measured the latency from sleep to wakefulness. We also stimulated mice immediately following 2 or 4 hours of sleep deprivation by gentle handling.
Results: We found that stimulation of Hcrt neurons increased the probability of an awakening event throughout the entire circadian period but that this effect was lost with sleep pressure induced by 2 or 4 hours of sleep deprivation. Interestingly, photostimulation of Hcrt neurons was still sufficient to increase activity in Hcrt neurons after sleep deprivation, even though this stimulation did not cause an increase in transitions to wakefulness. We also demonstrate that photostimulation of Hcrt neurons increases neural activity in the downstream arousal-promoting locus coeruleus and tuberomammilary nucleus, but not after 2 hours of sleep deprivation. Finally, stimulation of Hcrt neurons was still sufficient to increase the probability of an awakening event in histamine-deficient HDC KO animals.
Conclusion: These results suggest that the Hcrt system promotes wakefulness throughout the circadian period by exciting downstream targets, which themselves are inhibited with increased sleep pressure.

0060

QUANTIFYING CONVENTIONAL AND ECG-SPECTROGRAPHIC SLEEP ARCHITECTURE WITH MARKOV STATE TRANSITION MODELS

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Introduction: Improved characterization of sleep architecture and state transition patterns may enhance clinical phenotyping of sleep disorders, with the goal of increasing predictive value for pertinent end-points such as sleepiness, cognitive function, cardiovascular events and cerebrovascular events. As long-term monitoring in the home setting becomes increasingly available, metrics that capture sleep dynamics may provide important diagnostic and/or prognostic information to clinicians.
Methods: We retrospectively studied, in 374 patients from the Sleep Heart Health Study who were free of medications, sleep apnea, medical co-morbidities, or sleepiness: 1) Conventional sleep states, and 2) Sleep states from a novel ECG-derived cardiopulmonary coupling algorithm that distinguishes "stable" sleep, "unstable" sleep, and a composite "wake-REM" state (high, low, and very low frequency coupling, respectively).
Results: We confirm prior studies demonstrating that the distribution of time spent in PSG-defined states is exponential. The frequency distribution histograms for standard scoring stages were distinct from those using spectrogram-defined states, in terms of both the number and time constant value of the best-fit exponential functions. We propose Markov state transition models that recapitulate the standard and spectrogram-delineated sleep-wake state architecture in this control population. Model parameters were constrained by the time constants derived from the frequency histograms for each state, as well as adjacent-interval analysis of state transition patterns. The Markov schemes are amenable to dynamic modulation using the classic 2-process model as an input function, allowing incorporation of circadian and sleep drive variables into the model.
Conclusion: Markov state transition models can recapitulate normal human sleep architecture. We are currently applying this strategy to patients with a range of sleep disordered breathing, clinical symptoms, and co-morbidities. We hypothesize that Markov "fingerprints" of sleep dynamics (number, connectivity, and transition probability of states) will distinguish between normal and pathological clinical states, and may demonstrate improved correlation with clinically relevant endpoints.

0061

ACTIVATION DIFFERENCES DURING ASCENDING AND DESCENDING TRENDS IN Δ-WAVE POWER WHILE SLEEPING

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Introduction: We attempted to identify differences in brain activation as measured by fMRI during periods of sleep with ascending or descending trends in δ-wave (1 - 3.9 Hz) activity. Increasing δ-wave activity is associated with increasing "depth of sleep" and its prevalence is a key criterion for the transition between sleep stages. Spatial localization of activation differences in the brain between periods of increasing and decreasing δ-wave power should allow us to better understand brain regions involved in sleep stage transitions over the course of a night's sleep.
Methods: EEG and fMRI data were collected concurrently during sleep from 10 subjects at the National Institutes of Health. Scans were conducted after 44 hours of sleep deprivation and the maximum length of the scan was 3 hours. Mutually exclusive monotonic trends of ascending and descending δ power were identified for each individual and then modeled in regression analysis with Analysis of Functional NeuroImages (AFNI) software. Periods of non-varying δ-wave activity served as the baseline. The coefficients from these regressions were then submitted to a single factor ANOVA.
Results: During periods of descending δ power, increased activation was seen in the left middle frontal gyrus, the right postcentral gyrus, and the right superior temporal gyrus relative to periods of non-varying δ-wave power. Periods of increasing δ power were associated with increased activation in the right thalamus and the culmen.
Conclusion: Broadly speaking, the results indicate that increasing δ power and increasing "depth of sleep" is associated with increasing subcortical activation, whereas decreasing δ power and decreasing "depth of sleep" is associated with increasing cortical activation. This finding is consistent with literature in this field. Additional analyses are underway to identify differences in neural activation during periods of increasing and decreasing δ power within specific sleep stages.

0062

PROLONGED SLEEP FRAGMENTATION INDUCES DELAYED HIPPOCAMPAL-DEPENDANT LEARNING DEFICITS

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Introduction: Sleep fragmentation is prevalent in human sleep-related disorders. In rats, sustained sleep fragmentation has a potent suppressive effect on adult hippocampal dentate gyrus (DG) neurogenesis. Normally, newly-generated DG neurons progressively mature over at least 4 weeks, and are hypothesized to participate in hippocampal-dependent learning. However, a prediction that suppression of neurogenesis would impair hippocampal-dependent learning at the time when neurons are expected to reach maturity has not been tested.
Methods: Sprague-Dawley rats were surgically-prepared with EEG and EMG electrodes for sleep state detection. We used a computer controlled treadmill system to induce sleep-dependent sleep fragmentation for 12 days, and used both yoked controls (YC), on the same treadmill, and cage controls (CC). The rats were injected with 5-bromo-2-deoxyuridine (BrdU, 200 mg/Kg) to label proliferating cells half on days 5 and 11 of the procedures or only on day 5. Rats then rested in their home cages for 14 days prior to cognitive testing. Cognitive performance was then tested in a Barnes maze for 7 days, 5 trials a day, with 5 days at a constant escape tunnel position followed by 2 days with a rotated position (1350 to the right). All groups were perfused the day after completion of the Barnes maze and DG sections were immunolabeled for both BrdU and NeuN to identify mature cells.
Results: The use of random search strategies was significantly elevated in sleep fragmented (SF) compared to both YC and CC groups. In groups injected on days 5 and 11, SF and YC animals had significantly higher BrdU cell counts (YC were highest) than CC animals.
Conclusion: Sustained sleep fragmentation induced a spatial learning deficit when tested 2 weeks after terminating the procedure. The altered performance of the SF rats could be due to the abnormality of hippocampal DG neurogenesis.

0063

PROJECTIONS FROM THE AMYGDALA TO THE ACTIVE (REM) SLEEP EXECUTIVE AREA OF THE NUCLEUS PONTIS ORALIS IN THE GUINEA PIG

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Introduction: There is a consensus that active sleep (AS) occurs as a result of the activity of executive AS-on neurons that are located in the nucleus pontis oralis (NPO). It is also accepted that the AS-on neurons of the NPO are activated by excitatory cholinergic projections from the laterodorsal and pedunculopontine nuclei (LDT/PPT). In the present study, we examined the hypothesis that, in addition to input from the LDT/PPT, neurons that are located in the amygdala project to AS-on neurons in the NPO and thereby participate in the control of AS.
Methods: Eight adult guinea pigs were utilized in these studies. Under general anesthesia, the retrograde tracer Cholera toxin subunit-b (CTb) was microinjected into the NPO, unilaterally, by iontophoresis (+5 μA, in 5 seconds ON/OFF, for 30 minutes). Subsequently, the animals were euthanized and perfused with a mixture of fixatives; frozen coronal sections (20 μm) were then obtained from the amygdala and brainstem. Immunohistochemical procedures were utilized to identify CTb.
Results: Large numbers of retrogradely-labeled (CTb+) neurons were found ipsilaterally in the central nucleus of the amygdala following the injection of CTb into the nucleus pontis oralis. The CTb-labeled neurons were principally oval shaped. Their diameters were approximately 20 μm. In addition, CTb+ neurons were also found in the ipsilateral as well as the contralateral LDT/PPT.
Conclusion: We determined that there are direct projections from the central nucleus of the amygdala to the NPO. Therefore, we suggest that the central nucleus of the amygdala is capable of regulating AS by activating neurons that comprise the AS-generator in the NPO.
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0064

INTERLEUKIN-1B AND NERVE GROWTH FACTOR ARE DIFFERENTIALLY ALTERED IN THE RAT SOMATOSENSORY CORTEX DEPENDING ON TIME OF DAY

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Introduction: Interleukin-1β (IL1β), tumor necrosis factor α (TNF) and nerve growth factor (NGF) expression are activity-dependent and affect sleep. Electroencephalographic (EEG) slow wave activity (SWA) during non-rapid eye movement sleep (NREMS) gradually increases in the rat somatosensory cortex (Sctx) during the dark, a time of high whisker afferent activity, and peaks at light onset. Neuronal activity increases TNF expression in the Sctx in the dark. We hypothesize that the natural use of whiskers that occurs with rats during the dark will also enhance Sctx expression of IL1β and NGF.
Methods: Five-6 rats under a 12:12 h light:dark cycle were killed 6 or 11 h after dark or light onset. NGF & IL1β immunohistochemistry was performed and IL1β- and NGF-immunoreactive (IR) cells were counted. EEG SWA was characterized in four rats.
Results: EEG SWA during NREMS decreased during the light hours then increased initially during the dark. Six hours after dark onset, the number of IL1β-and-NGF-IR cells in the Sctx was significantly lower in layers II, V and VI for IL1β and layer IV and V for NGF (p= 0.04, 0.002, 0.001, and 0.02, 0.01) when compared to 6 h after light onset. However, IL1β increased significantly 11 h after dark onset in layers IV and V (p= 0.04, 0.01) compared to 11 h after light onset. NGF-IR cells increased significantly when comparing 6 h and 11 h after dark using an ANOVA followed by a post-hoc test for layers II-V (p= 0.013, 0.0002, 0.001).
Conclusion: These data support, in part, our hypothesis that increased SWA is associated with an increase in IL1β expression in the Sctx. However, increases in IL1β and NGF in the dark were delayed until the end of the dark period suggesting that natural vs manual stimulation have distinct time courses of action on cytokine expression.
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0065

BASAL GANGLIA CONTROL OF AROUSAL

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Introduction: The basal ganglia controls motor, learning, emotion and addictive behaviors, all of which operate on the basis of wakefulness. The most prominent structure in the basal ganglia is the striatum comprised of 98% medium spiny neurons (MSN) and 2% interneurons. The MSN receiving massive glutamatergic inputs from the cortex/thalamus and dopaminergic inputs from the midbrain. The MSN fire synchronously with cortical pyramidal neurons, alternating between an excitatory up-state and an inhibitory down-state. Through direct and indirect projections to the substantia nigra pars reticulate (SNr) and thalamus, the striatal MSN neurons can shape the activity of the thalamo-cortical arousal network. We hypothesized that the striato-thalamo-cortical loop plays an important role in the regulation of wakefulness.
Methods: To test this prediction, we made cell-body specific lesions in the striatum of 8 rats using ibotenic acid. Six additional rats received saline injections to serve as controls. Following seven days of surgical recovery, we recorded the EEG/EMG in all rats for 48 hrs.
Results: We found that rats with bilateral striatal (caudoputamen) lesions (up to 75% cell loss, but sparing the caudal striatum) exhibited a ca. 20% reduction in wakefulness as compared with controls. Furthermore, the striatal lesions produced fragmentation of wakefulness (and sleep) as indicated by an increase in bout number and duration, and a decrease in the diurnal amplitude of wakefulness (and sleep).
Conclusion: These results suggest that the striatum is a major component of the arousal system and is involved in the consolidation and promotion of wakefulness.
Support (optional): NIH

0066

ANESTHETIC EMERGENCE IS A USEFUL TOOL TO STUDY AROUSAL AND WAKEFULNESS IN A DROSOPHILA MELANOGASTER MODEL SYSTEM

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Introduction: Volatile Anesthetics (VA) induce a hypnotic state that shares important similarities with sleep. In fact, it has been shown that VA act on neuronal loci and circuits important for sleep regulation to produce their effect. In addition, drugs with hypnotic properties are commonly used in clinic as sleep promoting agents. We propose to study anesthetic emergence in a Drosophila melanogaster model system as a tool to improve our understanding of the neuronal circuits that regulate and promote arousal and wakefulness.
Methods: Female flies were individually loaded into cylindrical tubes with a volume of 0.75 mL that were connected to a gas manifold delivery system. Locomotor activity was measured using an automated system. Flies were housed in a 12 hour L:D cycle. VA (Isoflurane and Halothane) were delivered at ZT 10-12. Flies were then simultaneously exposed to progressive increasing and then decreasing concentrations of

VA. Cessation of locomotion for 5 minutes was defined as our anesthetic endpoint. Experiments were conducted with 3 wild type strains and the Shaker mns (minisleep) mutant line that has been previously shown to have reduced sleep.

Results: Dose response curves were obtained for induction and emergence from the anesthetized state. In Iso31 flies, curves yielded the following results. For Isoflurane, Induction EC50 Induction was 0.42%(CI 0.41-0.44) and Emergence EC50 was 0.29% (CI 0.27-0.31) For Halothane Induction EC50 was 0.51% (CI 0.50-0.53) and Emergence EC50 was 0.21% (0.18-0.24) These results indicate that the emergence curve was shifted in comparison to the induction Curve. In Shaker mns flies Isoflurane Induction EC50 was 0.49 (CI 0.48-0.51) and Emergence EC50 was 0.47 (CI 0.44 to 0.49) reflecting mildly increased resistance to induction and a significant reduction in the induction to emergence EC50 differential.

Conclusion: Anesthetic emergence appears to be a distinct process that requires the participation of arousal pathways/circuits rather than the passive dissipation of the VA at its action site in the central nervous system as shown by tissue measurements. In addition anesthetic emergence can be manipulated by a single gene mutation in a potassium channel involved in membrane repolarization and is also leads to markedly reduced sleep. We believe that further studies of anesthetic emergence will allow us to further elucidate the neural substrates that mediate arousal.

Support (optional): Harold Amos Medical Faculty Development Program from the Robert Wood Johnson Foundation, Parker B Francis Fellowship, ITMAT Transdisciplinary Award Program from the University of Pennsylvania, NIH NIGMS, NIH T32 Training Grant Awarded to the Department of Anesthesiology and Critical Care at the University of Pennsylvania and Howard Hughes Medical Institute.

0067

SURVIVAL ANALYSES OF SLEEP AND WAKE BOUTS REVEAL DIFFERENTIAL REGULATION OF THE MAINTENANCE OF NREM AND REM SLEEP

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Introduction: Survival analyses of sleep and wake bout lengths were used to quantify the statistical characteristics of bout lengths and the effects of prior wake, circadian phase and length of time within a sleep episode on sleep architecture.

Methods: Polysomnographic sleep recordings were obtained from healthy subjects during inpatient forced desynchrony protocols with 20-hr, 28-hr, or 42.85-hr cycles. Circadian phase was defined using plasma melatonin. Two consecutive 30-second epochs of NREM sleep, REM sleep, Sleep (NREM or REM) or Wake were required to initiate a "bout" of that state; this bout lasted until a bout of another state began. Kaplan-Meier survival analyses were performed using SAS PROC LIFETEST with Cycle-length as a strata variable. Analyses were performed for Sleep-Wake or NREM-REM-Wake transitions.

Results: The survival of Sleep, Wake, NREM sleep and REM sleep bouts lengths had non-normal statistical distributions. The "hazard" or rate of transitioning from that state depended on bout length. For all types of bouts, the hazard rate was much higher for the first ~5 minutes. Sleep and REM sleep bouts had an exponential shape for bout lengths longer than ~5 minutes, indicating that the probability of transitioning out of that state was independent of bout length. In contrast, Wake bouts had a power-law shape for bout lengths: the probability of falling back to sleep decreased with increasing Wake bout length. In Sleep bouts, there was a non-linear dose response to different durations of prior scheduled wake episode length. There was a significant variation in hazard with respect to circadian phase and length of time within a sleep episode for all bout types.

Conclusion: Survival analyses demonstrate differential regulation of Sleep, Wake, NREM sleep and REM sleep maintenance. Further exploration of these differences and the effects of different pathophysiology or pharmacologic agents on these measures may be fruitful in identifying physiological mechanisms and evaluating hypnotics.

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0068

FEAR-CONDITIONED ALTERATIONS IN REM PHASIC ACTIVITY MEASURED BY MUSCLE TWITCHES IN STRESS-SENSITIVE WISTAR-KYOTO (WKY) VERSUS WISTAR (WIS) RATS

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Introduction: We have previously reported greater REM fragmentation resulting from fear conditioning in WKY compared to WIS. In order to explore underlying causes of this difference, we investigated the effect of fear conditioning on the frequency of muscle twitches during REM (MT) as a measure of REM phasic activity. We hypothesized that fear-conditioned WKY would show greater alterations in MT number.

Methods: Animals were implanted with EEG and EMG electrodes and habituated to the recording procedure. They had baseline sleep recorded over 4 hrs in the light, and the next day were fear-conditioned to ten presentations (30s ISI) of a tone co-terminating with a foot shock (1.0 mA, 0.5s). The following day (Day 1) and 14 days later, three tones were presented every 30s, without shock, and sleep was recorded over 4 hrs. We visually analyzed MT from the neck muscle EMG during REM sleep, with artifacts excluded.

Results: A significant day x strain interaction was found in total number of MT [p=0.0056]. In WKY, total MT increased from 19.3 ± 2.7 at baseline to 48.2 ± 14.1 on Day 1 [p=0.03]. In WIS, no significant change in total MT was found on either test day. Significant strain differences in MT were found at baseline (WKY: 19.3 ± 2.7; WIS: 120.0 ± 16.7; [p=0.0001]), on Day 1 (WKY: 48.2 ± 14.1; WIS: 76.3 ± 21.2; [p=0.02]) and Day 14 (WKY: 27.2 ± 6.3; WIS: 81.8 ± 8.5; [p=0.002]).

Conclusion: Lower MT number in WKY is consistent with reports of a baseline norepinephrine (NE) deficiency. The increase in REM phasic activity on Day 1 in WKY may be due to a stress-induced surge in NE that activates alpha motor neurons. The lack of change on Day 14 in WKY may be associated with a maladaptive coping response to repeated stress.

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0069

TIME COURSE OF WHISKER -STIMULATION-INDUCED INCREASES IN INTERLEUKIN-1 BETA- AND NERVE GROWTH FACTOR-IMMUNOREACTIVE CELLS IN RAT SOMATOSENSORY CORTEX

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Introduction: Interleukin-1 beta (IL1β) and nerve growth factor (NGF) are examples of activity-dependent sleep regulatory substances. Unilateral manual brushing of the rats' mystacial vibrissae for 2 h increases the number of IL1β- and NGF-immunoreactive (IR) cells in the somatosensory cortex (Sctx). We now determine the time course of whisker stimulation-induced increases in IL1β- and NGF-IR cells.
Methods: Rats were gradually (increasing by 15 min/day) habituated to being placed on inverted flower pots (to avoid whisker self-stimulation) and having the whiskers on one side of the face manually stimulated by hand over 8 days. On the ninth day, rats received either 1 or 2 h of whisker stimulation while on the inverted flower pot. Immunohistochemistry was performed using NGF or IL1β antibodies. An individual blind to the experimental conditions counted NGF- and IL1β-IR cells in 3 sections from each rat on stimulated and unstimulated sides. NGF- or IL1β-IR cell numbers from the control side were compared to those on the side receiving whisker-stimulated input. A paired Students' t-test was used to compare the cell counts between control and stimulated sides in the 5-6 rats. A one-way ANOVA was used to analyze the differences between the 1 and 2 h of stimulation on each side.
Results: With whisker stimulation, the number of NGF-IR cells increased significantly in layers IV and VI at 1 h and layer V at 2 h on the stimulated side. Similarly, the number of IL1β-IR cells increased in layers II-IV at 1 h and IV-VI at 2 h on the stimulated side. A significant increase between 1 and 2 h occurred in the number of IL1β-IR cells, but not NGF-IR cells, in layers V and VI on the stimulated side.
Conclusion: Collectively, these data support the hypothesis that expression of NGF and IL1β is dependent, in part, on neuronal activation.
Support (optional): NIH NS 25378 and NS 31453

0070

DYNAMIC EXPRESSION OF PURINE TYPE 2 RECEPTORS (P2Y1 R) AND THEIR CO-LOCALIZATION WITH INTERLEUKIN-1 BETA AND TUMOR NECROSIS FACTOR ALPHA IN RAT PYRAMIDAL NEURONS

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Introduction: Adenosine triphosphate (ATP) released during neurotransmission is posited to be the initial event in a larger mechanism by which the brain keeps track of sleep/wake history within local neuronal networks. Somnogenic doses of interleukin-1β (IL1β a substance implicated in sleep regulation, given centrally enhances purine type 2 receptor (P2Y1R) mRNA levels. P2Y1R protein levels in the somatosensory cortex (Sctx) increase 3 h after dark onset compared to 9 h after light onset as determined by Western blot analyses. IL1β and tumor necrosis factor α (TNF) expression respond to whisker stimulation and increase in the Sctx during the dark. These data are compatible with the hypothesis that natural stimulation of whiskers during the dark enhances Sctx release of ATP which acts via purine type 2 receptors to release of IL1β and thereby increase the number of P2Y1 receptors in specific layers of the Sctx. In this study we evaluate whether the increased P2Y1 receptor-expressing cells are neurons and whether they colocalize with IL1β and TNF.
Methods: Five-6 rats under a 12:12 h light:dark cycle were killed at 3, 6 or 9 h after dark or light onset. P2Y1 receptor immunohistochemistry was performed and double-labeled with the neuronal marker, NeuN, or with the cytokines, IL1β or TNF. P2Y1 receptor-immunoreactive (IR) cells were counted in the layers of the Sctx.
Results: P2Y1 receptor-IR cells co-localized with NeuN as well as IL1β and TNF. A significant increase in the number of P2Y1 receptor-IR cells in Sctx layers II-III occurred at 3 h after dark relative to 9 h after light onset.
Conclusion: P2Y1 receptors are localized on neurons that show cytokine-IR. Further, the number of P2Y1 receptor-IR cells increase in the Sctx layers II-III after natural stimulation in the dark, suggesting an activity-dependent increase in these purine receptors.
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0071

RECURRENT HYPOGLYCEMIA DECREASES GABA(A) RECEPTOR (GABA-AR) SUBUNIT PROTEIN IN AROUSAL-PROMOTING HYPOTHALAMIC REGION OF JUVENILE RATS

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Introduction: Recurrent hypoglycemia (RH) in children with type 1 diabetes mellitus (DM1) can lead to hypoglycemia unawareness and hypoglycemia-associated autonomic failure (HAAF). Sleep exacerbates HAAF, and during sleep, individuals with DM1 fail to arouse to hypoglycemia. We now investigated whether RH in prepubertal rats alters expression of peptidergic and GABAergic system components in posterior hypothalamic arousal-promoting perifornical (PF) region and glucose-sensing ventromedial (VM) region.
Methods: Male Sprague-Dawley rats were treated with insulin (RH, n=21) or saline (sham control, n=18) for three days, starting on postnatal day 27. Three or twenty one days after the last injection, rats were sacrificed, and two pairs of 700 μm tissue micropunches were cut bilaterally, one from the PF region and the other from the VM region. One of the samples from each pair was subjected to quantitative RT-PCR, and the other sample was used for protein quantification by dot-blot immunodetection.
Results: Three days post-RH, immunoreactivity for α5 subunit of GABA-AR significantly decreased ($p<0.004$) in the PF region, whereas its mRNA levels were increased ($p<0.007$). In this region, RH caused an increase in melanin-concentrating hormone (MCH) and GAD67 mRNA levels ($p<0.02$; negatively correlated with blood glucose levels during treatment), whereas prepro-orexin (PPO) mRNA was not affected. No significant changes in PPO, MCH and GAD immunoreactivity were detected. In the VM region, GABA transporter (GAT-1) mRNA ($p<0.04$) was reduced after RH, whereas GABA-AR subunit mRNAs were not altered. These changes were no longer significant 21 days post-RH.
Conclusion: Juvenile RH results in a reversible region- and subunit-specific decrease in GABA-AR subunit immunoreactivity in the PF region. This can result from arrested translation or increased protein degradation since the corresponding mRNA levels are increased. Decrease in GABA-AR function may compensate loss of hypoglycemic arousal because these receptors mediate sleep-promoting role of GABA in the PF region.
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0072

PREFRONTAL HEMODYNAMIC SIGNALS MEASURED BY NEAR-INFRARED OPTICAL TOPOGRAPHY ARE CORRELATED WITH ATTENTIONAL LAPSES ON A PSYCHOMOTOR VIGILANCE TEST

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Introduction: Near-infrared optical topography (NIROT) can be applied to noninvasively measure regional brain hemodynamic signals during performance of a task. NIROT recordings of the prefrontal cortex were made during performance on a psychomotor vigilance test (PVT) during sleep deprivation. We compared hemodynamic signals during periods of alert task performance vs. periods of attentional lapsing.
Methods: As part of a larger study, 6 healthy young adults (ages 22-32y, 4 females) underwent 62h total sleep deprivation in a laboratory. At 2h intervals throughout most of the sleep deprivation period, subjects performed a 10min PVT. Concurrently, bilateral prefrontal hemodynamic signals were measured (0.17Hz) with NIROT (Hamamatsu NIRO-200); head position was fixed with a chin rest. Relative changes in left and right prefrontal oxygenated and deoxygenated hemoglobin (O2Hb-L, O2Hb-R, HHb-L, HHb-R) were recorded; movement artifacts were removed after visual inspection. NIROT signal analyses focused on times of PVT lapsing, which were defined by RT>3.0s. Lapses were matched with alert responses, defined by RT<0.5s—and no RT>0.5s was to occur within 30s. To account for homeostatic, circadian and time-on-task effects, a matching alert response had to occur 1min earlier or later in the same test bout as the lapse, or at the same time-on-task in a test bout 2h earlier or later. A total of 42 matching pairs were identified in the data set. Using mixed-effects ANOVA, NIROT signals were compared between the lapse state and the alert state across the 3s intervals leading up to the PVT responses.
Results: There were significant effects of state for O2Hb-L ($F=63.3$), HHb-L ($F=25.8$), O2Hb-R ($F=9.3$), and HHb-R ($F=5.8$), with all these signals being higher in the lapse state (all $P<0.01$). Effects of time (across the 3s intervals) and interactions were not statistically significant (all $P>0.95$).
Conclusion: The present results indicate an overall increase in blood volume of the prefrontal cortex during attentional lapsing relative to alert responding on the PVT. This effect of attentional lapsing has also been seen in experiments with rats, where the increase in regional blood volume was found to be associated with a localized sleep-like brain state. A similar mechanism involving local sleep states may mediate PVT attentional lapsing.
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0073

AN ATP AGONIST PROMOTES AND AN ATP ANTAGONIST INHIBITS SLEEP

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Introduction: We have known for 100 years that waking activity enhances the production of sleep regulatory substances (SRS) but the literature has failed to characterize what it was about wakefulness that causes enhanced SRS activity. There are large literatures demonstrating that; a) ATP (adenosine triphosphate) is co-released in brain with neurotransmitters such as glutamate, GABA, acetylcholine and noradrenalin and b) that P2R activation by ATP releases cytokines from immunocytes and glia. Two cytokines, interleukin-1 and tumor necrosis factor are implicated in sleep regulation. We test the hypothesis that ATP, released during neurotransmission, acting via purine type 2 receptors (P2R), promotes sleep.
Methods: Mature male Sprague-Dawley rats (250-300g) were provided with EEG and EMG electrodes and an intracerebroventricular cannula. After recovery, BzATP, an ATP agonist (0.4, 4, and 40 nmoles), or OxATP, an ATP antagonist (4 nmoles), were injected ICV within one hour of light onset and EEG and EMG were recorded for the next 22 hours. Rats were kept on a 12:12 L:D cycle at 22°C. Records were scored for sleep states using standard methods.
Results: BzATP enhanced duration of NREMS for 2-12 hours depending upon dose after a latency of 2 hours. The 4 and 40 nmole doses enhanced EEG delta wave activity during NREMS and inhibited duration of REMS during daylight hours. In contrast, OxATP inhibited duration of NREMS after about a 6 hour delay. OxATP also inhibited REMS although this effect was small and confined to daylight hours. OxATP, like BzATP enhanced EEG SWA during NREMS.
Conclusion: Activation of P2Rs affects sleep. Results are consistent with the hypothesis that synaptic release of ATP during neurotransmission initiates a series of steps that ultimately provide a mechanism by which the brain keeps track of prior sleep/wake history.
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0074

DECREASED EVOKED HEMODYNAMIC RESPONSES DURING INCREASED BASELINE ELECTRICAL ACTIVITY

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Introduction: We examined the effects of urethane anesthesia on the evoked hemodynamic response of the barrel cortex following whisker stimulation. High levels of urethane anesthesia suppresses spontaneous cortical bursting activity. We hypothesize that increased burst suppression is accompanied by decreased cortical perfusion, due to decreased metabolic demands. Conversely, increased basal levels of cortical perfusion might blunt the evoked hemodynamic response, if perfusion can saturate. Therefore, we predict that rats with a greater level of burst suppression will experience a larger hemodynamic response following stimulation of the barrel cortex.
Methods: Seven Sprague-Dawley rats were anesthetized with urethane (1.5-2.5 g/kg) and implanted with EEG electrodes, an LED (660nm) light source, and a photodiode over the whisker barrel cortex. Whisker barrel stimulation was accomplished by providing 100 bursts of 5 whisker twitches, to whiskers B0,1,2 and C0,1 and D0 (twitch frequency = 10 Hz, burst frequency = .04 Hz). We continuously recorded optical and electrical responses during the entire recording session.
Results: Consistent with our hypothesis, the evoked hemodynamic response to whisker barrel stimulation was proportional to the evoked bursting activity elicited by whisker barrel stimulation, but inversely proportional to baseline spontaneous bursting activity of the barrel cortex.
Conclusion: Spontaneous bursting activity appears to be a significant predictor of the evoked hemodynamic response following whisker barrel stimulation. We hypothesize that basal perfusion to the cortex is depressed in animals with a greater level of burst suppression. As a corollary to this hypothesis, animals with increased spontaneous bursting activity would have an increased basal level of cortical perfusion, and would be more likely to saturate with higher levels of electrical activity.
Support (optional): This work was supported by NIH MH60263 and grants from the Keck Foundation and the Poncin Foundation.

0075

CIRCUITRY UNDERLYING RAPID EYE MOVEMENTS DURING REM SLEEP IN RATS

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Introduction: Rapid eye movement (REM) sleep is characterized by rapid eye movements (REMs), atonia of non-respiratory musculature, active dreaming and electroencephalographic (EEG) desynchronization. Surprisingly, the origin of actual rapid eye movements (REMs) during REM sleep is not known. We systematically lesioned inputs of the abducens nucleus to identify the premotor region mediating REMs.
Methods: Brain lesions were made by microinjection of neurotoxins: Orexin- or anti-vesicular acetylcholine transporter-saporin. Rats were equipped for recording EEG, EMG, EOG and masseter activity. REM periods were extracted for scoring of REMs and generation of cumulative sum plots.
Results: Bilateral lesion of the main abducens nucleus nearly abolishes horizontal REMs, including both medial and lateral movements, suggesting that REMs most likely do not depend upon the accessory abducens nucleus and that medial rotation of the globe during REM depends upon the abducens nucleus. Lesions of the region immediately rostral to abducens only partially reduced REMs; lesions ventrolateral to it were without effect. However, retroabducens lesions, immediately caudal from the abducens nucleus and extending laterally, reduced REMs proportionally to lesion size (cumulative sum deviated from controls by 2-3 SD), but did not alter the amount or bout duration of REM sleep (total REM of 7.8 vs. 8.7 %; bout duration 99±50 vs. 94±55 s), suggesting that this region is not critical for REM sleep, but only the associated eye movements. Jaw and neck muscle activity were also unaffected.
Conclusion: Horizontal REMs are likely driven by premotor inputs from the retroabducens area to the principle abducens nucleus in the rat. Lesions of this pathway do not alter REM sleep, or neck or masseter phasic activity. Because the retroabducens area overlaps with the rostral part of the DPGi area of Luppi and colleagues, REM related activity in this region may be related to driving REMs, not REM sleep itself.
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0076

CHOLINERGIC MODULATION OF FAST SYNAPTIC TRANSMISSION IN PEDUNCULOPONTINE THALAMIC PROJECTING NEURONS

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Introduction: The PPN is the cholinergic arm of the reticular activating system (RAS), which is most active during waking and REM sleep. Cholinergic modulation of this area is known to be crucial for the regulation of sleep-wake cycles. We determined the effects of exposure to the nonspecific cholinergic agonist carbachol (CAR) on PPN cells with efferent projections to the thalamus. We quantified changes in excitatory and inhibitory post-synaptic currents during the application of CAR to determine the cholinergic modulation of fast glutamatergic and GABAergic activity.
Methods: Green fluorescent retrobeads were injected into the thalamus of 9-14 day old rats 1 or 2 days before recording. Whole-cell voltage clamp recordings were performed on fluorescent labeled thalamic projecting PPN neurons in 10-15 day rat parasaggital brainstem slices and their responses to the cholinergic agonist CAR were determined. Immunohistochemical labeling was conducted to identify the bNOS positive neurons, considered to be cholinergic PPN neurons.
Results: In the presence of TTX or Cadmium, an outward current was induced by CAR in 64.5% (n=20/31) of PPN output neurons; 19.4% (n=6/31) of cells showed an inward current, and 16.13% (n=5/31) of them had a fast outward current followed by a slow inward current. One half of CAR-excited PPN neurons demonstrated spikelets, indicating the presence of electrical coupling, which were found to be bNOS negative. CAR induced an increase in spontaneous EPSCs, but not miniature EPSCs, mostly in large bNOS positive efferent neurons. These neurons were significantly inhibited by CAR (n=28, 90.6 ±10.2 pA outward currents). However, a significant increase in spontaneous IPSCs was observed in neurons with small CAR-induced outward currents (n=5, 17.5 ±2.1 pA outward currents), although their neurotransmitter phenotype has not been identified.
Conclusion: PPN neurons with efferent projections to the thalamus include three subgroups: small non-cholinergic neurons are excited by cholinergic input and some of them are electrically-coupled; large cholinergic neurons are inhibited by cholinergic input (large outward currents), however, glutamatergic neurons projecting to these appear to be excited by cholinergic input; and an unidentified third group includes smaller cells inhibited by cholinergic input (small outward currents), while, gabaergic neurons projecting to these appear to be excited by CAR. Cholinergic input to the PPN effects separate populations of output cells differentially.
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0077

A HODGKIN-HUXLEY-TYPE MODEL OREXIN NEURON

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Introduction: The excessive daytime sleepiness, sleep-onset REM, and, in some cases, cataplexy that constitute the phenotype for the human sleep disorder narcolepsy are associated with a loss of signaling in the orexin (also known as hypocretin) system. Orexin neurons, located in the hypothalamus, are wake-active and have widespread projections to other arousal-promoting neuronal populations. Synaptic input to orexin neurons comes from other sleep/wake regulatory populations and from local interactions within the orexin neuron field: the neuropeptides orexin and dynorphin appear to be colocalized in orexin neurons, but, interestingly, these peptides exert opposite auto-effects. Although recent experimental work has sought to characterize orexin neuron electrophysiology, the link between electrophysiologic properties of orexin neurons and their function in regulating sleep/wake behavior is not well understood.
Methods: To complement ongoing experimental characterization of electrophysiology in these cells, we developed a Hodgkin-Huxley-type mathematical model of the orexin neuron. We modeled each of the seven experimentally-identified intrinsic currents, and these currents governed the change in membrane potential in the model orexin neuron. To explore local synaptic effects in orexin neurons, we simulated small networks of orexin neurons with colocalized orexin/dynorphin coupling.
Results: The properties of the model orexin neuron are consistent with several key features of reported orexin neuron electrophysiology including a relatively depolarized resting membrane potential that allows spontaneous spiking at a rate of 3-4 Hz. In response to various depolarization/hyperpolarization protocols, model orexin neurons can fire at very fast frequencies, display low-threshold calcium spikes, and demonstrate an h-current-related sag. Our analysis of local synaptic effects in the small network suggests that the time dynamics of dynorphin desensitization determine network behavior.
Conclusion: This theoretical approach provides a novel framework for detailed analysis of orexin neuron electrophysiology and for investigating the relationship between electrophysiology and the role of orexin neurons in promoting arousal, consolidating sleep, and preventing cataplexy.
Support (optional): KSW was supported by an NSF summer REU grant.

0078

PRE-ADOLESCENT RATS EXPOSED TO ALCOHOL DURING PERINATAL PERIOD HAVE REDUCED GLUTAMATE DECARBOXYLASE (GAD) LEVELS IN SLEEP- AND WAKE-REGULATING HYPOTHALAMIC REGIONS

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Introduction: Human victims of prenatal alcohol exposure (AE) and rodents treated with alcohol during perinatal period exhibit sleep abnormalities that may extend into adulthood, but the underlying neural substrate(s) are unknown. We investigated whether early AE alters GABAergic system in hypothalamic regions important for the regulation of sleep and motor activity.
Methods: Male rats received 5.25 g/kg/day of alcohol via intragastric intubations during postnatal days (PD) 4-9, a period equivalent to human brain development during the third trimester of pregnancy (AE group). Control pups were sham-intubated (S group). On PD15-16, total RNA and protein were bilaterally extracted from 700 μm tissue micropunches from the wake-promoting, perifornical (PF) region of the posterior hypothalamus and sleep-promoting, ventrolateral preoptic (VLPO) region of the anterior hypothalamus. GAD levels (mRNA and protein) and mRNA levels for eleven subunits of $GABA_A$ receptor ($GABA_AR$) were quantified using RT-PCR and immunoblotting, respectively (n=5-7/group). In additional animals (n=9-10/group), motor activity was recorded for 30 min using infrared beam-splitting technique.
Results: In the PF region, GAD65/67 immunoreactivity and GAD67 mRNA levels were significantly lower (by 44% and 24%, respectively; $p<0.01$ for both), and in the VLPO region, GAD65/67 immunoreactivity (but not mRNA) was lower (by 8%; $p<0.05$) in the AE group. $GABA_AR$ α4 and δ subunit mRNA levels were higher in the PF region and α3 and γ2 subunit mRNA levels were higher in the VLPO region ($p<0.05$) in the AE group. The total number of movements was significantly higher in AE than S rats (by 36%; $p<0.05$).
Conclusion: Perinatal AE results in reduced levels of hypothalamic GABA enzymatic precursor, GAD, in both sleep- and wake-related hypothalamic regions, and opposite changes in expression of mRNA for $GABA_ARs$, when measured five days after the exposure period. Deficient hypothalamic GABAergic mechanisms may contribute to motor hyperactivity and disrupted sleep in victims of perinatal AE.
Support (optional): HL-071097

0079

ADULT RATS EXPOSED TO ALCOHOL DURING PERINATAL PERIOD HAVE ALTERED REM SLEEP AMOUNTS AND SLEEP INITIATION

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Introduction: We previously reported that perinatal alcohol exposure (AE) alters molecular components of GABAergic signaling in hypothalamic regions important for the regulation of sleep in juvenile rats (Volgin DV, *Neurosci. Lett.* 439:182-186, 2008). Using the same rat model of fetal alcohol spectrum disorders (FASD), we investigated whether perinatal AE leads to changes in sleep-wake behavior in adult rats.
Methods: Alcohol (5.25 g/kg/day) was administered to male rats via intragastric intubations during postnatal days (PD) 4-9, a period equivalent to human brain development during the third trimester of pregnancy (AE group; N=4). Control pups were sham-intubated (S group; N=3). On PD 52-78, rats were instrumented for EEG and nuchal EMG recording. Following recovery and habituation, sleep-wake behavior was recorded on PD 70-97 during one 24 h-long session that started at 9-10 AM. Wake, slow-wave sleep (SWS), and rapid eye movement sleep (REMS) were distinguished in 10 s epochs covering six h of recording during the lights-on (12PM-6PM) and six h during lights-off (12AM-6AM) period.
Results: During the lights-off phase, REMS percentage was significantly lower in AE than S rats (4.3%±1.2 (SE) vs. 9.7%±0.6 in S group; $p=0.02$), whereas the percentages of SWS were not significantly different (24.6%±4.7 vs. 29.1%±3.6 in S group). During the lights-on period, sleep did not differ between the groups (total sleep in AE rats: 63.1%±3.0 vs. 59.4%±1.3 in S rats), but AE group tended to have higher SWS latency, and had significantly higher REMS latency (147±17 vs. 60±21 min in S rats; $p=0.02$).
Conclusion: Perinatal AE leads to changes in sleep-wake behavior in a rat model of FASD that extend into the adulthood and are suggestive of problems with sleep initiation during the rest period and REMS generation and/or maintenance during the active period.
Support (optional): HL-071097

0080

AN INVESTIGATION OF THE ASSOCIATION BETWEEN SLOW-WAVE OSCILLATIONS AND FAST AND SLOW SLEEP SPINDLES USING 256-CHANNEL EEG

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Introduction: Sleep spindles and slow-wave oscillations (SWO) (<1Hz) are characteristic EEG patterns observed during non-REM sleep. Sleep spindles (SS) have been characterized into two types: slow spindles (11-13Hz) and fast spindles (13-15Hz). The positive half-wave (PHW) of the SWO recorded with scalp EEG is believed to reflect cortical depolarization and has been shown to be associated with SS activity. We investigate the relation between SS and the PHW of SWOs recorded in humans using dense-array EEG technology.
Methods: Sleep EEG was acquired from 10 subjects using a 256-channel sensor array. Non-REM sleep stages were identified and SS and SWOs were scored. To evaluate the association between events, we grouped fast and slow spindles that occurred in the presence (within +/- 1 sec) and absence of SWO and performed statistical analysis. Source distribution of these two spindle types and their overlap with SWO sources were also compared by transforming the scalp data to source space using a realistic head model and linear-inverse method.
Results: We observed a relationship between the PHW of the SWO and the SS frequency band (11-15Hz). There was an increase in activity in the spindle frequency band during this phase of the SWO. During the PHW, there was a larger increase in the slow spindle band (compared to the fast spindle band).
Conclusion: We can conclude that there is a stronger association between the PHW of the SWO and the slow spindle frequency band. There may be a significant physiological reason for the temporal relationship of these EEG oscillations.

0081

LIMBIC NEUROPEPTIDERGIC INNERVATION OF BRAIN REGIONS INVOLVED IN THE MODULATION OF REM SLEEP

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Introduction: Emotions modulate the amount and density of REM sleep, and these effects are mediated by the limbic system, mainly the central nucleus of the amygdala (CeA) and the bed nucleus of the stria terminalis (BST). Lesions of the CeA decrease REM sleep under normal or stress conditions, whereas lesions of the BST revert the REM suppression induced by a psychological stressor. We previously showed that the CeA and BST project directly to regions involved in REM control

and indirectly via projections to intermediate regions, such as the lateral hypothalamus-perifornical region (LH-PeF), parasubthalamic nucleus (PSTh), and lateral parabrachial nucleus (LPB). The CeA and BST neurons contain GABA and different neuropeptides, some of them known to exert an effect on REM sleep. Thus, corticotropin-releasing hormone (CRH) inhibits REM sleep whereas neurotensin (NT) enhances it. Enkephalin (Enk) acts on mu receptors, which mediate opioid-induced REM inhibition and are expressed in the majority of REM areas. The aim of this study was to determine: 1) whether CeA or BST neurons that project to regions involved in REM control contain CRH, Enk or NT, and 2) whether projections from CeA or BST are in close apposition with CRH-, Enk- or NT-positive fibers in areas involved in REM control.

Methods: Colchicine-treated rats were injected with the retrograde tracer cholera toxin B subunit (CTB) into the sublaterodorsal nucleus (SLD; REM-on area) or the lateral pontine tegmentum (LPT; REM-off area). Double fluorescence immunohistochemistry was used to detect neurons labeled with CTB (green) and CRH, Enk, or NT (red). Another group of rats was injected with the anterograde tracer adeno-associated virus conjugated with GFP (AAV-GFP) into the CeA or BST. Apposition of limbic afferent fibers (green) with CRH, Enk, or NT-positive fibers (red) was detected with double immunofluorescence.

Results: CTB-CRH neurons were observed in the CeA, BST and LH-PeF after injection into the LPT, and in the BST, LH-PeF and PSTh after injection in the SLD. After CTB injection in the LPT, CTB-NT neurons were found in the BST and CTB-Enk neurons in the LPB. There were dense CRH-, Enk-, and NT-fibers intermingled with limbic fibers in all regions involved in REM modulation, including the LH-PeF, PSTh, and LPB, as well as the CeA and BST.

Conclusion: These results suggest that the limbic modulation of REM sleep might be mediated by several neuropeptides that can be co-released with GABA in specific areas of the REM circuitry.

0082

CIRCADIAN AND SLEEP/REST DISTURBANCES IN OLDER MICE UNDERGOING CHRONIC ETHANOL TREATMENT

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Introduction: Chronic ethanol exposure causes disruptions in circadian rhythmicity and sleep consolidation. The magnitude of ethanol-induced disruption increases with age. To study this, we assessed circadian activity patterns in C57BL/6J mice undergoing chronic, long-term ethanol treatment.
Methods: Older mice (22 wks.) received water (n=4) or 10% ethanol (n = 4) ad libitum. The experiment was conducted under a 1 min light pulse (25 lux) skeleton photoperiod to characterize ethanol's effects on photic entrainment capacity. General circadian locomotor activity entrained to the 1 min pulse was measured using a passive infrared motion detector interfaced with a computerized data acquisition system. Activity measurements were averaged over a 3 day period beginning immediately after ethanol introduction. Activity bouts were defined as periods of activity separated by at least 10 min of quiescence.
Results: Ethanol drinkers had later activity onsets vs. water drinkers (6.36 h +/- 0.62 vs. 4.60 h +/- 0.30, respectively; $p<0.04$). Ethanol drinkers had marked disturbances of their rest period as indicated through more bouts of activity during this period than water drinkers (repeated measures ANOVA; $p<0.02$). Frequencies of bout durations (bin size = 15 min) throughout the rest period revealed ethanol-induced disruptions in sleep consolidation; ethanol drinkers had more bouts 0-15 min in duration than water drinkers (10.75 +/- 1.14 vs. 6.33 +/- 0.89, respectively; $p<0.02$). The amount of solution consumed during treatment did not differ between ethanol and water drinkers (repeated measures ANOVA; $p<0.81$).
Conclusion: This analysis revealed that older mice drinking ethanol have significant circadian and sleep/rest disturbances. Although sleep per se was not directly measured, these results are evidence that in this animal model, circadian rhythmicity and sleep consolidation are greatly altered by chronic ethanol consumption.
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0083

A SECONDARY REFLEX SUPPRESSION PHASE IS PRESENT IN GENIOGLOSSUS BUT NOT TENSOR PALATINI IN RESPONSE TO NEGATIVE PRESSURE PULSE STIMULI

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Introduction: It has recently been reported that the genioglossus (GG) negative pressure reflex consists of an initial excitation phase followed by a secondary state-dependent suppression phase. Prior research had overlooked this secondary phase due to the use of signal averaging techniques. The mechanistic origin and functional role of GG suppression is unknown. This suppression has been hypothesized to arise from global inhibition of respiratory active neurons as a protective reflex to brief airway occlusion to prevent aspiration as is seen in other respiratory muscles (i.e. scalene and diaphragm). Unlike GG, the tensor palatini (TP) is a tonic muscle with minimal respiratory phasic activation during basal breathing. Thus, this study aimed to compare the reflex responses of GG vs. TP to the same negative pressure stimulus. We hypothesized that reflex suppression would be present in GG but not TP.
Methods: Raw GG and TP EMGs were recorded in 12 awake, healthy subjects (6 female). Reflex responses were generated via 250 ms pulses of negative upper-airway pressure (-16 cmH_2O at the mask) delivered in early inspiration.
Results: GG and TP demonstrated reflex activation in response to negative pressure (peak latency 31±4 vs. 31±6 ms; peak amplitude 318±55 vs. 314±26 % baseline, respectively). A secondary suppression phase below baseline was present in 8/12 subjects for GG (nadir latency 54±7 ms, nadir amplitude 64±6 % baseline) but was not present in any subject for TP.
Conclusion: These data provide further support for the presence of both excitatory and inhibitory components to the GG (phasic muscle) to brief pulses of negative airway pressure. Conversely, no reflex suppression below baseline was observed in the tonic TP muscle to the same stimuli. These differential responses support the hypothesis that reflex suppression in GG may originate from inhibition of respiratory neurons innervating the hypoglossal motor nucleus.
Support (optional): HIH and NHMRC Biomedical Fellowship

0084

INFLUENCE OF DISTRIBUTION OF ENERGY AND MACRONUTRIENTS INTAKE UPON BODY COMPOSITION

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Introduction: Some evidences suggest that the time of day that meals are eaten may influence body composition. The aim of this study was to evaluate distribution of energy and macronutrients intake, both in health men and women, and correlate it with anthropometric variables.
Methods: Fifty-two (24 men and 28 women) healthy volunteers (20-45 years) participated in the study. Food intake was analyzed by a three-day food record. Anthropometric measurements included weight, height, Body Mass Index (BMI), body fat percentage (BF%) and waist circumference (WC). Student's t test and Pearson's correlation coefficients were used for statistical analyses and $P < 0.05$ was considered statistically significant.
Results: Negative correlations were found between morning energy intake and BMI ($r = -0.48$, $P < 0.05$), BF% ($r = -0.56$, $P < 0.05$) and WC ($r = -0.53$, $P < 0.05$); morning carbohydrate intake and BMI ($r = -0.47$, $P < 0.05$), BF% ($r = -0.56$, $P < 0.05$) and WC ($r = -0.51$, $P < 0.05$); morning protein intake and BF% ($r = -0.46$, $P < 0.05$) and WC ($r = -0.44$, $P < 0.05$); and morning fat intake and BMI ($r = -0.43$, $P < 0.05$), BF% ($r = -0.49$, $P < 0.05$) and WC ($r = -0.47$, $P < 0.05$), only in men.
Conclusion: These data suggests that morning food intake can be associated with reductions in anthropometric variables like BMI, BF%, and WC, at least in men.
Support (optional): CEPID/FAPESP (#998/14303-3), FADA/ UNIFESP, AFIP, CNPQ.

0085

SLEEP PATTERNS IN AN EXPERIMENTAL MODEL OF SYSTEMIC LUPUS ERYTHEMATOSUS

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Introduction: Chronic sleep deprivation is a common occurrence in modern society and has been observed in a number of chronic inflammatory conditions, such as systemic lupus erythematosus (SLE). New Zealand Black/New Zealand White (NZB/NZW) F1 mice develop an autoimmune disease that strongly resembles SLE in humans, exhibiting high titers of antinuclear antibodies associated with the development of rapidly progressive and lethal glomerulonephritis. The current study evaluated the sleep pattern during the onset and progress of lupus in NZB/NZWF1 mice.
Methods: Female mice (n=12) were implanted with electrodes for recording of sleep-wake cycle (light and dark periods lasting 12 h each)

during the entire experimental period (9, 19 and 29 week of age). In each time-point, blood samples were collected from the orbital plexus to evaluate serum antinuclear antibodies which are important sorologic parameters of disease evolution. Proteinuria, pain perception (sensitivity to thermal stimuli) and body weight were also assessed.
Results: The sleep recording data showed that during the disease activity (29 wk of age) the sleep architecture is altered. Lupus-prone mice exhibited increased sleep stage transitions and number of awakenings during the light period. These sleep disturbances were also observed in the dark period as well as reduced wake time.
Conclusion: According to these results, increased sleep fragmentation, increased disease activity and pain sensitivity are features observed in these mice as well as in SLE patients.
Support (optional): FAPESP/CEPID and AFIP.

0086

CONTROL AND FUNCTION OF THE HOMEOSTATIC SLEEP RESPONSE BY ADENOSINE A1 RECEPTORS

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Introduction: Sleep is modeled by two process, one of which is homeostasis. Homeostasis is the process by which sleep drive increases during waking and dissipates during sleep. Slow wave activity (SWA), a 0.5-4.5 Hz oscillation in membrane potential, is often used as a measure of sleep drive since SWA increases during waking and dissipates during sleep. Adenosine has been hypothesized to be involved in homeostasis by modulation of SWA, with adenosine A1 receptors gaining attention due to their activity in cholinergic nuclei controlling arousal. We tested the hypothesis that adenosine A1 receptors (AdoA1R) are necessary for increased SWA following sleep restriction and that attenuating SWA rebound during chronic sleep loss, impairs working memory.
Methods: Floxed AdoA1R homozygotes (AdoA1Rf/f) were crossed with CamKII-Cre mutants to produce AdoA1R-/- mice. The AdoA1R-/- show a lack of CNS AdoA1R, while AdoA1Rf/f show normal distribution. Mice were implanted with EEG and EMG electrodes, given 1 week to recover, then placed on a slowly moving treadmill (3 cm/sec) and forced to walk for 4 hrs followed by 2 hrs recovery, setting a 6 hr cycle that was repeated 8 times over 2 days. SWA across states and during slow wave sleep (SWS) was compared between groups. In a second experiment, f/f and -/- mice were trained on an 8 arm radial maze working memory task to retrieve food rewards from each of the arms and tested during sleep restriction. Errors were scored when an animal returned to a previously visited arm and compared between groups.
Results: AdoA1R-/- mice showed decreased SWA across states and especially within SWS, however the amount of SWS was unchanged. Decreased SWA was seen with acute sleep restriction (1, 6 hr cycle) and with chronic sleep restriction (8, 6 hr cycles). Additionally, AdoA1R-/- committed significantly more errors on the working memory task compared to controls.
Conclusion: AdoA1Rs are necessary for the full expression of SWA following acute and chronic sleep restriction, however mice lacking AdoA1Rs are still able to show increased SWA, indicating that AdoA1Rs have a modulatory influence on SWA expression. Mice lacking AdoA1Rs are not able to achieve the same magnitude of SWA during a 2 hr recovery period, associated with working memory deficits during subsequent waking. Mice with functional AdoA1Rs have no deficit in working memory performance during chronic sleep restriction, suggesting a compensatory role in cognition for AdoA1R induced SWA rebound during the recovery period.

0087

ALLOPURINOL AMELIORATES CARDIAC DAMAGE AND OXIDANT STRESS OF CHRONIC INTERMITTENT HYPOXIA

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Introduction: Obstructive sleep apnea (OSA) is associated with chronic intermittent hypoxia (CIH), oxidant stress (OS), and cardiac deterioration. OS may be wholly or in part generated via the xanthine oxidase pathway. Allopurinol (ALLO) is a xanthine oxidase inhibitor, free radical scavenger, antioxidant, and binds to myeloperoxidase. Previously in rats, we showed that CIH leads to OS and deterioration in cardiac function. We hypothesized that ALLO decreases OS associated with and prevents cardiac deterioration with CIH.
Methods: CIH was produced in rats by exposure to nadir FiO2 4-6%, once per minute, 8 hours per day for 10 days and compared with similarly handled normoxic controls (HC). A was given as 1% in the drinking water. Four groups (8 to 10 each) were studied: CIH/ALLO, CIH/placebo (P), HC/ALLO, HC/P. Outcomes at the end of the exposure period included total myocardial lipid peroxides (LPO), fractional LV shortening (echo - FS%), and myocardial apoptosis (TUNEL assay).
Results: LPO was lower in CIH/ALLO than CIH/P: 179+/-102 vs. 589 +/-68 micron/mg protein ($p<0.05$), without significant effect for HC. FS% was greater with ALLO than P for both CIH and HC: CIH/ALLO 48.6 +/- 2.3% vs CIH/P 38.0 +/- 1.4% ($p<0.05$); HC/ALLO 64.9 +/- 1.8% vs HC/P 51.5 +/- 1.5 % ($p<0.05$). The number of TUNEL positive cells per HPF was less in CIH/ALLO than CIH/P: 38.0+/-1.4 vs 48.6/-2.3 ($p<.05$) with no difference for the HC groups. For HC animals the differences between ALLO and P for all outcomes were also significant ($p<.05$).
Conclusion: In CIH, ALLO OS and preserves LV function compared to P. Because even without CIH, ALLO led to less OS and improved LV function, this may be part of an overall nonspecific action of ALLO on OS. ALLO may have a role in treating OS associated with OSA.
Support (optional): American Heart Association

0088

SLEEP-WAKE-LIKE PERIODIC CHANGE IN EEG PATTERN ACCOMPANIED BY SUDDEN INCREASE IN BREATHING RATE IN URETHANE ANESTHETIZED MICE

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Introduction: We previously found a marked, sudden increase in BR (SIBR) of up to >100% appears during REM sleep in humans and freely-moving mice (Sato et al., 2007). On the other hand, urethane-anesthetized rats were found recently to exhibit a periodic alteration in EEG pattern, which closely resembles its change during sleep-wake transition (Elizabeth et al., 2008). In the present study, we examined whether the SIBR also appears in synchrony with EEG alteration in urethane-anesthetized mice.
Methods: Mice were anesthetized with urethane (1.8 g/kg) by intraperitoneal injection and their heads were fixed with ear bars of a stereotaxic frame for drilling two holes on the skull at adjacent of bregma and lambda, then bolts (1.3 mm in diameter) with connector for EEG recording were screwed into the holes. Cardiorespiratory activity and body temperature were noninvasively monitored and maintained by a piezoelectric-transducer (PZT) sensor with heater placed under the body, respectively. After 1.5-8 h of surgery, EEG and cardiorespiratory activity were recorded and stored in a computer, and changes in heart

rate (HR), breathing rate (BR) and EEG power spectrum by using Fast Fourier Transform (FFT) were analyzed.
Results: Periodic amplitude alteration in EEG at an interval of 2.5-5 min occurred in all 8 urethane-anesthetized mice examined; slow (delta wave: 0.5-4 Hz) and fast (beta wave: 30-50 Hz) wave alternatively increased during large and small amplitude EEG, respectively. HR increased and decreased in parallel with EEG amplitude alteration in 5/8 mice, while SIBR appeared synchronously with low-amplitude EEG (i.e. period of low delta power) in 6/8 mice. HR and BR showed periodic increase by ~20 and ~100 % in amplitude at maximum, respectively.
Conclusion: Urethane anesthetized mice showed several EEG patterns and SIBRs similarly to those of sleeping mice, except HR that seemed to be increased during NREM sleep. Thus, urethane anesthesia in mice may be a valuable tool, at least in part, for the study in mechanisms of peculiar physiological phenomenon that occurs during REM sleep in mice and humans.

0089

SLEEP CHARACTERISTICS IN PREGNANT WOMEN OF DIFFERENT RACIAL BACKGROUNDS

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Introduction: Epidemiological studies suggest that racial background may be a risk factor for sleep disturbances. African Americans have higher risk for sleep-disordered breathing (SDB) than Caucasians and may be at higher risk for insomnia. Data suggest that sleep disorders in pregnancy may impact maternal and fetal health. No study has addressed racial differences in sleep during pregnancy.
Methods: A multi-ethnic sample of adult women attending a large academic obstetric clinic were recruited during their last trimester and invited to complete several sleep questionnaires. These included the General Sleep Disturbance Scale (GSDS, Lee 1992), the Berlin Questionnaire, and a 4-item scale about restless legs (RLS) symptoms. A mean score ≥ 3 on the GSDS or any of the sub-scale scores (e.g., sleep quality or daytime functioning) is consistent with DSM-IV criteria for insomnia.
Results: In total, 575 women have been studied as part of an ongoing investigation. Racial background was 71% Caucasian, 15% African American, 6% Asian, 4% Hispanic, and the remainder of mixed race. Overall, mean age was 30.2±5.8 years and 20% were obese prior to pregnancy, with African Americans having the highest and Asians having the lowest pre-pregnancy BMI (30.1±8.0 vs. 21.6±4.0kg/m^2). Asians were least likely to report habitual snoring (17% compared to 40% of African Americans and 33% of Caucasians and Hispanics). After adjusting for pre-pregnancy BMI, race was not a predictor of habitual snoring. Regardless of race, the majority of women reported symptoms consistent with insomnia: poor sleep quality (74% African Americans, 72% Caucasians, 57% Asians, and 81% Hispanics) and poor daytime functioning (72% African Americans, 73% Caucasians, 51% Asians, and 71% Hispanics). Symptoms of RLS were more common in Caucasians than African Americans (37% vs. 24%; $p<0.05$).
Conclusion: Sleep disturbances are commonly reported during pregnancy. Racial differences are apparent in some sleep disorders although pre-pregnancy BMI likely accounts for the differences in habitual snoring. These findings may have relevance to the management of pregnant women.
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0090

ANALYSIS OF SLEEP ABNORMALITIES IN FATAL FAMILIAL INSOMNIA (FFI) USING MATHEMATICAL MODELS OF THE HUMAN SLEEP/WAKE CYCLE

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Introduction: FFI, a rare prion disease, constitutes by their wake and sleep abnormalities a unique pathophysiological model of disease (Montagna, P. Sleep Medicine Reviews 2005; 9: 339). Recently, a neurobiological-mathematical model of the human sleep/wake cycle (NMM) developed by Rempe MJ et al. (Mathematical Bioscience Institute 2008, Technical Report 72, 1-24) reconciles circadian/homeostatic influences with new findings like the proposed sleep/wake flip-flop switch and REM-NoREM switch (Saper CB et al. TINS 2001, 24:726). We attempt now to modeling sleep abnormalities seen in FFI patients with the hypothesis that different degrees of perturbation (activation/deactivation) of circadian and homeostatic drives are related with sleep findings previously reported (Provini F. et al. Rev. Neurol (Paris) 2008, 164(8-9-):692).
Methods: We used two modeling approachs, the well known limit cycle reciprocal interaction model (LCRIM) in which we introduced modifications on the Lotka-Volterra system and the NMM, where, briefly, the ventrolateral preoptic neurons (VLPO) and monoaminergic neurons (AMIN) inhibit each other and are modeled as a system of two ordinary differential equations. A similar interaction between REM-on and REM-off was also implemented. Both models were able to produce simulations that we confront with reanalyzed polysomnograms of a proven case of FFI (Reder AT et al. Neurology 1995, 45: 1068; Garay A. et al. Neurology 1996, 46: A121).
Results: IntraREM sleep fragmentation can be simulated according the NMM by increasing random and Poisson perturbations on circadian and/or REM-on inputs. This was made by modifying the term I AMIN that corresponds to REM-on equations of this model. A cyclic alternating pattern reported in REM sleep in our case of FFI was characterized by 30-60 seconds centered bursts (Kruskall-Wallis NP Test, Dunns NC Test, p less than 0.05) that can be simulated with an increase of frequency in d(circ) using LCRIM.
Conclusion: These mathematical models support the hypothesis that in FFI the extended neuronal network that regulates sleep and wakefulness could be disrupt by altered circadian/homeostatic and REM inputs.

0091

RELATIONSHIP BETWEEN THE PHASIC ACTIVITIES OF THE GENIOGLOSSAL AND NUCHAL MUSCLES IN REM SLEEP IN RAT

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Introduction: Rapid eye movement (REM) phasic events are thought to be coordinated by a pontine generator. However, phasic diaphragmatic activity during apnea in the mechanically ventilated cat is poorly related to ponto-geniculo-occipital waves. We hypothesize that phasic activity of a respiratory muscle, the genioglossus, in REM sleep (and here we mean not the rhythmical or phasic activity related to breathing but instead activity that appears episodically in REM sleep) and the phasic activity of a non-respiratory muscle, a nuchal muscle, are not coordinated by a single generator. Accordingly, we tested the hypothesis that phasic genioglossal acivity and phasic nuchal muscle activity are unrelated in REM sleep.
Methods: Adult male Wistar rats were anesthetized and electrodes were implanted to record electroencephalogram and electromyograms of the diaphragm, genioglossus and neck muscle. After recovery and adapta-

tion, the animals were head restrained and recorded during REM sleep. Recording were digitized (Spike2) and analyzed off-line.
Results: Genioglossal activity in REM sleep showed a unimodal pattern with a delayed onset, a gradual rise to peak in the last half of the REM period and a decline prior to the end of the period. Analysis of variance of 26 REM periods confirmed this profile ($p<0.0001$). Genioglossal activity emerged on an atonic background an average of 20s (±2 SEM) after the onset of REM sleep. This activity developed to a peak 2-3 fold higher than the average level of activity present during the preceding NREM period. Genioglossal activity correlated with an increased rate of breathing and diaphragmatic muscle activity. However, genioglossal phasic activity in REM sleep, unlike NREM sleep, was predominantly nonrespiratory, that is, not correlated with breathing. Analysis of variance of neck muscle activity across REM periods did not reveal an effect of time in the REM period. Thus, nuchal activity in REM sleep was not related to genioglossal activity.
Conclusion: These results indicate that genioglossal activity in REM sleep does not correlate with phasic nuchal activity. These results do not support the idea that a single generator produces the phasic events of REM sleep. They suggest instead that these activities have separate generators, and in particular that there may be a system that generates activity specifically in respiratory muscles during REM sleep.

0092

THE IMPACT OF DAYTIME CHALLENGES ON BEHAVIORAL SLEEP IN THE HOUSE SPARROW, *PASSER DOMESTICUS*

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Introduction: An organism's sleep behavior may change seasonally depending on life-history stage, or nightly in response to daytime experiences, which are comprised of psychological, social, and physiological influences. To investigate the adaptive nature of sleep in different seasons, we experimentally tested the effects of ecologically-relevant stressors on the daytime and nighttime behavior of birds housed under naturalistic conditions.
Methods: For one year, we kept a flock of ten male birds in a large, outdoor aviary and recorded seasonal changes in sleep behavior using specialized-nestboxes equipped with infrared videocameras. We also recorded changes in physical activity using small radiotransmitters, attached to birds with elastic leg harnesses. We recorded baseline sleep behavior and rest-activity patterns during each season, as well as after presenting birds with a psychological challenge during winter (predation risk), a social challenge during spring (conspecific competition), and a physiological challenge during fall (increased foraging effort).
Results: Sleep characteristics changed across the annual cycle: Sleep duration was longest in winter, sleep continuity was greatest in spring, and daytime sleep was greatest in fall. Further, different types of daytime experiences impacted sleep significantly in different seasons ($p < .05$). A psychological challenge during winter increased sleep duration. A social challenge during spring decreased sleep duration but increased sleep continuity. Here, we also found an effect of social status: Food-dominant birds decreased sleep duration but increased sleep continuity, while non-dominant birds showed smaller decreases in sleep duration and decreased sleep continuity. In the fall, a physiological challenge increased sleep duration, decreased sleep continuity, and increased daytime rest.
Conclusion: Daytime experiences may impact sleep in different ways in order to best facilitate "recovery" from waking experience and maintain homeostatic balance in the organism. Further, we found that sleep modification varied with season, such that the aspect of sleep that was already "maximized" under baseline conditions increased further in response to a challenging situation. We raise the idea that sleep may have different allostatic set points between seasons and responds accordingly to stress in a context-dependent manner. However, future work needs to test the same challenges across seasons in order to confirm this hypothesis.
Support (optional): NSF Doctoral Dissertation Improvement Grant IOB 0608262, and research grants from: Animal Behavior Society, American Ornithologist's Union, and Society for Integrative and Comparative Biology.

0093

INDIVIDUAL REACTIVITY AND THE ROLE OF CORTICOSTERONE IN MEDIATING STRESS-INDUCED SLEEP CHANGES IN THE HOUSE SPARROW, *PASSER DOMESTICUS*

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Introduction: Daytime stress can impact sleep behavior, yet individuals often show different sleep responses to the same stressor. Research across animal taxa has repeatedly revealed individual variation in behavioral and physiological reactivity to stress. These individual differences have also been linked to nighttime sleep characteristics, but it is unclear as to how these changes are physiologically mediated. We sought to determine whether there is individual variation in post-stress sleep modification in the house sparrow, and whether these changes relate to an individual's behavioral or physiological reactivity.
Methods: In order to ascertain behavioral reactivity (BR), we paired male birds in a small cage during the pre-breeding season and observed daytime aggression and activity. We then obtained sleep behavior and compared this to sleep under control conditions. Based on the magnitude and direction of change in several sleep characteristics, we classified birds into two reactivity groups. We then performed a corticosterone stress series to ascertain individual physiological reactivity (PR). Finally, we blocked corticosterone production with mitotane, and examined post-stress sleep behavior in the same birds between conditions.
Results: Individual BR and PR showed no direct relationship. After stress, birds with higher BR showed greater increases in sleep duration ($r_s=.91$). In contrast, birds with higher PR showed an increased sleep latency ($r_s=.79$) and decreased sleep continuity ($r_s=-.78$). Birds classified in reactivity Group 1 had significantly higher body conditions, were more physically active during stress, and showed greater post-stress increases in sleep duration and continuity ($p<.05$). We found that blocking corticosterone production significantly delayed post-stress rise time (thereby increasing sleep duration) and increased nighttime respiration rate ($p<.05$). Further, birds with higher PR showed greater increases in sleep duration and depth ($r_s>.72$) after injection with mitotane.
Conclusion: The direct relationship between behavioral and physiological reactivity is unclear. Taken separately, high BR appears to increase sleep duration, while high PR appears to decrease sleep duration and quality. Blocking corticosterone production in individuals with higher PR appeared to reverse stress-induced decreases in sleep parameters. Corticosterone may also play a role in avian sleep by decreasing nighttime physiological parameters such as respiration and metabolic rate.
Support (optional): NSF Doctoral Dissertation Improvement Grant IOB 0608262, and research grants from: Animal Behavior Society, American Ornithologist's Union, and Society for Integrative and Comparative Biology.

0094

VISCERAL ADIPOSE TISSUE RELEASES MUCH MORE IL-6 AND MCP-1 THAN SUBCUTANEOUS ADIPOSE TISSUE

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Introduction: Excessive daytime sleepiness (EDS) and sleep apnea are associated with obesity and elevation of interleukin-6 (IL-6), tumor

necrosis factor-alpha (TNFα) and monocyte chemoattractant protein-1 (MCP-1) in the serum. Compared with peripheral obesity, visceral obesity is a stronger risk factor for EDS and sleep apnea. We tested the hypothesis that visceral adipose tissue (VAT) has a greater capacity to release inflammatory markers than subcutaneous adipose tissue (SAT). Since members of mitogen-activated protein kinase (MAPK) including p38, c-Jun N-terminal kinase (JNK) and extracellular signal-regulated kinase (ERK) are involved in inflammatory activities and display higher activities in VAT than SAT, we also determined whether MAPK is involved in the differential inflammatory activities between VAT and SAT.

Methods: Adipose tissues were collected from C57BL/6 mice and cultured in the medium with or without inhibitors of p38 (SB203580), JNK (SP600125) or ERK (U0126) for 24 h. Preadipocytes isolated from the tissue samples were chronically cultured to detect the release of inflammatory markers. The levels of IL-6, TNFα and MCP-1 from adipose tissue/preadipocytes were measured with enzyme-linked immunosorbent assay.

Results: VAT released over 10 fold more IL-6 [$F(1,4)=27.212$, $p=0.006$] and MCP-1 [$F(1,9)=110.520$, $p<0.001$] than SAT, whereas the visceral preadipocytes released only 2-3 fold more IL-6 [$F(1,4)=572.840$, $p<0.001$] and 30-40% less MCP-1 [$F(1,4)=21.086$, $p<0.01$] than the subcutaneous preadipocytes. TNFα release was not significantly different between VAT and SAT and was undetectable in preadipocyte culture. IL-6, MCP-1 and TNFα releases were decreased by SB203580, SP600125 and U0126 with slightly greater inhibition in SAT than VAT.

Conclusion: These results indicate that: 1) VAT has greater capacity to secrete IL-6 and MCP-1 than SAT, and 2) this difference is primarily not due to preadipocytes, and is not mediated by MAPK. Our results support the idea that increased inflammatory activities is involved in the increased risk for sleep apnea and EDS in visceral obesity.

Support (optional): This research was supported by NIH grant HL64415.

0095

INTRACRANIAL CORRELATION OF SCALP EEG IN CHARACTERIZING SLEEP ARCHITECTURE

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Introduction: There is abundant information of the origin of sleep architecture (spindles, vertex waves, K-complex and slow waves) from animal data; however there is less data available in humans, and even minimal to no data of similar correlations in children. The objective of this study is to correlate sleep architecture on scalp EEG (Cz electrode) with different areas of the cortex during intracranial monitoring via strips and grids placed for phase 2 monitoring of intractable epilepsy. Extensive areas of frontal, parietal and temporal regions including mesial regions were sampled.

Methods: We analyzed data from four children, ages of 4 to 21 years, 3 males and 1 female, correlating sleep architecture on Cz electrode with areas of the cortex on implanted electrodes showing maximum amplitude.

Results: We found that spindles were visualized maximally in the central peri-sulcal region at times arising a few milli-seconds earlier, but also seen in the frontal regions, including the mesial areas; they were not seen in electrodes representing the hippocampus and mesial temporal areas. Interestingly, we found slow waves of sleep in a more extensive distribution across the cortex, more pronounced over the frontal areas. The spindle component of the K-complex was visualized maximally over the central sulcus region, while the slow wave component was seen persistently with higher amplitude in the contacts anteriorly in the frontal cortex. In-spite of postulated acoustic origin, K complexes were not visualized in the temporal cortex. Vertex waves were seen maximally and persistently over the frontal-central regions.

Conclusion: Preliminary data from our study shows that there is a good cortical representation of sleep architecture correlating with traditional scalp electrodes. Additional information exploring abnormalities or differences in scalp/depth correlation not only in non-REM but also REM sleep need to be done.

0096

INFLUENCE OF THE TRANSITION FROM WAKEFULNESS TO SLEEP, SLEEP STAGE AND RECOVERY SLEEP ON ENERGY EXPENDITURE IN HUMANS

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Introduction: Little is known about how sleep processes influence energy expenditure (EE) in humans. The aim of the current analysis was to test the hypothesis that EE would decrease during the transition from wakefulness to sleep and that EE would be influenced by sleep stage and recovery sleep.

Methods: Seven healthy participants (5 men, 2 women), aged 22.43±4.76 (Mean±SD), maintained an ~8h per night sleep schedule for one week at home, verified by actigraphy recordings. Participants consumed an outpatient isocaloric diet for three days prior to an ~90h GCRC protocol. Following an 8h sleep disorders screening night, subjects lived in a whole room indirect calorimeter and were scheduled to a 16h wakefulness:8h sleep baseline, followed by 40h of sleep deprivation and 8h recovery sleep. Meal, sleep and wake times were scheduled relative to habitual wake time, calculated from the week prior. EE was calculated every minute. Rate of change in EE during the sleep transition was calculated with linear regression. Rate of change, percent sleep stage and EE during sleep were examined with repeated measures ANOVA.

Results: Sleep onset latency, percent of stage 1 and wakefulness, and number of arousals significantly decreased, whereas percent SWS increased during recovery versus baseline nights ($p<0.05$). EE decreased across the sleep transition and rate of change during the transition was faster on recovery versus baseline nights ($p<0.05$). EE was significantly lower during recovery versus baseline nights ($p<0.05$). No significant differences in EE were seen between sleep stages, but EE on both nights was higher for wakefulness during the scheduled sleep episode compared to all sleep stages.

Conclusion: The sleep transition, recovery versus baseline sleep, and sleep versus wakefulness reduced energy expenditure. The finding that energy expenditure did not significantly differ between sleep stages suggests that sleep continuity contributes more to lower energy expenditure during recovery sleep than does sleep stage.

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0097

A DUAL OREXIN RECEPTOR ANTAGONIST MODULATES THE SLEEP/WAKE CYCLE IN WHITE-CROWNED SPARROWS

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Introduction: The orexin/hypocretin system modulates the sleep/wake cycle in mammals but little is known of the function of orexin in birds. Recently in pigeons, orexin A injections had arousing effects and decreased sleep postures. We hypothesized that a dual orexin receptor an-

tagonist would increase sleep postures and decrease daytime activity in sparrows.
Methods: White-crowned sparrows kept in a short day photoperiod (8L:16D) were injected intramuscularly with a low (6mg/kg) or a high (30mg/kg) dose of almorexant. Sleep postures and daytime activity were monitored by video and behavior was analyzed. We compared behaviors immediately after injection and throughout the day and night.
Results: There was a significant increase in sleep postures exhibited by the sparrows in the high dose group immediately after injection ($P<0.05$). Total activity and sleep postures did not significantly change during the day or night.
Conclusion: This study indicates the orexin system may modulate the sleep/wake cycle similarly in mammals and birds. Additionally, these data support previous findings in another species of bird.

0098

THE EFFECTS OF FLUOXETINE ON THE SLEEP/WAKE CYCLE OF MIGRATING SPARROWS

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Introduction: Nocturnally migrating birds exhibit disrupted sleep/wake cycles during exposure to long photoperiod. During this time, they display migratory restlessness characterized by a decrease in daytime activity and an increase in nighttime activity and arousals. Serotonin is known to modulate sleep cycles; therefore, we wondered how increased serotonin would affect the sleep/wake cycles in White-crowned sparrows. We hypothesized administration of fluoxetine, a serotonin reuptake inhibitor, during early and late subjective day, would regulate activity.
Methods: White-crowned sparrows were exposed to long day photoperiod (16L:8D); A stimulus known to induce migratory activity in captive sparrows and was confirmed by video recording. Birds were divided into low dose (10mg/kg fluoxetine in 25% DMSO), high dose (30mg/kg in 25% DMSO), and saline groups. Injections were given intramuscularly at early subjective day and at late subjective day. Video recordings were taken after injections through most of the day and the night. Analysis of videos included comparison between groups of duration of sleep, low activity, and high activity.
Results: Our results indicate that fluoxetine had no immediate regulatory effect on early and late subjective day activity or sleep behavior. Likewise, results were similar between the early and late subjective groups that received fluoxetine. However, there was a strong trend in high activity found in late subjective day. Finally, the overall course of day and of night also did not show any significant differences.
Conclusion: Our pilot data suggests that increased serotonin activity does not modulating sleep/wakefulness in captive white-crowed sparrows given migratory cues. These results are surprising given that serotonin is a known to modulate sleep/wake cycles. Further analysis could be done through using more test subjects, comparing activity within individual subjects, or by observing ingestive behaviors.

0099

PATHOLOGICAL GAMBLING IN PATIENTS ON PRAMIPEXOLE FOR RESTLESS LEGS SYNDROME- A CASE SERIES AND REVIEW OF THE CURRENT LITERATURE

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Introduction: There is growing evidence to show that pramipexole causes compulsive behaviors when used in Parkinson's disease. It is argued that these patients have neurodegenerative changes predisposing them to develop these behaviors. There are recent reports of similar behaviours occurring in patients on pramipexole for restless legs syndrome (RLS). We report two cases with no previous psychiatric history who developed pathological gambling after starting on pramipexole for RLS.
Methods: Mr S, a 61-year-old male, was started on 0.125 mg of pramipexole to treat his RLS. Following this he reported an increase in sexual desire. Three years later the dose was raised to 1 mg. He then developed amphetamine abuse and pathological gambling. He spent a total of $120,000 on his habit. His gambling stopped soon after discontinuing pramipexole. Mr D, a 65-year-old male, was started on pramipexole for RLS secondary to chronic renal failure. He developed pathological gambling on 1.5 mg of pramipexole, spending $400,000 on his habit. His medication was changed to 2 mg of ropinorole. His gambling continued for one year after stopping pramipexole. He was able to stop gambling while remaining on 2 mg of ropinorole.
Results: The doses of pramipexole used in RLS are smaller than those in Parkinson's disease. There is conflicting evidence on the relationship between the dose of pramipexole and pathological gambling in patients with Parkinson's disease. Our cases developed compulsive behaviours on a mean dose of 1.25 mg. In previous reports of pathological gambling in RLS the doses were between 0.125 mg to 0.5 mg. This series adds to the growing literature of compulsive behaviors occurring in patients with RLS on pramipexole.
Conclusion: Clinicians prescribing these medications must be aware of these side effects and inform patients and their families accordingly to prevent long-term financial loss and social morbidity.

0100

ARMODAFINIL IN SHIFT WORK DISORDER: NORMALIZATION OF THE MSLT

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Introduction: Wake-promoting agents can improve alertness as measured by the MSLT in patients with shift work disorder (SWD). However, in samples selected using laboratory criteria (i.e., MSLT <6) alertness does not normalize. SWD patients with a symptom-based diagnosis (i.e., subjective sleepiness) unselected based on MSLT may respond differently to wake-promoting agents. In order to obtain an unbiased indication of the response to a wake-promoting agent in SWD, this study evaluated the effect of armodafinil on MSLT in patients with SWD unselected for MSLT at baseline.
Methods: All subjects met ICSD-2 criteria for SWD (n=5). Symptoms of sleepiness were determined by the Epworth Sleepiness Scale (ESS>10). Patients worked a minimum of 10 night shifts/month and were screened out for additional sleep and medical disorders. Armodafinil (150 mg) or placebo was administered (2300) in a randomized, double-blind, placebo-controlled cross-over design. Daytime polysomnograms were performed at baseline for all patients. MSLT naps were done at 0130, 0330, 0530, and 0730hrs.
Results: PSG data at baseline was consistent with a SWD diagnosis (sleep latency=13.2±9.8 minutes; wake after sleep onset =125.5±111.6 minutes; sleep efficiency =70.6%±23.0). Patients with SWD had a mean MSLT of 5.68±3.83 minutes (range 1.5-11.8) following placebo and improved to 12.65±3.13 minutes (range 7.5-16) following 1 night of treatment with armodafinil (p<.05).
Conclusion: Objectively measured nocturnal alertness on the MSLT improved to well within normal limits following 1 night of treatment with armodafinil 150 mg in patients with SWD. These results represent a larger improvement in MSLT (+7.0 minutes) compared to previous studies (+1.7 to 3.0 minutes) using MSLT selected patients, but similar doses of medication.
Support (optional): Cephalon Inc.

0101

CHRONIC HYPNOTIC USE: RISK OF REBOUND INSOMNIA

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Introduction: Rebound insomnia is a worsening of sleep following drug discontinuation. Few studies have assessed the risk of rebound insomnia as a function of duration of use. The withdrawal literature suggests that withdrawal can occur at therapeutic doses with chronic use. This study is the first to repeatedly test for rebound insomnia with chronic nightly therapeutic dose hypnotic use for 4 months.
Methods: Primary insomniacs, meeting DSM-IV criteria were recruited. Randomly assigned participants received, double-blind, either zolpidem or placebo for 4 months. On nights 1, 2 and 7 zolpidem efficacy was assessed and rebound on month 1 nights 8, 9, & 14 and month 4 nights 1, 2, & 7, with 8-hr NPSG. To test rebound, placebo substitution occurred for zolpidem. No night differences occurred within the three assessments and data are 3-night averages.
Results: Zolpidem produced a significant increase relative to placebo in total sleep time (TST), 7.0 vs. 6.2 hrs, [F(1,26)=8.93; p=0.01]. Month 1 and 4 placebo substitutions TST did not differ between zolpidem and placebo groups (6.5 vs. 6.3 hrs; p=0.515) and (6.6 vs. 6.2 hrs; p=0.326). Both sleep latency (SL) and min of wake after sleep onset (WASO) were improved by zolpidem SL:17.0 vs. 32.3 min, [F (1, 26)=6.288; p=0.019] and WASO:48 vs. 90 min, [F(1,26)=8.163; p=0.008]. Placebo substitutions returned measures to placebo level in month 1 (SL:20.74 vs. 26.18 min, (p=0.379) and (WASO:78 vs. 78.6 min, (p=0.892) and in month 4 (SL:26.75 vs. 40.56 min, p=0.311) (WASO:72 vs. 91 min, (p=0.278). Month 1 and 4 substitution data did not differ in either group.
Conclusion: Zolpidem improved sleep initiation, maintenance, and duration at month 1. The therapeutic dose, (10mg) did not produce rebound insomnia or increase its likelihood as a function of chronic nightly administration for 4 months.
Support (optional): NIDA, grant#: R01DA17355 awarded to Dr. Roehrs.

0102

CHRONIC HYPNOTIC USE: ITS ABUSE LIABILITY

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Introduction: Primary insomnia is considered a chronic disorder, but concerns about chronic hypnotic abuse remain. Short-term studies suggest that hypnotics have a low abuse liability, but no studies have assessed liability beyond 2 weeks. This study evaluated abuse liability in insomniacs using clinical doses of hypnotics nightly for 4 months.
Methods: Primary insomniacs, meeting DSM-IV criteria and a screening sleep efficiency of <85% were recruited. Randomly assigned participants received, double-blind, either 10mg zolpidem or placebo nightly for 4 consecutive months. In months 1 and 4, one-week self-administration

occurred in the sleep laboratory. The zolpidem group had color coded zolpidem (10 mg) or a placebo capsule on sampling nights 1 and 2. The capsule colors and drug administration were in counter-balanced order. The following 5 nights, choice of either 1, 2, or 3 zolpidem (5mg each) or placebo capsules occurred depending on sampling night experiences.
Results: The zolpidem group selected zolpidem more often than placebo (X2=12.1; p=0.001). The percentage of insomniacs in the zolpidem group choosing zolpidem over the 5 nights did not differ significantly from month 1 to month 4 (69% to 89%), X2=0.841; p=0.359. The percentage of available zolpidem capsules self-administered by the zolpidem group did not differ significantly from self-administration of placebo capsules by the placebo group at month 1 (46% and 53%; X2=0.107; p=0.743) or at month 4 (43% and 45%; X2=0.841; p=0.359). On average, the zolpidem group self-administered a 7.25 mg nightly dose in both month 1 and 4.
Conclusion: Nightly zolpidem, 10 mg, use for 4 months did not increase the number of capsules self-administered over 5-day tests in month 1 and month 4. On average a 7.25 mg dose was self-administered on the two tests.
Support (optional): NIDA, grant#: R01DA17355 awarded to Dr. Roehrs.

0103

EVALUATIONS OF WAKE PROMOTING EFFECTS OF PARAXANTHINE IN OREXIN/ATAXIN-3 NARCOLEPTIC MICE

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Introduction: Caffeine is the world's most widely consumed stimulant and wake-promoting agent. Caffeine's effects are mediated by antagonism of adenosine A1 and A2A receptors. Caffeine is also used for the treatment of hypersomnia, but wake-promoting potency of caffeine is often not strong enough, and high doses may induce various side effects such as anxiety, tremors, headache, and GI irritation. Caffeine is metabolized extensively (80% on average) to paraxanthine and small portions to theobromine and theophylline. Caffeine and paraxanthine have similar anti-adenosine actions, but paraxanthine exhibits a slightly higher potency, lower toxicity, and lesser anxiogenic effects than caffeine. In addition, paraxanthine provides protection against dopaminergic cell death via ryanodine receptor stimulation. Paraxanthine may thus be a better wake-promoting formula in normal and neurological conditions. In the current study, we evaluated the wake-promoting efficacy of paraxanthine in mice model of narcolepsy, a prototypical disease model of hypersomnia.
Methods: Orexin/ataxin-3 TG narcoleptic mice and their littermate wild type (WT) mice were used (n=8 each group). The mice were surgically prepared for EEG and EMG, locomotor activity and core body temperature recordings by telemetry transmission. The mice were subjected to oral administration, at ZT 2 and ZT14, of three doses of paraxanthine (6.25, 25. 100 mg/kg p.o.) or vehicle. A reference wake-promoting compound, modafinil (50, 100, 200 mg/kg, p.o.) was also administered. Data for the six-hours post drug administration were analyzed, and each 10-second epoch was scored visually as wake, REM, or NREM sleep, and direct transitions from wake to REM sleep (DREM).
Results: Paraxanthine and modafinil increased wake and reduced NREM and REM sleep in both narcoleptic and WT mice in a dose dependent manner. Both compounds had no effect on DREM. Both narcoleptic and WT mice responded similarly, but wake-promoting effects of paraxanthine (100 mg/kg p.o.) were more potent than those of modafinil (200 mg/kg p.o.). Wake-promoting effects of paraxanthine and modafinil were associated with increase in locomotor activity and temperature, and greater effects on temperature were observed with paraxanthine administration.
Conclusion: If paraxanthine exhibits a lower toxicity than caffeine and provides neuroprotection, paraxanthine may be a better formula as a wake-promoting agent in neurological conditions, such as narcolepsy and Parkinson's disease.
Support (optional): This study was supported by Institut de Recherche Pierre Fabre

0104

THE EFFICACY OF METHYLCOBALAMIN IN NORMAL SUBJECTS: EVALUATION BY MEANS OF CYCLIC ALTERNATING PATTERN

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Introduction: It is well-known that methylcobalamin (VB12) is one of the cure for circadian rhythm sleep disorder (CRSD). However, the mechanisms of action have not been revealed enough. Several studies suggested that VB12 has sleep-promoting effects in rats and human. The aim of this study is to examine the effect of VB12 on sleep microstructure in normal subjects using Cyclic Alternating Pattern (CAP).
Methods: Subjects were 8 normal males (mean age; 36.5±11.2y). All subjects gave written informed consent. Sleep-wake rhythm of each subject was regularly controlled to their habitual schedule for a week before PSG recording and confirmed by actigraphy and sleep diary. All subjects received a single dose of placebo and VB12 500μg in a single-blind method 30min before starting PSG measurement, and there was at least 1week washout interval between the PSG recordings of the same patient. All recordings were scored by means of R&K methodology (macrostructure) and CAP methodology (microstructure). The subjective sleep evaluations were The St Mary's Hospital sleep questionnaire (SMH), Visual analog scale (VAS), Stanford sleepiness scale (SSS), and Spaceaeromedicine Fatigue check-list (SAM). Furthermore, psychomotor vigilance task (PVT) and Pauli test were performed to evaluate response rate. Each evaluation was carried out every two hours after polysomnograms. Analysis: Cross-over ANOVA was used for each variable of VAS, SSS, SAM and PVT. R&K and CAP parameters were evaluated by Wilcoxon singled-ranks test.
Results: By intravenous administration of VB12, CAP time (106.4±16.6 →85.1±16.7min, p=0.046) and CAP rate (37.3±6.3→ 30.2±7.1%, p=0.043) significantly decreased. There was no significant difference in the subjective sleep evaluations, mental performance, and each sleep parameter of R&K method between placebo and VB12.
Conclusion: Our findings suggested that peripherally infused VB12 may have the ability of enforcing sleep stability even in subjects without CRSD. Further study in insomniacs is necessary to clarify the sleep promoting effect of VB12.

0105

EFFECTS OF EPLIVANSERIN, A NON-SEDATIVE AGENT, ON DRIVING AND COGNITIVE/PSYCHOMOTOR PERFORMANCE: A RANDOMIZED PLACEBO- AND ACTIVE-CONTROLLED TRIAL IN INSOMNIA PATIENTS WITH DIFFICULTIES MAINTAINING SLEEP

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Introduction: Eplivanserin, an Antagonist of Serotonin Two A Receptors (ASTAR) developed at 5 mg/day for chronic insomnia characterized by nocturnal awakenings, has no affinity for GABA receptors, unlike benzodiazepines. The objective of this study was to assess next-day driving and cognitive/psychomotor performance after 3-week repeated administration of eplivanserin 5 mg to differentiate it from classical

hypnotic agents, such as flurazepam 30 mg (active control), which may produce residual sedative effects in the morning due to their mechanism of action.

Methods: This is a single-center, randomized, double-blind, placebo- and active-controlled, double-dummy study, in which patients (n=28) with sleep maintenance insomnia underwent a 3-way crossover with placebo, eplivanserin 5 mg and flurazepam 30 mg (active control). A 3-week washout separated each 21-day treatment period. After final administration on Day 20, a monotonous driving test evaluated standard deviation of lane positioning (SDLP) and number of lane crossings (NLC) at 2, 12, 16, 20 and 23 hours post-administration, and a driving test with distractors evaluated the brake reaction time (BRT) and distance from infront vehicle (DFV) at 14, 18 and 22 hours post-administration. Cognitive/psychomotor performance was evaluated by a Cognitive Drug Research test battery including power of attention (PA), and quality of episodic secondary memory (QESM) composite scores.

Results: Flurazepam increased SDLP ($p<0.0001$) and NLC over the 24-h test period. No alteration in these parameters or in BRT or DFV occurred after repeated eplivanserin dosing. Over the 24-h test period, flurazepam produced significant impairment reflected in the composite scores for PA ($p<0.05$) and QESM ($p<0.0001$) vs placebo, but neither PA ($p=0.1335$) nor QESM ($p=0.1027$) were significantly altered by eplivanserin. Frequent adverse events with eplivanserin were somnolence, headache and fatigue.

Conclusion: Eplivanserin 5 mg for 21 days, at steady state, did not alter driving performance or cognitive and psychomotor functioning in patients with insomnia characterized by sleep maintenance difficulties. Eplivanserin was well tolerated.

Support (optional): Supported by sanofi-aventis.

0106

EFFECTS OF EPLIVANSERIN, A DEEP SLEEP ENHANCER, ALONE AND IN COMBINATION WITH ZOLPIDEM, ON PSYCHOMOTOR AND COGNITIVE PERFORMANCE IN HEALTHY SUBJECTS

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Introduction: Eplivanserin, Antagonist of Serotonin Two A Receptors (ASTAR), a non-sedative sleep agent increases slow wave sleep. Eplivanserin, being developed at 5 mg/dose for chronic insomnia characterized by nocturnal awakenings, unlike benzodiazepines, has no affinity for GABA receptors. Eplivanserin, without effect on sleep onset, may be combined with zolpidem, a sleep inducer, in patients with both sleep onset and maintenance insomnia; so the effect of coadministration on psychomotor/cognitive performance was investigated.

Methods: This is a two-part, single-center, double-blind, randomized, placebo- and active-controlled, 4-way crossover study in 24 healthy subjects (age 19-49 years), who were administered (Part A) one 30-mg dose of flurazepam (positive control) or placebo, followed by the reverse treatment after a 21-day washout; (Part B) then eplivanserin 5 mg or placebo for 21 days in the evening followed by coadministration with a single 10-mg dose of zolpidem-IR, and followed by the reverse treatment. Next-day tests included: Critical Flicker Fusion (CFF); Choice Reaction Time (CRT); Immediate and Delayed Recall of Supraspan Word Lists (IDR); Compensatory Tracking Task (CTT); and Bond-Lader Visual Analog Scale (VAS) of Alertness.

Results: Part A: Flurazepam significantly impaired global psychomotor/cognitive performance vs placebo ($p=0.0001$). Part B: Eplivanserin had no significant effect vs placebo on CRT, IDR, CTT, or alertness; however, CFF was decreased (-1.01 Hz; $p=0.0002$). The effects of eplivanserin+zolpidem-IR on psychomotor/cognitive performance were not significantly different from placebo+zolpidem-IR, except for CFF, which was again decreased (-1.07 Hz; $p=0.002$) after eplivanserin+zolpidem-IR. Eplivanserin alone for 21 days and in combination with zolpidem-IR was well tolerated.

Conclusion: Eplivanserin had no effect on psychomotor/cognitive performance when administered alone or in combination with zolpidem-IR. The decreases in CFF (seen both with eplivanserin+placebo and eplivanserin+zolpidem-IR) confirm that eplivanserin affects CFF, likely caused by miosis (observed with other 5-HT2 antagonists) and not caused by sedation.

Support (optional): Supported by sanofi-aventis.

0107

THE EFFICACY OF METHYLCOBALAMIN IN PSYCHO-PHYSIOLOGICAL INSOMNIAC PATIENTS: EVALUATION BY MEANS OF CYCLIC ALTERNATING PATTERN (CAP)

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Introduction: It has been reported that Vitamin B12 is one of the cure for CRSD via sleep promoting effect. The aim of this study is to examine the therapeutic efficacy of methylcobalamin (VB12) on psycho-physiological insomniac patients by means of CAP.

Methods: The subjects were patients with psycho-physiological insomnia (7 women 36.9±12.8 y). All subjects received a single dose of placebo and methylcobalamin 500μg in a single-blind method 30min before starting PSG measurement, and there was at least 1week washout interval between the PSG recordings of the same patient. All recordings were scored by means of R&K methodology (macrostructure) and CAP methodology (microstructure). The subjective sleep evaluations were The St Mary's Hospital sleep questionnaire (SMH), Visual analog scale (VAS), Stanford sleepiness scale (SSS), and Spaceaeromedicine Fatigue check-list (SAM). Furthermore, psychomotor vigilance task (PVT) and Pauli test were performed to evaluate response rate. Each evaluation was carried out every two hours after polysomnograms. Analysis: Cross-over ANOVA was used for each variable of VAS, SSS, SAM and PVT. R&K and CAP parameters were evaluated by Wilcoxon singled-ranks test.

Results: By intravenous administration of VB12, CAP time (174.8±29.3min→127.0±37.5min:$p=0.011$), CAP rate (62.6±10.3%→53.4±10.4% :$p=0.021$), total cycle (381±63→304±111:$p=0.028$) and the number of A1 phases (214±79→134±50:$p=0.008$) significantly decreased. There was no significant difference in the subjective sleep evaluations, mental performance, and each sleep parameter of R&K method between placebo and VB12.

Conclusion: These results suggested that a single intravenous administration of VB12 improved sleep stability in psycho-physiological insomniac patients. Even though the effect of VB12 on subjective evaluations were not clarified, repetitive administration of VB12 may improve subjective sleep evaluation, which has been reported to be closely associated with CAP rate in insomniacs.

0108

NITRIC-OXIDE DONOR MICRODIALYSIS IN THE BASAL FOREBRAIN PRODUCES IMPAIRMENTS IN THE RAT-PSYCHOMOTOR VIGILANCE TASK THAT ARE REVERSED BY AN ADENOSINE A1R ANTAGONIST

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Introduction: Evidence indicates that adenosine (AD) is a key mediator of the behavioral sleepiness seen following sleep deprivation (SD). The following neurobiological model has been proposed: SD leads to a rise in extracellular AD in the basal forebrain (BF) and cortex. This rise in AD is produced by nitric oxide (NO). The elevated levels of AD

produce sleepiness and impaired vigilance (sustained attention) by inhibiting wake active cortically projecting BF neurons (as well as acting directly on cortical neurons). Here we test the effect of BF microdialysis application of an NO donor on vigilance performance in rats.
Methods: Adult male Fischer-Norway rats were trained on the rat-Psychomotor Vigilance task (rPVT) and then surgically prepared for bilateral microdialysis perfusion in the BF. Drugs were locally administered in the BF via reverse dialysis using a counter balanced repeated measures design. Three doses of an NO donor (DETA/NO; 1, 3, 10 mM)) were bilaterally dialyzed in the rat BF for 2h immediately prior to rPVT testing.
Results: DETA/NO produced dose-dependent behavioral impairments in rPVT performance, similar to those produced by 24 h of total sleep deprivation. Finally, to test the prediction that the behavioral effects of the NO donors dialyzed in the BF are mediated by AD, we co-dialyzed the AD antagonist CPT (1 μM) with 1, 3 and 10 mM DETA/NO. DETA/NO vigilance impairments were blocked by co-perfusion with CPT.
Conclusion: In summary, pharmacological elevation of NO in the BF of rats produces reversible vigilance deficits that closely resemble the vigilance impairments produced by sleep disruption in rats and humans. These findings support the global hypothesis that sleep disruption produces elevated levels of NO in the BF, and that these changes may be the biochemical mediators of the homeostatic sleep drive.
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0109

LATE-DAY PLASMA CONCENTRATIONS FOLLOWING MULTIPLE-DOSE ADMINISTRATION OF ARMODAFINIL

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Introduction: Armodafinil (NUVIGIL®) is the *R*- and longer-lasting isomer of modafinil. Armodafinil is a non-amphetamine, wakefulness promoting medication that is approved for excessive sleepiness associated with obstructive sleep apnea, shift work disorder, and narcolepsy. A study in healthy subjects with acute sleep deprivation showed that a single dose of armodafinil produced higher plasma concentrations 5 hours after dosing compared with modafinil. The objective of this study was to compare steady-state plasma concentrations of armodafinil and modafinil on a milligram-to-milligram basis.
Methods: Post-hoc analyses of steady-state pharmacokinetic data from two studies of healthy adult subjects administered armodafinil (n=34) or modafinil (n=18) compared average late-day (3-7 PM) plasma concentrations, concentration swing, and fluctuation after 7 days of once-daily dosing. Swing was defined as the variation in drug concentration from peak to trough over the dosing interval ($[C_{max} - C_{min}]/C_{min}$) and fluctuation was defined as the variation in drug concentration from peak to trough relative to the average steady-state concentration over the dosing interval ($[C_{max} - C_{min}]/C_{avg}$). Doses of both agents were normalized to 200 mg and pooled within study prior to analysis.
Results: Average late-day plasma concentrations and AUC (3-7 PM) were ~43% higher for armodafinil than for modafinil. Across the 24-hour dosing interval, plasma concentration swing and fluctuation were 42% and 28% less, respectively, with armodafinil versus modafinil.
Conclusion: After multiple dosing, armodafinil produced higher steady-state plasma concentrations and less variability in plasma concentrations across the dosing interval than modafinil when compared on a milligram-to-milligram basis. The greatest differences were observed later in the day. Armodafinil once daily may provide improved wakefulness throughout the day compared with modafinil.
Support (optional): Study sponsored by Cephalon, Inc.

0110

ARMODAFINIL AND MODAFINIL: SIMILAR TERMINAL HALF-LIVES, SUBSTANTIALLY DIFFERENT PHARMACOKINETIC PROFILES

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Introduction: Armodafinil (NUVIGIL®), the *R*- and longer-lasting isomer of modafinil, is a non-amphetamine, wakefulness promoting medication. Armodafinil produces higher late-day plasma concentrations than modafinil despite similar terminal half-lives ($t_{1/2}$). The objective of this analysis was to identify the pharmacokinetic parameters underlying these higher late-day plasma concentrations following armodafinil administration versus modafinil.
Methods: Individual subject data from multiple studies in healthy subjects administered a single dose of either armodafinil or modafinil were dose normalized to 200 mg and then pooled for each compound. Pharmacokinetic parameters assessed included $t_{1/2}$, maximum plasma concentration (C_{max}), time to C_{max} (t_{max}), and area under the plasma concentration-versus-time curve (AUC).
Results: The $t_{1/2}$ for both armodafinil and modafinil was about 13 hours. The two agents also had comparable mean values for C_{max} (5.44 μg/mL and 4.61 μg/mL for armodafinil and modafinil, respectively) and median tmax values (1.8 and 2.5 hours, respectively). However, after reaching C_{max}, armodafinil concentrations declined monophasically while a biphasic decline in modafinil concentrations was observed due to more rapid elimination of the *S*-isomer within the racemate+. This difference in elimination was also apparent in the higher AUC for armodafinil (95.8 μg h/mL) versus modafinil (68.5 μg h/mL) on a milligram-to-milligram basis.
Conclusion: Armodafinil and modafinil have similar early profile parameters and terminal half lives. These results indicate that the monophasic elimination observed with armodafinil differentiates it from modafinil, resulting in higher total systemic exposure and late-day concentrations relative to those for modafinil on a mg-to-mg basis. Once-daily administration of armodafinil may result in improved wakefulness that is maintained throughout the day.
Support (optional): Study sponsored by Cephalon, Inc.

0111

SPECTRAL PROFILE OF EPLIVANSERIN DIFFERS FROM OTHER SWS-ENHANCING AND HYPNOTIC DRUGS

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Introduction: Eplivanserin, a 5-HT2A antagonist under development as treatment for chronic insomnia, has been shown to increase slow wave sleep (SWS). This analysis examined the spectral NREM EEG profile of eplivanserin to determine if the profile is similar to other SWS-increasing drugs such as tiagabine or gaboxadol.
Methods: Screen (run-in placebo) and eplivanserin treatment (nights 41-42) polysomnography (PSG) of 102 primary insomnia patients (52 women, 50 men) who completed a 6-week clinical trial were randomly selected for spectral analysis (Vitascore 1.30). Absolute power in quarter-Hz bins was obtained for NREM central EEG and summed into 1-Hz bins, as well as delta, theta, alpha, sigma, and beta bands. Screen and treatment PSG log-transformed absolute power estimates were compared, as were relative (to baseline) power estimates between sexes.
Results: Absolute power in 1- and 2-Hz bins was significantly greater after eplivanserin treatment than at baseline, as were sub-delta (0.25-0.75 Hz) and delta (0.75-4.5 Hz) power. Power in 1-Hz bins from 12 to 23 Hz and within the sigma (12-15 Hz), beta-1 (15-20 Hz), and beta-2 (20-25 Hz) bands was significantly lower with eplivanserin. Relative

power did not differ between males and females in any 1-Hz bins or standard bands.
Conclusion: Power-density increases with eplivanserin occurred in the 1- and 2-Hz bins; power was reduced in many beta frequency bins. This contrasts with BzRAs, which reduce power in slow wave and theta frequencies, and with other SWS-enhancing drugs, which increase power throughout the slow wave and theta bands. Finally, contrary to sex differences observed with other SWS-enhancing drugs, men and women treated with eplivanserin show identical relative spectral power density. These findings indicate that eplivanserin produces a NREM spectral profile that differs from both hypnotics and other SWS-enhancing drugs, consistent with a different mechanism of action of eplivanserin.
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0112

THE EFFECTS OF ZOLPIDEM ON PSYCHOMOTOR AND SUBJECTIVE EVALUATION IN HEALTHY ELDERLY PERSONS

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Introduction: Many problems have been reported in the use of hypnotics in the elderly, such as balance disturbance, falling, and memory disturbance. A safer use of hypnotics is being anticipated.
Methods: We performed a double-blind crossover trial on 14 healthy elderly subjects in order to investigate the residual effect of a single administration of Zolpidem (5mg). The subjects were given either Zolpidem or a placebo at 23 o'clock before going to bed. Objective assessments (Sway pass, Functional Reach Test (FRT), Up and Go Test, Choice reaction time (CRT), Critical Flicker Fusion Test (CFF), memory test) were conducted at 22 o'clock before the subjects took the hypnotic, and at 4, 6, 10, and 14 o'clock the next day. Also, subjective assessments (Stanford Sleepiness Scale (SSS), alertness, well-being, fatigue) were conducted once every two hours from 4 o'clock on the next day of the hypnotic administration. This experiment protocol was approve by Akita University Ethical Committee. The repeated-measures ANOVA with a grouping factor (placebo vs. drug sessions) for objective and subjective assessments was conducted to verify main effects and interactions of time and/or drug. A p-value less than 0.05 was considered significant.
Results: There was no change in objective and subjective ssessments on the following day in the Zolpidem night compared to the placebo night. Especially in the CFF and memory test, the results of Zolpidem were significantly better than those of placebo ($p<0.05$).
Conclusion: Zolpidem has a hypnotic activity without disturbing objective and subjective performance on the following day when given to healthy elders. Therefore, Zolpidem may be useful in healthy elders to adjust their insomnia without balance disturbance, falling and memory disturbance.

0113

EFFECTS OF BAICALIN & WOGONIN IN THE REGULATION OF SPONTANEOUS SLEEP

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Introduction: Baicalin and wogonin are active compounds originated from the root of traditional Chinese herb Scrutellaria baicalensis Georgi. They have been used in anti-inflammation, anti-bacteria, anti-hypertension, anti-allergy and sedative actions since ancient China. Baicalin and wogonin possess abilities to decrease the expression of pro-inflammatory cytokines and NF-κB activity. Cytokines play an important role in the regulation of slow wave sleep (SWS). However, there is a lack of evidence linking baicalin and wogonin to the sleep regulation. This study is designed to investigate the mechanisms of baicalin and wogonin on spontaneous sleep.
Methods: We respectively i.c.v. injected baicalin and wogonin into brain and EEG-defined sleep-wake activities were collected.
Results: Our results indicated that both baicalin and wogonin exhibited a biphasic effect on spontaneous sleep, an initiate phase and a late phase of sleep regulation. In the initiate phase, the time spent in SWS during hours 1~2 of the light period were decreased from 63.19 ± 3.62 %, obtained after vehicle (DMSO), to 47.73 ± 6.88 % acquired after administration of baicalin 20 mins prior to light onset. Besides, the time spent in SWS were increased during hours 8~12 of dark period from 17.03 ± 1.86 %, obtained after DMSO, to 26.6 ± 2.63 % acquired after injection of baicalin prior to dark onset. Wogonin also exhibited a similar sleep-wake regulation as that of baicalin.
Conclusion: The observation elucidated that both wogonin and baicalin exhibited dual responses to regulate sleep-wake activity; an initiate phase to suppress SWS during the light period and a late phase to enhance SWS during the dark period. We hypothesized that the anti-inflammatory effect of wogonin and baicalin may be involved in the regulation of the initial phase, and corticotrophin-releasing hormone (CRH) and/or GABA may mediate the late phase response. However, these hypotheses need to be further investigated.

0114

ATYPICAL ANTIPSYCHOTICS AND SEVERITY OF OBSTRUCTIVE SLEEP APNEA

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Introduction: Weight gain is a common complication of atypical antispychotic (AA) administration and may exacerbate obstructive sleep apnea (OSA). We hypothesize that AAs independently affect severity of OSA.
Methods: Historical, demographic and physiologic data of 842 adult (age > 18 yrs) patients receiving polysomnography (PSG) for sleep-related complaints were analyzed.
Results: Mean age of patients was 49.09 y, 55.1% were male and mean body mass index (BMI) was 33.82 kg/m2. 68 (8.0%) patients were taking AA at the time of PSG. There were no differences in age, gender, neck circumference or BMI of AA vs. non-AA patients. 77% of the patients had OSA (apnea hypopnea index; AHI >5/h). The AHI was 29.26+/-3.3/h in AA patients and 21.94+/-0.9/h in non-AA patients (P= 0.03). 34% of AA patients had severe OSA (AHI>30/h) compared to 23% of non-AA patients (P=0.04). When adjusted for BMI, gender, use of benzodiazepines and sleeping aids, the odds of severe OSA in AA patients were 1.7 times those of non-AA patients (95%CI=1.03-3.03). Further dividing AHI into Culminate obstructive index (COI; Obstructive apnea index plus Hypopnea index plus Mixed apnea index) and Central apnea index (CAI),COI of 27.65+/-4.4/h and 20.35+/-1.5/h was noted in AA patients and non-AA patients respectively (p= 0.04) There was no difference between the mean CAI of the two groups.
Conclusion: Atypical antipsychotic medication use is independently associated with increasing severity of OSA. This increased severity of OSA is primarily due to increased frequency of obstructive events during sleep.

0115

ANTIDEPRESSANT AND ANXIOLYTIC POTENTIAL OF NEU-P11 IN ANIMAL MODELS

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Introduction: Neu-P11 is a novel melatonin agonist currently in development for the treatment of insomnia. Neu-P11 demonstrated antidepressant-like activity in rats (learned helplessness). The aim of the present study was to further evaluate the antidepressant (forced swimming rat model) and anxiolytic (elevated plus-maze mouse model) potential of Neu-P11.

Methods: Forced swimming test: rats (12 per group) were injected intraperitoneally with Neu-P11 (25, 50, 100 mg/kg) imipramine (32 mg/kg, positive control) or vehicle, and dropped 2h later into a water cylinder for 5 minutes. Immobility during the test phase was assessed by video recordings. Elevated plus-maze test: mice (12 per group) were injected intraperitoneally with Neu-P11 (50 mg/kg) melatonin (50 mg/kg) or vehicle in the morning or in the evening and tested 2 h later. The percentage of entries and time spent in the open arms of the maze apparatus during a 5 minutes test were assessed.

Results: Compared to vehicle treatment rats treated with Neu-P11 at 25, 50 and 100 mg/kg, showed significantly lower immobility times ($p<0.01$, $p<0.05$ and $p<0.01$, respectively) in the forced swimming test. Imipramine 32 mg/kg had a similar effect ($p<0.05$). In the elevated plus-maze test mice with Neu-P11 showed higher percentage of entries and time spent in the open arms compared to vehicle when tested at both times of day (($p<0.001$ for both) whereas melatonin was effective only in the evening test.

Conclusion: The results demonstrate significant antidepressant and anxiolytic potentials of Neu-P11. Unlike melatonin, the anxiolytic effect of Neu-P-11 appears to be independent of the time of day.

Support (optional): Neurim Pharmaceuticals Research Grant (to ST).

0116

NEU-P11, A NOVEL MELATONIN AGONIST INHIBITS WEIGHT GAIN AND IMPROVES METABOLIC PROFILES IN HIGH-FAT/HIGH-SUCROSE-FED RATS

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Introduction: Neu-P11 is a novel melatonin agonist developed for insomnia. Accumulating body of evidence indicates that sleep disorders increase risk of obesity and insulin resistance ("metabolic syndrome"). Furthermore, recent studies associated polymorphism in MT2 melatonin receptors with risk of diabetes in humans. There is a medical need for new drugs that effectively manage both insomnia and insulin resistance. Neu-P11 demonstrated sleep promoting effects in rats. Neu-P11 improved glucose transport in an in-vitro model of insulin resistance in mouse adipocytes. The aim of the present study was to characterize the potential metabolic effects of Neu-P11 in vivo in obese rats.

Methods: Obese rats with hyperglycemia/hyperlipimia induced by in high-fat/high-sucrose-fed (HFSD) were injected intraperitoneally daily, at 20:00h for 8 weeks with Neu-P11 (10mg/kg), melatonin (4mg/kg) or saline (n=10 per group). Glucose and lipid plasma levels were then tested. Body weight, temperature and food consumption were monitored weekly.

Results: Administration of Neu-P11 or melatonin to the diet-induced obese rats inhibited body weight gain and abdominal fat ($P<0.01$ for all) with no influence on food intake. Plasma glucose, total cholesterol, triglycerides levels significantly decreased and HDL-cholesterol increased in the Neu-P11 and melatonin treated compared to the HFSD rats ($P<0.05$ for both). The body temperature was significantly higher from week 3 on in the Neu-P11 treated group compared to the HFSD group ($P<0.01$). Melatonin was less effective.

Conclusion: These data suggest that Neu-P11 even more than melatonin improve metabolic profiles in HFSD-induced obesity model in rats. Neu-P11, a novel melatonin receptor agonist may potentially improve metabolic profiles in obesity.

Support (optional): Neurim Pharmaceuticals Research Grant (to WY).

0117

NEU-P11, A NOVEL MELATONIN AGONIST IMPROVES INSULIN SENSITIVITY IN HIGH-FAT/HIGH-SUCROSE-FED (HFSD) RATS

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Introduction: Neu-P11 is a novel melatonin agonist currently in development for insomnia. Recent evidence link sleep disorders, melatonin receptors and diabetes risk. In animal studies Neu-P11 demonstrated sleep promoting effects. The aim of the present study was to characterize the potential metabolic effects on insulin sensitivity in vivo and gain further insight into the molecular basis of Neu-P11 effects on insulin signaling pathway.

Methods: Obese rats with hyperglycemia/hyperlipimia induced by in high-fat/high-sucrose-fed (HFSD) were injected intraperitoneally, at 20:00h for 8 weeks with Neu-P11 (10mg/kg), melatonin (4mg/kg) or saline (n=10 per group). Glucose tolerance (intragastric 2g/kg glucose bolus) and insulin tolerance (subcutaneous injection 0.5 units/kg insulin) were tested. Insulin receptor substrate 1 (IRS-1) and ser307-phosphorylated IRS-1 as well as PKC-θ were tested in gracilis muscle, liver and fat tissues by western blots.

Results: At the end of the 8 weeks treatment Neu-P11 attenuated insulin intolerance as indicated by the changes in glucose and insulin concentrations after the glucose load in the HFSD rats and improved insulin sensitivity as indicated by a significantly lower 30-min glucose level after insulin injection ($p<0.05$). Neu-P11 treatment significantly decreased Ser307-phosphorylated IRS-1 in muscle, liver and fat (51.5%, 50.5%, 57.4% respectively) and depressed the activity of PKC-θ by inhibiting threonine phosphorylation. Melatonin had similar effects.

Conclusion: PKC-θ activation during hyperlipidemia is necessary for inhibition of IRS-1 tyrosine phosphorylation and insulin-stimulated glucose uptake. Our results show that Neu-P11 and melatonin improve the impaired insulin sensitivity in obese rats probably via the inhibition of PKC-θ and Ser307-IRS-1 phosphorylation.

Support (optional): Neurim Pharmaceuticals Research Grant (to WY).

0118

PREGABALIN IMPROVES FATIGUE IN FIBROMYALGIA PATIENTS AS MEASURED BY FIQ FATIGUE AND SF-36 VITALITY SUBSCALES

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Introduction: Fatigue is a disabling symptom common in patients with fibromyalgia (FM). Pregabalin has been demonstrated to improve pain,

function and sleep disturbance in FM, but pregabalin's effect on fatigue symptoms has not been fully described.
Methods: Pooled analyses of 3 RCTs (2228 FM subjects) were performed in patients receiving placebo, 300, 450, or 600 mg/day of pregabalin for 13-14 weeks. Fatigue data was evaluated using the FIQ fatigue subscale which asks patients to rate (VAS scale) "How tired you have been?" and the SF-36 Vitality Scale (0-100), comprising 4 questions asking how much of the time patients felt "full of life", "worn out", "tired" and "had a lot of energy." Changes of 0.8310 on the FIQ fatigue subscale and 5-10 points on the SF-36 Vitality Scale are reported to represent clinically important differences.
Results: The baseline mean FIQ fatigue subscale score (all patients) was 7.9. The endpoint mean FIQ fatigue subscale scores were 6.75, 6.58, 6.39, and 6.54 for placebo, 300, 450, and 600 mg/day pregabalin, respectively ($p<0.05$ for 450 mg/day). In severely impaired patients, with baseline FIQ total score >70, a nearly 1-point placebo-corrected improvement in fatigue was observed at 450 mg/day (-0.99, $p=0.0026$). The baseline mean SF-36 Vitality score (25.2) was the worst of any SF-36 subscale. Endpoint mean SF-36 Vitality scores were 32.4, 35.1, 35.6, and 35.6 for placebo, 300, 450, and 600 mg/day pregabalin ($p<0.05$ for all). An SF-36 Vitality 10-point responder analysis demonstrated significant improvement ($p<0.05$) in patients treated with 300 and 450 mg/day pregabalin (45.9%, 45.2%) compared to placebo (39.0%). Consistent with previous research, dizziness and somnolence were the most common adverse events.
Conclusion: This pooled analysis of 3 RCTs in FM reveals that pregabalin treatment results in improvement in fatigue as assessed by the FIQ fatigue and SF-36 Vitality subscales.
Support (optional): Supported by Pfizer Inc.

0119

THE EFFECTS OF GAMMA-HYDROXYBUTYRATE ON VIGILANCE STATES AND EEG: ROLE OF $GABA_B$ RECEPTORS

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Introduction: Gamma-hydroxybutyrate (GHB) and its precursor gamma-butyrolactone (GBL) have wide-range effects on vigilance and behavior. However, the mode of action of GHB remains unclear. Evidence indicates that GHB acts mainly through $GABA_B$ receptors that consist of two subunits; $GABA_{B1}$ and -$_{B2}$. $GABA_{B1}$ has two isoforms; 1a and 1b. To elucidate the mechanisms by which GHB affects vigilance states and the role of different $GABA_B$ receptor subunits, the electroencephalogram (EEG) of different $GABA_B$ receptor subunit knock-out (KO) mice was studied before and after GBL administration.
Methods: Adult male wild-type (WT) BALB/c, $GABA_{B(1a)}$ -/-, $GABA_{B(1b)}$ -/-, $GABA_{B1}$ -/- and $GABA_{B2}$ -/- mice were implanted with EEG and EMG electrodes. Mice were recorded during 24hr baseline followed by daily injections with saline and 3 doses of GBL (50, 100 and 150 mg/kg i.p.).
Results: Under baseline conditions, $GABA_{B1}$ -/-, $GABA_{B2}$ -/- and $GABA_{B(1a)}$ -/- mice exhibited spontaneous seizure. Sleep amount, sleep quality and the EEG were differentially affected in the different KO mice. GBL induced EEG slow waves (1-4Hz) with a spike-like EEG pattern at high doses in $GABA_{B(1b)}$ -/-, $GABA_{B(1a)}$ -/- and WT mice, but no behavioral or EEG changes were observed in mice without any functional $GABA_B$ receptors ($GABA_{B1}$ -/- and -$_{B2}$ -/- mice). The duration of the 'GBL-induced state' and the prevalence of EEG slow-waves (delta power) during this state increased with dose in each genotype. $GABA_{B(1a)}$ -/- mice showed 2-fold higher values of delta power than the 2 other genotypes. Although GBL suppressed sleep dose-dependently after injection and induced a dramatic but non-physiological high delta power, none of the 3 genotypes clearly compensated this sleep loss and/or modified the kinetic of delta power.
Conclusion: Our results demonstrate that $GABA_{B(1a)}$ plays an important role in epilepsy, sleep and thalamo-cortical synchronization. GBL acts only through $GABA_B$ receptors to induce behavioral and EEG effects. The lack of a compensatory response to the sleep time lost due to GBL indicates that sleep need does not change during the GBL-induced state. Moreover, the slow waves that accompany this state do not seem to lower subsequent sleep need. Thus, the homeostatic regulation of sleep seems temporarily suspended during the GBL-induced state and the delta activity induced by GBL might functionally be different from delta activity expressed during 'physiological' sleep.

0120

HYPNOTIC EFFECTS OF SB-649868, AN OREXIN ANTAGONIST, AND ZOLPIDEM IN A MODEL OF SITUATIONAL INSOMNIA

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Introduction: Several lines of evidence support the role of orexin in the control of sleep and suggest that orexin antagonism may be a novel treatment for insomnia. SB-649868 is a potent orexin antagonist which has demonstrated hypnotic properties in multiple preclinical models.
Methods: This was a randomised, double-blind, double dummy, placebo-controlled, four-way crossover study to investigate the effect of single oral doses of SB-649868 and of zolpidem in a model of noise induced situational insomnia in 48 healthy male volunteers. SB-649868 (10 or 30mg) was administered after food, 90 minutes before bedtime, while zolpidem 10mg was administered 30 minutes before bedtime. Polysomnographic (PSG) recordings were obtained for 8 consecutive hours. Psychometric tests were administered upon awakening to assess next day residual effects.
Results: Statistically significant increases were observed in total sleep time (TST) for both the SB-649868 10 mg and 30 mg doses and zolpidem 10mg compared with placebo. The increase in TST observed after the administration of SB-649868 30 mg was significantly greater than that observed after the administration of zolpidem 10 mg. SB-649868 10 mg and 30 mg induced statistically significant reductions in latency to persistent sleep and statistically significant increases in sleep efficiency. A statistically significant reduction in wake after persistent sleep onset was observed with SB 649868 30 mg but not 10 mg. A dose-dependent increase in REM sleep was observed with SB-649868, while a reduction was observed with zolpidem. Both compounds were well tolerated with no evidence of next day residual effects.
Conclusion: SB-649868 demonstrated a robust hypnotic effect in the noise-disturbed sleep model of situational insomnia. The hypnotic effects of SB-649868 were comparable to, or stronger than those of zolpidem 10 mg
Support (optional): This study was sponsored by GlaxoSmithKline.

0121

A RANDOMIZED DOUBLE-BLIND PLACEBO-CONTROLLED 12-WEEK TRIAL OF EPLIVANSERIN IN INSOMNIAC PATIENTS WITH SLEEP MAINTENANCE DIFFICULTIES

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Introduction: Eplivanserin, Antagonist of Serotonin Two A Receptors (ASTAR), is a novel sleep compound developed at 5 mg/day for chronic insomnia characterized by nocturnal awakenings. Eplivanserin increases slow wave sleep and, in contrast to benzodiazepines, does not bind to GABA receptors.
Methods: In this multicenter, Phase III, double-blind, randomized, placebo-controlled, parallel-group study, 962 patients with primary insomnia and sleep maintenance difficulties received eplivanserin 5 mg (617 patients) or placebo (345 patients) orally for 12 weeks. The primary efficacy parameter was the change from baseline of patient-reported wake time after sleep onset (pr-WASO) on Week 12. The main secondary parameters assessed the consequences of the treatment of insomnia on daytime functioning using the Functional Outcomes of Sleep Questionnaire (FOSQ). Additional assessments were total sleep time (TST), number of awakenings (NAW), sleep onset latency (SOL), sleep quality, and refreshing sleep quality from the patient's sleep questionnaire. Potential next-day effects were assessed on pr- sleepiness in the morning and on pr-ability to concentrate.
Results: Eplivanserin reduced WASO from baseline significantly more than placebo at 12 weeks (LS mean difference -11:32±2:49 min:s; 95% CI -17:03 to -6.02; $p<0.0001$). Meaningful improvements also at week 12 were: TST (+10:56 min:s; 95% CI 3:06 to 18:45), NAW (-0.33; 95% CI -0.48 to -0.19), sleep quality (-0.10; 95% CI -0.19 to -0.02), and refreshing sleep quality (-0.09; 95% CI 0.18 to -0.01) compared with placebo; SOL was unaffected. A favorable effect of eplivanserin for sleepiness in the morning and ability to concentrate (next-day effects) was observed in comparison with placebo. Eplivanserin was well tolerated as compared to placebo. The most frequently reported TEAEs were an incidence of ≥1% in eplivanserin-treated patients (at least 1% higher than in the placebo group) were dizziness, upper respiratory tract infection, dry mouth, anxiety, depression, gastroenteritis, diverticulitis, urinary tract infection, pharyngolaryngeal pain and vertigo. No rebound insomnia nor meaningful withdrawal symptoms were observed during the 2-week run-out period.
Conclusion: Eplivanserin 5 mg daily for 12 weeks was effective in improving insomnia associated with sleep maintenance difficulties and it had no detrimental effect on next-day effects. Eplivanserin was globally well tolerated.
Support (optional): Supported by sanofi-aventis.

0122

A RANDOMIZED DOUBLE-BLIND PLACEBO-CONTROLLED 12-WEEK TRIAL OF EPLIVANSERIN WITH LONG-TERM OPEN EXTENSION IN INSOMNIAC PATIENTS WITH SLEEP MAINTENANCE DIFFICULTIES: RESULTS FROM THE DOUBLE-BLIND TREATMENT PERIOD

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Introduction: Eplivanserin is a novel sleep compound developed at 5 mg/day for chronic insomnia characterized by nocturnal awakenings. Eplivanserin is an Antagonist of Serotonin Two A Receptors (ASTAR) and has no affinity for GABA receptors, unlike benzodiazepines.
Methods: In this multicenter, Phase III, double-blind, randomized, placebo-controlled, parallel-group study, 1145 patients with chronic insomnia and sleep maintenance difficulties received eplivanserin 5 mg (N=850) or placebo (N=295) orally for 12 weeks, followed by a 40-week open-label extension with eplivanserin 5 mg. The primary and main secondary efficacy parameters were the change in baseline of patient-reported wake-time after sleep onset (pr-WASO) and of daytime functioning items of the Functional Outcomes of Sleep Questionnaire (FOSQ) at 12 weeks. Additional parameters were total sleep time (TST), number of awakenings (NAW), sleep onset latency (SOL), sleep quality and refreshing sleep quality from patient's questionnaire. Potential next-day effects were assessed on pr-sleepiness in the morning and on pr-ability to concentrate.
Results: At 12 weeks, eplivanserin decreased WASO from baseline significantly more than placebo (LS mean difference -13:31 min:s; 95% CI -19:19 to -7:43; $p<0.0001$). A positive effect of eplivanserin compared with placebo was observed regarding the improvement of activities related to work and hobbies at 12 weeks. Meaningful improvements were seen in NAW (-0.35; 95% CI -0.50 to -0.19), TST (+16:20 min:s; 95% CI 9:14 to 23:27), sleep quality (-0.14; 95% CI -0.21 to -0.06) and refreshing sleep quality (-0.15; 95% CI -0.23 to -0.07) compared with placebo; SOL was unaffected. A favourable effect of eplivanserin for sleepiness in the morning and ability to concentrate (next-day effects) was observed in comparison to placebo. Eplivanserin was well tolerated as compared to placebo. The most frequently reported treatment emergent adverse events (TEAEs) in the eplivanserin group (≥1% and at least 1% higher than placebo) were dizziness, diarrhea, somnolence, dry mouth, constipation, diverticulitis, and upper abdominal pain. No rebound insomnia was observed in the 2-week run-out period.
Conclusion: Eplivanserin was an effective and globally well-tolerated treatment that improved insomnia characterized by sleep maintenance difficulties with no evidence of next-day residual effects.
Support (optional): Supported by sanofi-aventis.

0123

POST SURGERY PATIENT CONTROLLED ANALGESIA IN SMOKERS AND NON SMOKERS

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Introduction: Patient controlled analgesia (PCA) use in women after post cesarean surgery was higher in smokers compared to non-smokers. In joint-replacement patients PCA use was inversely related to pre-surgery sleep. This study assessed sleep and PCA use in smokers vs non-smokers undergoing joint replacement surgery.
Methods: Thirty three joint-replacement patients, 40-84 yrs old, (11 smokers, 2M, 9F; 22 non-smokers 8M, 14F), volunteered. They completed a questionnaire that included questions about sleep, nicotine use, other drug use, and co morbid disorders. Smokers reported using 3-30 cigarettes/day. Nicotine use was discontinued on entering the hospital the day of surgery. After surgery and anesthesia recovery, each received pain medication with a PCA device that limited doses of morphine to 1mg every 10 min. PCA number of injections and denials (requests during 10 min lockouts), was recorded for 24 hrs post-surgery.
Results: The 24-hr average number of denials ($p<.002$) and injections ($p<.008$) was greater in smokers than non-smokers (62 vs14 and 46 vs 27). By hour, smokers had more denials ($p<.007$) and more injections ($p<.014$) in the first 6 hrs, while not differing in the last 18 hours. Plots of denials and injections as a function of time-of-day revealed a spike in denials ($p<.001$) in smokers vs non-smokers that was coincident with their self-reported time of arising. Pre-surgery sleep and drug use reports did not differ between groups.
Conclusion: These data show a history of smoking and acute abstinence over the 24-hr surgery and recovery period is associated with increased

analgesia seeking (morphine denials and injections) behavior. Hourly and time-of-day patterns of analgesia seeking suggest that both pharmacologic (hrs of abstinence) and behavioral factors (smoking at time of arising) are mediators of analgesia seeking in smokers.
Support (optional): The Fund for Henry Ford Hospital, B10914 awarded to Dr Roehrs

0124

RAPID ONSET OF ACTION AND LONG-TERM EFFICACY OF EPLIVANSERIN, A NOVEL SLEEP AGENT, IN PATIENTS WITH CHRONIC INSOMNIA CHARACTERIZED BY SLEEP MAINTENANCE DIFFICULTIES

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Introduction: Eplivanserin, a novel non-sedative sleep agent, is being developed at a 5 mg/dose for chronic insomnia characterized by nocturnal awakenings. Eplivanserin is an Antagonist of Serotonin Two A Receptors (ASTAR) that, unlike benzodiazepines, has no affinity for GABA receptors.
Methods: In two phase III, double-blind, randomized, placebo-controlled, parallel-group studies, 2107 patients ≥18 years of age with chronic insomnia and sleep maintenance difficulties received eplivanserin 5 mg (N=617/962, Study 1; N=850/1145, Study 2) or placebo (N=345, Study 1; N=295, Study 2) orally for 12 weeks. Patient-reported wake-time after sleep onset (pr-WASO) was assessed daily. Study 2 had an additional 40-week open-label (OL) extension (total 52 weeks), available to all patients who completed the double-blind period, during which all patients received eplivanserin 5 mg. A total of 911 patients were treated in the OL extension (673 from the eplivanserin group and 238 from the placebo group).
Results: Efficacy analyses revealed that in both studies, eplivanserin immediately decreased pr-WASO from day 1, more than placebo (Study 1, LS Mean Difference =-13:54 min:sec [95% CI: -20:29 to -7:19]; Study 2, LS Mean Difference =-14:42 min:sec [95% CI: -22:10 to -7:14]), and up to the end of the 12-week double-blind period (Study 1, LS Mean Difference =-11:32 min:sec, $p<0.0001$; Study 2, LS Mean Difference =-13:31 min:sec, $p<0.0001$). During the open-label period of Study 2, the decrease in pr-WASO persisted through Week 52.
Conclusion: The efficacy of eplivanserin on sleep maintenance occurs after the first night of administration and persists up to 12 months of treatment with no tolerance phenomenon.
Support (optional): Supported by sanofi-aventis.

0125

PRECLINICAL PHARMACOLOGY OF SB-649868: A NOVEL OREXIN OX_1/OX_2 RECEPTOR ANTAGONIST POSSESSING POTENT HYPNOTIC ACTIVITY IN RODENTS AND PRIMATES

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Introduction: Orexins (OX) are hypothalamic neuropeptides that appear to have an important role in sleep/wake control and other physiologic functions. SB-649868 is a novel OX receptor antagonist that demonstrates high functional affinity for recombinantly expressed OX_1 and OX_2 receptors (fpKi rat and human OX_1/OX_2=9.8/9.3), and is 1000-fold selective over other targets. The compound has been characterised as a potential novel hypnotic agent in preclinical sleep models using telemetric recording of EEG and EMG.
Methods: SB-649868 was tested in the following preclinical models over a dose range of 1-30mg/kg: orexin-A induced grooming (rat), circadian time (CT) 18 sleep model (rat), rotarod (rat), passive avoidance (rat) and acoustically-disturbed sleep in a non-human primate model (marmoset).
Results: SB-649868 (3 and 10mg/kg p.o.) inhibited i.c.v. orexin-A induced grooming in the rat. In the CT 18 sleep model, SB-649868 (3, 10 and 30mg/kg p.o.) potently reduced sleep latency and increased total sleep time after both acute and chronic (14 days) administration. In the marmoset acoustically-disturbed sleep model, SB-649868 (1, 3, and 10 mg/kg p.o.) decreased arousal and increased deep sleep producing similar hypnotic efficacy to zolpidem but did not suppress duration of REM sleep. Unlike benzodiazepine receptor modulators, SB-649868 did not cause motor incoordination (alone or combined with ethanol) in the rat rotarod model and failed to impair acquisition in the passive avoidance paradigm.
Conclusion: These studies demonstrate that SB-649868 is a centrally active OX_1/OX_2 receptor antagonist which possesses potent hypnotic activity in the rodent and non-human primate. The pharmacological profile of SB-649868 suggests that this agent may be differentiated from hypnotic agents acting via the benzodiazepine receptor in terms of both hypnotic profile and side effect potential. Clinical findings to date with SB-649868 have been encouraging and appear to validate the preclinical models which have driven the early development of this orexin OX_1/OX_2 antagonist.

0126

EFFECTS OF AMITRIPTYLINE ON AHI

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Introduction: Amitriptyline is a tricyclic antidepressant used in the pharmacologic management of depressive illness. Although not a labeled indication, amitriptyline is widely used as an atypical treatment of insomnia and mild sleep apnea. This is significant due to the fact that the comorbidity between insomnia and sleep related breathing disorders is substantial. Amitriptyline is believed to help mild sleep apnea by improving pharyngeal tone. This study will determine the effect of amitriptyline on the AHI.
Methods: A sample of 29 patients diagnosed with insomnia that attended nPSG without amitriptyline as well as nPSG with amitriptyline were selected. The sample consisted of both males and females between the ages of 18-65. AHI was independently calculated for both diagnostic and therapeutic studies and statistical analysis performed.
Results: The average difference between the diagnostic and therapeutic AHI is an increase of 4.97. For n=29 a one-tailed test was used where Ho: amitriptyline has no effect on AHI and H1: amitriptyline increases AHI. The $\mu = np = (29)(0.7) = 20.3$, $\sigma = 2.46$, $z = 5-\mu/\sigma = -6.199$, $\alpha = 0.9998$. Therefore 99.9 % of all sample size 29 would lead to rejection of Ho.
Conclusion: Based on the above results it would appear that taking amitriptyline increases the AHI. We acknowledge that the sample size is small and parameters such as increased sleep efficiency were not considered. The practice of prescribing amitriptyline in insomnia patients with mild AHI needs further examination.

0127

MELATONIN AGONIST TASIMELTEON IMPROVES SLEEP IN PRIMARY INSOMNIA CHARACTERIZED BY DIFFICULTY FALLING ASLEEP

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Introduction: Tasimelteon is a dual MT1/MT2 receptor melatonin agonist. Tasimelteon has previously been shown to improve sleep onset and sleep maintenance in two transient insomnia studies. In this Phase III trial, the efficacy and safety of tasimelteon was studied in primary insomnia characterized by difficulty falling asleep.

Methods: A randomized, double-blind, placebo-controlled, multi-center study investigated 20 mg, 50 mg, or placebo in primary insomnia in 322 patients over a 5-week double-blind treatment period using polysomnography (PSG) measures of sleep. Subjects underwent PSGs on Nights 1, 8, 22 and 29. Entry criteria emphasized enrollment of primary insomnia patients with difficulty falling asleep. Subjective sleep latency was ≥45 minutes based on sleep history and sleep diary and on two consecutive screening PSG nights, patients had a mean latency to persistent sleep (LPS) of ≥30 minutes with no night having an LPS less than 20 minutes.

Results: On the primary end point, the mean improvement in LPS from baseline to the average of Nights 1 and 8 was 44.9 minutes (20 mg) and 46.3 minutes (50 mg) versus 28.2 minutes (placebo) ($p<0.001$). Improvements in LPS persisted through the last time point (Nights 22 and 29, $p<0.01$). Tasimelteon did not cause next-day cognitive or mood changes and did not cause rebound effects after discontinuation.

Conclusion: Tasimelteon improved time to sleep onset (LPS) beginning on the first night of treatment and this effect continued for the duration of the study. Tasimelteon was well-tolerated with no next-day residual effects observed.

0128

A NEW 0.5 MG MELATONIN PHASE RESPONSE CURVE IN HUMANS

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Introduction: We published a phase response curve (PRC) to 3.0mg melatonin, a dose often used for its soporific effects (J Physiol 2008). Here we present a new PRC to 0.5mg melatonin, a lower dose often used for phase shifting the circadian clock.
Methods: So far 18 young healthy subjects participated in two 5 day laboratory sessions. Each session began with a phase assessment, to measure the dim light melatonin onset (DLMO), followed by 3 days in an ultradian light-dark cycle (LD 2.5:1.5), and then a final phase assessment. Each subject received one pill per day at the same clock time each day, during the 3 ultradian days (melatonin or placebo, double blind, counterbalanced). Each individual's phase shift to melatonin was corrected by subtracting their phase shift to placebo (a free-run).
Results: The resulting PRC illustrates how 0.5mg melatonin can phase shift the circadian clock in the absence of conflicting light exposure. The results suggest that if 0.5mg melatonin is taken about 3 hours before the DLMO (about 5.5 hours before habitual bedtime) for 3 days, the circadian clock will advance by about 1.3 hours. Similarly, 0.5mg melatonin taken about 12 hours after the DLMO (shortly after habitual waking) for 3 days, can phase delay the clock by about 1.5 hours. These numbers may change slightly as more subjects complete the study. When 0.5mg melatonin is taken at usual bedtime, minimal phase shifts result.
Conclusion: This PRC demonstrates (1) the best times to administer a low dose of melatonin to achieve desired phase shifts, (2) that even a low dose of melatonin can phase delay as well as phase advance, (3) that using a low dose of melatonin as a sleep aid at night has minimal phase shifting effects, (4) that PRCs to different doses of melatonin have different shapes.
Support (optional): NIH grant R01 HL086934.

0129

A COMPROMISE CIRCADIAN PHASE POSITION FOR PERMANENT NIGHT WORK IMPROVES NIGHT SHIFT ALERTNESS AND IS COMPATIBLE WITH LATE NIGHTTIME SLEEP ON DAYS OFF

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Introduction: This is the final study in a series designed to produce and maintain a compromise phase position for permanent night work, in which the sleepiest circadian time is delayed out of the night work period and into the first half of daytime sleep, improving night shift alertness and subsequent daytime sleep, but not precluding late nighttime sleep on days off.
Methods: Subjects underwent 3 night shifts (23:00-7:00), two days off, 5 more night shifts, and two more days off. During night shifts, an experimental group (n=9) received four 15-minute pulses from light boxes (~ 4,100 lux, ~1,200 μW), interspersed by 45 minutes of room light. The first pulse began at 00:45 and the last ended at 4:00. Subjects wore dark sunglasses (~15% transmission) when outside. Home sleep episodes in darkened bedrooms occurred from 8:30-15:30 after night shifts, 8:30-13:30 after the last night shift in a block, and 3:00-12:00 on days off. Subjects went outside for ≥15 minutes after awakening to receive a "light brake" to keep them from delaying past the compromise phase position, defined as a dim light melatonin onset (DLMO) of 3:00. A control group (n=10) remained in room light during night shifts, wore lighter sunglasses (~36% transmission), and had unrestricted sleep and outside light exposure.
Results: The final DLMO for the experimental group was close to the target compromise phase position, and significantly later than the control group (3:22 ± 2.0 vs. 23:24 ± 3.8 h, $p < 0.001$). Subjects who phase delayed close to the target phase performed better during night shifts.
Conclusion: A compromise circadian phase position for permanent night shift work improved performance during night shifts, allowed sufficient sleep during the daytime after night shifts and during the late nighttime on days off, and can be produced by feasible interventions.
Support (optional): R01 OH003954.

0130

DIURNAL VARIABILITY OF C-REACTIVE PROTEIN (CRP) IN OBSTRUCTIVE SLEEP APNEA (OSA)

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Introduction: Inflammation is a hallmark of the pathophysiology of OSA and represents a pathway linking OSA to increased cardiovascular morbidity. CRP is an acute phase response protein implicated in broad range of cardiovascular diseases. This study examined the diurnal variability of CRP in OSA.
Methods: Forty-four individuals with untreated OSA (mean apnea/hypopnea index = 37.5, SD ± 28) and 23 healthy adults with no OSA were studied at the UCSD Gillin Laboratory of Sleep and Chronobiology. Over a 24-hour period, blood was collected every two hours and CRP levels were determined. Participants had their sleep monitored with polysomnography to verify OSA diagnosis. The time-course of CRP levels over the 24-hour period was analyzed using a linear mixed-effects model fitted with restricted maximum likelihood methods.
Results: There were significant main effects for body mass index (BMI) (with higher BMI being associated with higher CRP levels; regression coefficient = 0.094, $p < 0.001$) and gender (with CRP levels being higher in women; regression coefficient = 0.667, $p = 0.04$) for the 24-hour period. Adjusting for age and gender, a group by time interaction (regression coefficient = 0.081, $p = 0.01$) showed that patients with apnea had higher CRP levels during the daytime (8:00am - 8:00pm) versus the nighttime (10:00pm until 6:00am) ($p < 0.001$). Non-apneics showed no change in CRP levels during the 24 hours.
Conclusion: Studies in OSA show increased risk for cardiovascular events in the daytime and this risk is attributed to several mechanisms, including local and systemic inflammation. Our findings indicate that OSA patients have disproportionately elevated CRP levels in the day versus the nighttime, possibly as a result of carryover effects of nighttime arousal into the daytime. Our findings suggest that fine-grained chronobiological analysis with frequent blood sampling is invaluable to better understand inflammatory variables in OSA.
Support (optional): Supported by NIH grants HL073355, HL44915, HL36005, and CA23100

0131

EARLY MORNING NADIR IN ENDOTHELIAL FUNCTION

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Introduction: There is a growing awareness of the importance of the endothelium in regulating vascular tone via the production of the potent vasodilator nitric oxide. Endothelial dysfunction is a reliable biomarker of future cardiovascular events and poor clinical outcomes. Previous studies demonstrated circadian rhythm in vascular tone with a nadir at the early morning hours. The purpose of the present study was to investigate the 24-h pattern of endothelial function under different sleep-wake conditions.

Methods: Ten subjects, 5 men (age:22-29 yrs; BMI: 20-27.7 Kg/m2) and 5 women (age: 21-24 yrs; BMI: 19-22.2 Kg/m2) participated. All were healthy, non smokers and without complaints about sleep. Each subject was tested during three 24-h periods, spaced one week apart, under the following conditions: sleep deprivation, nocturnal (23:00-0600) and diurnal (0700-14:00) sleep periods. Endothelial function was measured every 4 hours during the waking hours by the peripheral arterial tonometry (PAT) technique. Subjects consumed standardized liquid food at predetermined times. The device consists of two finger-mounted probes that measure the pulse volume amplitude in the test and control fingers. The test comprises: 5-min baseline, 5-min occlusion, and 5-min post-occlusion recording. The reactive hyperemia PAT (RH-PAT) index is the ratio between the average amplitude of the PAT signal after occlusion and the average amplitude before occlusion, normalized to the concurrent signal from the non-occluded hand.
Results: The results demonstrated a distinct 24-h pattern of the RH-PAT index with a nadir at 0200-0600 and maximal values during the afternoon hours. The nocturnal nadir in endothelial function was observed in both the sleep deprivation and diurnal sleep conditions. In the nocturnal sleep condition the nadir occured just after waking up from sleep at 0700. Women showed significantly lower RH-PAT index than men but had a similar 24-h pattern with an early morning nadir.
Conclusion: The present results confirmed the existence of circadian rhythm in endothelial cell function with blunting of endothelium dependent vasodilation in the early morning hours. These results may explain the early morning peak in the frequency of cardiovascular events.

0132

THE NON-24 HOUR PERIOD OF THE REST/ACTIVITY CYCLE IS IDENTICAL TO THAT OF THE FREE-RUNNING MELATONIN RHYTHM IN BLIND AND SIGHTED INDIVIDUALS

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Introduction: The majority of blind individuals without light perception have free-running circadian melatonin rhythms. Such blind free-runners (BFRs) often attempt to maintain a 24-hour sleep/wake schedule and consequently suffer from recurrent sleep disruption and daytime somnolence. In contrast, sighted individuals with free-running disorder (FRD) demonstrate pronounced free-running sleep/wake schedules. We compared the free-running melatonin period to the period of the rest/activity cycle in BFRs and one sighted individual with FRD.
Methods: Subjects (6 F, 7 M; 8-78 y.o.) were totally blind individuals in good health and a 39 y.o. sighted woman with FRD. Subjects wore an actiwatch (AW-64, Minimitter) for 117-364 days while maintaining a sleep/wake schedule of their choosing. Plasma or saliva samples were collected every 1-2 h for 14-25 h at the Oregon Health & Science University Clinical and Translational Research Center (CTRC) every 6-44 days. Melatonin concentrations were measured by radioimmunoassay (ALPCO) and the plasma and salivary melatonin onsets (MOs) were assessed using a 2 or 0.7 pg/ml threshold, respectively. Melatonin period was calculated by linear regression through a series of MOs. Rest/activity period was calculated using chi-squared periodogram of the actigraphy data (ClockLab 2.6, Actimetrics).
Results: Twelve of the 13 BFRs had a significant ($p < 0.001$) non-24-hour rest/activity period. There was a robust correlation between the non-24-hour rest/activity period and the melatonin period ($r = 0.956$, $p < 0.0001$) with a slope near unity (0.996). The average (± SD) non-24-hour rest/activity period and the average melatonin period were virtually identical (24.30 ± 0.32 versus 24.34 ± 0.33, $p = 0.78$, respectively). In the BFRs, the amplitude of the 24-hour component of the rest/activity cycle was greater than that of the non-24-hour component in all cases (average ± SD of 18,401 ± 7,577 versus 5,452 ± 3,228, $p < 0.001$, respectively). In the sighted subject, the non-24-hour rest/activity period was the same as the melatonin period (both 24.67 h) and the amplitude of the 24-hour component of the rest/activity cycle was greater than that of the 24.67 h component (12,360 versus 5,457, respectively).
Conclusion: The non-24-hour component of the rest/activity rhythm in both blind and sighted free-running individuals precisely reflects the free-running endogenous circadian pacemaker. This may have implications for the diagnosis and treatment of both sighted and blind individuals with FRD.
Support (optional): Sleep Research Society Foundation Gillin Award, K23RR017636, and NARSAD Young Investigator Award (JSE); R01 EY018312-09A1, R01 HD42125, and R01 AG21826 (AJL); and MO1 RR000334 and UL1 RR024120.

0133

THE EFFECT OF DIURNAL PREFERENCE ON SUBJECTIVE ALERTNESS AND PERFORMANCE DURING EXTENDED WAKEFULNESS

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Introduction: Previous reports in morning (M) and evening (E) types identified using the Horne and Östberg Morningness-Eveningness Questionnaire (MEQ) have found differences in circadian rhythms and in sleep homeostasis between the types. In the present study, we aim to compare alertness and performance between M and E types during extended wakefulness.
Methods: Twenty-five healthy adults, 17 M types (6 females; 23.76 ± 3.35 years) and 8 E types (2 females; 22.75 ± 3.24 years), were selected based on their MEQ score. They completed an inpatient study consisting of 3 baseline days followed by a 40-h extended wake episode in constant conditions. The Karolinska Sleepiness Scale (KSS) was given every 30 minutes and the Psychomotor Vigilance Task (PVT) was given every 2 h throughout the study. Data were binned in 1-h (KSS) or 2-h bins (PVT), and a mixed model analysis with repeated measures (SAS 9.1) was used to compare the self-rated sleepiness and performance between the groups.
Results: Results from the KSS showed that both M and E types reported growing progressively sleepier across the 40-h wake episode, and that overall E types rated themselves as sleepier than M types. PVT results showed a slower reaction time (RT) and more lapses in M types compared to E types. We next divided the 40-h extended wake into 2 parts, the first 16 h equivalent to a normal day and hours 17-40, representing the extended wake/sleep deprivation. Both groups were sleepier during the extended wake portion than during the first 16-h segment, but there was greater difference between groups in alertness during the first 16 h, with E types reporting greater sleepiness. In contrast, the greatest performance difference between two groups was during the extended wake segment, with the E types showing faster RTs and fewer lapses.
Conclusion: Although E types reported themselves to be sleepier as a group than M types, they showed faster RTs and fewer lapses, particularly during extended wakefulness. We plan to study additional E types to determine whether there are differences between these types under standard daytime conditions or under conditions of sleep deprivation, and to extend our analysis to data collected across different circadian phases.
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0134

CIRCADIAN PHASE IN PATIENTS WITH SHIFT-WORK DISORDER (SWD): INFLUENCE ON NIGHTIME SLEEPINESS, PERFORMANCE AND DAYTIME SLEEP

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Introduction: Shift Work Disorder (SWD) is characterized by complaints of insomnia during displaced sleep or excessive sleepiness during work or commuting hours that occur in relation to work hours scheduled during the usual sleep episode (ICSD-2). We evaluated the influence of circadian phase on daytime sleep and nighttime sleepiness in participants with SWD.
Methods: Participants with SWD (125 males, 79 females), aged 18-60, were assessed in the laboratory after three consecutive night shifts. Timing of salivary dim light melatonin onset (DLMOn) or offset (DLMOff) was assessed from 2000-0800h to estimate circadian phase. Severity of sleepiness during the night shift/commute to and from work was assessed with clinical global impression of severity of disease scale (CGI-S). MSLT and PVT were assessed every 2h and KSS every 1h across the simulated nightshift; daytime PSG was performed from 1000-1800h.
Results: Of 204 participants, 45% (n=91) showed DLMOn indicating minimal circadian adaptation (MCA) to the night shift. Another 14% (n=29) showed DLMOff indicating a circadian phase advance (CPA). Nocturnal melatonin was absent (ANM) in 41% (n=84). Average nighttime MSLT scores were below 5 min and differences due to circadian phase were small with ANM better than MCA at 0800h ($P<0.05$; MSLT 2.0+0.3 min versus 1.2+0.2 min;+SEM). Compared to MCA, CPA showed less sleepiness (KSS, $P<0.05$) and better performance (PVT lapses, $P<0.05$) the latter part of the night; KSS was also lower in CPA versus ANM and ANM versus MCA ($P<0.05$). Average daytime sleep efficiency (SE) was <76% with worse SE in CPA versus MCA and ANM ($P<0.05$). More severely/extremely ill subjects comprised MCA versus CPA (CGI-S, $P<.05$).
Conclusion: MSLT sleepiness during the night shift and daytime insomnia were severe regardless of circadian phase relative to the work schedule. Differences in circadian phase among participants with SWD had influence on sleepiness, performance, and daytime sleep.
Support (optional): Cephalon, Inc.

0135

ATTENUATING NOCTURNAL LIGHT INDUCED DISRUPTION IN ENDOCRINE, GENETIC AND BEHAVIORAL CIRCADIAN RHYTHM PHASE MARKERS BY FILTERING SHORT WAVELENGTHS

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Introduction: Numerous physiological processes follow a circadian rhythm synchronized to the geo-physical light dark cycle. Nocturnal shift work alters the timing of light exposure and induces circadian rhythm disruption. Interestingly, recent studies suggest that short optical wavelengths (440-480 nm) have a pronounced disruptive effect on circadian rhythms.
Methods: We used a single blind, crossover, placebo controlled study to test if filtering optical wavelengths below 480 nm would be effective in preventing circadian rhythm disruption and resulting neuropsychometric changes reported in shift workers. Healthy volunteers (n=13) were kept in darkness (control), or subjected to simulated shift work in bright light (780 Lux) or filtered bright light (780 Lux) between 2000 h and 0800 h. Light was filtered using identical standard spectacle frames fitted with optical filter lenses that blocked wavelengths below 480 nm or similar colored lenses (placebo). Saliva samples were collected hourly and RNA from buccal swabs was collected every 4 h. Every 2 h during light exposure, subjects completed validated testing of alertness, sleepiness, and fatigue, and vigilance was tested every 4h. Melatonin and free cortisol in saliva and gene expression was measured by ELISA and real time RT-PCR, respectively.
Results: Exposure to light at night suppressed the nocturnal rise in melatonin, increased cortisol secretion, and disrupted Per2 and Bmal1 clock gene expression. The disruptive effects of nocturnal light exposure on endocrine and gene expression rhythms were prevented by filtering wavelengths below 480 nm but not by the placebo lenses. Furthermore, subjective alertness, vigilance and mood were improved between 0400 h and 0800 h, without adversely affecting sleepiness and fatigue in individuals with normalized circadian rhythms.
Conclusion: The myriad of health disorders associated with rotating shift work can be attributed to recurrent disruption of endogenous circadian rhythms. These findings may have important implications for the pathogenesis of diseases affecting shift workers.
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0136

INCIDENT CARDIOVASCULAR DISEASE AND REST/ACTIVITY RHYTHM DISTURBANCES IN OLDER MEN: MROS SLEEP

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Introduction: Disruptions in circadian rhythms, especially among night-shift workers, have been associated with increased risk of cardiovascular disease (CVD). Whether this association exists in a general population of older adults is uncertain.
Methods: To test the hypothesis that disturbed rest/activity rhythms are associated with increased risk of incident CVD, we measured 5 days (range 3-12.4) of activity patterns using wrist actigraphy in a cohort of 2986 community-dwelling men aged 67 and older. Parameters included: acrophase (time of peak activity), amplitude (peak-to-nadir height), mesor (mean activity), F-value (rhythm robustness), minimum (lowest activity value), alpha (peak-to-trough width ratio) and beta (steepness of curve) and were expressed as quartiles. The primary outcome was a composite of incident CVD events (coronary heart disease, cerebrovascular events and peripheral arterial disease [PAD]) verified by medical records. All analyses were adjusted for age.

Results: There were 505 composite CVD events, 182 (36%) in men without a history of CVD. Quartiles of rhythm robustness were associated with increased risk of incident CVD (HR=1.34,95%CI 1.04-1.71 for quartile 1 vs. quartile 4), but there was no association after adjusting for history of CVD (p-trend=0.34). These results were driven by an association between quartiles of rhythm robustness and incident PAD, with men in the lowest quartile of F-value at a 2.2-fold increased risk (HR=2.21,95%CI 1.20-4.09), compared with the highest quartile. After further adjustment for race, education, multiple indicators of health status and history of CVD events, this association remained statistically significant (HR=1.91,95%CI 1.01-3.62). There were no associations between quartiles of rhythm parameters and incident coronary heart disease or cerebrovascular disease. Analyses excluding men with prior history of CVD events were generally consistent.
Conclusion: Among older men, rest/activity rhythms were not strongly associated with overall CVD events. Only reduced rhythm robustness was moderately associated with increased risk of PAD.
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0137

THE MELANOPSIN-MEDIATED DIRECT EFFECTS OF LIGHT ON SLEEP AND THE EEG INTERACT WITH THE CIRCADIAN AND HOMEOSTATIC DRIVE

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Introduction: Light influences sleep and alertness either indirectly through a well-characterized circadian pathway or directly through yet poorly understood mechanisms. Melanopsin (Opn4) is a retinal photopigment crucial for conveying non-visual light information to the brain.
Methods: Under various light-dark regimens including 12h:12h light-dark (LD), single 1h L- or D-pulses during the 12h D- or 12h L-period, respectively, and one day under short LD1h:1h cycles), we analyzed sleep-wake time, the EEG, and light-induced c-FOS immunoreactivity in wild type (n= 10) and melanopsin deficient (Opn4-/-) mice (n=10).
Results: In contrast to wild type, light failed to induce sleep in Opn4-/- mice and the D-pulse-induced increase in EEG theta and gamma activity (EEG correlates of alertness and cognition) was delayed. Analysis of the LD1h:1h cycle revealed that only in Opn4-/- mice the light and dark effects greatly depended on circadian time. Light induced c-Fos immunoreactivity in galanin positive sleep-active neurons of the VLPO and in the retino-recipient part of the SCN was importantly reduced in Opn4-/- mice. In addition to these acute light effects, Opn4-/- mice slept 1h less during the 12h L-phase. Despite this reduction in sleep time, EEG delta activity, a marker of sleep need, was decreased in Opn4-/- mice for most of the (subjective) D-period and the level of delta power reached after 6h sleep deprivation was significantly lower in Opn4-/- mice indicating that lack of melanopsin alters sleep homeostasis.
Conclusion: Our study demonstrates that melanopsin mediates the direct effects of light on sleep and alertness, more likely through pathways including the VLPO and the SCN. The findings that melanopsin mediated direct effects of light are modulated in a circadian fashion and that melanopsin affects the sleep homeostat in a light independent fashion call for a re-evaluation of the role of light on human behavior and performance.
Support (optional): National Institutes of Health (grant MH67752 to PF), American Sleep Medicine Foundation (grant 31CA-05 to PB), Howard Hughes Medical Institute (URO grant to support JWT)

0138

EFFECT OF CIRCADIAN SYSTEM AND BEHAVIORAL STRESSORS ON PLATELET ACTIVITY AND REACTIVITY: IMPLICATIONS FOR THE MORNING PEAK IN CARDIOVASCULAR INCIDENTS

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Introduction: The risk of adverse cardiovascular events has a day/night pattern peaking in the morning (~09:00), possibly related to increased platelet activation and aggregability at that time. We tested the effects on platelet function of the circadian system, potential behavioral triggers, and their interaction.
Methods: 12 healthy adults (6 female) underwent a 13-day Forced Desynchrony protocol, wherein subjects were scheduled to 12 recurring 20-hour 'days' in dim light. On each 'day' subjects underwent a test battery consisting of 10-min mental stress (serial addition), 15-min postural stress (60° head-up tilt) and 15-min physical exertion (cycling 60% HRmax), preceded and followed by 20-min rest periods. Body temperature was used to assess circadian phase (fitted minimum assigned 0°). Data were binned in 60°-bins and analyzed with Mixed Model ANOVA.
Results: Across the whole test battery, there were significant circadian rhythms in platelet surface activated glycoprotein (GP) IIb-IIIa (monoclonal antibody PAC1 binding; peak 60°; equivalent to ~9 AM in these subjects; P=0.03), GPIb (60°; ~09:00; P=0.007), whole blood aggregability (180°; ~17:00; P=0.03) and platelet count (240°; ~21:00; P=0.004), but not in platelet surface P-selectin (reflecting platelet degranulation). Remarkably, we found no effect of any behavioral stressor on activated GPIIb-IIIa or GPIb and only a change (increase) in P-selectin with mental stress. There were significant increases in whole blood platelet aggregability with each stressor and increases in platelet count with postural stress and exercise (all P<0.001). There was no statistical interaction between circadian and behavioral effects.
Conclusion: These data demonstrate significant effects of the circadian system on hemostatic function in healthy subjects. Most importantly, platelet surface activated GPIIb-IIIa, the final common pathway of platelet aggregation, showed no effect of any behavioral stressor, but a significant circadian rhythm with a peak at the time of habitual awakening and of increased risk for cardiovascular incidents.
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0139

CIRCADIAN RHYTHMS, PHYSICAL ACTIVITY AND THEIR INFLUENCE ON SLEEP-WAKE REGULATION DURING AN ANTARCTIC SUMMER EXPEDITION

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Introduction: The present investigation was conducted during two Antarctic summer expeditions, the BELARE (Belgian Antarctic Research Expedition) campaigns 2007-2008 and 2008-2009. First, this experiment aimed at investigating how well the subjective complaints of par-

ticipants were related to objective measures of sleep quality. Second, we hypothesized that participants with a more intense physical activity would increase their sleep pressure, and therefore suffer less from the possible circadian disruption due to the constant daylight conditions.
Methods: 8 subjects were investigated in the first expedition. Actigraphy data were collected for 48 hrs every ten days. Sleep efficiency (sleep time/lying down time) as well as sleep fractionation were computed, and related to active energy expenditure. 15 subjects participated during the second campaign. Data were collected every 2 weeks for each subject. These included 48 hrs actigraphy, a sleep diary, one night polysomnography, morning and evening Profile of Mood States and Karolinska Sleepiness Scale and morning Psychomotor Vigilance Test. Morning and evening saliva samples were taken to determine melatonin levels. Circadian rhythms were determined with 2hrs-spaced cortisol sampling.
Results: First year data showed poor sleep efficiency and high sleep fractionation, in concordance with participants' subjective evaluations. Furthermore, there was a strong correlation between sleep efficiency and active energy expenditure (Pearson's r = 0,63; p = 0,015), as well as a strong relationship between active energy expenditure and sleep fractionation. Second year data collection is still ongoing until February 2009.
Conclusion: Results from the first campaign confirmed both our hypotheses, namely the lower sleep quality (lower efficiency and higher fractionation) during the expedition and the relationship between sleep quality and active energy expenditure. Data from the second campaign will confirm whether a decreased melatonin secretion is a causal mechanism of the impaired sleep quality, and how strong is the impact upon mood and performance.

0140

BRIGHT BLUE-ENRICHED AND WHITE LIGHTS PRODUCE SIMILAR MAGNITUDE PHASE DELAYS OF THE HUMAN CIRCADIAN CLOCK

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Introduction: Laboratory studies have shown that the circadian system is most sensitive to short wavelength (blue) light. We previously reported no difference in the magnitude of phase advances produced by bright white versus bright blue-enriched light in a practical protocol that could be used in the real world. Since the spectral sensitivity of the circadian system may vary with a circadian rhythm, we tested whether the results of our phase advancing study hold true for phase delays.
Methods: In a within-subjects counterbalanced design, 13 healthy subjects received a 2-hour phase delaying light pulse combined with a gradually delaying sleep/dark schedule on each of 4 consecutive treatment days. The light pulse began 3 hours after the dim light melatonin onset (DLMO) on the first treatment day. An 8 hour sleep episode began at the end of the light pulse. The light pulse and sleep schedule were delayed 2 hours on each subsequent treatment day. The bright light was produced by single fluorescent light boxes (~56 x 56cm) placed on a desk ~40cm from subjects' eyes. The blue-enriched (17,000K, ~ 4000 lux) and white (4,100K, ~ 5000 lux) light boxes emitted the same number of total photons (4.2 x 10^{15} photons/cm^2/sec). The blue-enriched light box emitted three times the number of photons in the blue range, between 400-490nm, than did the white light box (19.0 versus 6.4 x 10^{14} photons/cm^2/sec).
Results: Phase delays of the DLMO in the blue-enriched and white conditions were not significantly different (-4.45 ± 2.02 versus -4.48 ± 1.97 hours, respectively).
Conclusion: At commonly used light levels bright blue-enriched polychromatic light is no more effective than standard bright white light for phase delaying the circadian clock. Standard bright white light treatment may contain a saturating level of short wavelength light.
Support (optional): R01 NR007677.

0141

NEUROBEHAVIORAL PERFORMANCE IN YOUNG ADULTS LIVING ON A 28-H DAY FOR SIX WEEKS

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Introduction: Performance on many cognitive tasks varies with time awake and with circadian phase, and the forced desynchrony (FD) protocol can be used to separate these influences on performance. Some performance tasks show practice effects, while the Psychomotor Vigilance Task (PVT) has been reported not to show such effects. We aimed to compare performance on the PVT and on an addition test (ADD) across a six-week FD study, to determine whether practice effects were present, and to analyze the circadian and wake-dependent modulation of the two measures.
Methods: Data from nine healthy adults (7 men, 2 women; mean age: 24.4 yrs) who took part in a six-week 28-h FD study were included in our analysis. For two baseline days and across six weeks of FD, we gave a test battery (ADD, PVT, PEERS: Performance Evaluation and Effort Rating Scale) every two hours. Both the baseline and FD data were analyzed using mixed model analyses testing for the main effects of time awake, circadian phase and FD week, and their interactions.
Results: There were significant main effects of time awake, circadian phase and FD week in all performance measures. Across the six-week FD there was a significant ($p<0.0001$) improvement in ADD performance (more correct calculations completed), while PVT performance (mean RT, fastest 10% RT, lapses) significantly ($p<0.0001$) declined week-by-week. Subjective ratings of PVT performance improved across the study ($p<0.0001$), but the subjects' rating of whether they could have performed better with greater effort did not change across the study ($p>0.05$).
Conclusion: The decline in PVT performance suggests a cumulative effect of sleep loss across the six-week study. Subjects did not accurately detect their declining PVT performance, and a motivational factor could not explain this decline.
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0142

THE USE OF RAMELTEON TO ADVANCE SLEEP TIMING AND MELATONIN PHASE IN DELAYED SLEEP PHASE DISORDER

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Introduction: Ramelteon, a melatonin receptor agonist, has demonstrated both phase-shifting and sleep-promoting effects in previous clinical trials. The goal of the current study was to evaluate the ability of ramelteon to advance sleep timing and melatonin phase in individuals with delayed sleep phase disorder (DSPD).
Methods: Adults (>=18 years) meeting diagnostic criteria for DSPD were administered ramelteon 1 mg, 4 mg, 8 mg, or placebo 30 minutes before desired sleep time nightly for 2 weeks, followed by a 1-week placebo run-out period. Sleep was measured using polysomnography during an initial screening period and on Nights 6, 7, 13, and 14 of the treatment period. The primary endpoint was mean latency to persistent sleep (LPS) for Nights 6 and 7. Complete 24-hour endogenous melatonin profiles were collected during the screening period and after the 2-week treatment period to compare dim-light melatonin onset time (DLMO) with placebo before and after ramelteon treatment.

Results: A total of 132 individuals were included in the study (32 placebo, 32 ramelteon 1 mg, 33 ramelteon 4 mg, 35 ramelteon 8 mg). Mean LPS was reduced at Nights 6 and 7 with ramelteon 4 mg compared with placebo; however, the results did not reach statistical significance (P=0.084). Ramelteon 1 mg and 8 mg did not significantly reduce mean LPS. DLMO was advanced 1 hour 50 min with ramelteon 1 mg compared with placebo. No significant phase shifts were detected with ramelteon 4 mg or 8 mg.
Conclusion: Ramelteon 1 mg significantly advanced the timing of the circadian rhythm of melatonin and there was a trend towards a reduction in LPS with ramelteon 4 mg in subjects with DSPD. Further studies are needed to determine the efficacy, timing, and dosage of ramelteon for the treatment of DSPD.
Support (optional): This study was supported by funding from the Takeda Pharmaceuticals Company, Ltd.

0143

POSTPARTUM SLEEP: THE IDEAL SLEEP SCHEDULE?

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Introduction: Few studies have examined postpartum mothers' 'normative' sleep patterns. Because infant sleep periods are distributed across the 24-hour day, postpartum mothers' sleep is presumed to be constrained by the infant's lack of schedule. The purpose of this study was to evaluate the preferred and actual timing of postpartum mothers' nocturnal sleep.
Methods: Two items from Horne and Ostberg's Morningness-Eveningness Scale were used to identify preferred bed ("If you were entirely free to plan your evening and had no commitments the next day, at which time would you choose to go to bed?") and rise ("If you had no commitments the next day and were entirely free to plan your own day, what time would you get up?") times. Actual sleep/wake times were determined by averaging across actigraphy recorded during postpartum weeks 9-10.
Results: The 24 participants were 30.5(+5.2) years, white (92%), married/cohabitating (96%), 50% primiparous, and breastfeeding (67%), with incomes $65,808(+4,1398). Preferred and actual bed times were positively correlated ($r=0.720;p<0.001$), as were preferred and actual wake times ($r=0.562;p<0.01$). When divided, primiparous mothers' actual and preferred sleep ($r=0.707;p=0.015$) and wake times ($r=0.684;p=0.020$) were significantly correlated. While multiperous mothers' actual and preferred sleep times were significantly correlated ($r=0.795;p=0.003$), actual and preferred wake times were not ($r=0.392;p=0.233$).
Conclusion: Our findings demonstrate that, contrary to the presumption that the timing of maternal sleep is severely impacted after childbirth, postpartum mothers' sleep/wake times remain in synch with self-reported preferred sleep/wake times. The exception is multiparous mothers' actual wake times, which may be earlier than preferred due to being awakened by older children. Though postpartum mothers' sleep is disturbed and leads to significant daytime consequences, our data suggest that the timing of sleep may be preserved.
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0144

NONPARAMETRIC MODELING OF FORCED DESYNCHRONY DATA: SUBJECT-SPECIFIC EVALUATION OF PERFORMANCE

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Introduction: We used modern statistical methods to build subject-specific models for the effects of circadian phase and homeostatic sleep drive on individual neurobehavioral performance. The model allows (1) conducting hypothesis tests on the significance of effect of circadian phase and homeostatic sleep drive effect on an individual's neurobehavioral performance, (2) assessment of the functional form of these effects and (3) testing for the presence of inter-individual differences. Our objective was to develop a method that could be used to statistically assess an individual's response (rather than a group average response) to a work schedule that includes different combinations of circadian phase and length of time awake, such as occurs for workers in transportation.
Methods: When an individual lives on a 24h day, two covariate processes, circadian phase and homeostatic sleep drive (related to length of time awake), covary. This does not allow reliable estimation of the effects of the two covariates under different sleep/wake schedules on different physiologic measures, including performance and alertness. Therefore, a forced desynchrony protocol is used, whereby subjects are scheduled to live on non-24h days, for example, a 42.85h day with 28.56h awake and 14.28h asleep. This protocol allows neurobehavioral testing at different combinations of circadian phase and homeostatic sleep drive. We estimated subject-specific effects of circadian phase and homeostatic sleep drive on neurobehavioral performance using smoothing spline ANOVA models with restricted number of knots. We developed a unified framework for conducting hypothesis tests to assess goodness-of-fit and test for inter-individual variability via a permutation approach.
Results: The functional estimates for the effects of circadian phase and homeostatic sleep drive revealed that, for most subjects, the two variables have statistically significant effects on performance. In addition, there are statistically significant inter-individual differences in the effects of circadian phase and homeostatic sleep drive on performance.
Conclusion: The new method of functional estimation and hypotheses testing is reliable, allows estimation of subject-specific effects as well as assessment of inter-individual variability. It has better estimation properties than previously used methods, such as parametric ANOVA models, and can be used to assess effects of multiple factors on human performance, alertness and fatigue for individuals.

0145

SLEEP-WAKE CYCLE PATTERNS EVALUATED BY ACTIMETRY IN AN ADULT SAMPLE OF SAO PAULO CITY POPULATION

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Introduction: The aim of this study was to evaluate the sleep-wake cycle patterns by actimetry in the Sao Paulo Epidemiological Sleep Study.
Methods: A population based survey adopting a probabilistic three-stage cluster sample of the Sao Paulo city was used to represent the population according to gender, age (20-80 years), and socioeconomic classes. The volunteers were invited to wear the actimetry and completed a sleep diary for at least three consecutive days.
Results: From a total of 1101 volunteers selected to represent the adult population from Sao Paulo city, 397 properly wore the actimetry (mean period of use=5.5 days). Mean age was 43±14 years and 59% were women. Most volunteers (92%) had monophasic rest-activity cycles (RAC); 4% had biphasic and 1% had polyphasic RAC. The mean of the total sleep time was 370±61 minutes (6.2 hours), sleep efficiency was 81±7%, sleep latency was 12±11 minutes, and wake time after sleep onset was 54±21 minutes.
Conclusion: The results suggest that the association of monophasic RAC and short sleep time could be a factor to chronic partial sleep deprivation in a sample of adult inhabitants of Sao Paulo city. Additional analyses are necessary to better comprehend such sleep disorder within this population.
Support (optional): AFIP, FAPESP, CNPq

0146

MENSTRUAL CYCLE INFLUENCE ON THE CIRCADIAN VARIATION OF SLEEP IN HUMANS

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Introduction: Sleep propensity and organization vary across circadian phase. We hypothesize that the expression of core body temperature (CBT) and melatonin, two reliable circadian markers, may influence changes in sleep at different phases of the menstrual cycle.
Methods: Eight women with regular menstrual cycles participated in an ultra-rapid sleep-wake cycle (URSW) designed to assess the circadian variation of sleep during the mid-follicular (MF) and mid-luteal (ML) phases of the menstrual cycle. After a 3-week stabilization of the sleep-wake cycle to an 8-hr sleep episode, participants entered the laboratory for a nocturnal polysomnographic (PSG) sleep recording, followed by a 72-hr URSW (36 cycles of 60-min wake episodes in constant conditions alternating with 60-min naps) at MF and ML. PSG sleep and CBT were recorded, and salivary melatonin was sampled (1x/hr).
Results: During nocturnal sleep episodes in ML compared to MF, sleep efficiency (SE) and REM sleep decreased significantly, whereas significant increases were observed in sleep onset latency (SOL) and non-REM sleep. Throughout the URSW, total sleep time, SE, SOL, REM onset latency (ROL), stage 2, SWS, REM and non-REM sleep showed a significant circadian variation. A significant main effect and a trend for a menstrual phase difference was observed for ROL and REM sleep, respectively. A trend for a menstrual phase x time interaction was observed for ROL. During ML compared to MF, ROL in naps at 15h00 and 05h00 was significantly lengthened, whereas REM sleep was significantly decreased in naps at 01h00 and 05h00. The circadian profile of salivary melatonin was similar at both menstrual phases; however in ML, participants demonstrated significantly increased CBT and decreased CBT amplitude.
Conclusion: We observed moderate but significant sleep changes across the menstrual cycle in healthy women. The variation of body temperature and/or sex hormones across the menstrual cycle may interact with circadian processes to alter sleep characteristics.
Support (optional): Research supported by the Canadian Institute of Health Research (CIHR).

0147

SLEEP ARCHITECTURE IN MORNING AND EVENING TYPES AT BASELINE AND FOLLOWING SLEEP DEPRIVATION

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Introduction: Diurnal preference (for early/late sleep) is associated with differences in the circadian timing system and differences in sleep homeostasis. In this study we tested whether sleep architecture is different between Morning Types [M-types] and Evening Types [E-types] under baseline conditions or following sleep deprivation.
Methods: Eighteen subjects, 10 M-types (2F, 23.1±3.28 years) and 8 E-types (2F, 22.75±3.24 years) were selected using the Horne-Östberg Morningness-Eveningness Questionnaire. The inpatient study included three 8-hour nights scheduled at each subject's preferred times, 40 hours of acute sleep deprivation, and a 9-hour recovery night. We examined sleep architecture in terms of stages (minutes and %) and latencies, and compared data from the third baseline night (BN) and the recovery night (RN) within each group and between the groups.
Results: M-types had significantly earlier bedtimes and waketimes than E-types [bedtimes: 22:52+/-0:58 vs. 01:41+/-01:01; waketimes: 06:56+/-0:57 vs. 09:46+/-01:04], and significantly earlier circadian phase of core body temperature [03:25+/-01:05 vs. 06:22+/-01:58] and plasma DLMO25% [21:25+/-0:59 vs. 00:03+/-01:51], with no significant difference in phase angle. In both groups, latency to Stage 4 and amount and percentage of Stage 4 and slow wave sleep (SWS) were increased on the RN compared with the BN. There were no significant differences in sleep architecture between M and E types on either night, and no significant difference in how sleep architecture changed between BN and RN between the groups.
Conclusion: These preliminary results reveal that when sleeping at habitual times, M and E types do not show significant differences in sleep architecture or differences in response to a night of sleep deprivation. Further quantitative analysis of the sleep and waking EEG during and after sleep deprivation, and/or sub-dividing our subjects into those with and without extreme phase angles may reveal differences in sleep homeostatic factors between the types.
Support (optional): Studies supported by NIH grant HL08978, RR02635 (BWH GCRC), and RR025758 (Harvard Catalyst CTSC).

0148

A 12 MONTH OR MORE OPEN-LABEL STUDY OF THE EFFICACY AND TOLERABILITY OF ARMODAFINIL

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Introduction: In 12-week studies, armodafinil (NUVIGIL®) significantly improved wakefulness compared with placebo and was generally well tolerated in patients with excessive sleepiness (ES) associated with obstructive sleep apnea (OSA), shift work disorder (SWD), or narcolepsy.
Methods: In this 12-month or more (extension period), open-label, flexible-dose study, adult patients (n=328) who had a complaint of ES associated with a current diagnosis of OSA (n=170), SWD (n=108), or narcolepsy (n=50) received armodafinil 100 to 250 mg once daily (OSA and narcolepsy) or before night shifts (SWD). Patients with OSA were required to be regular users of nasal continuous positive airway pressure (nCPAP) therapy. Safety and tolerability was the primary objective of this study. Secondary measures of efficacy included the clinician-rated Clinical Global Impression of Change (CGI-C) for all patient groups and, in patients with OSA or narcolepsy, the Epworth Sleepiness Scale (ESS).
Results: The most commonly occurring adverse event was headache (17%). Nightly duration of nCPAP therapy decreased slightly from 6.7±1.1 hours at baseline to 6.3±1.2 hours postbaseline. There were no clinically meaningful trends in mean changes from baseline for laboratory variables, vital signs measurements, ECG, or physical examination findings. At final visit, 80% (95% CI, 74.1, 86.7) and 84% (95% CI, 72.7, 94.8) of patients with OSA and narcolepsy, respectively, were rated on the CGI-C as at least minimally improved with regard to overall clinical condition; 98% (95% CI: 95.2, 100.0) of patients with SWD were rated as improved with regard to sleepiness during night shifts, including the commute to and from work. Armodafinil improved mean ESS total scores in patients with OSA (mean [SD; 95% CI] change from baseline) (-7.3 [5.6; -8.39, -6.30]) or narcolepsy (4.7 [6.0; 7.41, 1.93]).
Conclusion: Armodafinil was generally well tolerated. Administration of armodafinil for 12 months or more was associated with sustained improvements in wakefulness in patients with ES associated with OSA,

SWD, or narcolepsy and overall clinical condition of patients with OSA or narcolepsy.
Support (optional): Study sponsored by Cephalon, Inc.

0149

MUTUAL INFLUENCE OF MATERNAL AND INFANT CIRCADIAN RHYTHM AND SLEEP-WAKE PATTERN

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Introduction: The purpose of this project was to explore relations of timing and strength of circadian activity rhythm with sleep amount, consolidation, and night slept in mothers and infants.
Methods: Home-based actigraphy and sleep-wake diaries were recorded continuously over a four day period from 20 mothers and their 4-10 week old infants. Actiwatch 64 (MiniMitter, Sun River, OR) actigraphy monitors were attached to maternal non-dominant wrist and infant ankle. The diary was recorded in 15 minute epochs. Actigraphy rhythm was determined by cosinor analysis using linear regression. Circadian rhythm strength and timing were defined as R2 and acrophase respectively. Diary information was summarized. Sleep consolidation was defined as number of sleep bouts and longest sleep bout while sleep occurring between 2200-0600 was defined as night sleep. Mutual influence among maternal and infant circadian rhythm and sleep-wake pattern were examined using bivariate correlations.
Results: As expected, maternal circadian rhythm and sleep pattern were related. Maternal R2 correlated with maternal longest sleep bout ($r = 0.487$, $p < 0.05$), total sleep ($r = 0.463$, $p < 0.05$), and sleep bouts ($r = -0.548$, $p < 0.05$). Increased mother night sleep was associated with acrophase occurring earlier in the day ($r = -0.677$, $p < 0.01$). Infants did not demonstrate significant relations of rhythm strength with total sleep and night sleep. Infant acrophase occurring earlier in the day was associated with fewer infant sleep bouts ($r = 0.587$, $p < 0.01$). Significant correlations were found between: maternal total sleep and infant R2 ($r = 0.448$, $p < 0.05$), and maternal R2 and infant total sleep ($r = 0.645$, $p < 0.01$).
Conclusion: While the effects of infant sleep on mother sleep are well known, knowledge of the mutual influence of maternal and infant circadian rhythm and sleep may inform entrainment of infant sleep.
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0150

CIRCADIAN ACTIVITY RHYTHMS FOR MOTHERS WITH AN INFANT IN ICU

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Introduction: Circadian rhythms (CR) influence sleep and wakefulness. CR of activity is altered in dementia and seasonal affective disorder. To date, studies exploring CR and sleep in postpartum women are rare. Having a medically ill infant hospitalized in an intensive care unit (ICU) can intensify sleep disturbances. The purpose of this report is to 1) describe relationships between CR, sleep disturbances, and fatigue among mothers with an infant cared for in ICU, and 2) compare differences in activity CR between good sleepers and poor sleepers.
Methods: A total of 50 mothers of infants hospitalized in ICU were included in this descriptive exploratory study. Participants completed the General Sleep Disturbance Scale (GSDS), Numerical Rating Scale for Fatigue (NRS-F), and a sleep diary. The objective sleep data included total sleep time (TST), wake after sleep onset (WASO), and circadian equation (amplitude/mesor) averaged from at least 48-hours of wrist actigraphy monitoring.
Results: TST was less than 7 hours (M=380 minutes, SE=12) and the average WASO was 16.3% (SE=1.8). Overall mothers general sleep disturbance scores were borderline (M=2.6; SD=0.8). The mean score for the sleep quality subscale was 4.4 (SD=1.9), indicating mothers experienced poor sleep quality for more than 4 nights per week. The fatigue mean scores were 4.8 and 6.5 for morning and evening respectively, indicating moderate fatigue severity. The amplitude and mesor was 59.7 (SD= 27.9) and 90.56 (SD= 36.5). The CR of activity determined by circadian equation was .67 (SD=.18), indicating that CR was disturbed. A higher circadian equation was associated with higher TST ($r = .83$, $p<.001$), less WASO ($r = -.50$, $p< .001$), less self-reported sleep disturbances ($r = -.35$, $p = .01$), and less morning fatigue ($r = -.26$). The good sleepers (GSDS < 3) had better circadian equations compared to poor sleepers (GSDS > 3) ($t [48] = 2.5$, $p< .03$).
Conclusion: Findings indicate that mothers with a hospitalized infant have both nocturnal sleep problems and disturbed circadian activity rhythms. Factors responsible for these sleep and rhythm disturbances, the adverse effects on mother's physical and mental well-being, and mother-infant relationship require further study.
Support (optional): The first author of this study was supported by NINR T32NR 07088, Association of Women's Health, Obstetric and Neonatal Nurses.

0151

SLEEP CHARACTERISTICS IN SUBJECTS RECRUITED FOR A JET LAG STUDY

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Introduction: According to the National Sleep Foundation, approximately 50 million people in the United States chronically suffer from sleep problems and disorders that affect their productivity, safety, health and relationships - both on the job and at home. The objective of this analysis was to evaluate the sleep characteristics in men and women, 18 through 65 years of age, who had a history of jet lag and who were undergoing screening to determine eligibility for participation in a clinical study of armodafinil (NUVIGIL®) for the treatment of excessive sleepiness associated with jet lag.
Methods: Subjects must have experienced jet lag symptoms associated with a time zone change of 6 hours or fewer at least once during the past 5 years. Subjects were required to have bedtime hours between 2100 and 2400 and an average of between 6.5 and 9 hours of total sleep time per night during the past month. Subjects were excluded from the study if they had an Epworth Sleepiness Scale (ESS) score of 10 or greater or had a history or diagnosis of narcolepsy, obstructive sleep apnea/hypopnea syndrome, shift work disorder, hypersomnia, insomnia or any other sleep disorder. Travel across time zones with a 4-hour or more difference, in the 2 weeks prior to screening was prohibited. Any medication with sleep or wakefulness effects was prohibited. Assessments included nocturnal polysomnography (PSG), Multiple Sleep Latency Test (MSLT) 20 minute version (at 1000, 1200, 1400, and 1600), Karolinska Sleepiness Scale, Patient Global Impression of Severity, and Epworth Sleepiness Scale.
Results: The results of sleep parameters in approximately 800 subjects who had a history of jet lag disorder will be evaluated and presented.
Conclusion: This is the first analysis that measures sleep characteristics, including excessive sleepiness, in subjects who were recruited for a jet lag study.
Support (optional): Study sponsored by Cephalon, Inc.

0152

A PROSPECTIVE, OBSERVATIONAL ONE YEAR STUDY MONITORING SLEEP QUALITY, MOOD AND QUALITY OF LIFE OF THE CALGARY POLICE SERVICE HYBRID 12-10-8 PATROL WORK SCHEDULE PILOT PROJECT

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Introduction: The 12-10-8 Patrol Work Schedule Pilot Project is a hybrid shift design, developed by police officers to address concerns between management and officers with regards to shift configuration. Purpose was to monitor prospectively sleep quality, mood and quality of life using metrics with established psychometric properties and to develop a method for future comparative studies.
Methods: Repeated measures design was used; baseline testing was followed by 4 testing sessions repeated at 12 week intervals over 52 weeks. Subjects completed the Pittsburgh Sleep Quality Index (PSQI) for night sleep/day shift and day sleep/night shift, the Profile of Mood States (POMS), and Short-Form 36 Health Survey (SF-36). Test scores were compared using analysis of variance and Greenhouse-Geisser adjustment. Mean component scale scores were compared for differences across time using Friedman's test.
Results: Ninety-four members were eligible to participate. Analysis was performed on participants (n=25) who completed all five testing sessions (response rate 26.6%). PSQI Global Scores did not change substantially over the 52 weeks; however the trend was positive. PSQI Sleep Duration subscale (night sleep/day shift) showed a significant decrease across time ($p = 0.0013$). The POMS Total Mood Disturbance Score ($p = 0.0022$), Tension ($p = 0.0006$) and Fatigue ($p = 0.0004$) subscales suggest improvements across time. The SF-36 Vitality subscale improved across time($p < 0.0001$).
Conclusion: Poor response rates limits the generalizability of the observations/results. The general direction of change over time, while not statistically significant, was positive for sleep quality, tension, fatigue and vitality. More importantly the parameters did not decline as a result of this hybrid shift design. Future research should employ a control group and substantial effort should be made to improve response rates.
Support (optional): The Calgary Police Service, City of Calgary, Calgary, Alberta, Canada The Centre for Sleep and Human Performance, Calgary, Alberta, Canada

0153

ARMODAFINIL FOR EXCESSIVE SLEEPINESS ASSOCIATED WITH JET LAG DISORDER

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Introduction: Two-thirds of international travelers experience jet lag disorder, a disturbance of circadian rhythms associated with excessive sleepiness, reduced concentration and alertness, fatigue, and impaired function. Armodafinil (NUVIGIL®), a non-amphetamine, wakefulness-promoting medication, is the *R*- and longer lasting isomer of modafinil and has been shown to improve wakefulness in shift work disorder, another circadian rhythm sleep disorder. The objective of this study was to assess the effects of armodafinil on patients with a history of jet lag disorder. This is the first known study of an intervention which is intended to improve wakefulness in this patient population.
Methods: Patients who had previously experienced jag lag disorder (as defined by the International Classification of Sleep Disorders) on at least 1 occasion during the past 5 years underwent baseline evaluations at US centers. Patients then boarded eastbound nighttime flights originating in US cities to destination cities in Europe, with a time-zone change of 6 hours. The following morning, patients were randomized to armodafinil (50 or 150 mg/day) or placebo for 3 days and underwent repeat assessments as inpatients. On the fourth day, patients returned to their originating cities where final physical exams were performed. Patients were contacted 48 hours and 7 days later for follow-up. Primary assessments included the Multiple Sleep Latency Test (MSLT) and Patient Global Impression of Severity (PGI-S). Secondary assessments included the Karolinska Sleepiness Scale (KSS) and nocturnal polysomnography (PSG). Safety and tolerability were evaluated throughout the study.
Results: Armodafinil compared with placebo on MSLT, PGI-S, KSS, and PSG will be reported, along with safety and tolerability data.
Conclusion: This the first study of armodafinil in patients with jet lag disorder.
Support (optional): Study sponsored by Cephalon, Inc.

0154

A COMPARATIVE ANALYSIS OF AUTOMATED VERSUS MANUAL SCORING OF ACTIGRAPHY IN SHIFT WORKERS DOING 12-HOUR ROTATING SHIFTS

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Introduction: Actigraphy is convenient and cost-effective for assessing sleep/wake, but methodological issues continue to limit its applicability, especially in shift workers. Automated scoring was observed to overestimate total sleep time (TST), (>8 hours), inconsistent with a shift work population (<7 hours). Estimated time in bed (TIB) from sleep logs further demonstrated inconsistency with the automated scoring. Therefore, a manual scoring method was developed and applied to better estimate TST is this group of shift workers (N=9).
Methods: Actigraphy data was collected using Proportional Integrating Measures. Data was used to compared automated (University of California, San Diego (UCSD) algorithm) and manual scoring (UCSD algorithm, sleep logs and event marker information) to estimate TST over 14 days of rotating 12-hour shifts. TST is defined as the number of epochs (1 minute) scored as sleep within 24-hours (06:00-06:00).
Results: Comparative analysis of the automated and manual scoring methods was conducted. TIB was used as a benchmark for the comparison. Average estimated TIB per day for 14 days was 415 minutes (6.9 hours). TST (group means) was calculated across 14 days. Average TST for automated was 502 minutes (8.4 hours); manual was 391 minutes (6.5 hours). A discrepancy of 111 minutes (1.85 hours) was detected between the automated and manual scoring; with automated overestimating TST.
Conclusion: Manual scoring provided a better estimate of TST in this group of shift workers. This analysis exemplifies the importance of utilizing sleep logs and event markers in conjunction with actigraphy. Limitations included small sample size and lack of validation of the manual scoring method.
Support (optional): The Calgary Police Service, City of Calgary, Calgary, Alberta, Canada The Centre for Sleep and Human Performance, Calgary, Alberta, Canada

0155

TIME OF DAY CHANGES IN MOTOR BRAIN ACTIVITY

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Introduction: Performance to several tasks changes according to time of day or circadian phase, including motor tasks. However time of day changes in human motor brain activity are largely unknown.
Methods: Twenty four young subjects performed a control motor task (CTR) during one visit to the laboratory and a visual motor adaptation task (ADAPT) during another visit (counterbalanced order). For both tasks, subjects used a mouse to reach targets displayed on a computer screen. Directions of the pointer were inverted as compared to direction of the mouse for ADAPT while they remained unchanged for CTR. Twelve subjects performed the tasks at 9AM (morning group) and 12 performed them at 9PM (evening group). After a training session, subjects were scanned while performing the task. Functional MRI data were acquired using a 3T MR scanner (TRIO, Siemens) and analyzed using SPM2 (http://www.fil.ion.ucl.ac.uk).
Results: Performance for ADAPT was significantly higher in Evening than in Morning. No time of day effect on performance was found for CTR. ADAPT was associated with significantly higher activity in the Evening than Morning in the thalamus, primary motor cortex, dorsolateral premotor cortex, supplementary motor area, and in the deep nuclei and lobe 6 of the cerebellum. These differences were abolished when activity of the control task was subtracted from the adaptation task indicating that they may be related to motor activity per se rather than the adaptation aspect of the task.
Conclusion: These data suggest that brain activity in brain structures associated to alertness regulation and motor brain structures is modulated by time-of-day. Future studies should investigate to which extend these effects are associated to homeostatic and circadian regulatory mechanisms.
Support (optional): IRSC/CIHR

0156

SLEEP AND DIETARY PATTERNS IN NURSES UNDER SHIFT WORK

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Introduction: Shift work has great impact on biological clock to alter nurses' sleep and dietary patterns. This study investigated nurses' sleep and dietary patterns under shifts and their consequences on sleep quality and health.
Methods: Sixty-seven nurses were recruited from a medical center in Taiwan. They were grouped into fixed day (DS, n=18), fixed evening (ES, n=17), fixed night (NS, n=15) and rotating shifts (RS, n=17). Shift was lasting for one month. Participants filled out questionnaires of the "Pittsburg Sleep Quality Index (PSQI)," the"3-day Sleeping diary," the "3-day dietary record," and the "GI dysfunction checklist" in the middle 3 days of their shift.
Results: There were 52.9%~82.4% of nurses reported their sleep as poor (PSQI≥5). Sleep quality in the RS group was the worst. Most of the NS (80.0%) and the RS (100%) groups lived in DS or ES patterns in their off shift. The ES group has the longest sleep hours (8.9 hrs vs. 7.3~7.9 hrs). Sleep fragmentation significantly happened in most of the NS (46.7%) and the RS (23.5%) groups. The 3-day average of total caloric intake in the ES and NS groups (1193-1409 Kcal) were significantly less than the DS and RS groups (1643-1684 kcal) ($F=10.8$, $p<.001$). Nurses in the ES group also took less protein, fat, and carbohydrate significantly than the others. Moreover, there were 26.8%-47.1% of nurses reported various G-I dysfunctions, but no significant differences among groups.
Conclusion: More than half of nurses perceived their sleep as poor, and nurses in the rotating shift and night shift are the worst. Live pattern in off shift may play a role to disturb their circadian rhythm. Moreover, the total caloric intake in nurses under evening shift is less than the recommended. Findings in this study provide information for nurses to better adapt their shift work.

0157

ATTENTIONAL FAILURES ARE MORE PRONOUNCED IN THE LATTER HALF OF A WAKE EPISODE FOLLOWING AN INVERSION OF THE SLEEP-WAKE SCHEDULE

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Introduction: Our ability to attend to the environment is critically dependant on our circadian rhythms being appropriately aligned with our sleep-wake schedule. We tested the hypothesis that brief attentional failures would increase significantly during the latter half of the waking day, when it coincides with adverse circadian phase, a hypothesis based on the finding that the wake-dependant deterioration in alertness worsens at the circadian nadir.
Methods: Seven healthy young adults participated in a 71-day inpatient protocol. We compared performance on the Psychomotor Vigilance Task (PVT) administered during the morning and evening of an entrained 24 h day (Baseline Day 1), on the first day following an inversion of the sleep-wake schedule (Experimental Day 1), and 3 weeks later, after participants had entrained to the new schedule (Experimental Day 22).
Results: Prolonged circadian misalignment persisted following the sleep-wake schedule inversion. The average phase angle on the 6th experimental day was still 5.87 +/- 2.39 h (baseline: -1.36 h). By Experimental Day 20, participants had entrained to the imposed sleep-wake schedule at an appropriate phase angle of -2.1 +/- 0.23 h, and thereafter entrainment persisted. A comparison of PVT performance between Baseline Day, Experimental Day 1, and Experimental Day 22 indicated no significant differences in performance in the first part of the waking day ("morning"). However, towards the latter half of the Experimental Day 1 ("evening") there was more than a twofold increase in attentional failures ($p< 0.01$) compared to the other two entrained days.
Conclusion: Individuals are particularly vulnerable to attentional failures during the latter half of a waking episode when it coincides with adverse circadian phase. This finding underscores the potent influence of the circadian and homeostatic (wake-dependent) systems on attention, and has implications for overnight operations, shift work, and transmeridien travelers.
Support (optional): National Space Biomedical Research Institute through the National Aeronautics and Space Administration (NCC 98-58) to CAC, and NIH grant M01 RR02635 (BWH GCRC).

0158

EFFECTS OF THE MT1/MT2 MELATONIN AGONIST RAMELTEON ON THERMOREGULATORY PHYSIOLOGY AND DAYTIME SLEEP

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Introduction: A reduction in core body temperature and an increase in peripheral heat loss are reported to be associated with shorter sleep onset latencies (SOL) and better sleep quality. Ramelteon is a novel sleep promoting therapeutic approved for the treatment of insomnia. At night, Ramelteon has been reported to shorten SOL. The influence of Ramelteon on thermoregulatory physiology and daytime sleep in humans is unknown. Therefore, we tested the hypothesis that Ramelteon (8mg) would reduce core body temperature, increase peripheral heat loss, as well as shorten SOL, reduce wakefulness after sleep onset (WASO) and increase total sleep time (TST).
Methods: Fourteen healthy adults (5 females), BMI (22 ± 2 kg/m2) aged (23 ± 4 yrs) participated in a randomized, double-blind, placebo-controlled, cross-over within-subjects study. Participants completed two laboratory visits, each preceded by one week ~8h consistent sleep-wakefulness schedules verified by call-ins to a time stamped recorder, actigraphy (Actiwatch-L, Mini Mitter Respironics) and sleep logs. Subjects were studied under modified constant routine conditions to control for influences of activity, posture, and lighting. Ramelteon/placebo was administered 2h prior to a 4h afternoon sleep opportunity. Core and skin (clavicle and foot) body temperatures (Vital Sense, Mini Mitter Respironics) were analyzed for 2.67h prior to the polysomnography recorded (Siesta, Compumedics) sleep opportunity.
Results: As hypothesized, repeated measures ANOVA revealed Ramelteon significantly reduced core temperature and increased the distal-proximal skin temperature gradient (both $P<0.05$). Furthermore, Ramelteon increased TST, Stage 2 sleep, and sleep efficiency and reduced WASO (all $P<0.05$).
Conclusion: Ramelteon improved daytime sleep, perhaps in part by reducing core temperature and increasing heat loss. These findings suggest that Ramelteon may have applications for the treatment of circadian sleep disorders.
Support (optional): Takeda Pharmaceuticals North America, Inc., the Howard Hughes Medical Institute Bioscience Grant in collaboration with the Biological Sciences Initiative at the University of Colorado—Boulder and NIH MO1-RR00051.

0159

CONTRIBUTION OF HOMEOSTATIC, CIRCADIAN AND SLEEP INERTIA PROCESSES ON HIGHER ORDER COGNITIVE FUNCTIONS USING A FORCED DESYNCHRONY PROTOCOL

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Introduction: Length of wakefulness and circadian phase have been shown to modulate simple reaction time, working and long-term memory, mood and alertness. We sought to extend understanding of sleep-wake processes regulating cognition by examining selective visual attention and the inhibitory control component of executive function in a forced desynchrony protocol(FD), assessing the influence of time awake, circadian phase and sleep inertia.
Methods: Six healthy subjects [5 males (aged 26.8±5.2;mean±SD)] were studied in a 28h FD (scheduled 18.66h wakefulness and 9.33h sleep) for 12 days. The FD permits cognition assessment across the circadian cycle and time awake. Cognition was assessed beginning at scheduled awakening and every 2h thereafter until 18h wakefulness. Selective visual attention (conjunction search) and executive function (inhibitory control—Stroop Color Word and working memory—Mathematical Addition) were examined. Data were averaged into 60° circadian bins, with temperature minimum assigned to 0°, and into 2h time awake bins. Deviations from the mean were analyzed with repeated measure ANOVA.
Results: Significant effects of circadian phase and time awake were observed for all tasks ($P<0.05$). Cognition was best ~240° and worst ~60° after the temperature minimum. Cognition was impaired upon scheduled awakening and improved over the next 2-4h of wakefulness, worsening thereafter until scheduled bedtime. Relative modulation for visual search and inhibitory control tasks by time awake and circadian phase were similar for this time awake; when averaged across all circadian phases, impairment by sleep inertia was less than that induced by circadian phase misalignment or 18h wakefulness. Modulation of working memory was greatest for time awake; working memory impairments by circadian phase and sleep inertia were similar to that produced by ~16h wakefulness.
Conclusion: Length of time awake, circadian phase and sleep inertia each modulate higher order cognitive functions. These findings reveal that these three processes affect components of selective attention and executive function that are critical for decision making.
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0160

CHRONOTYPE PREFERENCE IS ASSOCIATED WITH MEMORY, SELF CONCEPT, AND SOCIAL FUNCTIONING IN HEALTHY MEN

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Introduction: Circadian preference has been associated with attention and daytime functioning, however, there is little information regarding the impact of circadian preference on attention, memory and daytime functioning in normative population. The objective of the current study was to determine the association between adults' circadian preferences and their daytime attention, memory and social functioning. We hypothesized that adults with an evening preference will present more daytime impairments associated with their cognitive and social functioning.
Methods: The sample consisted of 53 men 39.8 years of age that completed the Horne-Ostberg Morningness-Eveningness Questionnaire (MEQ) to determine their circadian rhythm patterns and the Conners' Adult ADHD Scale (CAARS) to determine daytime attention, memory, social relationships, and self confidence.
Results: Subjects were divided into 2 groups based on their chronotype score, with subjects above and below the mean (M= 55.6) placed in the Morning Preference Group (MPG) and Evening Preference Group (EPG), respectively. Multiple Analysis of Covariance (MANCOVA) was computed with the Chronotype Group (MPG or EPG) taken as the between-subject independent factors, the scores on the CAARS as the dependent variables, and SES as a covariate. Significant differences were found between the MPG and EPG groups on the men's CAARS scores [$F(1,44) = 2.95$, $p<.05$]. Univariate analyses indicated that men in the MPG Group reported significantly better memory functioning [$F(1, 44) = 5.86$, $p<.02$] and higher "self-concept", i.e., better social relationships, higher self-esteem and more self confidence [$F(1, 44) = 10.45$, $p<.001$] compared to subjects in the EPG Group.

Conclusion: The findings of the present study support the hypothesis that circadian preference is associated with daytime social and memory functioning. This could have significant impact on work performance and on the ability to keep up with job demands and relationships.
Support (optional): This study was supported by Canadian Institutes of Health Research (CIHR) grant number 153139 and Fonds De La Recherche en sante (FRSQ) grant number 10091.

0161

CHRONOTYPE, SLEEP HYGIENE, AND ACADEMIC PERFORMANCE IN HIGH SCHOOL AND COLLEGE

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Introduction: Chronotype has been related to academic performance in young children, early adolescents, and medical students with evening types performing more poorly. The relationship in college students has only been examined in a military academy. Although influenced by genetics, chronotype may be modulated by environmental factors. We examined the relationship of chronotype to college performance and its longitudinal persistence as students transitioned from high school to college.
Methods: During pre-freshman summer, entering freshmen at a liberal arts college were solicited for participation. 89 students (17-20 yrs, 57 women) completed questionnaires regarding their high school sleep habits and gave access to their high school and college academic records. 34 of them completed the same questionnaires at the end of their freshman year. The questionnaires included demographic information, Epworth Sleepiness Scale, Horne and Ostberg Morningness-Eveningness Questionnaire, Sleep Timing Questionnaire, and The Sleep Hygiene Index.
Results: Evening types compared to morning and intermediate types combined had lower first year college GPA (evening: M=2.84, SD=1.03; morning & intermediate: M=3.18, SD=.73; $p<.05$), a greater decline in high school to college GPA ($t(76)=-1.67$; $p<.05$), poorer sleep hygiene ($t(87)=-2.42$; $p<.05$), and slept on average 41 minutes less on school nights ($t(87)=-2.79$; $p<.05$). Sleep hygiene was poorer in college ($t(33)=-4.44$; $p<.05$) and poor sleep hygiene was associated with lower GPA ($r(80)=-.277$; $p<.05$). In transitioning from high school to college, participants made small but not significant shifts to more evening type.
Conclusion: Evening chronotype is associated with lower academic performance in college and a decline in academic performance from college to high school. This may be related to reduced sleep hygiene. Sleep hygiene for all students was related to academic performance. Education about possible negative effects of poor sleep behaviors on academic performance may help students' academic performance, particularly those at risk because of their chronotype.

0162

EPIDEMIOLOGY OF BEDTIMES: AGE, GENDER, AND ETHNICITY

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Introduction: Little epidemiological data exist on bedtimes in the general population, particularly with respect to ethnicity and gender. The present study attempts to address this gap by analyzing the bedtimes reported in 2 weeks of sleep diaries from our epidemiological survey.
Methods: 772 participants from a metropolitan community were enrolled using random-digit dialing. The population was nearly equally comprised of males and females. Participant ages ranged from 20 to 98 and were grouped into decades. The majority of the population was Caucasian or African-American. Participant bedtimes for 14 days were obtained via 2 weeks of sleep diaries and analyzed for circadian patterns. Participant demographic data from our database was also included in our analysis. T-tests were performed to analyze group differences in mean bedtimes.
Results: The differences in mean bedtimes between young and elderly individuals, middle-aged and elderly individuals, and young and middle-aged individuals were all statistically significant ($t[205] = -10.0$, $p < 0.01$; $t[214] = -7.1$, $p < 0.01$; and $t[214] = -3.2$, $p < .01$ respectively). Females had, on average, slightly earlier bedtimes than males but this difference was not statistically significant ($t[725] = -1.5$, $p = 0.14$). African-Americans had a slightly earlier mean bedtime than Caucasians but this too was not statistically significant ($t[347] = -0.6$, $p = 0.54$).
Conclusion: Earlier bedtimes are associated with aging. Significant gender and ethnicity differences in bedtimes were not apparent in this study.
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0163

ASSOCIATION OF CIRCADIAN GENE POLYMORPHISMS WITH DIURNAL PREFERENCE, SLEEP TIMING, SLEEP QUALITY AND DEPRESSION IN JAPANESE POPULATION

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Introduction: A system of self-sustained biological clocks regulates 24-hour (h) rhythms of behavioral and physiological processes such as the sleep-wake cycle, body temperature and hormonal secretion. The circadian clock system also influences sleep timing and diurnal preference. A number of polymorphisms in the circadian clock genes have been reported to correlate with sleep disorders. For example, PER2 functional polymorphisms show strong association with familial advanced sleep phase syndrome, and a variable number tandem repeat (VNTR) and a haplotype in PER3 influence diurnal preference and susceptibility to delayed sleep phase syndrome.
Methods: 925 Japanese people (274 males, 651 females, average age 36.45 years) were surveyed by questionnaires; morningness-eveningness questionnaire (MEQ), Pittsburgh Sleep Quality Index (PSQI), and Center for Epidemiological Studies Depression Scale (CES-D). Furthermore, functional polymorphisms in the circadian clock genes, PER2, PER3, TIM, and NPAS2 were determined in the 925 subjects. These clock gene polymorphisms were tested for association with MEQ score, PSQI score, and CES-D scale and multiple sleep parameters including sleep onset, wake time, sleep duration.
Results: A PER2 haplotype influenced diurnal preference and a missense polymorphism in PER2 was associated with depressed mood. Eveningness preference and poor sleep quality were strongly associated with a PER3 haplotype, and sleep onset correlated with a PER3 missense variation. Depression was influenced by two functional TIM polymorphisms. A NPAS2 missense variation correlated with sleep duration.
Conclusion: Our study demonstrates that these functional polymorphisms in the circadian clock genes are significantly associated with diurnal preference, sleep quality, depression and sleep timing. The results of the current study suggest that the circadian clock genes may not only regulate daily cycles of behavior and physiology but also modulate sleep quality and mood in human.

0164

MOLECULAR INSIGHTS INTO HUMAN DAILY BEHAVIOR

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Introduction: Human beings exhibit wide variation in their timing of daily behavior. We and others have suggested previously that such differences might arise because of alterations in the period length of the endogenous human circadian oscillator.
Methods: Using dermal fibroblast cells from skin biopsies of 28 subjects of early and late chronotype (11 "larks" and 17 "owls"), we have studied the circadian period lengths of these two groups, as well as their ability to phase-shift and entrain to environmental and chemical signals.
Results: We find not only period length differences between the two groups, but also significant changes in the amplitude and phase-shifting properties of the circadian oscillator among individuals with identical "normal" period lengths. Mathematical modeling shows that these alterations could also account for the extreme behavioral phenotypes of these subjects.
Conclusion: We therefore conclude that human chronotype may be influenced not only by the period length of the circadian oscillator, but also by cellular components that affect its amplitude and phase. In many instances, these alterations may be investigated in peripheral tissues.

0165

THE EFFECTS OF BEHAVIOURAL INDUCED SLEEP DISRUPTION ON CIRCADIAN PARAMETERS IN MICE

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Introduction: The mammalian sleep-wake cycle is under homeostatic, circadian and cognitive control; however, the mechanism(s) by which each executive is influenced by any disruptions in this sleep-wake cycle remains unclear. Previous animal models of induced insomnia have relied on purely physiological stressors, which may not have provided analogous characteristics of insomnia found in humans. In the present study, we employed a model of induced insomnia that generates, in rats, a pattern of sleep disturbance that resembles the sleep changes observed in humans with stress-induced insomnia (Cano et al, 2008). The present experiments examine the effects of behavioural induced sleep disruption on the response of the circadian pacemaker, and test the possible involvement of the histaminergic input from the tuberomammillary nucleus in mediating the effects of sleep deprivation on the circadian clock.
Methods: The present experiments examine the effects of behavioural induced sleep disruption on the response of the circadian pacemaker, and test the possible involvement of the histaminergic input from the tuberomammillary nucleus in mediating the effects of sleep deprivation on the circadian clock.
Results: Wild type mice were exposed to the behavioural induced insomnia protocol during their inactive portion of their cycle. Under this protocol, mice that were housed individually were transferred into another animal's cage (dirty cage exchange). Circadian parameters, including total volume of activity and temporal distribution of activity within the active period, demonstrated significant changes following the behavioural induced model compared to controls. There is strong evidence to suggest that the histaminergic neurons are involved in the regulation of the circadian input in the sleep-wake cycle. Sleep deprived mice (8 hours) exhibited a significant reduction of almost 40% in the phase delaying response to light at ZT14 compared to controls. Following treatment with mepyramine (acting as a H1 receptor antagonist) sleep deprivation was no longer able to attenuate the phase delays to light.
Conclusion: Taken together, the present findings suggest that disruptions in the sleep wake patterns can affect the regulation of intrinsic circadian parameters and these effects may be mediated by changes in histamine transmission.

0166

CIRCADIAN RHYTHM OF REACTION TIME IN TOTALLY BLIND ATHLETES

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Introduction: Light can phase-shift the biological clock, synchronizing it with the environmental cycles of light and darkness. Studies show that peak of simple reaction time occurs in the afternoon, at the same time as the peak in body temperature. In constant routine condition, the reaction time in sight people shows a free-running rhythm. However the reaction time in totally blind people has remained unclear. The present study aimed at analyzing the behavior of reaction time during psychomotor vigilance task (PVT) in totally blind people with free-running circadian rhythm.
Methods: Six totally blind people with free-running rhythm attended three sessions in laboratory at two consecutive weekends and one after a weekend of rest. In each session, body temperature and reaction time were collected at 6 different times of day (02:00h, 06:00h, 10:00h, 14:00h, 18:00h, 22:00h). Statistical analysis employed the cosinor method to determine acrophases. The acrophases were converted into relative data. Relative acrophases were pooled across all 6 subjects and linearly regressed as a function of days from start, using the slope as a gauge of average daily shift.
Results: The results show that the endogenous period of temperature, mean reaction time and fastest reaction time were longer than 24 hours. Slowest reaction time and lapses show endogenous period longer than 24 hours but confidence interval include zero value.
Conclusion: We found that totally blind people show a free-running rhythm in mean and fastest reaction time, like as slight people when they stay in constant routine condition. Therefore, the implications to know the behavior of performance on PVT for this people is relevance for acquisition and improvement of skills, for the prevention of impairment performance and errors in some kind of work, for improve athletic performance and for optimize school timetables (most favorable time of day for teaching).
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0167

THE RELATIONSHIP BETWEEN MELATONIN AND LUNG FUNCTION IN ASTHMATIC AND HEALTHY SUBJECTS

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Introduction: The circadian system contributes to the diurnal change in lung function seen in healthy individuals. While the amplitude of lung function rhythm is greater in asthma than in health, it is unknown if the endogenous circadian system has a role in the development of asthma. The aim of the current study is to explore whether melatonin, a marker of central circadian rhythm, and lung function rhythms are desynchronized in asthmatic as compared to healthy subjects.
Methods: Two healthy (average age=43.5), 3 NNA (age=48), and 2 NA (age=26.5) participants maintained regular habitual sleep times for one week prior to the laboratory study. After a night of adaptation, subjects completed a 28 hour constant routine protocol, with serial blood

sampling for melatonin every 30 minutes and spirometry every 2 hours. Results were expressed as clock time and as circadian time (relative to habitual wake time), and the phase angle between melatonin midpoint and lung function nadir was calculated. One way ANOVA was used for statistical analyses.
Results: The average melatonin midpoint in clock time was 3:12(±2:35) for healthy, 1:32(±0:14) for NNA, and 2:56(±1:51) for NA subjects. Melatonin midpoints in circadian time were 19:44(±1:49), 18:44(±0:16), and 19:01(±0:55), respectively. Average clock times of lung function nadir were 1:27(±3:35) for healthy, 4:08(±4:42) for NNA, and 2:54(±0:28) for NA subjects. Circadian times of lung function nadir were 18:00(±2:49), 21:20(±5:02), and 19:00(±1:24), respectively. The phase angles between melatonin midpoint and lung function nadir for the healthy, NNA, and NA subjects were 1:44(±0:59), -2:35(±4:45), and 0:01(±2:20).
Conclusion: These preliminary findings indicate that the phase relationship between the circadian rhythm of melatonin secretion and lung function may differ by more than 4 hours between asthmatic and healthy subjects. We are continuing to enroll more participants to determine the role of circadian regulation in the expression of asthma phenotypes.
Support (optional): 5R01HL069988

0168

THE EFFECT OF CIRCADIAN PREFERENCE AND DAYTIME SLEEPINESS ON ACADEMIC PERFORMANCE MAY BE MEDIATED BY ACADEMIC MOTIVATION IN SENIOR HIGH SCHOOL STUDENTS

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Introduction: Teenagers tend to shift their time of day preferences from morningness to eveningness during the age of puberty. Various studies have found associations between the progressive reduction of morningness during adolescence and insufficient sleep, daytime sleepiness, poorer academic achievement. The current study tried to explored whether circadian preference and daytime sleepiness is related to academic performance via achievement motivation among senior high school students.
Methods: A questionnaire regarding sleep pattern and daytime functioning was administered to 1650 students from the 10th grade to 12th grade. The participants were recruited form senior high schools in Taipei using stratified cluster sampling method. There were 1308 valid questionnaires obtained. Structural Equation Model (SEM) was used to examine the relationship among the variables.
Results: The results showed that evening tendency and daytime sleepiness are associated with low achievement motivation and academic performance. The effect of circadian preference and daytime sleepiness to academic performance is indirect, through the mediation of achievement motivation. The circadian preference and daytime sleepiness accounted for 15.3% of the variation of achievement motivation. The model of mediation effect of achievement motivation on the effect of circadian preference and daytime sleepiness to academic performance could explain 12.4% of the variance in academic performance.
Conclusion: The current study supported the hypothesis that the association between circadian preference, daytime sleepiness and academic performance was mediated by achievement motivation. Therefore, academic motivation, which is the key predictor of academic performance, may be decreased by the evening tendency and daytime sleepiness which in turn affect academic performance. It is important that parents, educational fields, and health professionals should pay attention to the sleep duration and diurnal preference to facilitate the learning among adolescents.

0169

GENDER DIFFERENCES IN ENTRAINED CIRCADIAN PHASE IN HUMANS

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Introduction: There have been conflicting results from studies of gender differences in the timing of entrained circadian phase in humans. This may be because none of the studies conducted to date have controlled for the masking effects of the rest-activity cycle on circadian phase markers.
Methods: We examined circadian phase data from 60 adult subjects (18-34 yrs) studied in a Constant Routine (CR) protocol designed to minimize masking effects. We matched female and male participants with similar wake times. Participants maintained a regular sleep schedule at home for a week prior to study. After three baseline days, participants began a 27-50h CR during which time they remained awake in a semi-recumbent posture in constant dim lighting, while core body temperature (CBT) and plasma samples for melatonin assessment were collected. Phase estimates for CBT minimum, and dim light melatonin onset and offset were calculated.
Results: The timing of all three circadian phase markers were significantly earlier in the women relative to the men, though habitual sleep and wake times were not different. The relative phase relationship between sleep and circadian phase was therefore different between genders, with sleep occurring at a significantly later circadian phase in women than men.
Conclusion: This difference in entrained circadian phase in women may reflect a shorter circadian period and/or a decreased sensitivity to phase delaying light. Additional research is needed to determine the biological basis for this gender difference.
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0170

COMPARISON OF CIRCADIAN PHASE AND MID-SLEEP TIMES IN MORNING AND EVENING TYPES

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Introduction: The Horne-Östberg morningness-eveningness questionnaire (MEQ) has been used to study differences in physiologic and performance parameters in morning (M) and evening (E) types for over 30 years. The Munich Chronotype Questionnaire (MCTQ) is a newer questionnaire to determine chronotype, but there are fewer reports of physiologic measures from subjects taking the MCTQ. A key measure from the MCTQ is mid-sleep time on "work" days (MSW) vs. mid-sleep time on "free" days (MSF). The aim of the present study was to compare the timing of circadian rhythms, MSW, and MSF in M and E types identified by the MEQ.
Methods: Data from 100 healthy young adult subjects (18-34 yrs, mean 22.7±3.8; 37 F) who took part in a circadian rhythm study were included. During pre-study screening each subject completed the MEQ and indicated their bedtime and wake time on week days and weekends. While these subjects did not take the MCTQ, weekday and weekend sleep times were used to calculate MSW and MSF. Each subject's inpatient study had 3 baseline days followed by a constant routine where we assessed circadian phase of core body temperature nadir (CBT) and plasma dim light melatonin onset (DLMOn).

Results: Of the 100 subjects, there were 18 M types (9 females) and 13 E types (2 females) according to the MEQ. CBT and DLMOn phases were significantly earlier in the M than the E types (CBT: 04:32±1:35 vs. 07:00±1:12, $p<0.05$; DLMOn: 22:48±1:14 vs. 00:14±1:30, $p<0.05$). MSW and MSF were also significantly earlier in the M types than the E types (MSW: 03:25±0:54 vs. 04:42±1:29, $p<0.05$; MSF: 04:29±1:01 vs. 06:27±1:09, $p<0.05$).
Conclusion: The circadian phase results are consistent with prior reports from young adult M and E type subjects. While average phase was significantly earlier in the M types, there was overlap in the circadian phase measures between M and E types. There was also overlap between the M and E types in their mid-sleep times. Further study is needed to determine whether MSF is a better measure than MEQ score at identifying whether an individual is an extreme chronotype.
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0171

PER3 POLYMORPHISM, MOOD AND DELAYED SLEEP PHASE DISORDER

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Introduction: Alterations in circadian clock function have been implicated in sleep and mood disturbance. A variable number tandem repeat (VNTR) polymorphism in the coding region of the circadian clock gene PERIOD3 (PER3) has been reported to result in alterations in sleep structure, performance during sleep deprivation and to be associated with depression and circadian rhythm sleep disorders. The aim of the study is to examine the relationship between this PER3 polymorphism, mood and sleep quality in individuals with delayed sleep phase disorder (DSPD) and controls subjects.
Methods: 21 DSPD (mean age 30 years) and 12 control subjects (mean age 31 years) participated. Subjects were screened using interviews and questionnaires, including the Center for Epidemiological Studies depression scale (CES-D) and Pittsburgh sleep quality index (PSQI). Blood was drawn for determination of PER3 genotype by PCR. One way ANOVA and ANOVA with 2 factors, genotype (4/4, 4/5, 5/5 repeat) and group (DSPD, Control) were used for analysis.
Results: DSPD subjects had significantly higher CES-D (15 vs 3.4, $p<0.001$) and PSQI (7.5 vs 2.4, $p<0.0001$) scores compared to controls. There was no significant difference in genotype distribution between groups ($p=0.19$), 100% of 5/5, 55% or 4/4 and 60% of 4/5 were DSPD. For CES-D, significant main effects were seen for genotype ($p=0.03$) and group ($p=0.0005$), without significant interaction ($p=0.34$). CES-D scores tended to be higher for those with DSPD and for both the 4/4 and 5/5 repeats, as compared to the 4/5 repeat. For PSQI there was a significant group effect ($p<0.00001$) but no genotype effect ($p=0.13$) and no interaction ($p=0.29$).
Conclusion: The PER3 polymorphism is associated with depressive symptoms independent of a sleep disorder diagnosis or poor sleep quality. These data further support a role for alterations in circadian clock function in mood.
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0172

CIRCADIAN AND SLEEP-WAKE STATE DEPENDENT REGULATION OF HEART RATE IN HUMANS

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Introduction: Recent evidence suggests that a complex interaction between sleep and the endogenous circadian oscillator modulates heart rate (HR) in humans. Using an ultra-rapid sleep-wake cycle procedure (URSW), we investigated the effect of circadian and homeostatic processes on heart rate variability (HRV).
Methods: Five healthy participants (3 men, 2 women, mean age ± SD: 27.1 ± 3.2 years) were studied for 5 days in time isolation. After an 8-hour baseline sleep episode, participants underwent a 72-hour URSW consisting of 60-min waking episodes in dim light (<10 lux) alternating with 60-min nap episodes in total darkness. During the procedure, participants remained in a semi-recumbent posture and were served balanced iso-caloric snacks. HR was monitored continuously throughout the procedure. RR interval, high and low frequencies (HF, LF) and LF/HF ratio were calculated using wavelet transform. Data were binned per waking and napping episode then folded per day. Two-way ANOVA (factors: Time of day x Sleep-wake state; i.e. wake and nap episodes) was used to analyse HRV data.
Results: For all parameters analyzed, there was a significant main effect of sleep-wake state (RR, HF, LF/HF: $F(1,4)\geq 9.79$, $p<0.05$), and of time of day (RR, HF, LF/HF: $F(11,44)\geq 3.78$, $p<0.05$). However, none of these parameters showed a significant interaction of time of day and sleep-wake state.
Conclusion: HRV parameters have been shown to be affected by time of day and sleep-wake state. Naps promote parasympathetic modulation and reduction of HR, and this effect seems to be constant throughout the day. Sleep stages will be analyzed to further address the interaction between these factors on HRV.
Support (optional): This work was supported by the Canadian Institutes of Health Research (CIHR) and the National Sciences and Engineering Research Council of Canada (NSERC). P. Boudreau and D. B. Boivin are supported by IRSST and FRSQ, respectively.

0173

SLEEP, HEALTH, AND WORK OUTCOMES FOR SHIFT WORKERS: RESULTS FROM THE 2008 SLEEP IN AMERICA POLL

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Introduction: Of the 15% of U.S. workers employed in shift work (SW), 10% report symptoms of shift work sleep disorder (SWSD). Using results from the National Sleep Foundation's 2008 "Sleep in America" poll, we assessed differences on sleep-, health-, and work-related outcomes among SW, SWSD, and day workers (DW).
Methods: Data were obtained from the NSF's 2008 "Sleep in America" poll, which evaluated sleep-, health-, and work-related outcomes in a nationally-representative sample of 1000 U.S. workers. Participants reporting work start times between 1800 and 0600 hours were classified as SW. SW who reported symptoms of insomnia or excessive daytime sleepiness (ICSD-2 diagnostic criteria) were considered at-risk for

SWSD. Chi-square tests and logistic regressions (adjusted for age, gender, and BMI) were used to evaluate group differences.
Results: Seven percent of participants were classified as SW, and 21% of SW were at-risk for SWSD. Compared to DW, a larger percentage of SW reported sleeping less than 6 hours per night over the past two weeks (33% vs 15%, p=.001) and impairment due to sleepiness (21% vs 13%, p=.001). Odds of a work accident over the past year were 3x higher for SW (95% CI=1.27-6) and 4x higher for SWSD (CI=1.15-16.48) compared to DW. As compared to DW, the odds of drowsy driving at least once per month were 2x higher for SW (CI=1.28-3.61) and 4x higher for SWSD (CI=1.43-15.37). Relative to DW, SWSD participants were more likely to report current treatment for heart disease (p=.005), diabetes (p=.013), and GERD (p=.005). Relative to SW, SWSD participants were 26x more likely to report treatment of diabetes.
Conclusion: In this nationally representative sample of U.S. workers, SW reported sleeping less and more impairment due to sleepiness than DW, as well as an increased risk for work accidents and drowsy driving. SWSD was associated with several chronic health conditions.

0174

THE CIRCADIAN VARIATION IN SWIM PERFORMANCE IS NOT ALTERED BY THE TIME OF HABITUAL TRAINING

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Introduction: Some studies have reported better athletic performance at the usual time of training relative to other times of day. However, other studies have provided equivocal or negative results. The purpose of this study was to examine whether the circadian rhythm of swim performance differs between individuals who habitually train at a certain time(s) of day compared to those who do not.
Methods: 25 swimmers were assessed for 50-55 consecutive hr while adhering to a 3-hr ultra-short sleep/wake cycle. Swimmers performed 6 maximal 200-m swims, with each trial separated by 9 hr. Performances were z-transformed and expressed relative to time of day. Each swimmer's time of habitual training was obtained via pre-study questionnaire. Estimates of swim performance rhythm amplitude, acrophase, and mesor were obtained via cosinor analysis and compared between groups with independent sample t-tests. Group data were analyzed via ANCOVA with trial number as a covariate and time of day and habitual training time status as fixed factors.
Results: Twelve individuals reported no usual time of training. The half (n=13) with habitual swim times trained daily between 0600-0900 hr, 1600-1800 hr, or at both of these times. Those with a habitual time of training had lower mesors (i.e., faster swim time; p<0.001), but did not have different rhythm acrophases or amplitudes compared to those without a specific time of training. No between-group differences were found when analyzed via ANCOVA.
Conclusion: This study found minimal evidence of different swim performance rhythm characteristics between those who habitually trained at a particular time of day versus those who did not, nor for performance improvement at the time of training. However, the data do not discount the possibility that such an advantage might be observed via a non-circadian adaptation under usual diurnal conditions, due to variations in diet, sleep, rest, and performance preparation.

0175

THE MELANOCORTIN-3 RECEPTOR IS INVOLVED IN FOOD ENTRAINMENT OF SLEEP

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Introduction: Food availability has powerful influences on the timing of behaviors including sleep. Rodents display food anticipatory activity 1-2 h before the food is available in a restricted feeding (RF) schedule. The mechanism for food entrainment of sleep is not clearly understood. Melanocortins are known to regulate energy homeostasis through melanocortin receptors 3 and 4 (Mc3r, Mc4r) and sleep through unknown mechanisms. We hypothesized that Mc3r are involved in food entrainment of sleep.
Methods: WT mice (n=9) and melanocortin-3 receptor-deficient Mc3r-/- C57BL/6J mice (n=6) were implanted with EEG and EMG electrodes and maintained on a 12-12 h light-dark cycle with food and water available ad libitum. After recovery from surgery, baseline EEG and EMG were recorded for 24h. Food availability was then restricted by giving 2 grams of food from the 7th hour after light onset. The mice typically consume all available food within 2 h. EEG and EMG were recorded on the 4th day of RF.
Results: Baseline wakefulness (W), rapid eye movement sleep (REMS) and non-NREMS (NREMS) were not different between WT and Mc3r-/- mice. Both WT mice and Mc3r-/- mice showed increased W and decreased NREMS and REMS during a 2-h period after food presentation, and rebound of sleep during the subsequent dark period. WT mice but not Mc3r-/- mice displayed increased W [$F(11,88)=11.479$, $p<0.001$; $q(2,88)=6.902$, $p<0.001$] and decreased NREMS [$F(11,88)=10.255$, $p<0.001$; $q(2,88)=6.098$, $p<0.001$] 2 h before the food was available. REMS was reduced in WT mice during a 4-h period before food intake [$F(11,88)=13.338$, $p<0.001$; $q(2,88)=4.260$, $p=0.003$, 3-4 h before food; $q(2,88)=9.629$, $p<0.001$, 1-2 h before food intake] and in Mc3r-/- mice during a 2-h period before food intake [$F(11,55)=2.344$, $p<0.02$; $q(2,55)=3.019$, $p<0.05$].
Conclusion: These data indicate that food entrainment may influence W and NREMS through Mc3r-dependent mechanism, and REMS through both Mc3r-dependent and Mc3r-independent mechanisms.
Support (optional): This work was supported by the Pennington Biomedical Research Foundation (A.A.B) and NIH grant DK073189 to A.A.B, and NIH grant R41 HL084990-01 to J.F.

0176

DECLARATIVE MEMORY RECALL AND CIRCADIAN PHASE IN ADOLESCENTS: PRELIMINARY FINDINGS

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Introduction: Effects of sleep on memory consolidation have been a research focus; however, circadian phase has received limited study. Here we examine performance on a declarative memory task at different circadian phases in adolescents.
Methods: Ten participants (ages 10 to 16 yrs; 2 male) successfully performed a paired associates (6 pairs) word task during three 24-hr Cycles living on a 4-hr day (1.5 hr sleep). All recalled at least 2 pairs on more than one-third of trials. The first task occurred at 1630 on Cycle 1 after a short (5 hr) night of sleep. Immediate recall occurred 12 minutes after learning; delayed recall 4 hours later.
Results: Average time of Cycle 1 melatonin onset phase was 2122 (sd=24 min) and melatonin offset was 0721 (sd=25 min). Repeated mea-

sures ANOVAs were used to examine number of correct pairs recalled at 6 Times for each of 3 Cycles. Immediate recall showed no effect of Cycle ($F(2,18)=1.126$, $p=0.346$) but significant effects of Time ($F(5,45)=2.52$, $p=0.043$) and interaction of Cycle and Time ($F(10,90)=2.19$, $p=.025$). Analysis of Cycles 2 and 3, without Cycle 1, removed the interaction effect ($F<1$); Time remained significant ($F(5,45)=4.339$, $p=0.003$). For Cycles 2 and 3, immediate recall was best at 0830. Delayed recall showed no effect of Cycle ($F(2,18)=1.262$, $p>0.307$) or Time ($F(5,45)=1.82$, $p=0.406$) and a marginal interaction ($F(10,90)=1.822$, $p=.068$). Analysis of only Cycles 2 and 3 removed any interaction effect ($F<1$) and revealed a significant Time effect ($F(5,45)=2.542$, $p=0.041$). Delayed recall was best for the word list learned at 0830 (recalled at 1230).

Conclusion: We found best Immediate recall at 0830 at the start of the circadian day and best Delayed recall for word pairs learned at 0830. This finding indicates that caution should be used interpreting overnight learning if circadian phase is not controlled. Future analyses will examine effects of sleep.

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0177

EFFECTS OF SLEEP LOSS AND CIRCADIAN MISALIGNMENT ON PERFORMANCE AND ALERTNESS: A COMPARISON OF OBJECTIVE AND SUBJECTIVE MEASURES

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Introduction: Neurobehavioral performance and alertness are influenced by circadian and homeostatic processes. Whether different domains of performance and alertness are differentially affected by these processes has not been investigated systematically. This study assessed the wake-dependent and circadian effects on objective and subjective measures of performance, alertness and mood.

Methods: Nineteen healthy subjects (12 males) aged 18-29, underwent a 36 hour Constant Routine during which performance was assessed 24 times. Working memory and executive function were assessed through N-Backs and Paced Visual Serial Addition Task (PVSAT); sustained and selective attention through the Sustained Attention to Response Task (SART); visuomotor skill was quantified by a pursuit tracking task (PTT). Subjective alertness and mood were assessed by the Karolinska Sleepiness Scale (KSS) and by the Positive Affect Negative Affect Sale (PANAS). The data were analyzed by nonlinear regression analysis using PROC NLIN (SAS®) comprising a linear component modeling the wake-dependent process and a sinusoidal component modeling the circadian process.

Results: All aspects of performance, subjective alertness and negative affect deteriorated significantly during the CR. Estimates of both linear (homeostatic) and rhythmic (circadian) components were statistically significant ($P<0.05$) for all dependent variables except for positive affect. The nadir of performance measures, whether defined as the timing of the minimum in the raw data or the minimum of the fitted function, varied widely between measures. The earliest nadir was observed for the KSS at approximately 6 am and the latest nadir was located at approximately 10.30 am for the SART, with intermediate timings for other measures. The minimum of the subjective measures occurred three to five hours earlier than objective measures.

Conclusion: The findings confirm that many aspects of performance and alertness are modulated by circadian and homeostatic processes and suggest some dissociation between objective and subjective measures.

0178

THE INFLUENCE OF MORNINGNESS-EVENINGNESS ON LATENCY TO PERSISTENT SLEEP IN A MODEL OF TRANSIENT INSOMNIA

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Introduction: A series of studies have investigated self-reported Morningness-Eveningness and its association with scored sleep parameters. The current study evaluated a treatment for transient insomnia in a 5-hour phase advance model. A post hoc analysis examined whether a tendency toward morningness or eveningness would (1) predict latency to persistent sleep (LPS) among participants receiving placebo treatment, and (2) moderate the effect between treatments.

Methods: This was a multi-site, double-blind, randomized, parallel-group, sham-controlled trial carried out at 7 sites in the United States. The subjects were 282 healthy normal sleepers who were randomized to receive active or placebo treatment on a night where they underwent a 5-hour sleep phase advance. A subset of the population (n=162) completed the 19-item Morningness-Eveningness questionnaire (MEQ) rating their tendency to be a morning type (M), evening type (E), or intermediate (I). This subset was distributed as follows: M: 41.4%, I: 53.1%, E: 5.5%. A t-test compared morning to intermediate/evening types within the placebo population. An ANOVA model assessed the interaction between treatment and MEQ classification.

Results: Within placebo treated subjects, the LPS among intermediate/evening types was 20.1 ± 24.50 (mean ± SE) minutes greater than among morning types. Though this difference was not significant ($p=0.415$), it is comparable to other normals in phase-advance studies. Further, a nearly significant interaction was observed between the MEQ classification and treatment effect: The reduction in LPS tended to be greater for intermediate/evening types (-49.38 ± 18.29,) than for morning types (-17.5 ± 23.53) ($p=0.066$).

Conclusion: These results suggest that MEQ classification moderates response to treatment in a phase-advance model of transient insomnia. Inclusion of morning types in such models may dilute the observed treatment effect.

Support (optional): This study was funded by Respironics.

0179

THERAPEUTIC EFFICACY OF A MELATONIN AGONIST, RAMELTEON, AND A BENZODIAZEPINE, TRIAZOLAM, IN A MOUSE GENETIC MODEL OF ADVANCED SLEEP PHASE SYNDROME

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Introduction: We previously described the early runner variant of mice, a model of advanced sleep phase syndrome. The advanced phase of onset of these mice may be a self-reinforcing process, wherein wakefulness and locomotor activity during the latter portion of daily light phase of the LD cycle causes an advance of the circadian clock. If so, experimental manipulations that suppress waking and locomotor activity might be expected to delay the early onset of activity in these mice. Accordingly, we tested the hypothesis that timed daily administration of the melatonin agonist ramelteon normalizes the timing of daily wheel running rhythms in early runner mice.

Methods: The daily profiles of wheel running activity of these mice were assessed before, during and after timed daily administration of saline vehicle (p.o., n=12), ramelteon (10 mg/kg p.o., n=12), or triazolam

(1 mg/kg, p.o., n=12). The phase of onset of the daily wheel running rhythms was used as a measure of early morning awakenings.
Results: Early runner mice entrained to a light/dark cycle at an advanced phase, approximately 3 h before dark onset on average. Triazolam, but not ramelteon, suppressed wheel running acutely when administered prior to the time at which wheel running onset had occurred under baseline conditions. On a washout day under a light/dark cycle subsequent to one week of once daily administration, the onset of wheel running was delayed relative to baseline in both ramelteon-treated mice and triazolam-treated mice. In constant dark subsequent to a second week of daily administration, the onset of wheel running activity was not affected by either compound.
Conclusion: Ramelteon and triazolam caused a shift the timing of wheel running rhythms upon drug washout in an LD cycle. Only ramelteon did so without causing a profound suppression of wheel running. Both compounds were without long-term effects on the functioning of the circadian clock.
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0180

THE INFLUENCE OF LIGHT ON SLEEP ONSET AND ARCHITECTURE DURING DAYTIME SLEEP

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Introduction: Greater understanding of the effect of light and other sensory input on sleep could lead to breakthrough treatments for individuals with chronic or acute circadian disruption, or dysrhythmia related to shiftwork and jet lag. Daytime sleep, by necessity, often takes place under some light exposure. The effect of light during human sleep, however, has been almost completely ignored in scientific research. The present study focuses on ideal lighting conditions under which to nap to minimize sleep latency, increase sleep quality, and facilitate schedule adjustment. We hypothesized that more intense lighting during the nap would increase lighter sleep and inhibit SWS.
Methods: We examined the effect of four levels of green (495nm) light that approximate, in intensity, physiological darkness (0 lux), moonlight (1 lux), dim indoor lighting (80 lux) and bright light (6,400 lux) to determine the effect of constant light on sleep latency and architecture during daytime sleep. Participants slept for a period of 90 minutes in each condition wearing light masks with green LEDs, and napped at consistent times and days of the week for four weeks. Light conditions were counterbalanced across weeks. Actigraphy was monitored throughout to ensure the participants were not sleep deprived.
Results: Light exposure during sleep resulted in a mean reduction in Stage 2 sleep of approximately 20%, and a mean increase in SWS of approximately 23%, across conditions. Exposure to the light did not reduce total sleep time or efficiency, and participants were able to achieve both REM and SWS even under the brightest condition.
Conclusion: The data suggest that light has an unexpected effect on daytime sleep architecture. Specifically, more intense lighting conditions increased deep sleep and decreased lighter sleep. The implications of this extend from those who nap habitually to alleviate the symptoms of dysrhythmia to any individual who sleeps during daylight hours.

0181

SLEEP DURING PHASE RESTRICTED FEEDING IN C57BL/6 MICE

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Introduction: Recently we discovered that feeding a 60% high fat diet only during the 12 hour light phase caused a significantly greater weight gain in C57BL/6 (B6) mice than feeding only during the dark phase. Here we examine sleep during a similar phase restricted feeding (PRF), however using a regular chow diet. Due to the interconnectivity of sleep, circadian timing and metabolism, and evidence supporting sleep deprivation contributing to weight gain, it is necessary to assess sleep disturbance during PRF.
Methods: Six-week old male B6 mice (N=27) underwent 5 weeks of PRF. Mice were equally divided into three groups: ad libitum (ADLIB), where regular chow food was provided ad libitum in both the light and dark phase, dark-fed (DARK), where regular chow was only provided during the 12 hour dark phase, and light-fed (LIGHT), where regular chow was only provided during the 12 hour light phase. During the fifth week, sleep was recorded for 48 hours. Body weights were monitored twice a week, food intake once a week and locomotor activity was measured continuously during the fifth week.
Results: Using regular chow instead of high fat significantly impacted body weight. The LIGHT group was significantly lighter than the DARK group ($p < 0.05$) and only began to match the DARK groups' weight 4 weeks into the diet. This is most likely due to the sudden introduction of the diet. However, food intake was similar beginning week 2 of the diet ($p = 0.92$). Preliminary sleep and locomotor data suggest that the LIGHT group slept more than the DARK or ADLIB group in the dark phase.
Conclusion: These data indicate phase restricted feeding as both a metabolic and a sleep disturbance protocol.
Support (optional): This research was supported by NIA-PPG Grant P01 AG 11412 and NIH/NHLBI Grant T32 HL007909.

0182

DIURNAL CHRONOTYPE VARIABILITY IN SHORT TIME PRODUCTION AND GENERAL ACTIVATION

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Introduction: Internal timing is crucial for human activities. Its accuracy may depend upon unknown weightings between the interactions of biological circadian and sleepiness factors with psychological mood changes.
Methods: Ten Evening-type (ET) and 10 Morning-type (MT) chronotypes, selected by MEQ and BALM scale scores, completed five equally-spaced test sessions across the day beginning and ending within one hour of subjects' usual bed and wake times. At each session responses to computerized time production, PAB Mood Scale, and Stanford Sleepiness Scale (SSS) tasks were recorded. Subjects were asked to produce time intervals of 13, 27, 43, and 57 seconds, each repeated five times randomly.
Results: Repeated measures ANOVA results indicated that when compared with MTs the ETs had increased mean overproduction (perceived slower time) for 13- and 27-sec intervals with means = 13.19 ($p=.024$) and 27.71 ($p=.004$), respectively. Similar diurnal sleepiness (SSS) changes were found for both chronotypes ($p=.003$) who were most alert around five hours after waking. Fatigue subscale profiles differed for chronotypes ($p=.009$), linearly increasing for MTs across the day, but for ETs highest during the first hour after waking, while lowest for MTs at that time ($p<.020$). Although slight, the active and happy subscales scores of MTs decreased from session 1 to 5, while for ETs they peaked around six hours after awakening. Mood subscale scores for alleged depression, fear, and anger showed no diurnal or chronotype effects. However, lower anger scores (perhaps lower frustration) correlated with higher overproduction for 27-, 43-, and 57-sec intervals ($p<.05$). The 57-sec interval at session 4 particularly was influenced by mood, with lower depression, anger, and fatigue, and higher happy subscale scores associated with greater overproduction.
Conclusion: Biological chronotype status appears to influence shorter interval productions while for longer interval productions psychological mood appears the more prominent influence.

0183

DIURNAL RHYTHMS OF HIGH MOLECULAR WEIGHT ADIPONECTIN AND LIPOCALIN-2 IN MEN UNDER FED AND FASTED CONDITIONS

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Introduction: The adipocyte hormone adiponectin is negatively associated with obesity and stimulates insulin sensitivity, which makes it of potential therapeutic interest. Conversely, lipocalin-2 has been proposed to be positively associated with obesity and to inhibit insulin sensitivity. Considering the epidemiological and experimental association between sleep duration and glucose metabolism, we assessed effects of the sleep/wake cycle and the fasting/feeding cycle on the active form of adiponectin (high molecular weight adiponectin, HMWA) and lipocalin-2.
Methods: Ten lean men underwent a 3-day study, either fed (n=8, age: 20.9±2.1 years, BMI: 22.8±2.3 kg/m2) or fasted (72-h fast, n=4, 25.3±3.9 years, 23.3±2.2 kg/m2). Two subjects participated in both studies. Subjects were scheduled to sleep between 23:00 and 07:00. Blood was sampled every 15 min during sleep and wake on the third day. Data were grouped in 30-min bins, expressed as percentage of each individual's mean and analyzed with Mixed Model ANOVA.
Results: During fed conditions, HMWA and lipocalin-2 had significant daily rhythms with a trough in the middle of the sleep episode and, for HMWA, with a clear rise preceding scheduled awakening by several hours (HMWA: trough ~04:00, peak-to-trough amplitude 36%; lipocalin-2: ~04:00, 40%). Remarkably, following a 3-day fast, the phase and amplitude of the daily rhythms in HMWA and lipocalin-2 were almost identical (HMWA: trough ~04:00, peak-to-trough amplitude 38%; lipocalin-2: ~05:00, 38%).
Conclusion: These data demonstrate significant diurnal variations in both HMWA and lipocalin-2 that are not caused by the fasting/feeding cycle. Future studies are required to investigate whether other behavioral factors or the endogenous circadian system causes these rhythms, which may play a role in energy homeostasis and insulin sensitivity, especially in shiftworkers.
Support (optional): NIH-K24 HL076446 in support of SAS; NIH-R21 AT002713 in support of FAJLS

0184

MEDIATIONAL EFFECT OF SLEEP QUALITY IN THE RELATIONSHIP BETWEEN CIRCADIAN SLEEP PHASE PREFERENCE AND DEPRESSIVE MOOD

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Introduction: Circadian sleep phase preference(Morningness-Eveningness) has been found to be associated with depression in many studies. However, we could not find any studies which explored the relationship between M-E and depression with sleep variables controlled. The present study explored the effect of sleep quality as a potential mediator in the association between circadian sleep phase preference and depressive mood.
Methods: 898 Korean college students(441 male; mean age of 21.04) completed PSQI(Pittsburgh Sleep Quality Index:Chronbach's α=.623), CES-D(Center for Epidemiologic Studies Depression Scale;Chronbach's α=.897), CSM(Composite Scale of Morningness;Chronbach's α=.845). Data was analyzed using structural equation modeling with AMOS 16.0, and a bootstrapping method(n=500) was conducted to estimate indirect effect.
Results: In the study model, sleep quality was tested as a mediator in the relationship between morningness and depression. In the original, unmediated model, the direct path from morningness to depression(total effect: C) was estimated to be β = -.365($p<.001$). In the mediational model, indices of the model fit were CFI=.936, TLI=.912, RMSEA=.063. Morningness was negatively and significantly linked to sleep quality(path a: β = -.454, $p<001$). Sleep quality was positively and significantly linked to depression (path b: β = .586, $p<.001$), and the direct effect of morningness on depression was also significant (path c': β = -.100, p=.015). And, the result of bootstrap showed that the indirect effect(a*b) was β = -.266, and confidence interval at 95% did not include zero (upper limit= -.144, lower limit=-.274), suggesting significant mediating effect of sleep quality. The present results show that sleep quality had partial mediating effect on the association between morningness and depression.
Conclusion: The present study provides a strong support for the mediational effect of sleep quality on the relationship between circadian sleep phase preference and depression. It indicates that evening type people's (E-types') lower sleep quality leads to more depressive mood. Furthermore, the present results also show that the mediational effect of sleep quality is partial. It needs to be explored in further detail whether and how the other possible mediational variables might be involved in the relationship between circadian sleep phase preference and depressive mood.
Support (optional): This research was supported by a grant from POSTECH Basic Science Research Institute.

0185

HYPERTENSION AND OSA IN CHILDREN

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Introduction: It has been well established that Obstructive Sleep Apnea (OSA) causes increased mortality and significant cardiovascular complications in adults. There are mixed reports regarding the prevalence of hypertension in children with OSA, in part due to methodological differences and mixed study populations. We performed echocardiography and 24-hour ambulatory blood pressure monitoring in otherwise healthy children with polysomnographic-proven OSA.
Methods: A prospective, cohort study design was performed on a group of consecutive, otherwise healthy children aged greater than four years, with polysomnography-proven OSA (apnea hypopnea index > 1.5 per hour). Echocardiography was performed on all subjects and left ventricular mass was calculated. Study subjects underwent additional investigation with 24-hour ambulatory blood pressure monitoring.
Results: 30 children (21 males) were studied. Mean age was 8.9 years (Range 4.5 - 15.5 years). Mean BMI was 19.87 (range 13.60-44.1). Only one child was obese. Mean apnea-hypopnea index was 14.3 per hour (range 1.5-125.2). 10/30 (33%) of the study population met criteria for pre-hypertension (n=3) or masked hypertension (n=7) based on standard ambulatory monitoring criteria. All 10 children had systolic hypertension throughout the night with 5/11 also having high daytime systolic readings. Only 2 of the 10 had elevated nocturnal diastolic readings. Two children had evidence of white coat hypertension only. There were no subjects with left ventricular hypertrophy and/or right ventricular hypertrophy.
Conclusion: There is a high prevalence of pre-hypertension and/or masked hypertension in otherwise healthy, non-obese children with OSA which is unlikely to be identified using standard office/clinic protocols which limit BP recordings to daytime, awake readings.
Support (optional): Alberta Children's Hospital Foundation

0186

OBSTRUCTIVE SLEEP APNEA (OSA) EXACERBATES ENDOTHELIAL DYSFUNCTION IN BOTH OBESE AND NON-OBESE CHILDREN

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Introduction: Obesity has recently emerged as a major risk factor of OSA in children, and both OSA and obesity are believed to impose adverse cardiovascular consequences, including endothelial dysfunction. However, the individual and joint effect of OSA and obesity on endothelial function has not been critically examined in a pediatric population.
Methods: Consecutive pre-pubertal non-hypertensive children participating in research sleep studies were recruited. Endothelial function was assessed in a morning fasting state, using a modified hyperemic test involving cuff-induced occlusion of the radial and ulnar arteries. The presence of OSA was determined by overnight polysomnograghy. All children had anthropometry performed and serum lipid and metabolic profiles determined.
Results: In total, 158 children (mean age 8.2±1.7 years), of which 89 (56%) were obese with a body mass index exceeding the 95th percentile. 50 children (32%) were determined by polysomnography to have OSA with an obstructive AHI>2 /hrTST. In general, obese children had significantly longer delays in peak capillary reperfusion post occlusion compared to non-obese children (46.3±18.2 sec vs. 32.8±13.1 sec, $p<0.01$). Similarly, OSA was associated with prolonged latencies to peak capillary reperfusion in both obese children (55.6±24.4 sec) and non-obese children children (49.03±33.9 sec, $p<0.05$). However, at any level of OSA severity, obese children had longer reperfusion times compared to non-obese children
Conclusion: OSA and obesity independently lead to disturbed vascular endothelial function in children. It is likely that OSA may further potentiate the magnitude of endothelial dysfunction in obese children through shared atherogenic pathways.
Support (optional): Supported by Jazz Pharmaceuticals Fellowship and NIH grant HL-65270.

0187

SUBTLE MEMORY IMPAIRMENTS IN OSA CHILDREN

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Introduction: Limbic structures such as amygdala, hippocampus, and cingulate gyrus underlie aspects of emotion, memory, and autonomic functions, and are adversely affected by OSA. However pediatric memory (M) impairments are often secondary, and associated with executive (AE), language (L) and visuospatial (VS) dysfunction, which further compromise encoding, consolidation, storage and retrieval. Thus, memory underperformance might be exacerbated when increased levels of processing are required.
Methods: After NPSG, memory and learning abilities (M) were assessed with NEPSY: memory for face (MF) and names (MN), sentence repetition (SR) and narrative memory (NM). 5- to 9-year-old children (6.6±0.51yr; 57.3% boys; 76.4% Caucasian; 20.8% African American; DAS-GCA≥85) who were either healthy (n= 43, OAHI≤2, snore never to rarely, low SaO2>90, arousal index TST <20, NPSG TST ≥7hr, full-term, within normal range L, VS and AE scores) or had OSA (OAHI>2, snore ≥3x/week);i.e., OSA without L, VS, AE (OSA^-, n= 22, OAHI: 5.5 ±2.8/hrTST) and OSA with L (n=6), VS (n=1), AE (n=3) (OSA^+, n=10, OAHI: 5.75± 2.07; 2.93-8.79).
Results: No age, gender, BMIz and ethnicity differences emerged between groups. Likewise for confounders: parental education & smoking, gestation period, child vision/hearing, snoring of father, but snoring of mother was more prevalent in the OSA+ [Chi-square(2)=14.6, p=0.00068]. NEPSY revealed no gross memory problems in OSA; however supplemental score analyses suggested subtle memory impairments. Over the 3 learning trials of cross-modal association learning of name with face, the OSA^- improved performance gradually whereas the OSA^+ failed to progress. Also, OSA^+ tended to benefit from verbal cues when recalling a story. No within-group differences between immediate and delayed MF and MN were apparent.
Conclusion: Refined memory processing analyses suggest slower information processing, and/or secondary memory problems, in the absence of retrieval or recall impairments. These findings suggest impaired integrity of myelination (with or without structural damage to interconnected limbic structures) leading to reduced neuropsychological performance of OSA children.
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0188

LONGITUDINAL MEASUREMENTS DEMONSTRATE DIFFERENT MATURATIONAL PATTERNS OF NREM DELTA AND NREM THETA EEG

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Introduction: Longitudinal studies can reveal maturational patterns not apparent in cross-sectional data. We studied longitudinally the maturational declines in NREM delta (1-4 Hz) and theta (4-8 Hz) EEG power. Both frequencies behave homeostatically and have been shown, in cross-sectional studies, to decline with age.
Methods: Using ambulatory (home) recorders, sleep EEG was recorded semi-annually for 5 years in 2 overlapping age cohorts. Cohort C9 (n=27)

began the study at age 9 years, and cohort C12 (n=32) began at age 12 years. EEG data were scored visually and analyzed with FFT. Data from a 6 year old cohort's (n=28) first recording was also analyzed.
Results: Between ages 9 and 11 years, NREM Delta power did not change (p=0.59), but NREM theta power declined by 11% (p=0.0006). After age 11 years, both delta and theta power declined steeply (by 66% and 60% respectively) and significantly (p<0.000001) until age 16.5 years when the rates of decline slowed. Comparing the first recordings from C6 and C9 shows no change between 6.1 and 9.3 yrs in delta power but a 27% decrease in theta power (p=0.01).
Conclusion: We have previously hypothesized that the adolescent declines of delta and theta reflect a late brain maturation driven by synaptic pruning. The later decline in delta power, compared to the decline in theta power, likely represents a later maturation of the brain structures or circuits responsible for delta EEG oscillations. These different EEG maturational trends might be related to recent longitudinal MRI findings showing different maturational patterns in the thickness of allocortical and isocortical brain structures. Our data show that adolescent maturation proceeds at a high rate across ages 11 to 16.5 yrs for both theta and delta, indicating that these years are crucial for the aspects of brain maturation reflected in these EEG frequencies.
Support (optional): Public Health Services grant R01 MH62521 supported this work.

0189

IMPACT OF SUPPLEMENTAL MELATONIN ON SLEEP AND BEHAVIOR IN CHILDREN WITH AUTISM SPECTRUM DISORDERS

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Introduction: We describe a prospective dose-response trial of supplemental melatonin in children with ASD. Our objectives are: (1) To identify optimal dose, tolerability, and adverse effects and (2) To study the impact of supplemental melatonin on sleep and daytime behavior.
Methods: We included children ages 4-10 years with a clinical diagnosis of ASD, confirmed by the Autism Diagnostic Observation Schedule and Autism Diagnostic Interview-Revised, who took 30 minutes or longer to fall asleep on 3 out of 7 nights per week. Parents completed sleep and behavioral survey forms at the beginning and again at the conclusion of all study procedures and children wore actigraphy watches (Mini Mitter, Respironics) for 17 weeks. After three weeks of baseline actigraphy, melatonin (Natrol ®) dosing was begun at 1 mg, and escalated every three weeks, to 3mg, 6mg, and 9 mg, until the child achieved a "satisfactory response," defined as falling asleep within 30 minutes of bedtime on 5 out of 7 nights per week. Baseline and treatment survey and actigraphy measures were compared using a Wilcoxon signed-ranks test.
Results: Ten children completed the study; all tolerated melatonin without adverse effects at relatively low doses—3 at 1 mg, 5 at 3 mg, 2 at 6 mg and none requiring 9 mg. Sleep latency decreased from 38.7(22.5) minutes (mean (SD)) to 21.8(7.9) minutes (p = 0.039) with treatment. Treatment improvements were noted in the Children's Sleep Habits Questionnaire domains of sleep onset delay (p = 0.008) and sleep duration (p = 0.004), repetitive behavior scale domains of compulsive (p = 0.002) and ritualistic (p = 0.004) behavior, and Parent Interview for Autism domain of affective responses (p = 0.02).
Conclusion: Low-dose melatonin is a well-tolerated treatment for insomnia in children with ASD, and appears to impact favorably on both sleep and daytime behavior. Randomized clinical trials appear warranted.
Support (optional): Autism Speaks/Dana Foundation NICHD 1R01HD059253 Vanderbilt CTSA grant 1 UL1 RR024975 from NCRR/NIH

0190

THE SYNERGISTIC EFFECTS OF IMPAIRED AUTONOMIC MODULATION AND SLEEP-DISORDERED BREATHING ON BLOOD PRESSURE IN CHILDREN

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Introduction: Sleep-disordered-breathing (SDB) is associated with elevated blood pressure (BP) and impaired cardiac autonomic modulation (CAM) in adults. Data from population-based children are very limited. We examined the inter-relationship between SDB, BP, and CAM in a population-based sample of 612 grade K-5 children randomly selected from Harrisburg, PA - the Penn State Child Cohort.
Methods: All participants underwent a one-night polysomnography (PSG) recording in our sleep laboratory. SDB was defined, by the hourly average Apnea Hyponea Index (AHI) from the PSG, as "no-SDB" if AHI is < 1, "mild-SDB" if 1 < AHI < 5, and "moderate-SDB" if AHI ≥ 5. CAM was measured by heart rate variability (HRV) analysis of 8-hour beat-to-beat RR data collected during PSG. Demographic, BP, and anthropometric measures were obtained from a standardized clinical examination. The HRV indices included time (SDNN, RMSSD, and HR) and log-transformed frequency (log-HF, log-LF, and LF/HF) domains.
Results: The mean (SD) age was 111 (21) months, with 49% male and 25% non-white. After adjusting for age, sex, race, BMI, REM sleep, sleep efficiency and snore, SDB was significantly associated with both BP and HRV. Compared to no-SDB group, mild- and moderate-SDB groups have 1.78 and 16.28 mmHg higher SBP, respectively. The interactions between AHI and HRV indices in relationship to SBP were significant (p<0.05) in the direction that higher AHI is associated with higher SBP at all levels of HRV indices, but the association was more pronounced among persons with impaired HRV profiles. For example, one (1) unit increase in AHI is associated with 2.00, 1.20, and 0.50 mmHg increases in SBP among persons with lowest HRV-HF (around 10th percentile), the median HRV-HF, and highest HRV-HF (around 90th percentile), respectively.
Conclusion: In children, SDB is associated with both impaired CAM and higher BP. Moreover, impaired CAM greatly enhanced the SDB effects on BP.
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0191

ADIPOCYTE FATTY ACID BINDING PROTEIN 4 (FABP4) POLYMORPHISMS, GENE EXPRESSION, AND MORNING PLASMA LEVELS IN CHILDREN WITH AND WITHOUT OBSTRUCTIVE SLEEP APNEA (OSA)

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Introduction: Children with either OSA or obesity exhibit endothelial dysfunction, and are at risk for accelerated atherogenesis and the metabolic syndrome. FABP4 plays a critical role in both atherosclerosis and insulin homeostasis. FABP4 expression is regulated by intermittent hypoxia, and inhibition of FABP4 effectively reduces atherosclerotic lesion formation, and increases insulin sensitivity.
Methods: Six SNPs of the human FABP4 gene (rs1051231, rs13269251, rs2305319, rs16909233 rs1690213, and rs1054135), corresponding to several critical regions of the encoding FABP4 gene sequence were used to genotype children with OSA or matched controls. BMI z score was also assessed, and z>1.65 was used as obesity criterion. FABP4 gene and protein expression were also assessed in fasting morning blood samples

using RT-PCR and ELISA. Linkage disequilibrium was analyzed for the 6 SNPs using Haploview version 4.0 software.
Results: Thus far, 178 children (4-10 years of age) have completed the study. Obese children and children with OSA had significantly higher FABP4 levels than corresponding controls ($p<0.01$). FABP4 mRNA expression was reduced in OSA, but was increased in obese children without OSA compared to non-obese controls. Of the 6 FABP4 SNPs, the rs1054135 polymorphism showed significantly higher frequency among OSA children ($p<0.02$), as well as among obese children ($p<0.01$), and was associated with higher FABP4 plasma levels.
Conclusion: Increased plasma FABP4 concentrations are associated with obesity and OSA in children. Specific FABP4 gene polymorphisms appear to be important determinants of resultant FABP4 plasma levels in the context of either obesity or OSA, and may potentially modulate FABP4-associated cardiovascular and metabolic morbidities. Assessment of FABP4 expression and genomic variation may assist in categorical risk assessment of end-organ morbidities associated with either obesity or OSA in children.
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0192

COGNITIVE DEFICITS IN CHILDREN WITH OBSTRUCTIVE SLEEP APNEA (OSA) AND APOLIPOPROTEIN E (APOE) SINGLE NUCLEOTIDE POLYMORPHISMS

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Introduction: Several studies have reported an association between OSA and the chromosomal region containing the ApoE gene. Furthermore, the ApoE4 allele is associated with increased cognitive vulnerability in children with OSA (Gozal et al., Neurology 2007;69(3):243.). In a recent study, several polymorphisms involving more than one locus in the ApoE gene and its regulatory region were associated with OSA in children (Kalra M, et al., Sleep Med 2008;9(3):260.). We hypothesized that some of the polymorphisms that exhibit reduced ApoE biological activity may account for neurocognitive susceptibility in pediatric OSA.
Methods: Seven SNPs of the human ApoE gene (rs405509, rs769452, rs12982192, rs429358, rs7412, rs28931579, rs157580), corresponding to several critical regions of the encoding sequence of the ApoE gene were used to genotype 116 children with OSA (47 with neurocognitive deficits (NC+) and 69 age-, gender-, ethnicity-, OAHI-, BMI-, and maternal education-matched children without cognitive deficits (NC-). Linkage disequilibrium was analyzed for the 7 SNPs. All samples were genotyped using a polymerase chain reaction system with pre-developed TaqMan allelic discrimination assay. The Haploview version 4.0 software was used to analyze the linkage disequilibrium structure, calculating D' to define haplotype blocks and to estimate haplotype frequencies.
Results: For the 2 sub-groups NC+ and NC-, mean age was 6.1 years, 50% were males, 30% were AA, 22% were obese, and their mean obstructive AHI was 14.7/hrTST. Of the 7 ApoE gene polymorphisms tested in this highly matched cohort, significant differences emerged in the frequency of rs405509 with (NC+>NC-; $p<0.04$) and rs7412 (NC->NC+; $p<0.02$).
Conclusion: Two previously identified ApoE polymorphisms that associate with OSA in children may underlie individual susceptibility components to the occurrence of neurocognitive deficits in the context of pediatric OSA. These findings may allow for improved prediction of which children are at increased risk for end-organ morbidity.
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0193

SLEEP IN CHILDREN WITH ATTENTION DEFICIT DISORDERS: EFFECTS OF COMORBID ANXIETY AND RESPONSE TO TREATMENT

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Introduction: Children with Attention Deficit Hyperactivity Disorder (ADHD) are reported to present more sleep difficulties than children from non clinical population but such differences could partly be accounted for by comorbid anxiety (Mick et al., 2000). The first goal of the present study was to further examine the impact of comorbid anxiety on sleep difficulties in children with ADHD. The second goal was to measure the effect of a cognitive-behavioral therapy (CBT) on sleep quality.
Methods: Forty-five children (37 boys, 8 girls) aged between 8 and 12 years were diagnosed by a semistructured diagnostic interview to form three groups (19 with ADHD, 17 with ADHD plus anxiety, and 9 Controls). Parents completed the Child Sleep Habits Questionnaire (CSHQ). Sleep measure in children with ADHD and anxiety was taken again after a 10-session cognitive-behavioral therapy program for anxiety.
Results: The ADHD children with comorbid anxiety presented more difficulties than the two other groups on the two global scales of the CSHQ, i.e., total disturbance score ($p < 0.01$) and total item problems ($p < 0.01$), and on three subscales: sleep onset delay ($p < 0.01$), sleep anxiety ($p < 0.01$), and daytime sleepiness ($p < 0.01$). The ADHD group without comorbid anxiety was different from the control group only on delayed sleep onset ($p < 0.01$). In ADHD children with comorbid anxiety, CBT reduced sleep onset delay ($p < 0.05$) and improved marginally the total disturbance score ($p < 0.07$).
Conclusion: Comorbid anxiety appears to increase sleep difficulties in children with ADHD and is sensitive to a CBT program specifically aimed at reducing anxiety.
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0194

SLEEP PATTERNS, EATING HABITS AND ELECTRONIC MEDIA EXPOSURE AMONG ADOLESCENTS

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Introduction: Poor health behaviors in adolescents, including poor eating habits, poor sleep patterns, and excessive use of the electronic media, constitute major public health problems in Westernized cultures. The aim of the current study was to assess the associations between these health behaviors.
Methods: Healthy, middle school Israeli adolescents, 224 males and 220 females, mean age 14±0.8 years, completed questionnaires regarding sleep-wake patterns, media exposure (television, computer) and eating habits.
Results: All participants had a TV and a computer in their homes, 59% and 60% had a TV/computer in their bedroom. Later sleep onset and less total sleep time were significantly associated with more total TV time ($r=.21$, $r=.16$), more evening TV ($r=.23$, $r=0.19$) and more time on the internet ($r=0.24$, $r=.19$) respectively ($p<0.01$). Participants with a TV in the bedroom had longer viewing hours (3.08±2.27 vs.2.15±1.65;

p<0.001), later sleep onset (23.17±0.9 vs. 22.80±0.9; p<0.001); and shorter night sleep (7.2±1.1 vs. 7.65±1.12; P<0.001) compared to those without a bedroom TV. Likewise, participants who had a computer in their bedroom showed longer internet use (2.7±2.4 vs. 2.01±2.0; p<0.001), later sleep onset (23.11±0.93 vs. 22.89±0.90; p<0.013) and shorter night sleep (7.29±1.17 vs. 7.52±1.03; p<0.04) compared to those without a bedroom computer. Furthermore, about 20% of the students reported that they regularly eat and 70% reported that they sometimes eat while watching TV; and 8% reported that they regularly eat and 40% reported that they sometimes eat while using the computer.

Conclusion: Electronic media exposure is highly prevalent in adolescents, and is associated with reduced sleep time. The presence of a TV/computer in the bedroom is associated with increased exposure and more disrupted sleep patterns. Furthermore, electronic media exposure is related to poor eating habits. These findings, although preliminary, highlight the need for an intervention promoting changes in these health behaviors in adolescents.

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0195

OBESITY IN CHILDREN IS ASSOCIATED WITH SUBJECTIVE BUT NOT OBJECTIVE SHORT SLEEP DURATION IN A REPRESENTATIVE POPULATION SAMPLE

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Introduction: It has been reported in many studies that in children as in adults obesity is associated with short sleep duration. In these published studies sleep duration was based on self-report (adults) or parent report (children). There is mounting evidence that in adults the self-reported estimate of sleep duration is significantly associated with many non-sleep issues including: age; lifestyle; SES; sleep complaint; and stress. To address the complex association between subjective and objective sleep duration and obesity, we performed this study using data from a representative population sample of young children.

Methods: A random sample of local elementary school children (K-5) was assessed using a two-phased strategy. Phase I was a brief questionnaire completed by a parent of all of the children in a specified elementary school (N=5,740) with a response rate of 78.5%. Phase II randomly selected children and a parent to spend a night in our sleep laboratory (N=700) with a response rate of 70.0%.

Results: In this sample 33.0% were considered obese (BMI≥85th percentile) and 52% were girls. As previously reported the subjective estimate of sleep duration based on the parent report indicated a reduced duration associated with obesity (P=0.009). This reduced sleep duration was observed primarily in boys (P=0.006) but not in girls (P=0.278) and remained significant when adjusted for age and SDB. In contrast, the association of sleep efficiency with obesity based on the PSG data was not significant (P=0.089).

Conclusion: These findings suggest that, similar to adults, the subjective estimate of sleep duration based on parent report of their child's sleep may not be that reflective of actual sleep but may be more of a marker of other dimensions within the family structure including parent-child interaction.

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0196

SLEEP-DISORDERED-BREATHING IS A RISK FACTOR FOR COMMUNITY ACQUIRED PNEUMONIA IN CHILDREN

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Introduction: Children with obstructive sleep apnea (OSA) experience significantly more lower and upper respiratory infections during early childhood. We aimed to assess the prevalence of sleep disordered breathing (SDB) in children with community acquired alveolar pneumonia (CAAP) as compared to frequency matched controls.

Methods: A prospective population based case-control study assessing children < 5 years with CAAP presenting to a Pediatric Emergency Room during a 24 months period (2006-8). Children were included if they were diagnosed based on WHO criteria following X-ray interpretation by a pediatrician and a pediatric radiologist independently. Controls were frequency matched healthy children admitted with non infectious etiology. Symptoms of SDB were documented using a structured questionnaire. A comparison was also made between the CAAP study database and the sleep lab database for children <5 years of age.

Results: 1546 children with CAAP (58% boys) and 441 controls (54% boys) were prospectively enrolled. Frequent snoring (≥ 2 nights/week) was reported in 18.6% vs. 2.9%; CAAP vs. controls respectively, p<0.0001. Movements during sleep were reported in 21.6% vs. 5.3% p<0.0001; respiratory problems during sleep reported in 5% vs. 1.4% p<0.0001; daytime abnormal behavior in 6.4% vs. 0.2%; p<0.001 and chronic rhinorrhea in 12.9% vs. 1.8%; p<0.0001. 50 (3.3%) of the children with CAAP vs. 3 (0.7%) of the controls previously underwent adenoidectomy; p<0.0001. 79 (5%) of the children with CAAP vs. 6 (1.3%) of the controls had had a previous polysomnographic evaluation diagnosing OSA; p<0.0001. Calculated odds ratio was 3.70 (1.61-10.0), P=0.001.

Conclusion: Sleep disordered breathing is more common and is diagnosed prior to, and more frequently in children diagnosed with CAAP. SDB is a predisposing risk for CAAP in children younger then 5 years of age.

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0197

PREVALENCE OF SLEEP DISORDERS IN PEDIATRIC PRIMARY CARE PRACTICE

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Introduction: Sleep problems are highly prevalent in children, however little research has been done on the recognition of ICD-9 sleep disorders in pediatric practice. The purpose of this study was to examine the diagnosis rate of sleep disorders by pediatricians in a large primary care network.

Methods: A chart review was conducted for all well-child visits between January 1 and December 31, 2007 at primary care pediatric practices affiliated with the Children's Hospital of Philadelphia (32 practices, 154,957 patients). Information was collected on new and existing sleep related diagnoses. Patients were 51% male, 57% white, 26% black, and ranged in age from 0 to 18 years.

Results: Overall, only 4% (n=6581) of patients had an ICD-9 diagnosis for a sleep disorder. Diagnoses were combined into groupings, with the following overall diagnoses rates: insomnia (0.5%), hypersomnia

(0.001%), parasomnias (0.06%), RLS/PLMD (0.02%), sleep disordered breathing (SDB, 1.03%), infant apnea (0.22%), enuresis (1.17%), bruxism (0.004%), circadian rhythm (0.005%), narcolepsy (0.002%), and sleep disorders NOS (SD-NOS, 1.46%). For infants (0-12 months) SD-NOS was the most common group of diagnoses (n=339,1.4%) followed by infant apnea (n=209, 0.9%). In toddlers (12-36 months) SD-NOS was the most frequent group of diagnoses (n=861, 2.4%) followed by SDB (n=466, 1.3%). Similar rates of diagnoses for sleep disordered breathing (n=360, 1.7%), SD-NOS (n=349, 1.6%) and enuresis (n=282, 1.3%) were found for preschoolers (4-5 years). School-aged children (6-12 years) were most commonly diagnosed with enuresis (n=1350, 2.6%), followed by SD-NOS (n=598, 1.2%) and SDB (n=593, 1.1%). Finally, adolescents (13-18 years) were most commonly diagnosed with enuresis (n=265, 0.9%) and SD-NOS (n=246, 0.9%).

Conclusion: This study is one of the first to examine ICD-9 sleep diagnoses given by primary care pediatricians in a large representative sample of children ages 0-18 years. The 4% of patients given an ICD-9 sleep diagnosis is significantly lower than prevalence rates reported in epidemiological studies. This suggests that primary care pediatricians may be under-diagnosing sleep disorders in children and adolescents. As sleep disorders are treatable when recognized, the results from this study suggest a significant need to provide education and support to pediatricians in the diagnosis and treatment of pediatric sleep disorders.

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0198

HIGH PREVALENCE OF OBSTRUCTIVE SLEEP APNEA IN CHILDREN WITH SICKLE CELL ANEMIA

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Introduction: Obstructive sleep apnea (OSA) is a common childhood condition that may play a causal role in adverse health outcomes in children with sickle cell anemia (SCA), but there is a paucity of data on its prevalence in these children. We report the prevalence of OSA and its relationship to risk factors and other clinical findings in children with SCA, ages 4 to 18 years, participating in an on-going multi-center, prospective cohort study. Participants were not selected for either asthma, OSA symptoms, or other adverse health conditions at baseline.

Methods: OSA was defined by obstructive apnea hypopnea indices (OAHI) from overnight full-channel polysomnography. Data from standardized questionnaires, anthropometric measures, and other laboratory tests (lung function, blood count) were used to examine the relationship between OSA and other risk factors or clinical findings in 122 children (mean age 11.9 ± 4.3 years, 52% female, 98% African heritage).

Results: The prevalence of OSA in children with SCA was 23% using a cutpoint of OAHI ≥ 2, and was 9% for OAHI ≥ 5. Habitual snoring at least 1-2 nights per week, household smoking exposure, lower oxygen saturation values awake or during sleep, lower forced expiratory volume at 1 sec (FEV1) percentile, and lower ratio of FEV1 to forced vital capacity were associated with OSA. Age, gender, enuresis, hemoglobin level, hayfever and asthma were not associated with OSA.

Conclusion: Children with SCA have a high prevalence of elevated OAHI. Lower baseline oxygen saturation values and reduced lung function are associated with higher OAHI in this cohort. Increased efforts to screen for and treat OSA in this vulnerable population may be warranted.

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0199

COMPARISON OF TWO NEW ACTIGRAPHS WITH POLYSOMNOGRAPHY IN CHILDREN AND ADOLESCENTS

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Introduction: The use of actigraphy is increasing in pediatric research, yet little is known about whether brands of actigraphs provide equivalent information, limiting comparisons of results across studies. In adults, studies comparing two brands of actigraphs have shown differences in estimates of sleep patterns, and no studies have directly compared actigraph devices in a large population of children and adolescents. The aim of this study was to determine the inter-device sensitivity, specificity, and accuracy of actigraphy in children and adolescents.

Methods: One-hundred fourteen patients 3-18 years (mean=8.8, SD=4.3) wore two actigraphs (Ambulatory Monitory Inc. MicroMotionlogger Sleep Watch [AMI] and Respironics Mini-Mitter Actiwatch 2 [RMM]) on the non-dominant wrist during one night of polysomnography (PSG) at the Children's Hospital of Philadelphia. Placement on the wrist was randomly assigned (i.e., AMI-RMM, RMM-AMI). Data was analyzed using existing algorithms on the Action-W and Actiware 5.0 software. Sensitivity, specificity, and accuracy were calculated from epoch-by-epoch comparisons between PSG and actigraphic data; paired t-tests were used to compare sleep efficiency across devices; and one-way ANOVA was used to examine developmental differences (preschoolers 3-5 years; school-age 6-12 years; adolescents 13-18 years).

Results: For the full sample, sensitivity to correctly identify sleep was similar to previous reports (AMI=.89, RMM=.93), specificity to correctly detect wake was higher than previous reports (AMI=.70, RMM=.67), and accuracy was good (AMI=.87, RMM=.89, inter-device=.89). Sleep efficiency for the AMI device (78%) was significantly lower than both PSG (83%, p=.01) and the RMM device (82%, p=.04). Developmental differences were found, with sensitivity significantly higher for both devices in adolescents (AMI=.92, RMM=.96) than preschoolers (AMI=.86, RMM=.92), p_{AMI}=.01 and p_{RMM}=.009. Specificity for the AMI device was significantly lower in adolescents (.60) compared to preschoolers (.79), p=.002.

Conclusion: This is the first large study to compare inter-device reliability for the new AMI and RMM actigraphs in children and adolescents. While both devices showed good sensitivity, specificity, and accuracy, the AMI device underestimated sleep. Further analyses are needed to determine if the current scoring algorithms remain valid for both new devices. In addition, more work is needed to determine the most appropriate algorithms for different developmental stages.

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0200

ADOLESCENTS LIVING THE 24/7 LIFESTYLE: EFFECTS OF CAFFEINE AND TECHNOLOGY ON SLEEP DURATION AND DAYTIME FUNCTIONING

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Introduction: Adolescents may not receive the sleep they need. New media technology and new hip-named energy drinks may be implicated in sleep deficits. This study quantified nighttime technology use and caffeine consumption to determine effects on sleep duration and day-

time behaviors in adolescents. Hypothesis: We hypothesized that with increased technology use, adolescents increase caffeine consumption, resulting in insufficient sleep duration

Methods: Subjects were recruited from a pediatric office in a proximal suburb of Philadelphia. Inclusion criteria were middle and high school subjects ages 12-18 years. The questionnaire, Adolescent Sleep, Caffeine Intake and Technology Use, was developed by the investigators to measure adolescents' intake of caffeinated drinks, use of nighttime media-related technology, and sleep behaviors. Descriptive statistics characterized the subjects, their caffeine and technology use, and sleep variables. Regression models assessed the relationships between caffeine, technology use and sleep variables, having adjusted for age, race, gender and BMI.

Results: Sleep was significantly related to the multitasking index (p=0.043). Teens getting 8-10 hours of sleep on school nights tended to have 1.5 to 2.0-fold lower multitasking indices compared to those getting less sleep. 33% of the teens reported falling asleep in school. Caffeine consumption tended to be 76% higher in those who fell asleep. The log-transformed multitasking index was significantly related to falling asleep during school (OR=69.9, 95% CI=8.8-556.1, <0.001) and with difficulties falling asleep on weeknights (OR=19.79, 95% CI=3.1-126.6, p=0.002).

Conclusion: Many adolescents used multiple forms of technology late into the night and concurrently consumed caffeinated beverages. Subsequently, their ability to stay alert and fully functional throughout the day was impaired by excessive daytime sleepiness. Future studies should measure more than just television hours and coffee or soft drink intake when evaluating the impact of nighttime activities on sleep patterns in adolescents.

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0201

INVESTIGATING SLEEP PROBLEMS IN CHILDREN USING DRAWINGS: AN EXPERIMENTAL PARADIGM

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Introduction: To date, examining sleep problems in children relies heavily on reports from caregivers. However, the concordance between caregiver reports of sleep problems in their children and actual sleep problems in the child is poor, and subject to interpretation based upon the caregivers' beliefs about sleep need, their own sleep pattern, and beliefs about the child's temperament. As such a valid and reliable tool, which uses the child's own reports of a sleep problem is required. The aim of the present study was to examine whether children's drawings can be used.

Methods: Eighty-seven children completed a structured drawing task, counterbalanced under two conditions; a bed or a table, after wearing an actigraph for the period of five days. Additionally, the primary caregiver was asked to complete measures of depression, anxiety, caregiver stress, and sleep-related dysfunctional thinking. Additionally, the caregiver completed a clinical interview regarding their own and their child's sleep.

Results: When grouped according to proxy report, It was found that children with disturbed sleep patters did not draw their bed pictures significantly differently with regards to size or colour than their normal sleeping counterparts. However, when grouped according to actigraphy data, there was a significant difference, with children with a sleep problem drawing a larger bed than children without a sleep problem. There were no within group differences on either split.

Conclusion: The results suggest that the use of children's drawings in identifying children with a sleep problem warrants further attention, however, significant refinements in the methodology must be made to ensure reliability and validity.

0202

PEDIATRIC APNEA IN THE MOUNTAIN WEST: CLINICAL NORMS FOR AHI AT ALTITIUDE

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Introduction: Recent publications include norms for the diagnosis of pediatric OSA of greater than 1.0 for apnea-hypopnea index (AHI) as based on polysomnography. These norms are derived based on evaluations conducted at low elevations. It is clinically suspected that elevation associated changes in ambient P02 are likely to affect pediatric PSG results. This study includes results from 78 pediatric patients (ages 3-16, mean age 10.0) referred for sleep disorders evaluation to two AASM accredited sleep laboratories at 5000 ft. and 6000 ft. elevation.

Methods: The patients in this IRB approved study included all pediatric patients referred for polysomnography except for those with previous t&a, cleft palate repairs, or Down's syndrome. Study subjects are divided into 4 groupings based on full night polysomnography for statistical analysis: AHI < 1.0 (N=6), AHI 1.0-2.5 (N=24), AHI 2.5-5.0 (N=19) and AHI > 5.0 (N=29). Symptom data for these patients from an 18 response yes=2/ no=1 pediatric sleep questionnaire (Chervin 2000) are statistically correlated with AHI results.

Results: Mean AHI was 6.2 (range 0.0-20.1). Only 6/78 (7.6%) of these patients had an AHI in the "normal" range (AHI < 1.0) For the entire group, questionnaire responses were highest for: dry mouth in morning (1.82), waking unrefreshed (1.72), daytime sleepiness reported by teacher (1.63), and hard to wake in morning (1.63); and lowest for: stop breathing (1.07), snores always (1.07) and stopped growing (1.07). Questionnaire data was found to significantly vary based on AHI grouping only for enuresis (1.17 for < 1.0 AHI, & 1.25 for AHI 1.0-2.5 compared to 2.65 for AHI > 5.0, p > 0.05) and reported obesity (0.0 for AHI < 1.0, 1.16 for AHI 1.0-2.5 compared to 1.39 for AHI > 5.0, p > 0.05). Mean low Sa02 was non-significantly lower (83.7, sd. 1.28) for the AHI > 5.0 grouping compared to a mean low Sa02 of 84.7, sd. 6.74, for the groups with AHI < 5.0.

Conclusion: Based on published norms and AHI results, 92.4% of pediatric patients evaluated in these laboratories could be appropriately referred for surgical treatment. Lower Sa02, obesity and enuresis occurred at higher frequency for the AHI > 5.0 group, suggesting a possible association between symptoms, signs and OSA diagnosis for the grouping with AHI > 5.0. It appears that the effects of lower ambient PO2 on sleep related breathing in pediatric patients are such that published norms for pediatric AHI may be inappropriate when applied in clinical settings at altitude.

0203

A LABORATORY STUDY OF SLEEP PHASIC ACTIVITY IN CHILDREN WITH HIGH-FUNCTIONING AUTISM

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Introduction: Adults with high functioning autism (HFA) show a reduction of rapid eye movements during REM sleep and a reduction of EEG sleep spindles during stage 2 (Limoges et al., 2005). The present study aimed at verifying the density of these sleep phasic activities in children with autism.

Methods: Four male children with HFA (8.3 ± 1.2 years) and five comparison participants (CN) (9.2 ± 1.2 years) were recorded for two consecutive nights. EEG sleep spindles and rapid eye movements were scored during stage 2 nonREM sleep and REM sleep, respectively. Results from night 2 were compared using t-tests. Data are shown as mean ± S.E.M.
Results: HFA participants had a lower index of stage 2 sleep spindles compared to controls (HFA = 89.1 ± 126.6, CN = 281.5 ± 57.9, $p<.05$). Analysis by thirds of night showed that this effect was significantly present mainly in the first two thirds (78.7 ± 129.2 vs CN = 263.5± 80.8, $p<.05$; 72.8 ±110.3 vs CN = 359.3 ± 110.4 $p<.05$; 116.0 ± 143.4 vs CN = 223.1 ± 49.8, $p=.16$). The index of rapid eye movements during REM sleep was not different between the two groups (HFA = 398.5 ± 12.0, CN = 370.31 ± 88.4, $p>.05$).
Conclusion: Although these preliminary results need to be replicated with a larger number of participants, they suggest that the neural substrates subserving stage 2 sleep spindles, namely the thalamocortical loop, is atypical at an early stage in autism but not that subserving REM sleep rapid eye movements, namely the frontal eye field/limbic cortex network.
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0204

SLEEP PATTERNS IN CHILDREN WITH ASPERGER SYNDROME OR HIGH-FUNCTIONING AUTISM: A LONGITUDINAL APPROACH

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Introduction: Persistent and severe disturbances of sleep are considered to be more common in children of normal intelligence who are diagnosed with autism spectrum disorders than in typically developing children. Yet, there is still sparse evidence to substantiate this notion. The aim of the present study was to compare the course of sleep patterns in children with Asperger syndrome (AS) or high-functioning autism (HFA) with that of typical controls.
Methods: Thirty-two school-age children with AS/HFA and 32 age- and gender matched controls participated at baseline, and 23/32 with AS/HFA and 22/32 controls participated at follow-up two to three years later. Data about sleep were obtained by use of parent report regarding globally assessed sleep problems, and by use of sleep diary and actigraphy.
Results: Parents responded that 10/23 children with AS/HFA, but only 1/22 control child had a sleep problem at both baseline and at follow-up. Diary and actigraphy showed longer sleep latencies on schooldays and earlier awakening times on weekends in children with AS/HFA than in controls at baseline as well as at follow-up. The course of other basic aspects of sleep patterns; timing, duration and maintenance did not differ between the two groups.
Conclusion: Persistent parent-reported sleep problems are far more common in children with AS/HFA than in controls. Diary and actigraphy data obtained at baseline and follow-up did however reveal merely subtle differences between the two groups. Further studies of larger samples are warranted in order to increase our understandning of the sleep development in children of normal intelligence who are diagnosed with autism spectrum disorders.

0205

HIGH DOSE DEXAMETHASONE DURING MAINTENANCE CHEMOTHERAPY FOR ACUTE LYMPHOBLASTIC LEUKEMIA LEADS TO AN INCREASE IN DAYTIME AND NIGHTTIME SLEEP IN PRE-PUBERTAL CHILDREN

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Introduction: Glucocorticoids are a mainstay in the chemotherapy of children with ALL and have been associated with behavior and sleep problems in children.
Methods: Twelve prepubertal children, ages 2-12 years on maintenance chemotherapy for standard risk ALL were monitored for 28 days using an AMI motionlogger actigraph. Three time periods were identified: 5 days of dexamethasone administration (3 mg/M2 given twice a day), 10 days of drug washout assuming a half-life of ~2 days and the remaining 13 days post-washout. Sleep parameters including sleep latency, bedtime, sleep minutes, wake episodes, wake time, daytime sleep minutes and number of naps were analyzed. The median for each time period for each patient was used for analysis. The non-parametric Friedman test was used to compare these parameters over the three time periods and the Wilcoxon Signed Rank Test was used for paired comparisons.
Results: Nighttime and daytime sleep parameters were significantly different between the three time periods. Dexamethasone treatment was associated with an earlier sleep onset, increased total nighttime sleep, decrease number of nighttime wake episodes, decrease in daytime activity, and increased duration of daytime sleep compared to the off dexamethasone interval. There were no changes in the time of morning awakening. The sleep/wake parameters during the washout period were intermediate between dexamethasone treatment and post washout.
Conclusion: In pre-pubertal children with ALL on maintenance chemotherapy, high dose dexamethasone is associated with an increase in daytime and nighttime sleep. These effects occur during drug treatment and persist over the ten days of drug washout. These changes are consistent with an increase in the homeostatic sleep drive occurring during dexamethasone treatment, which declines during the drug washout.

0206

AGE INFLUENCES BOTH THE OBSTRUCTIVE APNEA INDEX (OAI) AND THE OUTCOME OF SURGICAL TREATMENT IN YOUNG ALLERGIC CHILDREN SUSPECTED OF OBSTRUCTIVE SLEEP APNEA SYNDROME (OSAS)

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Introduction: To evaluate the use of a polysomnography (PSG) prior to adenotonsillectomy and to assess the potential factors that may influence the PSG results.
Methods: Between 2005 and 2007, 210 children suspected of OSAS were evaluated with PSG prior to surgery. A subset of 38 children had a second PSG one month after surgery, for one or more of the following indications: 1. Young age at the time of surgery 2. Persistence of OSAS symptoms 3. Underlying pathology.
Results: 42 children (22.1%) with a mean age of 4.4 years had no OSAS: 31% of them were treated surgically. 98 patients (51.6%) with a mean age of 3.2 years presented mild to moderate OSAS and 59.2 % of them were treated surgically. Finally, 50 children (26.3%) with a mean age of 2.8 years had severe OSAS and 94% of them were treated surgically. Amongst the allergic children, as the severity of the OSAS increased from no OSAS to severe OSAS, the age of the children decreased in a significant manner ($p=0.0326$). 22 (57.9%) of the 38 children who benefited from a second PSG after adenotonssillectomy could be considered cured. 5 children kept an OSAS>5. These children had

significantly higher OAI prior to surgery when compared with the cured children (p=0.0470). In all cases, there was an improvement in their OSAS. Amongst the allergic children, those who could be considered cured after surgery were statistically older than the ones who were not cured (p=0.0109).
Conclusion: The PSG prior to adenotonssilectomy allowed the identification of the children with severe OSAS, those who did not require surgical treatment and also gave an indication of surgical outcome: A young child with severe OSAS had less favorable surgical outcome when compared with an older one, especially if allergic. These children may need additional medical support.

0207

EFFECT OF OSAS ON MEMORY TASK ACQUISITION IN CHILDREN

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Introduction: OSAS is a common disorder in children and imposes detrimental consequences to the developing CNS. We therefore sought to examine whether OSAS would be associated with impaired acquisition of a pictorial-based memory task.
Methods: Children referred for a NPSG were asked to participate in a 15-minute pictorial memory acquisition task before their NPSG. Each subject looked at 26 consecutive cards with colorful animal pictures for 3 minutes, followed by a free recall period, repeated 4 times with 2 minutes intercalated rest. The sum of points was recorded for each trial. Trial performance over the 4 trials was computed and compared. Subjects were divided to 2 groups according to their AHI (OSAS >2/hrTST and control (CO) AHI<2/hrTST).
Results: Thirty-four subjects have been thus far recruited to the study, and when subdivided to OSAS and CO, matched for age (11.0 ± 3.2 yrs), ethnicity, and BMI z-score, with AHI of (6.8 ± 9.4 /hrTST) in OSAS group and (1.0 ± 0.5 /hrTST) in CO (p<0.0001). The mean progressive learning scores in CO over 4 consecutive trials were T1(9.1 ± 3.6); T2 (12.0 ± 4.6); T3 (14.1 ± 6.5); and T4 (14.0 ± 5.7) compared to OSAS T1 (9.8 ± 3.4); T2 (9.3 ± 4.8); T3 (11.4 ± 6.0); T4 (12.8 ± 5.5) (p<0.01 2-way ANOVA).
Conclusion: The differences in pictorial task acquisition trajectories suggest that children with OSAS require longer time and increased number of learning opportunities to reach the same level of recall performance compared to CO. These findings confirm and expand on the presence of cognitive deficits in OSAS.
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0208

SLEEP IN CHILDREN WITH CANCER: CASE SERIES OF 70 CHILDREN

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Introduction: Children undergoing treatment for cancer are under a great deal of stress, receive toxic therapies to treat their cancer, and are often imunocompromised because of their treatments. Sleep problems have not been well characterized in this population.
Methods: The records of all children with a diagnosis of cancer referred for a clinical sleep evaluation from 1994 to present were reviewed. All children had a comprehensive sleep history taken, sleep diagnostic studies performed were: PSG - 17, PSG & MSLT - 36, actigraphy -6.
Results: The cancer diagnoses of the 70 children were: brain tumor - 49 (41/46 -brainstem, hypothalamus, thalamus; cerebellum - 4/46; cerebrum - 4/46); blood cancer -18, other solid tumors - 3. The primary sleep diagnosis were: EDS - 29/70, Sleep disordered breathing - 27/70, Insomnia - 16/70, Circadian rhythm disorders - 2/70, Parasomnias - 6/70 (confusional arousals-2, sleep eating -1,seizures -3), Fatigue - 7/70. Twenty-nine children had EDS, 22 had tumors involving the brainstem, thalamus or hypothalamus. Twenty-seven children were treated with cranial radiation, 15 had EDS, and 17 had a pituitary hormone deficiencies. Twenty-seven children had sleep disordered breathing, 3 had central sleep apnea with respiratory failure requiring ventilation, all in children with brainstem tumors; 12 had OSA which was treated successfully with CPAP in 5. The OSA was dramatically worse in 4 children when they given conscious sedation for procedures. In the 18 children with blood cancers, the most common sleep problem was insomnia, seen in 8/18. Among these children, insomnia was associated with: sleep onset association disorders - 3/8, anxiety - 2/8, dexamethasone, DSPS and pain-1/8.
Conclusion: Children with cancer experience a unique constellation of sleep problems. Brain tumors, which account for 25% of cancer in children, accounted for 70% of the referrals to the sleep center. Excessive daytime sleepiness was the most common sleep problem overall and was seen most often in children with brain tumors involving the brainstem and hypothalamus, and in children treated with cranial radiation. Insomnia was most often related to poor sleep hygiene or anxiety. Respiratory insufficiency during sleep was only seen in children with tumors involving the brainstem. OSA was often present but unrecognized before the child was diagnosed with cancer and was often exacerbated by conscious sedation. Children with cancer deserve careful evaluation for sleep problems.

0209

GENETIC AND ENVIRONMENTAL INFLUENCES ON SLEEP PROBLEMS: A STUDY OF PREADOLESCENT AND ADOLESCENT TWINS

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Introduction: Sleep difficulties are experienced by 30-70% of children and adolescents. Although in adults sleep problems are known to be moderately heritable, the role of genetic and environmental influences on sleep difficulties in children and adolescents has not been well studied. Thus, the aim of this study was to examine the extent to which additive genetic, shared environmental, and nonshared environmental factors contribute to sleep problems in preadolescents and adolescents.
Methods: The sample consisted of a cohort of 125 monozygotic and 110 dizygotic twin pairs (61.1% female) ages 10-17 from the Michigan State University Twin Registry (MSUTR). Twins completed the Youth Self Report (YSR) and their mothers completed the Child Behavior Checklist (CBCL). The sleep outcome variable was created as a composite score derived from the four sleep-related questions on the CBCL and YSR. For each question, the higher score (parent or child) was used and the sum of these scores comprised the composite variable (range = 0 to 8).
Results: The mean sleep composite score was 0.92 +1.51 (range=0-8). Twin models demonstrated that sleep problems were primarily influenced by shared environmental factors (c2 =0.42, CI=.16, .58). The remaining variance was accounted for by additive genetic (a2 =0.32, CI=.05, .58) and non-shared environmental (r2 =0.28, CI=.22, .38) effects.

Conclusion: Genetic and environmental influences each appear to be important to adolescent sleep problems. The heritability of sleep problems in the current study is consistent with findings from the adult literature, suggesting that the degree to which genetic effects influence these difficulties across the ages remains relatively stable. Future research should aim to identify specific environmental factors that may contribute to the development of sleep problems. The significant influence of enviromental effects also indicates the importance of behavioral interventions in managing adolescent sleep problems.

0210

SLEEP PROBLEMS AND TEMPERAMENT IN ADOLESCENT TWINS: THE MEDIATING EFFECT OF SHARED ENVIRONMENT

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Introduction: Research in infants and adults has suggested that temperament is related to sleep problems; however, this relationship has not been established in adolescents. Given that approximately two-thirds of adolescents complain of poor sleep, it is important to examine the potential role that temperamental variables (e.g., negative affectivity, self-regulation) may play with regard to influencing the development of sleep problems. Furthermore, the genetic and environmental influences that underlie this relationship are important to examine.
Methods: The sample consisted of 125 monozygotic and 110 dizygotic twin pairs and their mothers from the Michigan State University Twin Registry (MSUTR). The sample ranged in age from 10-17 with a mean age of 12.68 +1.51 yrs, and was 61.1 % female and 86% white. All twins completed the Youth Self Report (YSR) and the Early Adolescent Temperament Questionnaire (EATQ) while their mothers completed the Child Behavior Checklist (CBCL). The sleep outcome variable was derived from four sleep-related questions on the CBCL and YSR. For each question, the higher score (parent or child) was used and the sum of these scores comprised the composite sleep variable (range = 0 to 8).
Results: The mean sleep composite score was 0.92 +1.51. Correlations demonstrated significant associations between sleep and effortful control/ self-regulation ($r=-.21$, $p<.001$), affiliativeness/ sociability ($r=.09$, $p<.05$), and negative affectivity ($r=.23$, $p<.001$). No significant relationship was found between sleep and surgency/ extraversion. Twin model fitting analyses indicated that common shared environmental influences predominately mediated the relationship between sleep and three of the temperament variables: effortful control (rC=-.97), affiliativeness (rC=.57), and negative affectivity (rC=.87).
Conclusion: Results demonstrate that there are associations between sleep and dimensions of temperament in adolescents. Twin analyses indicate that this association is mediated primarily by shared environmental factors. Future research is needed to identify the specific factors impacting both sleep and temperament.

0211

SLEEP AS A WINDOW ONTO BRAIN MATURATION: THE EFFECT OF NIDCAP CARE VERSUS TRADITIONAL CARE IN THE NEONATAL INTENSIVE CARE UNIT

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Introduction: In 1986, NIDCAP or Neonatal Individualised Development Care and Assessement Program was proposed by H. Als, with the aim to improve the hospital care of premature infants hospitalized in a intensive care unit (NICU). The aim of this study was to compare the sleep development of premature infants during their first year of life in relation to the neonatal care received: NIDCAP care versus classic care.
Methods: 43 children born between 1999 and 2003 participated in this study. 23 children sojourned in the NICU of Brussels Children's Hospital where classical neonatal care was applied. They formed the control group. They were compared with 20 children who benefited from NIDCAP care at St Pierre Hospital, Brussels. All the premature infants who participated in this study had a gestational age under or equal to 30 weeks, with a birth weight less than or equal to 1500g. The infants were selected on the basis of their visits to the Children's Hospital Sleep Unit. Only children with more than one polysomnography were selected to participate in the study. These children were then matched for sex, gestational age and birth weight with children who also had more than one polysomnography and who had sojourned at the NIDCAP unit in St Pierre's Hospital.
Results: Adjusted for post-conceptional age, NIDCAP treatment was associated with decreased AS density ($p=0.009$), increased QS density ($p=0.000$), decreased % AS and increased QS % ($p=0.000$), decrease arousal index (0.003) and decreased sleep stage shifts ($p=0.011$). These differences decreased with post-conceptional age. NIDCAP was associated with earlier cross-over of AS/QS %.
Conclusion: The treatment of extremely premature infants hospitalized in an intensive care unit by NIDCAP promotes less disturbed sleep and favors an optimal maturation of sleep.

0212

SLEEP ARCHITECTURE NREM SLEEP INSTABILITY IN CHILDREN WITH AUTISM WITHOUT SLEEP DISORDERS

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Introduction: Purpose of this investigation was to compare sleep macrostructure and NREM sleep microstructure (by means of CAP analysis), in a selected sample of narrowly defined autism without sleep disorders with (AUT-Regr) and without (AUT-NoRegr) developmental regression. We limited our cohort to children who were medication-free and did not have mental retardation. Typically developing children (TD) were included as a comparison group.
Methods: Ten children AUT-NoRegr, six AUT-Regr and nine TD, aged 4-8 years underwent polysomnographic recordings. After performing conventional sleep scoring according to Rechtshaffen and Kales criteria, CAP was visually scored according to Terzano criteria.
Results: Analysis of macrostructure showed that AUT-Regr had a significant less efficient sleep (81% vs 88.6% vs 94.43%; F 43.31, $p<.001$), more WASO (9.9% vs 8.5% vs 4.5%; F 6.47 $p<.05$), stage 2 sleep (50.4% vs 44.6% vs 43%; F 11.3, $p<.01$), less REM sleep (12% vs 20% vs21% F 22.3, $p<.01$) than Aut-NoRegr and TD group. CAP analysis showed a lower total CAP rates (23% vs 30% vs 31%, F 13.27, $p<.01$)

mainly during stage 1 and 2 sleep with a lower A1 (48% vs 55% vs 63% F 69.45, p<.01) as well as an increased A2 and A3 in AUT-Regr compared to Aut-NoRegr and TD children.
Conclusion: Our findings suggest that children with developmental regression showed disrupted sleep either from a macro or from a microstructural point of view. The low CAP rate with a lower amount of A1 during light sleep might be considered an expression of a dysregulation of arousal level during NREM sleep, particularly evident in children with autism and developmental regression, even in absence of clinically reported sleep disorders and mental retardation.

0213

CHILDREN SHOW INDIVIDUAL NIGHT-TO-NIGHT VARIABILITY OF PERIODIC LIMB MOVEMENTS IN SLEEP

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Introduction: Several adult studies have documented the occurrence of significant night-to-night variability of periodic limb movements in sleep (PLMS). The aim of this study was to investigate the night-to-night variability of childhood PLMS.
Methods: Two to four nights of polysomnography (PSG) were performed as part of a multisite study investigating the effects of carbidopa/levodopa on attention-deficit/hyperactivity disorder in CNS medication-free children. Baseline PSGs from all children and endpoint PSGs from children who were randomized to a placebo group were scored using International Restless Legs Syndrome Study Group criteria for PLMS. PLMS indices from 101 sleep studies of 36 children, ages 7 to 12 years, were compared.
Results: For all 36 children as a group, PLMS index on night 1 (N1) was predictive of PLMS index on night 2 (N2) (OR 7.0, 95% CI 1.4-38.4), suggesting overall diagnostic classification (PLMS index above or below 5/hr) was accurate. In addition, for the 15 children with PLMS >5/hr on either night, there was no significant group difference on N1 vs. N2 for mean PLMS index (10.6 vs. 8.5/hr, p = 0.92) or chance of PLMS >5/hr, indicating no first-night effect. When looking at individual data, however, 9 of these 15 children (60%) were under and over the 5/hr cutoff on one of these two nights. Of these 15, 10 had clinical diagnoses of restless legs syndrome (RLS) and 5 of periodic limb movement disorder (PLMD).
Conclusion: Considerable individual night-to-night variability of PLMS indices was observed. This finding has important clinical relevance for the diagnosis of pediatric RLS and PLMD, and may impact future studies that correlate individual PLMS severity with frequently associated symptoms such as negative affect, fatigue, and inattention. Our data, however, also suggest individual PLMS variability is random, and not likely to skew the group-level analysis of treatment outcome studies.
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0214

PARENT-REPORTED SLEEP PROBLEMS AND ASSOCIATED BEHAVIORAL SYMPTOMS IN CHILDREN WITH ASPERGER SYNDROME AND HIGH-FUNCTIONING AUTISM: A LONGITUDINAL APPROACH

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Introduction: Chronic disturbances of sleep are considered to be more common in children of normal intelligence who are diagnosed with autism spectrum disorders than in typically developing children. Yet, research data which substantiate this notion is still relatively sparse. The present study examined the prevalence of persisting parent reported sleep problems and associated behavioral symptoms in children with Asperger syndrome (AS) or High-Functioning Autism (HFA) and in typically developing controls.
Methods: Sixteen school-age children with AS/HFA and 16 age- and gender matched controls participated at baseline, and at follow-up two to three years later. Data about sleep were obtained by use of parent report to a pediatric sleep questionnaire and data about daytime behaviour were obtained by use of parent and teacher report to the Strengths and Difficulties Questionnaire (SDQ) and the Asperger and High-Functioning Autism Screeening Questionnaire (ASSQ).
Results: Parent-reported persistent sleep problems, i.e. sleep problems endorsed both at baseline and at follow-up, occurred in 7/16 children with AS/HFA, but in none of the 16 controls. The children with AS/HFA and persistent sleep problems had higher SDQ-scores than those with AS/HFA and without persisting sleep problems. Parent-reported total scores was 19.1 vs 14.00; p< 0.05), and teacher-rated hyperactivity subscore was 5.57 vs 3.78; p<0.05. Parent-reported persisting sleep problems were, however, not associated with higher ASSQ-scores.
Conclusion: Persistent parent-reported sleep problems were common in school-age children with AS/HFA. Moreover, the persistence of sleep problems was associated with higher scores of the behavioural problems, according to SDQ, but not with higher scores of core autistic symptoms according to ASSQ.

0215

THE ASSOCIATION OF SLEEP AND OBESITY AMONG PRESCHOOL CHILDREN: RESULTS FROM SHANGHAI PRESCHOOL CHILDREN SLEEP STUDY

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Introduction: With the rapid economic growth in China in past 30 years, Chinese people are experiencing two parallel trends, an increase in the prevalence of obesity and a decline in sleep duration. This phenomenon is not only limited to adults, but also to children. An association between reduced sleep and obesity has been recently demonstrated in adults, and children. The objectives of this study are to examine 1) the relationship of sleep duration and obesity among 3-4 years old children in Shanghai, China, 2) the impact of cosleeping on children's sleep duration.
Methods: Chinese children from 10 kindergartens in Shanghai, aged 3-4 years participating in the kindergarten entrance health examination in 2000 were included in the study. Body weight and height were measured. A questionnaire was given to parents to assess sleep, physical and social characteristics of children and their family. The main outcome measure was obesity, defined as body mass index (BMI, kg/m2) ≥95th percentile for the children.
Results: 1311 children were included in the study, mean age 3.8 ± 0.5 years for boys and girls. Obesity rate was 10.3% in boys and 6.9% in

girls. Compared to children reporting 11 hr or more of sleep per night, the odds ratio (OR) for childhood obesity was 4.76 (95% confidence interval (CI), 1.28-17.69) for those with <9 hr of sleep, and 3.42 (95% CI, 1.12-10.46) for those with 9-9.4 hr sleep, after adjustment for age, sex and other risk factors. Nighttime sleep durations over 10 hours were not consistently associated with either an increase or decrease in the risk of obesity. The prevalence of bed sharing with caregivers was 68.60% in these children. Regression analysis demonstrated that children's sleep duration was predicted by caregivers' sleep duration (P<0.001), caregivers' bedtime (P<0.001), cosleeping (P=0.008) and mothers' level of education (P=0.001)

Conclusion: In Chinese preschool children, short sleep duration is positively associated with obesity and with cosleeping with their caregivers. As cosleeping is common in China, increasing parental awareness of the importance of sleep, and helping parents to establish an appropriate sleep schedule for young children, may decrease childhood obesity.

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0216

DOLL PLAY: ACTIGRAPHY PORTRAYAL OF ACTIVITY AND SLEEP-WAKE PATTERN IN INFANTS EXPOSED TO EXTERNAL MOTION

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Introduction: External motion is a common experience for infants yet it is usually overlooked in studies that use actigraphy to assess infant sleep. The purpose of this study was to assess the activity count and sleep-wake identification by actigraphy when an infant doll was exposed to external motion. A doll was used in this study simulating an infant who is always in a sleep state with no activity.

Methods: Actiwatch-Score (MiniMitter-Respironics, Inc., Bend, OR) actigraphs were placed on both ankles of a 20-pound infant doll. Experiments involving different types of activities (e.g., swing, moving automobile, shopping cart, bouncer, etc.) which infants typically experience at a home environment were conducted. Each activity lasted for 5 to 15 minutes. The Actiwatch was programmed to store activity counts at 15-second intervals. At the end of each trial, the actigraphy data were scored as sleep or wake at low, medium, and high sensitivity settings using the Actiware-Sleep 3.4 analysis software. Descriptive statistics were calculated to summarize the activity counts generated by different types of activity for the left and right leg Actiwatch. The percentage of epochs scored as wake was also calculated for different types of activities.

Results: The low speed infant swing generated zero activity count; however, external motion generated by a moving car, stroller, shopping cart, and a vibrating bouncer as well as by a caregiver's bouncing resulted in 100% false wake identification even when actigraphic activity data were scored using low sensitivity settings (i.e., which require 80 activity counts to be scored as wake).

Conclusion: External motion typically experienced by infants increases activity counts and influences the accuracy of infant actigraphy for sleep-wake estimation. The extent of external motion influencing the actigraphic sleep-wake scoring depends on the type of external motion experienced and where the threshold activity count falls.

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0217

BEHAVIOR PROBLEMS AND WEIGHT GAIN AFTER CONTROLLING FOR SLEEP-DISORDERED BREATHING IN THE TUCSON CHILDREN'S ASSESSMENT OF SLEEP APNEA STUDY (TUCASA)

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Introduction: Behavioral or psychological problems in children have been associated both, as cause and effect of weight increase in children. The present study evaluates the association between baseline behavior problems and follow up weight gain adjusting for sleep disordered breathing (SDB).

Methods: The Conners' Parent Rating Scale-Revised and the Child Behavior Checklist List were used to obtain behavioral data as part of the baseline study. A total of 245 children aged 6 to 12 years who completed these questionnaires underwent unattended home polysomnogram at baseline and follow up approximately 5 years apart. Height and weight measurements were taken from the children at both surveys. BMI percentiles for age and sex were derived according to the US CDC 2000 reference.

Results: Children were 51% male, 63% Caucasian, and 37% Hispanic. Mean baseline and follow up values were: age 9 and 13.7 years, RDI3% 1.1 and 0.5 (p=0.0003), BMI percentile 60.6% and 63.4% (p = 0.05). Overall obesity increased from 15.9% to 18.7%. Percent obesity among girls increased from 11.3% to 16.9% while obesity in boys remained at 20.7%. At baseline, obese girls had significantly higher behavioral problems including anxious/depressed and social problems than non-obese girls. Contrarily, no differences were seen between obese and non-obese boys except for social problems. Follow up differences persisted for obese girls who had higher cognitive and social problems than non-obese girls. Obese girls at follow up also had significantly higher sleep latency (31.0 vs 18.5 min, p=0.01) and higher RDI3% (2.3 vs 0.87, p=0.04) than non-obese girls. Adjusted linear regression predicting difference in BMI percent showed that children with high anxious/depressed scores on average increased their BMI by 5.8% (p=0.06).

Conclusion: Emotional and behavioral difficulties in children may lead to weight gain in adolescence after adjusting for SDB. These difficulties are more pronounced in girls than boys.

Support (optional): HL 62373

0218

MORNING AND AFTERNOON ATTENTION AND IMPULSE CONTROL IN OVERWEIGHT OSA CHILDREN

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Introduction: Inattention, hyperactivity and executive dysfunction have been well documented in non-obese children with OSA. The rapidly expanding obesity rates in the pediatric population could affect ADHD-like symptoms during morning or afternoon and affect class-room learning tasks differently.

Methods: A preliminary sample of 99 children (age: 6.7±0.5 yr, 55.5% boys, 66% Caucasian, 24.5% African American, 9.6% other ethnicity, DAS-GCA≥85) was divided into 4 groups by OAHI (cut-off: 2) and BMI (cut-off: 85th percentile): OSA^-OB^- (n= 45) and OSA^-OB^+ (n=23) with OAHI≤2, snore never to rarely, low SaO2>90, NPSG TST ≥7hr), and OSA^+OB^- (n=15) and OSA^+OB^+ (n=27) with OAHI>2, snore ≥3x/week children. Clinical attention problem scale (CAPS) which assesses attention and impulse control symptoms in a classroom was assessed.

Results: Age and gender were similar among groups. Whereas throughout the day inactivity and overactivity increased in otherwise healthy

children (z=2.91, p=0.004), this is not the case for OSA^+OB^- and OSA^+OB^+ children. For the 4 groups, overactivity differences emerged in the morning only [H(3,N= 98) =10.03706 p =.0183], with mean scores ranging from 0 to 2: OSA^-OB^- (0.83±0.57), OSA^-OB^+ (0.72±0.57), OSA^+OB^- (1.11±0.57), and OSA^+OB^+ (1.20±0.48). Post-hoc analyses revealed significant differences between OSA^-OB^+ and OSA^+OB^+ (z'=2.71, p=0.04).

Conclusion: CAPS overactivity scores reflect non-verbal and verbal impulse control impairments. Results are suggestive that in the morning, OB children are less active, that OSA children are more active, and that OSA^+OB^+ are the most affected. Thus, morning overactivity appears to be associated with the child's health condition, and could impact on class-room learning tasks.

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0219

HOME LITERACY ENVIRONMENT: A BEDTIME STORY OR NOT?

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Introduction: Home literacy stimulates cognition. While sleep hygiene includes a multitude of sleep characteristics it might overlap partially with home literacy activities. Moreover, relationships between sleep quality and quantity, and academic achievement have been suggested. As such, we hypothesized that an association may exist between home literacy environment and sleep hygiene, potentially affecting learning abilities.

Methods: Parents of 489 children (age 6.0±1.3 yr, 57% boys, 79% Caucasian (C), 21% African American (AA)) enrolled in Jumpstart or the early elementary program within the Jefferson County Public School system completed our sleep questionnaire and literacy environment questionnaire. The latter included environment (E, max. score 15), reading activities (R, max 13), language tools (L, max. 10), and parent involvement (PI, max. 19). The morning after NPSG, neurocognitive performance was tested.

Results: AA children scored significantly lower than C on E (9.8±3.2 vs. 12.3±2.3, $p < 0.001$), L (6.8±2.3 vs. 7.3±1.9, $p < 0.05$) and PI (15.7±3.7 vs. 16.5, $p < 0.05$), but not for R. The average number of nights of shared reading with the parent was 4.3±1.9 nights/week, with AA on average 0.9 days less ($p<0.01$). In comparison to C, AA sleep hygiene was less sleep promoting; i.e. shorter sleep duration (8.5±1.6 hrs vs. 9.4±1.2hrs, $p<0.001$), later bedtimes (>9PM, $p<0.01$), more co-sleeping (51% vs. 62%, $p<0.05$). SEM (χ^2 (36) = 89.33, p = 0.00; AGFI = 0.94) revealed that neurocognitive performance was mediated by sleep hygiene (β = 0.29, $p < 0.01$), which in turn was strongly predicted by the home literacy environment ($\beta = 0.84$, $p < 0.01$).

Conclusion: Home literacy, sleep hygiene and neurocognitive performance are likely associated, with sleep hygiene acting as a potential mediator. Reinforcing home literacy as well as sleep hygiene might be a protective factor for neurodevelopment of the child.

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0220

RELATIONSHIPS BETWEEN PSYCHOSOCIAL, BEHAVIORAL, AND FAMILIAL FACTORS AND SLEEP DURATION IN CHINESE ADOLESCENTS

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Introduction: Recent research suggests that Chinese youth have shorter sleep duration, later bedtime, and earlier wake time when compared to American youths. However, little is known about the correlates of sleep duration in Chinese adolescents. Therefore, it is important to identify potential determinants for sleep duration in Chinese adolescents. The objective of this study is to investigate the associations between psychosocial (depression, perceived stress, school stress, and quality of life), behavioral (physical activity, sedentary behavior, and diet intake), familial (parenting style and parental monitoring), and demographic factors (school grade, gender, puberty status, weekly allowance, parental education, parental income, and self-perceived health status) with sleep duration among Chinese adolescents.

Methods: This study includes complete baseline data from a longitudinal smoking prevention and health promotion study (China Seven City Study) conducted in 7 cities in China (N=9023, 52.71% girls, mean age 15, mean sleep duration 7.97 hours). Relationships between psychosocial, behavioral, familial, and demographic factors and sleep duration were examined using multivariate multi-level linear regression model.

Results: Higher frequency of participation in vigorous physical activity, higher levels of perceived stress, and school stress were related to shorter sleep duration. Time spent on sedentary behavior, frequency of snack intake, and parental monitoring were positively associated with sleep duration. Adolescents who were overweight, female, in higher school grade, and in post-puberty status reported shorter sleep duration.

Conclusion: Identification of these potential determinants of sleep duration could be targeted to effectively change sleep behaviors in Chinese youths. Overweight status and poor mental health (higher level of perceived stress/school stress) were associated with shorter sleep duration. Greater participation in vigorous physical activity and less time in sedentary behavior were related to shorter sleep duration. Perhaps, youths who engage in vigorous physical activity more frequently generally might feel more energetic and they thus might not need as much as sleep as physically inactive youth need in order to maintain normal daily function. Future longitudinal studies are needed to clarify theses associations in Chinese youths.

0221

NOCTURNAL ENURESIS AND OBSTRUCTIVE SLEEP APNEA IN CHILDREN

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Introduction: A strong association between enuresis and obstructive sleep apnea (OSA) has been reported with a prevalence of between 26 to 47.8% in children undergoing adenotonsillectomy for OSA. We wished to identify the prevalence of OSA in children presenting with the primary complaint of enuresis to see if this relationship was reciprocal.

Methods: A prospective, cohort study design was employed. Otherwise healthy children i) aged four to six years, with secondary enuresis only or ii) aged six to 18 years with either primary or secondary enuresis presenting to pediatric outpatient clinics were invited to participate. All completed the Pediatric Sleep Questionnarie (PSQ) and those with a positive PSQ underwent laboratory polysomnography (PSG).

Results: 25 children (18 males) met inclusion criteria. Of these, 13 (9 males) agreed to participate in the study. Median age was 9.0 years

(Range 6.5. - 16 years). Of these, 6 had a positive PSQ (>8/22 positive responses). Four of these underwent PSG, the other two refused further study, noting there were no longer concerns regarding enuresis. One of four children had an abnormal PSG with an apnea-hypopnea index (AHI) of 10.9 per hour (overall prevalence of 4%). The remaining PSGs were normal with AHI< 1.0.
Conclusion: In this pilot project, the prevalence of OSA in children presenting with the primary complaint of enuresis was not increased above the general population prevalence of OSA in children.
Support (optional): Alberta Children's Hospital Foundation

0222

ENDOTHELIAL DYSFUNCTION ASSOCIATED WITH OBESITY AND OBSTRUCTIVE SLEEP APNEA (OSA) IN CHILDREN APPEARS TO BE INDEPENDENT OF NITRIC OXIDE PATHWAYS

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Introduction: Obesity and OSA in children have recently been identified as independent risk factors in the development of cardiovascular morbidity, including endothelial dysfunction. However, the putative mechanisms accounting for the endothelial dysfunction seen in non-obese children with OSA and in obese children without OSA have yet to be elucidated.
Methods: Consecutive non-hypertensive children participating in research sleep studies were recruited. Non-obese children without polysomnographic evidence of OSA were compared to obese children with OSA. Endothelial dysfunction was confirmed in a subset of 10 subjects using a modified hyperemic test involving cuff-induced occlusion of the radial and ulnar arteries performed after overnight fasting. Laser doppler determination of nitric oxide mediated cutaneous capillary vasodilatory responses was performed using skin iontophoresis of 2% acetylcholine during which baseline and hyperemic responses were measured.
Results: 26 children (mean age 11.4±3.8 years) have been studied thus far. 15 (58%) were obese (BMI> 95th percentile) and had OSA (obstructive AHI> 2/hrTST), and 11 were non-obese, and had normal sleep studies. Cuff-induced occlusion testing performed on a subset of 5 subjects with OSA+obesity revealed significantly longer delays in peak capillary reperfusion compared to 5 non-obese children without OSA (60.2±24.4 sec vs. 33.6±7.9 sec, $p<0.05$). However, peak capillary perfusion responses to 2% acetylcholine revealed no differences in the magnitude of vascular perfusion increases in the obese+OSA group compared to the non-obese-non-OSA group (4.3±2.0 fold vs. 3.9±2.1 fold).
Conclusion: The endothelial dysfunction induced by OSA and obesity in children does not appear to be attributable to alterations in vascular responses to acetylcholine, and hence unlikely to reflect derangements in nitric oxide-mediated vasodilation. It is likely that in children, OSA and obesity elicit endothelial dysfunction via alternative pathways, such as inflammation and/or oxidative stress.
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0223

SLEEP IN CHILDREN WITH FRAGILE X SYNDROME (FXS)-A PILOT STUDY USING ACTIGRAPHY

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Introduction: Although sleep problems are often reported by parents of children with FXS, there has been little objective study of sleep patterns in this population. This is an important set of issues because sleep problems in children with FXS may be contributing to problems with affect regulation, behavior, learning and memory consolidation, as well causing pragmatic burdens on family members. This pilot study employs actigraphy as an objective measure of sleep in children with FXS.
Methods: The cross sectional design focused on sleep patterns in home settings in a sample of youth with FXS (N = 7; Mean age = 8.4 years) and a comparison group (N = 14) of normal controls matched on age.
Results: Children with FXS had a longer sleep latency (p = .026); greater number of minutes awake after sleep onset (p = .024); greater number of contiguous wake episodes (p = .009); greater duration of longest wake episode (p = .031); higher activity level (p = .012); more total wake minutes (p = .010); lower sleep efficiency (p = .046) and a significantly longer time in bed (p =.016).
Conclusion: Children with FXS showed significantly different sleep patterns than a normal comparison group matched on age, and they appear to have significantly disturbed sleep. This study highlights the need for additional studies to better understand the specific nature of sleep problems in FXS and to inform future intervention studies that may have a positive impact on children with developmental disabilities, as well as the quality of life for their caretakers and families.

0224

CHARACTERISTICS OF REM SLEEP BEHAVIOR DISORDER IN CHILDHOOD

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Introduction: REM Sleep Behavior Disorder (RBD) has been well described in adults. There is insufficient information concerning the clinical and polysomnographic features of RBD in childhood. We therefore describe our experience in this regard.
Methods: A review of subjects below the age of 18 years who had been evaluated at our institution between 2000 and 2008 revealed 9 subjects who met diagnostic criteria for RBD, namely motor dream enactment behavior and polysomnogram evidence of REM sleep without atonia. The history, comorbidities, and concurrent medications at diagnosis were reviewed.
Results: The nine subjects had a mean age at diagnosis of 8.4 years (±4.9 years), with 5/9 or 56 percent being male. Nightmares were reported in all nine, and excessive daytime sleepiness in 5/9. Two children had caused bodily harm to bed mate siblings. Comorbidities (which were multiple in some) included anxiety in 4/9, attention deficit disorder in 3/9, non-specific developmental delay in 2/9, Smith-Magenis syndrome in 1/9, pervasive developmental disorder in 1/9, non-accidental trauma with skull fracture in 1/9, and Moebius Syndrome in 1/9. Abnormal MRI scans were seen in 2/9 subjects (Chiari I malformation 1/9 and pituitary cyst in 1/9). Eight of 9 patients were treated with clonazepam before bedtime, with resolution of nightmares and abnormal motor behaviors in 6/8. The ninth patient was treated with discontinuation of a concurrently administered tricyclic agent.
Conclusion: REM Sleep Behavior Disorder in children may be associated with neurodevelopmental disabilities, anxiety or structural brain lesions. In the short term, it seems to be modestly responsive to benzodiazepines.

0225

PERSISTENT SLEEP-RELATED HYPOVENTILATION IN CHILDREN AFTER TONSILLECTOMY AND ADENOIDECTOMY

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Introduction: One of the findings sometimes seen during nocturnal polysomnography (NPSG) in the pediatric population in addition to obstructive sleep apnea (OSA) is the elevation of the peak end tidal CO_2 ($PetCO_2$). This is assumed to be secondary to obstructive hypoventilation. Whether this hypercapnia resolves after tonsillectomy and ad-

enoidectomy (T&A) raises the question of whether follow up studies are indicated and what the persistence of hypoventilation implies.
Methods: This was a retrospective review of pediatric NPSGs done in 2007 and 2008 with a diagnosis of hypoventilation with or without signficant OSA prior to T&A who also had post-operative NPSG. Subjects were classified as having hypoventilation by either the old criteria (maximum $PetCO_2$ > 53 torr; $PetCO_2$ > 46 torr for > 60% of total sleep time [TST]) or the new criteria ($PetCO_2$ > 50 torr for > 25% of TST). We then reviewed the post surgical NPSG to evaluate the persistence or resolution of hypoventilation.
Results: A total of 8 subjects met inclusion criteria. The mean age was 7.5 ± 3.9 (SD) years. The mean BMI was 22.6 ± 5.2 kg/m^2. Four of the cases had a concurrent diagnosis of overt OSA with apnea index (AI) > 1 apnea/hour. The mean AI among these OSA subjects was 2.2 ± 0.94 apneas/hour of sleep. All the patients met the criteria for hypoventilation as per the old criteria and 4 subjects by the new criteria. Thus 4 subjects (50%) met only the older criteria. The mean time between the first and second studies was 5.3 ± 2 months. All cases of OSA resolved on post-operative NPSG. Among the 8 patients that were diagnosed by the old criteria three had resolution (37.5%) of hypercapnia by all criteria. Two of the four patients (50%) with hypoventilation only by the new criteria had resolution by all criteria on post-operative NPSG.
Conclusion: Children diagnosed with obstructive hypoventilation may not have resolution of sleep-related hypoventilation after T&A, despite elimination of OSA. This appears to be valid using either the older criteria of Marcus et al., or the new criteria of the American Academy of Sleep Medicine. This implies either persisting upper airway obstruction or a non-obstructive pathophysiology for some cases of hypoventilation.

0226

CLINICAL AND POLYSOMNOGHAPYC EVALUATION OF OBESE CHILDREN

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Introduction: The aim of this study was to compare clinical parameters and upper airway (UA) and facial skeletal alterations with the presence of obstructive sleep apnea syndrome (OSAS) in obese children
Methods: 31 children with a body mass index (BMI) over the 95th percentile were successively enrolled. All patients were submitted to anamnese, UA and facial skeletal examination, polysomnography and laboratorial exams (glicemy and Radio Allergo Sorbent Test - RAST)
Results: 14 (45.2%) of the patients were female and 17 (54,8%) were male. The average age was 7.6 ± 2.9 years. OSAS was present in 16 (51.6%) of the patients. The only laboratorial finding that had any statistical difference between the genders was glicemy (was higher in the men) (p= 0.047). Neck circumference and BMI z-score did not present statistical differences between genders and OSAS and no OSAS groups. The Polysomnographic findings that showed statistical differences between OSAS and no OSAS groups were: Apnea and Hypopnea index (p< 0.01), with minimum oxihemoglobin saturation (p< 0.01) and arousals index (p< 0.01). No Polysomnographic findings showed statistical difference between genders. The only UA anatomical alteration that showed statistical differences between the OSAS and no OSAS groups was the palatine tonsil hypertrophy degree III and IV (p< 0.01) and the modified mallampati index class III and IV showed a tendency (p= 0.05).
Conclusion: The occurrence of OSAS in the obese children of the group was higher, confirming the existent correlation between obesity and OSAS, although no correlation was established with degree of obesity. The laboratorial exam used to diagnosis allergic rhinitis (RAST) was not related to the presence of OSAS. The only anatomical UA alteration that was related to presence of OSAS was palatine tonsil hypertrophy, showing us that even in a group of obese children the anatomical factor can be preponderant.
Support (optional): AFIP, FAPESP, CNPQ

0227

SLEEP PATTERNS IN AUSTRALIAN INDIGENOUS CHILDREN: EFFECTS ON PERFORMANCE AND BEHAVIOUR

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Introduction: Sleep problems in Australian children are common and may affect school performance and behaviour. However, the effects of sleep on these factors has not been investigated in Australian Aboriginal or Torres Strait Islander (indigenous) children despite poorer academic performance compared to non indigenous children. This study compares pilot data of sleep in indigenous and non indigenous children and investigates effects on school performance and daytime behaviour
Methods: Subjects included 25 indigenous and 25 non indigenous children with a mean (SD) age of 8.8 (1.4), range 7-11 yrs 11 mths, in 6 Northern Territory primary school classrooms (years 2-10, n = 200). Parents completed the Sleep Disorders Scale for Children which produces a T-score [mean=50 (SD = 10)] for behavioural sleep disorders, sleep disordered breathing, parasomnias, excessive daytime sleepiness and night sweating. School grades were recorded, and behaviour was assessed with parent-reported Child Behaviour Checklist.
Results: Behavioural sleep problems of initiating and maintaining sleep and parasomnias were common in both groups (24%-40%) with indigenous children reporting more problems in 8-9 year olds and non indigenous children reporting more in 10-11 year olds. No between group differences were found in school performance. However, significant relationships between sleep quality and aggression were found particularly for indigenous children.
Conclusion: These data suggest that more than one third of Australian children may suffer from significant sleep problems. Associations between sleep disturbances and aggression, particularly among indigenous children, could be significant if sleep problems hamper prefrontal cortical regulation of behaviour.
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0228

HABITUAL SLEEP DURATION AND BODY MASS INDEX IN CHINESE SCHOOL AGED CHILDREN

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Introduction: Habitual short sleep duration has been found to be linked to greater body mass index (BMI) among all ages of the general population in the Western countries. The relationship between sleep duration and BMI has not been studied in Chinese children.
Methods: The random sample of 17,696 children (age 7-12 years old) participated in a cross-sectional survey. The survey was conducted over eight mainland Chinese cities. Chinese version of the Children's Sleep Habits Questionnaire was administered to collect sleep data. Height and weight were measured during the survey.
Results: The prevalence of obesity and overweight in Chinese school aged children was 5.9% (BMI was 30 or greater) and 28.1% (BMI was 25 or greater), respectively. Compared to girls, boys had significantly higher prevalence of obesity (6.4% vs. 5.5%) and overweight (31.6% vs. 24.8%). After controlling for the factors of age, gender and media-

use, hierarchical multiple linear regression models revealed a significant association between shorter sleep duration in weekdays and increased IBM. Multivariate logistic regression models showed that mean sleep duration < 9 hours per day was a significant risk factor for overweight/obesity (OR: 1.14, 95% CI: 1.04-1.68, p<0.01).
Conclusion: In consistent with previous reports, the results suggested that short sleep duration significantly linked to the increase of BMI and was a high risk factor for obesity/overweight among Chinese school aged children.
Support (optional): Shanghai Key Laboratory of Children's Environmental Health (06DZ22024); National Natural Science Foundation of China (30700670); Innovation Program of Shanghai Municipal Education Commission (09YZ92); Program for Excellent Young Teachers in Shanghai (jdy-07011).

0229

SELF-REPORTED COPING IN OVERWEIGHT CHILDREN WITH OSA

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Introduction: Psychological distress may occur in addition to physical health risks associated with being overweight and/or suffering from OSA. Children with OSA report increased impairments in quality of life and depressive symptoms. Behavioral and emotional adjustment in children has been associated with coping. Thus, we aimed to conduct preliminary assessment of the coping strategies and needs of children who are overweight and also suffer from OSA.
Methods: 20 children (9.9±1.4yrs, 60% boys; 50% Caucasian, 35% African American, 10% others, BMIz >85th percentile and AHI>2) completed the Child Observed Coping Scale (COCS) and Children's Depression Inventory (CDI). COCS evaluates approach coping by self-seeking support and self-reliance or problem-solving subscales, and avoidance coping by distancing, internalizing and externalizing. Internalizing and Externalizing subscales reflect emotional reaction coping. CDI measures the presence of depression by negative mood, interpersonal problems, ineffectiveness, anhedonia, and negative self-esteem subscales.
Results: Overweight OSA children preferentially relied on avoidance coping, more specifically emotional reaction. Their negative mood was coped with via externalizing such as taking it out on others, yelling (r=0.52), while interpersonal problems were dealt with through internalizing for instance 'I get mad at myself for doing something that I shouldn't have done...' (r=0.59). However, potential cross-situational coping was also inferred from the item-analysis; i.e., negative self-esteem was likely associated with seeking self support and problem-solving behaviors, whereas ineffectiveness was linked to distancing coping behaviors.
Conclusion: Coping via emotional reactions may characterize the strategy of overweight children with OSA, i.e., behavioral, cognitive, or emotional activities oriented away from a stressor. Therefore, not only assessment of depression but also coping strategies should be incorporated in the evaluation of children who are overweight and at risk for OSA.
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0230

SOCIAL SKILLS IN CHILDREN: PRELIMINARY RESULTS ON THE EFFECT OF OVERWEIGHT AND OSA

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Introduction: Socially accepted learned behaviors, i.e., social skills, enable a child to interact effectively. These behaviors are a blend of memory, language, and visuospatial functions. Both OSA and obesity in children have been implicated as leading to adverse outcomes in a wide range of neurobehavioral and cognitive functions, and frequently co-exist. In the present study, we aimed to assess the adverse sequelae of OSA and overweight with respect to social skills.
Methods: Ongoing recruitment from the Louisville public schools resulted in a preliminary sample of 123 children (mean age: 6.7±0.6 years; 51.1% boys; 65% Caucasian, 25% African American; DAS-GCA≥85). Based on obstructive AHI (cut-off: 2/hrTST) and BMI (cut-off: 85th percentile) 4 groups were formed; OSA^-OB^- (n= 54) and OSA^-OB^+ (n=24; AHI≤2/hrTST, snore never to rarely, nadir SaO2>90%, NPSG TST ≥7hr), OSA^+OB^- (n=18), and OSA^+OB^+ (n=27; AHI>2/hrTST, snore ≥3x/week). The parental social skills rating system was used and assesses cooperation, assertion, responsibility, empathy and self-control. Relationships were analyzed by GLZ, with age as covariate and gender as factor, with Bonferroni correction for p-values.
Results: Exploratory analyses thus far did not reach statistical significance; however, ineffective social functioning might be present in the OSA^+OB^+ group (Wald statistic p-values range from 0.02 to 0.04). Indeed within OSA cluster, item-analyses show a possible tendency of OSA^+OB^- girls of inviting more frequently friends to their home, and usage of appropriate tone of voice. Further, regardless of gender, OSA^+OB^+ vs. OSA^+OB^- might potentially make less easily friends. Within the OB cluster, OB^+OSA^+ boys potentially refuse more often requests from others.
Conclusion: This ongoing study is currently underpowered. Further recruitments and analyses of deficits in assertion and self-control behaviors for OSA cluster and responsibility for OB cluster might provide insights into social function profiling.
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0231

ACTIGRAPHY IN INFANTS: HOW VALID?

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Introduction: Actigraphy is often used to measure sleep duration and patterns among pediatric populations. Compared to polysomnography, actigraphy is attractive for use with children and infants who do not warrant overnight assessment, largely because it is less intrusive. However, few actigraphy device brands have undergone rigorous validation with infant participants. The purpose if this study was to examine the agreement between concurrent polysomnography and one brand of actigraphy among a group of healthy infants using the Bland-Altman concordance technique.
Methods: Twenty-one healthy infants (14.5±0.5 months) contributed one night of concurrent ankle actigraphy during research polysomnography at Kosair Children's Hospital Sleep Research Center in Louisville, Kentucky. Both bivariate correlation and the Bland-Altman concordance technique for agreement were used to analyze agreement between total sleep time and nocturnal wake time simultaneously measured by both actigraphy and polysomnography.
Results: There was a significant correlation (r=.87, p<0.001) between total sleep time measured by actigraphy and polysomnography. However, the Bland-Altman concordance technique for agreement revealed that actigraphy underestimated total sleep time by an average of 26.8(±48.8) minutes and underestimated total sleep time by >60 minutes among 33% of the infants. The range of differences between these measures was -122.5 to 82.5 minutes. Nocturnal wake time measured by actigraphy and polysomnography was not significantly correlated (r=.01, p>0.1). Furthermore, actigraphy overestimated nocturnal wake time by an average of 42.5(±46.4) minutes; the range of differences between these measures was -35.2 to 148.3 minutes.
Conclusion: Polysomnography is time consuming, expensive, intrusive, and its availability for infants and children is limited. Actigraphy

may serve as an alternative method to allow naturalistic recording of certain measures of infant sleep, including time spent in sleep and wake states. However, improved device and/or software development is needed before actigraphy can be considered as a universally valid method for measuring infants' sleep and nocturnal wake.
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0232

THE ASSOCIATIONS BETWEEN SLEEP PATTERNS AND DAYTIME SLEEPINESS IN SENIOR HIGH SCHOOL STUDENTS WITH DIFFERENT SLEEP CIRCADIAN TYPES

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Introduction: Excessive daytime sleepiness among high school students has become a major concern that may negatively affects daily performance and learning. The factors that were found to be associated with elevated daytime sleepiness included sleep patterns such as early school starting time, sleep deprivation, and delayed weekend sleep schedule, as well as individual trait such as evening circadian type. The objective of the current study was to further investigate the association between sleep patterns and daytime sleepiness in students with different circadian types.
Methods: Participants included 1650 students form the 10th to 12th grades, recruited form senior high schools in Taipei using stratified cluster sampling method. A sleep pattern questionnaire, a daytime sleepiness scale, and the Morningness-Eveningness questionnaire were administered. Regression analyses were conducted to investigate sleep pattern factors that are associated with level of sleepiness separately for different circadian types.
Results: In evening type students, the duration of sleep on the weekdays and difference between weekday and weekend bedtimes revealed significant explanatory power for daytime sleepiness (R=.220 and R=.268). The less the duration of sleep they got and the later they go to bed on the weekend, the higher the daytime sleepiness. In morning type participants, the differences between weekday and weekend wake-up time was found to predict daytime sleepiness (R=.309). The more delayed wake up in the morning on the weekend, the higher the level of sleepiness. In intermediate type students, the level of sleepiness can be explained by the difference between weekday and weekend wake-up time (R=.106). The more delay on weekend wake-up time they had, the higher the level of daytime sleepiness.
Conclusion: Daytime sleepiness in different circadian types was associated with different aspects of maladaptive sleep patterns. Thus, when giving sleep education to high schoolers, different strategies may be emphasized for students with different circadian types.

0233

GENOME-WIDE GENE EXPRESSION PROFILING OF CHILDREN WITH PRIMARY SNORING

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Introduction: Obstructive sleep apnea (OSA) is a multi-factorial and highly prevalent disorder in which both genetic and environmental factors are involved. Children who snore but do not have gas exchange abnormalities or alterations of sleep architecture have primary snoring (PS). Since there is increasing evidence that PS may not be as benign as previously thought, we hypothesized that genome-wide gene expression in peripheral blood leukocytes (PBL) will identify a distinct genetic signature in children with PS compared to controls.
Methods: Children (ages 4-9 years) with and without habitual snoring were polysomnographically ruled out for OSA and designated as PS or controls. Age-, gender-, ethnicity-, and BMI-matched control and PS children underwent blood draw under fasting conditions. Genome-wide expression profiles of PBL in 5 children with PS and 5 controls were compared. Since sample sizes were small, we initially identified differentially activated pathway using gene set enrichment analysis (GSEA) by permutation analysis of 1892 gene sets (false discovery rate ≤ 5%). Next, we integrated our pathway-focused approach with genetic network analysis to explore the details of putative mechanisms activated in PBL of children with PS.
Results: GSEA identified six gene sets that were significantly enriched in the PS group relative to the control children, many of them intricately involved in inflammatory and proliferative processes. Network analysis of interacting gene products revealed widespread activation of IL-2 signaling pathways. In the IL-2 interactome, several major hubs stood out, including transcription factors Fos, Myc, STAT5a, STAT5b, and signaling molecules involved in inflammation and proliferation such as HRAS, MAP Kinases, IRS1 (insulin receptor substrate).
Conclusion: Using an unbiased, whole-genome transcriptional profiling approach, we show that children with PS have distinct gene expression patterns compared to controls. By developing a novel computational framework, we map these differences to critical biological pathways and their respective transcriptional networks. Our integrative approach may therefore be useful in identifying putative targets for therapy or intervention in children with sleep disordered breathing.
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0234

BASAL AND ESOPHAGEAL PROVOCATION INDUCED REFLEXES IN PREMATURE INFANTS DURING SLEEP

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Introduction: Possible airway and digestive tract problems are commonly investigated in infants with life threatening events. The effect of sleep state on modulation of basal and adaptive esophageal reflexes is uncertain. We tested the hypothesis that there are differences in esophageal responses between sleep states vs. awake-state in healthy premature infants.
Methods: 16 neonates (29±1 wks gestational age, 37±1 wks corrected age) were evaluated using esophageal manometry synchronized with video-polysomnography. Subjects were feeding orally and did not have known neurological or pulmonary disease. Basal motility characteristics and abrupt responses to mid-esophageal stimulation with air, water and apple juice infusions (graded stimuli, 0.1 - 5 ml) given during sleep and awake states were analyzed. Mixed statistical models were used, and $P < 0.05$ was considered significant.
Results: 129 spontaneous swallows and 489 infusion-induced responses were evaluated (158 in active,236 in quiet sleep, and 95 in awake). Comparing active and quiet sleep, there were no differences in esophageal, upper esophageal sphincter (UES) and lower esophageal sphincter (LES) motility characteristics, therefore data were combined. Between awake vs. sleep states respectively, basal esophageal motility characteristics were significant for: a) Completely propagated peristalsis (88% vs. 64%, P<0.0001) b) Resting UES pressure (20±3.1 vs. 13±2.2, P<0.01) mmHg c) UES relaxation rate (57±11 vs. 34±8.5, P<0.02) mmHg/sec d) LES relaxation rate (24±3.3 vs. 7±1.8, P<0.0001) mmHg/sec and e) Swallow-LES nadir onset (2±0.3 vs. 3±0.2, P<0.01) sec. Resting LES pressure was similar (15±4 vs. 14±3) mmHg. Upon esophageal provocation, between awake vs. sleep states, the frequency occurrence of peristaltic reflexes was similar (73% vs. 68%) and UESCR were similar (52% vs. 49%). However, the distribution of deglutition response (DR):

secondary peristalsis (SP) reflexes, between awake vs. sleep states respectively, were different (43 DR: 57 SP vs. 26 DR: 74 SP, P < 0.005).
Conclusion: Centrally mediated basal esophageal motility characteristics are suppressed in active and quiet sleep states compared to the awake-state in healthy premature infants. Peripherally mediated esophageal mechano- (air), osmo- (water), and chemo- (apple juice) sensitive peristaltic reflexes and UESCR are preserved in sleep state and are similar to the awake-state. In sleep states, secondary peristalsis is the most frequent peristaltic reflex in neonates.
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0235

SLEEP ABNORMALITIES IN PATIENTS WITH MÖBIUS SEQUENCE

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Introduction: Möbius sequence (MbS) is a rare congenital disorder and its primary diagnostic criteria are congenital facial and abducens nerve palsy. Mental retardation and autism, involvement of other cranial nerves and limb malformations are also described in MbS. This sequence is frequently described as a sporadic condition, but dominant, recessive autosomal and even X-linked recessive inheritances have been described. In our series most cases are related to the misuse of misoprostol during the first three months of pregnancy. There is evidence of a lesion of the central pathways in the brainstem, as part of the syndrome. However, there are very few studies reporting neurophysiological aspects of MbS.
Methods: Twelve patients with MbS were evaluated. Age ranged from 4 to 16 years (8 girls and 4 boys, mean age: 8,58 ± 3,9). All patients underwent overnight polysomnography (PSG) with standard parameters. Sleep stages and respiratory events were scored according to standard criteria. All values are expressed in mean with standard deviation.
Results: PSG findings were: Sleep efficiency (%): 84,68 ± 5,35; Sleep distribution (%): S1 (5,22 ± 3,33), S2 (53,6 ± 8,41), S3 (1,63 ± 0,62), S4 (18,29 ± 7,33), REM (10,37 ± 5,41); Sleep latency (min): 22,88 ± 16,61; REM latency (min): 233,28 ± 67,95; Arousal index: 6,37 ± 1,94; Apnea-hypopnea index (AHI): 4,17 ± 4,12; SpO2(%): mean (97,29 ± 1,71) and lowest(90,42 ± 3,15).
Conclusion: Our study suggests that patients with MbS have reduced sleep efficiency, and a remarkably increased REM latency associated with reduced REM amount. As REM sleep is generated by a complex neuronal interaction in the brainstem, which is the principal site of lesion in these patients, it is quite challenging the understanding of sleep mechanisms in these patients.

0236

RESPIRATORY THERAPY (RT) AND PAP (POSITIVE AIRWAY PRESSURE) THERAPY ADHERENCE: DOES OUTPATIENT RT INVOLVEMENT IMPROVE ADHERENCE IN CHILDREN ON PAP?

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Introduction: Many pediatric patients need CPAP (continuous positive airway pressure) /BIPAP (bilevel positive airway pressure) for the treatment of obstructive sleep apnea(OSA). Adherence with regular use of CPAP/BIPAP equipment is often poor and not sustained long- term. In May of 2006 the Arkansas Children's Hospital Sleep Disorders Center added a Respiratory Therapist skilled in the use of PAP to Pediatric Sleep Disorders Clinic. The responsibilities of the Respiratory Therapist in clinic included down-loading CPAP adherence information including reasons for poor adherence if detected, equipment evaluation (mask, tubing, filters, and machine) and correspondence with the Durable Medical Equipment Company(DME). There is no published literature regarding the role of respiratory therapists in improving adherence with PAP utilization in children.
Methods: We identified children who have been followed in the Sleep Disorders clinic and had adherence download information before and after introduction of RT services. We collected information regarding demographic data, polysomnogram details and CPAP adherence downloads at the clinic visits.
Results: Five patients met criteria for inclusion. The age ranged from 6 to 19 years (Mean 17, SD 4.6). The apnea hypopnea index (AHI)ranged from 4.2 to 30.6. Two out of the 5 patients (40%) carried a diagnosis of morbid obesity. One patient had achondroplasia, one had chronic otitis media with effusion (COME) and one had Klippel-Feil syndrome. Other than addition of RT intervention, all patients continued to receive the same clinical services as before. Three of the 5 patients showed improved CPAP/BIPAP adherence. 1 patient maintained good adherence. The fifth patient is non-adherent. The mean percentage of nights with use more than 4hours before RT intervention was 58.7% (SD 19.4). The mean percentage of nights with use more than 4hours after RT intervention was 70.78% (SD 40.18).
Conclusion: Preliminary data indicated that involvement of a respiratory therapist in the routine clinic follow up of patients needing PAP therapy may help in improving adherence with use of the equipment.

0237

OBSTRUCTIVE SLEEP APNEA DECREASES INSULIN SENSITIVITY IN OBESE LATINO ADOLESCENT MALES

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Introduction: Although obstructive sleep apnea (OSA) and insulin resistance have been linked to the metabolic syndrome in adults, this has not been well established in children. In the current study, we asked whether the severity of OSA in obese children was associated with decreased insulin sensitivity, and whether this was independent of adiposity.
Methods: Polysomnography was performed on obese, otherwise healthy Latino males referred for snoring (age 11-17 years, BMI>95th percentile for age/gender). The frequently sampled intravenous glucose tolerance test was used to assess insulin sensitivity (SI). Total body dual energy X-ray absorptiometry (DEXA) was used to assess adiposity (total body fat).
Results: 7 males (mean age 13.3±0.8 years, BMI z score=2.44±0.17, fasting glucose 83±3 mg/dL, obstructive apnea hypopnea index (OAHI) 5.2±1.1 events/hour, and desat score (≥3% drop in oxygen saturation) 4.1±1.8 events/hour sleep) were studied. SI (3.8±1.4x10-4min-1/μU/mL) was not normally distributed and was log transformed. Log SI was inversely associated with OAHI (Pearson r= - 0.859, p=0.013) and the correlation remained significant after correcting for BMI or total body fat. Log SI was inversely associated with desat score(r= - 0.826, p=0.022) but did not remain significant after correcting for BMI or total body fat.
Conclusion: The severity of OSA is associated with decreased insulin sensitivity independent of the degree of obesity in Latino adolescent males. Our data suggest increased risk for obesity-associated dysfunction in insulin physiology even in children with mild to moderate OSA.

We speculate that OSA potentiates the risk for development of insulin resistance in the adolescent population.

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0238

THE RELATIONSHIP BETWEEN PAIN, SLEEP, AND QUALITY OF LIFE IN PEDIATRIC SICKLE CELL DISEASE

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Introduction: The relationship between sleep and quality of life (QoL) in chronic pain patients is a growing area of research; however, only a few studies have focused on pediatric sickle cell disease (SCD) samples. The purpose of this study is to examine the relationship between sleep and pain reports as well as the relationship between sleep and QoL in children with SCD.

Methods: During a routine clinic visit, 25 children ages 8 - 18 years completed baseline ratings of SCD pain intensity and sleep quality and duration as part of a 28-day diary. Participants also completed the Pediatric Quality of Life Inventory, which assesses physical and psychosocial functioning at baseline and at the end of the month. Because data collection is currently ongoing, only baseline data was analyzed for this study.

Results: Preliminary analysis revealed no correlation between pain intensity and sleep quality or duration. A significant relationship between sleep quality and QoL ($r = .51$, $p = .009$) did emerge, but no relationship was found between sleep duration and QoL. When examining individual QoL domains, significant associations were found between sleep quality and both emotional functioning ($r = .63$, $p = .001$) and school functioning ($r = .43$, $p = .036$).

Conclusion: Better sleep quality may be associated with better QoL in children with SCD, particularly in the areas of emotional and school functioning. The lack of relationship between pain intensity and sleep may be due to use of current day pain, which does not account for prior or future pain experience that may relate to sleep. Using the entire month of diaries, in which pain and sleep were recorded at night, may help to resolve this issue. By improving sleep quality through interventions aimed at sleep hygiene, it may be possible to improve QoL in children with SCD.

0239

MORNINGNESS-EVENINGNESS, SLEEP, AND HEALTH RISK FACTORS AMONG STUDENTS WHO WORK DURING THE SCHOOL YEAR: PRELIMINARY RESULTS

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Introduction: Adolescents and young adults are at high risk of excessive daytime sleepiness and occupational injuries. Also, students who work during the academic year are more likely to obtain insufficient sleep on a regular basis. This study sought to assess the relationship between morningness-eveningness, sleep, and health risks in students who work during the school year.

Methods: A total of 64 students (30 men) aged 19-20 years attending high-school (6%), college (67%) or university (27%) wore an actigraph and filled out the Social Rhythm Metric (SRM-5) for two consecutive weeks during the school year. Also, participants completed the Horne-Ostberg morningness-eveningness Questionnaire, a psychological distress symptom scale (Ilfeld), the Pittsburgh Sleep Quality Index (PSQI), and the Occupational Fatigue Exhaustion Recovery (OFER) scale that includes a chronic work-related fatigue subscale. ANOVAs were used to compare morningness-eveningness groups on sleep and health variables.

Results: Thirteen students were morning types (M-types), 39 were intermediary types (I-types), and 12 were evening types (E-types). Mean hours worked per week was 20.8 (SD=11.4). Morningness-eveningness did not vary significantly with work hours. E-types had later mean sleep onset and offset than M-types (2:10 vs 23:26, $p<0,001$ and 9:23 vs. 7:29, $p<0,001$). E-types also had lower SRM-5 score ($p<0.01$), indicating lower lifestyle regularity, higher PSQI scores ($p<0.01$), suggesting lower sleep quality, and higher levels of chronic fatigue ($p<0.05$) compared to M-types. Finally, a tendency was observed for E-types to report more psychological distress symptoms than M-types ($p=0.057$).

Conclusion: E-types students who work during the school year are particularly at risk of sleep deprivation. Given that previous studies in adult workers identified both chronic fatigue and sleeping difficulties as independent risk factors for being injured in an occupational accident, it is necessary that E-types students who work obtain sufficient sleep in order to reduce the risks associated with health and safety.

0240

SLEEP IN CHILDREN, ADOLESCENTS AND THEIR MOTHERS DURING CANCER TREATMENT

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Introduction: While the literature suggests parents are more involved in regulating the sleep/wake patterns of healthy children compared to adolescents, little is known about parental influence of sleep/wake patterns of children and adolescents newly diagnosed with leukemia. Because children are receiving weekly intensive chemotherapy and experiencing multiple symptoms at home, do mothers increasingly regulate sleep schedules and monitor their children more vigilantly at night? Increased understanding of sleep patterns in children and mothers will assist in developing appropriate research methods (e.g. parent/child report) and interventions for improving sleep and symptom management during this stressful period.

Methods: Thirty-one mother-child dyads were included in this analysis, part of a larger longitudinal study of symptoms in children with leukemia and their parents. Start time for sleep for each family member was measured by actigraphy. Diaries asked children if they experienced pain in the evening and if they told their parents.

Results: Few children/adolescents receiving chemotherapy were attending school during the first two months of chemotherapy. The average time to sleep was 2200 for 7-10 year olds and 2300-2400 for 11-19 year olds. Nine (27%) children went to bed after their mothers, 2(14%) of 7-10 year olds and 7(37%) 11-19 year. Thirteen (87%) of 11-19 year olds reported pain; 80% told their parents. Eleven (69%) of 7-10 year olds reported pain; 64% told their parents.

Conclusion: Children are not attending school in the initial months after diagnosis, and the data suggests sleep schedules are less regulated. The data suggests that more 11-19 year olds go to bed after their mothers indicating they are not appropriate reporters of these children's sleep patterns. While more 11-19 years olds are having and reporting pain to

their parents in the evening, the data does not indicate increased parental monitoring during the night.
Support (optional): National Institutes of Health, National Institute of Nursing Research (Grant#5R01NR008570).

0241

A LONGITUDINAL INVESTIGATION INTO THE RELATIONS BETWEEN PERSONALITY, SLEEP, CONDUCT PROBLEMS, AND SCHOOL PERFORMANCE IN ADOLESCENTS

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Introduction: Different lines of research suggest that disturbed sleep is particularly detrimental during adolescence because it may contribute to emotional and behavioral disorders (e.g., Dahl & Harvey, 2007) and impair school performance (e.g., Wolfson & Carskadon, 2003). However, previous investigations were often limited in three respects: (a) They used cross-sectional rather than longitudinal designs, thereby precluding causal inference; (b) they did not take into account possible interactions with personality dimensions, in particular, the different facets of impulsivity; and (c) they relied on self-reported rather than on actual school grades. The present study sought to overcome these limitations.
Methods: A sample of 202 7th to 9th graders aged 12 to 16 years completed five questionnaires at an interval of 6 months: the short version of the Big Five Personality Inventory (Rammstedt & John, 2007), the UPPS Impulsive Behavior Scale (Whiteside & Lynam, 2001), the Insomnia Severity Index (Morin, 1993), the Multidimensional Fatigue Inventory (Smets et al., 1995), and the Strengths and Difficulties Questionnaire (Goodman, 2001). In addition, the school provided the grades that the adolescents obtained during the ongoing scholastic year.
Results: Insomnia severity and fatigue were correlated to emotional and behavioral problems (r range = .48 to .65, $p<.001$), as well as to school grades (r range = .22 to .23, $p<.01$). Five domains of personality were also correlated to emotional and behavioral problems: agreeableness (r range = -.32 to -.38, $p<.001$), conscientiousness (r range = -.38 to -.42, $p<.001$), neuroticism (r range = .44 to .48, $p<.001$), impulsive urgency (r range = .57 to .60, $p<.001$), and lack of perseverance (r range = .45 to .51, $p<.001$). Moreover, the latter two facets were correlated to school grades (r = -.18 to -.28, $p<.01$). Follow-up longitudinal structural equation models were computed to map the relations between the variables of interest across time.
Conclusion: The present findings support the notions that (a) disturbed sleep contributes to emotional and behavioral problems and to poor school performance in adolescents, and (b) the relations between sleep and behavioral measures are impacted by interindividual differences in personality.

0242

DEFINING THE SLEEP PHENOTYPE IN CHILDREN WITH AUTISM—CONTRIBUTIONS OF POLYSOMNOGRAPHY AND ACTIGRAPHY TO PARENTAL CONCERNS

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Introduction: Sleep problems are highly prevalent in children with autism spectrum disorders (ASD), although a subset of children with ASD are reported by their parents to sleep well. Our goal was to identify objective measures that differentiate sleep in children with ASD with parental sleep concerns (poor sleepers-ASD-PS) from those without (good sleepers-ASD-GS).
Methods: Fifty eight children, ages 4-10 years, participated in this study. Forty-two had a clinical diagnosis of ASD confirmed by the Autism Diagnostic Observation Schedule, and were defined as ASD-PS (n = 27) or ASD-GS (n = 15) based on the Parental Concerns Questionnaire. Sixteen were typically developing (TD) and reported to be good sleepers. Sleep was measured with two nights of wrist actigraphy (Mini-Mitter AW64) and polysomnography (PSG); nights were averaged. Measurements obtained included total sleep time (TST), sleep latency (SL), sleep efficiency (SE), wake time after sleep onset (WASO), nighttime movement and fragmentation (MFI)-actigraphy only, and arousal index (AI)-PSG only. Kruskal-Wallis statistics were used to determine significance between all three groups, and Mann-Whitney U tests provided between group comparisons on the overall significant parameters.
Results: With actigraphy, the ASD-PS group differed significantly from the ASD-GS group on sleep latency [mean(SD)] [53.4(25.6) versus 23.0(19.0) minutes]; sleep efficiency [80.9(6.6) versus 88.3(5.1)%], and MFI [(12.5(3.4) versus 9.4(3.1)]. With PSG, the ASD-PS group differed significantly from the ASD-GS group on sleep latency [(54.0(41.7) versus 34.9(34.3)] minutes. The ASD-GS and TD children were comparable on sleep parameters, except that the TD children had a higher MFI [(14.0(3.3) versus (13.5(3.4)].
Conclusion: Our results support a phenotype of children with ASD who sleep well, defined by parent report and confirmed by objective measures of sleep, including PSG and actigraphy, which are complementary. Defining this phenotype provides the foundation for focused studies of pathophysiology and targeted interventions in autism and broader populations.

0243

CO-SLEEPING, PARENTAL PRESENCE, AND SLEEP IN YOUNG CHILDREN: A CROSS-CULTURAL PERSPECTIVE

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Introduction: The aim of this study is to characterize co-sleeping, sleep patterns, and problems in a large cross-cultural sample of young Asian and Caucasian children.
Methods: Parents of 29,287 infants and toddlers from Australia, Canada, China, Hong Kong, India, Indonesia, Korea, Japan, Malaysia, New Zealand, Philippines, Singapore, Taiwan, Thailand, United States, United Kingdom, and Vietnam completed an expanded version of the Brief Infant Sleep Questionnaire. Co-sleeping was grouped by bed-sharing (BS), room-sharing (RS; in separate bed), and sleeping in a separate room (SR).
Results: Significant variability in BS and RS were found across countries, with 11.8% bed-sharing and 22.0% room-sharing in predominantly Caucasian (PC) countries compared to 64.7% and 86.5% respectively in predominantly Asian (PA) countries. Overall, children who slept in a separate room obtained more sleep, woke less at night, had less difficulty at bedtime, fell asleep faster, and were perceived as having fewer sleep problems. However, these clinically significant differences across sleep location were primarily observed in PC children, and not in PA children. A possible mechanism for these differences is whether a parent is present at bedtime when the child falls asleep. In PC countries, 97.4% (BS) and 83.9% (RS) of parents were present at bedtime compared to 40.9% if the child slept in a separate room. Minimal differences, however, were seen in PA, with 98.2% (BS) and 97.5% (RS) of parents present at bedtime compared to 87.4% of SR.
Conclusion: Overall, young children in PA countries are more likely to bed-share and room-share than those in PC countries. Interestingly, there are minimal differences in sleep patterns and sleep problems based on sleep location in Asian countries, compared to significant differences in Caucasian countries. One explanation may be negative sleep asso-

ciations, as parental presence at bedtime appears to be the factor that impacts sleep more than literal co-sleeping.
Support (optional): This study was supported by Johnson & Johnson Consumer Products Company, Division of Johnson & Johnson Consumer Companies, Inc.

0244

AN ELECTROCARDIOGRAM-BASED TECHNIQUE TO ASSESS CARDIOPULMONARY COUPLING DURING SLEEP IN PEDIATRIC PATIENTS SUSPECTED WITH SLEEP DISORDERED BREATHING

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Introduction: To evaluate an electrocardiogram (ECG)-based cardiopulmonary coupling (CPC) technique in a pediatric population suspected of SDB, a retrospective analysis of polysomnographic (PSG) studies was performed.
Methods: The SleepTech database was searched for full in-lab pediatric (mean age: 5.5 ± 2.0 years) PSG studies of patients suspected with SDB having a minimum of 6 hours of recording performed in the previous 4 months. Forty PSGs met inclusion criteria for manually sleep staged and respiratory scored, thoracic respiratory effort and ECG signal with less than 5% artifact of total study time. Two studies were not included in the statistical analysis for PSG variables due to no REM sleep scored but were included for analysis of the CPC variables. RemLogic (Embla, Inc; Broomfield, CO) was used to calculate the CPC- a measure of autonomic and respiratory interactions. The 40 studies were subdivided into 5 categories based upon the apnea hypopnea index (AHI): Group I) ≤ 1 event/hour (n=4); Group II) >1 and < 5 events/hour (n=13); Group III) ≥5 and < 10 events/hour (n=13); Group IV) ≥10 and < 20 events/hour (n=6); Group V) ≥ 20 events/hour (n=4).
Results: MANOVA performed for CPC and PSG sleep variables showed significant differences between groups. Standard PSG variables were not statistically different. High frequency coupling (HFC) was significantly reduced in Groups III (67.4%; p=.02), IV (60.5%; p<.01) & V (62.3% p<.01) compared to Group I (89.7%). A significant increase of low frequency coupling (LFC) was also observed in Group III (23.8%; p=.03), IV (30.7%; p<.01) & V (34.4%; p<.01) compared to Group I (6.8%).
Conclusion: The RemLogic CPC analyzer provides automated characterization of disrupted sleep quality in a pediatric population suspected with OSA. The clinical utility of using a spectrogram to indicate the presence of OSA in this population is promising.

0245

PRENATAL AND PERINATAL COMPLICATIONS AS RISK FACTORS FOR CHILDHOOD SLEEP DISORDERED BREATHING: POSSIBLE BRAIN EFFECT

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Introduction: Previously conducted studies suggest that the pathophysiology of sleep disordered breathing (SDB) in children most likely involves several mechanisms including anatomic and metabolic components. In addition, recent research has yielded evidence of the negative impact that obesity, low socioeconomic status, minority race, prematurity and maternal smoking during pregnancy can have on children, and how these factors are related to the development of SDB. In this study, we investigated the association between parent reported prenatal and perinatal complications and SDB.
Methods: We conducted a cross-sectional study of 613 children (105 clinically referred and 508 community controls) ages 4-17 who all underwent an overnight polysomnography, and complete history and physical examination. A comprehensive child development questionnaire was completed by a parent. We compared clinically referred children with SDB as defined by an Apnea/Hyponea Index >5 (AHI) to healthy population based controls from The Penn State Children's Cohort (AHI<1).
Results: In unadjusted and adjusted (race and socioeconomic status) analyses, prenatal complications such as maternal high blood pressure and gestational diabetes, perinatal complications related to prematurity and labor and delivery as well as neurodevelopmental delay (i.e., motor milestones) were significantly associated the presence of childhood SDB.
Conclusion: These preliminary data suggest that there is a strong association between children who experience prenatal and perinatal distress and the development of moderate to severe childhood SDB even after adjusting for race and socioeconomic status. The developmental motor delays suggest that these stressors may result in brain injury which in turn may effect nighttime breathing.

0246

EXPLORING THE PEDIATRIC POSITIVE AIRWAY PRESSURE (PAP) EXPERIENCE TO DETERMINE FACTORS ASSOCIATED WITH PEDIATRIC ACCEPTANCE OF PAP

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Introduction: Obstructive sleep apnea syndrome (OSAS) occurs in approximately one to three percent of children. Though positive airway pressure (PAP) therapy is a viable treatment option for children with OSAS, there is a paucity of information regarding factors that facilitate the acceptance of PAP therapy in childhood. The principal aim of this study was to explore the patient and family experiences adapting to PAP. We hypothesized that critical components of pediatric PAP education include, parent confidence and understanding of treatment process and practice exposure for the child. Herein, we report the themes regarding the lived experiences of children and their parents the first month of PAP therapy.
Methods: A qualitative design utilizing content analysis was employed. Prior to initiation of PAP therapy all participants (4 male, 2 female; age 6-13) received a nurse education visit comprised of PAP education, mask fitting, exposure to device and pressure flow. Participants underwent semi-structured, audio-taped interviews at the time of their one month CPAP follow up visit. For all interviews a parent and child were both present; both provided input, with most questions directed to the parent. A researcher not involved in the nurse visit coded transcripts and grouped themes to reflect experiences of the patients.
Results: Themes identified from all participants included hopes for the future, wide ranges of parent/child experiences and reactions, positive surprises, and advice to others. The overall theme reflected commitment to continuing therapy whether there were successes or challenges.
Conclusion: The opportunity to practice with equipment and try on different interfaces was considered paramount in coping with initial challenges and reactions to therapy. Participants recognized the improvement in daytime functioning and reported a more favorable view of CPAP at one month than expected at diagnosis.
Support (optional): This study is funded by the Elizabeth C. Bonner Memorial Education Fund of the Mayo Foundation for Medical Education and Research.

0247

EEG SPECTRAL ANALYSIS OF RESPIRATORY EVENT TERMINATIONS IN CHILDREN WITH SEVERE SLEEP DISORDERED BREATHING

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Introduction: Obstructive sleep apnea (OSA) is known to disrupt sleep quality in adults due to frequent arousals. In children, conventional methods suggest sleep may be less disturbed, as only ~50% of apneic events terminate with an EEG arousal. The present study tested the hypothesis that EEG spectral analysis would be more sensitive in identifying EEG arousals at respiratory event terminations in children than standard visually scored assessment of sleep quality.
Methods: 20 healthy children aged 7-12y diagnosed with Moderate/Severe OSA were recruited. Standard polysomnography was performed with EEG bandpass filtered from 0.3Hz to 100Hz and sampled at ≥500Hz. Respiratory events were categorised into their associated arousal type: cortical arousal, sub-cortical arousal, and non-arousal using visual analysis. Spectral analysis using Fast Fourier Transform was run on consecutive 5s blocks for 10s before respiratory event onset (averaged for baseline) and for the 10s after event termination. 5 frequency bands were derived: Delta (0-4 Hz), Theta (4-8 Hz), Alpha (8-12 Hz), Sigma (12-14 Hz), and Beta (14-30 Hz). Statistical analysis was performed using 2-way ANOVA with Student Newman Keuls post hoc tests ($p < 0.05$ being considered significant).
Results: There was a significant decrease in both Delta and Theta power when comparing baseline to the 10s immediately following respiratory event termination in the cortical arousals ($p<0.05$ for both). No differences were seen when comparing 5s blocks to baseline in either the subcortical or non-arousal related events in any frequency band.
Conclusion: The data confirm that children are relatively unlikely to show a cortical arousal at the termination of a respiratory event. We speculate that in children, a stronger sleep-drive preserves sleep quality even in severe OSA.
Support (optional): National Health and Medical Research Council of Australia

0248

CARDIOVASCULAR RESPONSES TO HEAD-UP TILTING: CONSEQUENCES OF PRETERM BIRTH

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Introduction: Neuropathological and physiological evidence in Sudden Infant Death Syndrome (SIDS) victims demonstrates marked abnormalities in cardiovascular control. Preterm infants are at an increased risk for SIDS and have altered heart rate (HR) and blood pressure (BP) compared to term infants. As there is a paucity of information on BP control in preterm infants, we aimed to examine the effect of preterm birth on cardiovascular responses to head-up tilting (HUT).
Methods: 25 preterm infants (28-32wk GA) and 20 term infants (38-42wk GA) were studied in the supine position using daytime polysomnography at 2-4wk, 2-3mo and 5-6mo CA. BP was recorded non-invasively using a photoplethysmographic cuff. 15° HUTs were performed during quiet (QS) and active (AS) sleep. Data are expressed as % change from pre-HUT baseline.
Results: Preterm infants responded to HUT with increased HR and BP, followed by a reflex bradycardia and a subsequent return in HR and BP to baseline levels. Overall, HUT response patterns were similar between preterm and term infants at matched ages. However preterm infants had a considerably delayed BP restoration to baseline levels (~37 beats post-HUT) compared to term infants (~23 beats post-HUT) at both 2-4wk and 2-3mo CA ($p<0.05$).
Conclusion: For a given perturbation in BP, preterm infants are able to respond appropriately with reflex changes in HR. However, the subsequent delayed BP restoration at 2-4wk and 2-3mo CA, may be indicative of underlying alterations in vascular control. These subtle alterations in BP control evident of preterm infants may contribute to their vulnerability to SIDS.
Support (optional): National Health and Medical Research Council of Australia

0249

SLEEP DISORDERED BREATHING IN OBESE CHILDREN IS ASSOCIATED WITH EDS, INFLAMMATION AND METABOLIC ABNORMALITIES

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Introduction: In obese adults, sleep apnea is associated with excessive daytime sleepiness (EDS) and cardiometabolic risk factors, including visceral adiposity, insulin resistance and hypercytokinemia. In children, sleep disordered breathing (SDB) has been primarily associated with anatomic abnormalities and neurocognitive impairment, while studies on potential concurrent metabolic aberrations and EDS have been limited and inconsistent. In this study, we examined the joint effect of SDB and obesity in EDS, as well as proinflammatory and metabolic markers.
Methods: 150 children aged 5-17 years were consecutively recruited from our sleep disorders clinic and from a subset of the Penn State Children's Cohort. Every child had a thorough history and physical examination, 9-hour polysomnographic study and a morning blood draw for the assessment of IL-6, TNFa, sIL-6R, TNFR1, CRP, leptin and adiponectin using commercially available kits. In addition, parents completed a subjective questionnaire to assess EDS. Analysis of covariance was performed on four groups that were separated by SDB severity and BMI (Lean no SDB, Obese no SDB, Obese mild SDB, Obese moderate/severe SDB).
Results: There was a significant linear trend in plasma IL-6, TNFR1, CRP and leptin concentrations with lowest levels observed in lean controls and highest in obese with moderate/severe SDB ($P=0.012$, $P<0.001$, $P<0.001$, $P<0.001$, respectively). Adiponectin followed the opposite pattern, with highest levels in lean controls and lowest in obese with moderate/severe SDB ($P<0.001$). EDS frequency increased progressively and significantly in the four groups ($P=0.001$).
Conclusion: This study suggests that in obese children, sleep disordered breathing is associated with EDS, elevation of proinflammatory cytokines, increased leptin and decreased adiponectin. All these changes point to an inflammatory/insulin resistance state suggesting that SDB in obese children share many similarities with SDB in obese adults, and that the disorder in obese children may also be a manifestation of the metabolic syndrome.

0250

DECLARATIVE MEMORY CONSOLIDATION IN YOUNG GIRLS: EFFECTS OF ACUTE SLEEP RESTRICTION

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Introduction: In adults, sleep has been shown to be essential for consolidation of declarative memory (memory for facts), however little research has examined this relationship in children. The aim of this study was to examine the effect of one night of sleep restriction on declarative memory consolidation in school-aged children.

Methods: Fourteen girls (mean age = 10.6±0.3y) attended a sleep laboratory for an adaptation and two counterbalanced treatment (control and sleep restriction) nights. Treatment nights were separated by 7-days. Bedtime was delayed in sleep restriction (0200-0700 - 5hr TIB) compared to control (2100-0700 - 10hr TIB). Actigraphy was used to measure objective sleep parameters. Declarative memory was assessed via recall and recognition of previously learnt words (Auditory Verbal Learning Test; AVLT). AVLT testing times were identical across conditions (1900h and 0900h). To control for inter-trial differences, post-sleep values were expressed relative to maximum potential learning.

Results: Actigraphy results showed successful manipulation of sleep (total sleep time: 9.18±0.16h vs 4.81±0.06h). Repeated measures ANOVA found a significant effect over time ($p<0.0001$), but not condition, with no difference in word recall performance between sleep restriction and control. When expressed relative to maximum learning, delayed recall was worse after sleep in both conditions, however only reached significance in sleep restriction ($p<0.05$). Comparison of performance on the recognition task found no difference between sleep restriction and control.

Conclusion: No difference in recall or recognition between conditions suggests that declarative memory consolidation in children may be resilient to acute sleep restriction. However, the greater decay in post-sleep performance in the sleep restriction condition suggests that shortened sleep may make children more susceptible to pre-sleep interference. Given the reported increased prevalence of chronic sleep restriction, an understanding of the implications of inadequate sleep on memory in children is imperative, especially if the sequelae include impaired academic progress.

0251

THE EFFECT OF INCONSISTENT SLEEP ROUTINES AND SNORING ON NEUROCOGNITION AND BEHAVIOR IN CHILDREN AGED 5-10 YEARS

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Introduction: Recent research shows consistency of sleep routine may be important for daytime functioning. We aimed to determine if inconsistent routines were associated with neurocognitive and behavioral deficits in both snoring and non-snoring, healthy children.

Methods: Habitual snorers (HS; N=28) and controls (N=62), identified from the South Australian Paediatric Sleep Survey (mean age 8.1±1.5 yrs), participated in neurocognitive (DAS) and behavioral (CBCL) testing, preceded by 7-day sleep diary. Coefficient of variation (CV)- calculated as s.d./mean and expressed as a percentage - was the variation measure in bedtime, wake time, time in bed (TIB) and total sleep time (TST) across weekdays (Sun-Thurs) and weekends (Fri/Sat). ANOVA was used to test differences between groups and stepwise regression analysis determined predictive relationships.

Results: No differences were found between groups on sex, age, socioeconomic status or neurocognition. HS showed later mean wake time on weekends and greater CV in weekly wake time ($p<0.05$). HS also demonstrated more problematic behavior for seven CBCL subsets ($p<0.05$). Sleep routine was significantly correlated with verbal and spatial ability (DAS), social, thought, affective and total problems, and rule-breaking behavior (CBCL). After controlling for demographics and snoring, increased CV of TST on weekends was predictive decreased verbal ability ($\beta=-0.28$, $p<0.05$). CV of TST on weekdays predicted thought ($\beta=0.34$) and affective problems ($\beta=0.32$: $p=0.005$). CV of bedtime on weekdays predicted rule-breaking behavior ($\beta=0.25$, $p<0.05$). Snoring independently explained 11.1% and 20.1% of the variance of thought and affective problems respectively ($p<0.001$), but was not predictive of verbal ability or rule-breaking behavior.

Conclusion: These results show that an inconsistent sleep routine is associated with neurocognitive and behavioral deficits over and above that explained by habitual snoring. As inconsistent routines may exist independently, as well as concomitantly, with sleep disorders, this result has serious implications for daytime functioning and sleep education.

0252

TEENAGE SLEEP AND THE INTRUSION OF DIGITAL TECHNOLOGY INTO THE BEDROOM

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Introduction: For most teenagers, digital technologies have become a pervasive part of life with a subsequent impact on a range of social behaviours including pre-sleep behaviour and possibly sleep quality.

Methods: In the mid school year, 316 teenagers (F = 121; mean (SD) age = 17.3 (.98), range = 15-20.2y) from four metropolitan Australian schools volunteered to complete an omnibus questionnaire which included measures of sleep habits and use of digital technologies.

Results: Girls compared to boys were less likely to play electronic games (>5 nights/week 2.5/5.7%), listen to music (18.5/23.9%) and watch TV (6.6/16.0%) but more likely to talk on the phone (19.2/15.0%). Only 25% of teenagers reported sufficient sleep on school nights [never 12.4/13.2 (male/female); rarely 32.2/30.0; sometimes 27.3/32.6; usually 22.3/22.0; and always 5.0/2.2%]. A relatively high number of teenagers also reported daytime sleepiness: with 3.2% falling asleep in conversation, 25% on a bus/train, 7% at the movies, 27% watching TV, 18% studying, 3% doing a test, 20% in class, 6% working on the computer, 5% playing video games and 20% reading a book. Significant but weak correlations were observed between digital media use and sleepiness (all $r < .22$).

Conclusion: Almost 50% of Australian teenagers in the present study reported before falling asleep on school nights that they either sometimes or always played an electronic game, watched TV, listened to music or talked on the phone. A sizeable percentage also reported insufficient sleep and daytime sleepiness. We suggest that sleep may be unnecessarily shortened in a substantial number of students during a period where alertness and peak academic performance are at a premium. There is a need to educate adolescents, schools, parents and the community about sleep hygiene and managing the intrusion of digital technology at bedtime.

0253

RELATIONSHIP BETWEEN SLEEP DISRUPTION AND IOWA GAMBLING TASK PERFORMANCE IN OVERWEIGHT CHILDREN AND ADOLESCENTS

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Introduction: Although problem-solving deficits occur in individuals with sleep pathology, much of the literature has focused on tasks that are mediated by the dorosolateral prefrontal cortex. The impact of sleep pathology on tasks mediated by the ventromedial prefrontal cortex (e.g., tasks that involve the regulation of affect and risk assessment) has yet to be determined. In this study, we investigated the association between sleep disruption and performance on the Iowa Gambling Task (IGT), which is heavily dependent on ventromedial prefrontal cortical functioning, in a sample at high risk for sleep pathology.
Methods: Overweight 10-16 year-old subjects who were not actively taking psychiatric medication and had no neurological history were recruited from hospital-based weight-management or sleep medicine clinics. Subjects (N=99) underwent a week of actigraphy and afternoon neuropsychological evaluation which included the IGT. For the IGT, subjects were asked to select cards from four decks, using feedback to determine which decks resulted in the greatest rewards and smallest punishment over 100 trials. Sleep disruption was operationalized as the number of long (>5 min) arousals shown on actigraphy divided by the total sleep duration. Data were analyzed using SAS PROC MIXED.
Results: As expected, IGT performance tended to improve over the course of the task ($p<.01$). However, the degree of improvement covaried with sleep continuity, as reflected in the significant interaction between sleep disruption and time ($p=.01$). Follow-up analyses indicated that subjects who showed good sleep continuity improved their performance across trials, but those with disrupted sleep failed to do so.
Conclusion: These data suggest that sleep disruption is associated with a failure to appreciate or learn from feedback regarding risks during decision-making, consistent with impairment in ventromedial prefrontal functioning. This may be related to behavioral impairments in children and adolescents with sleep pathology, reflecting a relationship between sleep quality and neurological development.
Support (optional): Grants #K23 HL075369 and M01 RR 08084 from the National Institutes of Health.

0254

MAIN AND INTERACTIVE EFFECTS OF SLEEP PROBLEMS AND HIGH BLOOD PRESSURE ON ATTENTION AND PROBLEM-SOLVING IN OVERWEIGHT 10-16 YEAR-OLD CHILDREN AND ADOLESCENTS

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Introduction: Separate literatures have reported that neurobehavioral deficits can be caused by sleep pathology and high blood pressure (HBP) in adults and children. Given that sleep problems and HBP are disproportionately evident in overweight children, it is important to understand the primary and interactive effects of sleep pathology and HBP on cognitive development in this burgeoning subpopulation.
Methods: Overweight 10-16 year-old subjects who were not taking psychiatric or hypertension medication and had no neurological history were recruited from hospital-based weight-management or sleep medicine clinics. Subjects underwent a week of actigraphy, a physical exam and overnight polysomnogram, and afternoon neuropsychological evaluation. 119 subjects had complete data on all relevant variables. HBP was defined as systolic or diastolic blood pressure >95th%ile for age, gender, and height. Five sleep variables were chosen for analysis: actigraphy-based sleep duration and efficiency, and polysomnogram-based arousal index, apnea+hypopnea index, and mean oxygen saturation during sleep. Validated neuropsychological tests yielded age-normed measures of problem-solving and short-term and sustained attention. Using linear regression, each of these neuropsychological outcomes was predicted by the five sleep variables and five sleep-by-HBP interaction terms, with and without covarying for adiposity, socioeconomic status, and race.
Results: Predictors were non-collinear. Better short-term attention was predicted only by longer sleep duration, $p=.01$. Better sustained attention was predicted only by greater sleep efficiency, $p=.009$. Sleep efficiency interacted with HBP to predict problem-solving, $p=.001$: there was no association in non-HBP subjects, but higher sleep efficiency correlated with better problem-solving in subjects with HBP. These effects were unchanged after entry of covariates. Neuropsychological outcomes were not predicted by the main effects of polysomnography indexes, HBP, or their interaction.
Conclusion: These data confirm that attention and problem-solving are related to sleep duration and continuity, and further provide novel evidence that blood pressure can moderate the relationship between sleep and problem-solving.
Support (optional): Grants #K23 HL075369 and M01 RR 08084 from the National Institutes of Health.

0255

ESOPHAGEAL SENSATION IN PREMATURE NEONATES DURING SLEEP AS DETERMINED BY ELECTROCORTICAL AROUSALS AND VISCEROSOMATIC RESPONSES UPON ESOPHAGEAL STIMULATION

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Introduction: While it is known that in premature infants a variety of sensory stimuli in the mid-esophagus evoke esophageal peristaltic and upper esophageal sphincter contractile reflexes (UESCR)from the aerodigestive tract, recognition of cortical arousal as an effect of visceral stimulus during sleep has not been quantitated. Our aim was to test the hypothesis that esophageal stimuli can result in both esophageal neuromotor responses and electrocortical arousals during sleep in premature infants.
Methods: Esophageal stimulation (N=83 stimuli, air, water, apple juice infusions) and 27 sham infusions were given in active and quiet sleep to 11 healthy premature infants (27±0.8 wks gestational age, 37±0.8 wks postmenstrual age). Concurrent manometry, respiratory inductance plethysmography and video-polysomnography were used for evaluation. The response latency, frequency occurrence and duration of arousals, peristaltic reflex and UESCR were assessed. Observers blinded to esophageal manometry examined fluctuation in respiratory patterns and sleep state changes. Esophageal motility data were scored by observers blinded to the sleep data. Mixed statistical models were used, and $P < 0.05$ was considered significant.
Results: None of the sham stimuli resulted in esophageal responses or arousals. In contrast, 55% of infusions produced electrocortical arousals

(P < 0.0001). Between arousals vs. non-arousals, basal esophageal characteristics were as follows: a) Stimulus-Peristaltic Reflex Onset (5.8±0.8 vs. 4.4±0.8, sec, P<0.2) b) Stimulus-UESCR Onset (5.2±0.8 vs. 4.0±0.9 sec, P<0.3) c) Frequency of Peristaltic Reflex (78% vs. 65%, P<0.2) d) Frequency of UESCR (85% vs. 73%, P<0.2) e) Stimulus-Return to Quiescence (33.8±1.6 vs. 16.2±2.8, P<0.0001) f) UESCR Duration (15.5±2.7 vs. 6.5±3, P<0.04) g) Change in Breathing Pattern (30% vs. 0%, P<0.0002) and h) Sleep State Change (17% vs. 5%, P<0.09).
Conclusion: Premature infants can perceive visceral sensations during sleep resulting in electrocortical, respiratory changes and esophageal reflexes. Frequency occurrence of arousals is dependent on prolonged peristaltic reflexes and UESCR. Esophageal afferent stimulation can activate dormant supra-tentorial pathways and cortical activation, and restoration of esophageal quiescence may restore sleep.
Support (optional): Supported by NIH-RO1 DK 068158.

0256

YOUNG ADOLESCENTS' SLEEP PATTERNS ACROSS DIFFERENT NEIGHBORHOOD ENVIRONMENTS

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Introduction: Low socioeconomic status and exposure to adverse conditions may affect sleep. It is unclear, however, how SES and environmental disadvantages contribute to young adolescents' sleep disparities. Neighborhood limitations increase prevalence of substance abuse and health problems such as asthma and obesity in lower SES groups. This study examined the influence of neighborhood factors on adolescents' sleep patterns.
Methods: 7th graders (N = 155, 63 males) at 2 urban, public schools (SST: 8:37am) completed the School Sleep Habits Questionnaire and parents provided background information. Utilizing the Mendes de Leon Systematic Neighborhood Survey, researchers coded participants' neighborhoods (i.e., area between 2 cross streets) regarding dwelling types, block conditions, traffic levels, etc. Inter-rater reliabilities for neighborhood variables ranged from .70 to .97.
Results: Seventh graders came from diverse families. Income levels ranged from less than $20,000 (18%) to over $80,000 (14%). Nearly half were Caucasian (48%), 25% Hispanic, 9% Black/African American, 7% Asian. Only 16% of the neighborhoods were predominantly single family homes, whereas 30% resided in neighborhoods with duplexes/triple deckers. Nearly 25% of the 7th graders reported that they are in bed less than 9 hours on school nights (M = 9.2, SD = 1.0), with 20% spending less than 9 hours in bed on weekends (M = 10.1, SD = 1.6). Correlational analyses examined the relationships between sleep patterns and neighborhood factors. Students living in neighborhoods with more single family homes, greater percentage of trees, and better overall conditions (e.g., less litter, noise) reported more consistent bedtimes and school-night time in bed, and less delayed weekend midsleep times (.17 < r's <0.21, p's < .05).
Conclusion: Preliminary analyses provide a new avenue for understanding the effects of the environment on sleep patterns. Young adolescents' sleep patterns were significantly associated with neighborhood environment such as, housing type, percentage of trees, and overall conditions.

0257

CELLULAR PROLIFERATIVE SIGNALING IS INDUCED BY A SERINE/THREONINE PHOSPHATASE IN TONSILS FROM CHILDREN WITH OSA

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Introduction: Adenotonsillar hypertrophy (AT) is the major pathophysiological contributor to OSA in children. However, exact mechanisms of adenotonsillar proliferation are poorly understood. Regulation of the phosphorylative state of proteins modulates both proliferation and death in multiple cellular systems. Since serine/threonine phosphatase (PSPH) signaling is a critical effector of intracellular phosphorylation pathways, we hypothesized that inhibition of PSPH would reduce proliferative activity in tonsils from children with OSA.
Methods: A previously described mixed cell tonsil culture system was used. Tonsil cultures were incubated in basal conditions or treated with several PSPH inhibitors (10-6M to 10-9M) including okadaic acid, calyculin A, and PPI2. Tonsils cultures were also transfected using a nucleofection technique to genetically knock-down PSPH gene expression using with small interfering RNAs (siRNA). Total cell proliferation was initially determined using a non-radioactive proliferation assay. To detect T-cell and B-cell specific proliferation and apoptosis induced by PSPH inhibitors, bromodeoxyuridine pulsed proliferation analysis and annexin V assay were used along with flow cytometry. Expression of PSPH mRNA and protein were assessed by real-time RT-PCR and western blotting, respectively.
Results: Treatment with chemical inhibitors of PSPH induced significant dose-dependent reductions in the proliferative rates of tonsillar cells derived from children with OSA. Of the 3 compounds, calyculin A was most effective. Moreover, calyculin A significantly reduced the proliferation of both CD3+ cells (T-cells) and CD19+ cells (B-cells), and also increased apoptosis, when compared to basal conditions. These findings were further corroborated following PSPH knock-down experiments with specific siRNAs.
Conclusion: PSPH plays an important role in the tonsillar proliferation of children with OSA. PSPH targeted disruption may provide novel non-surgical approaches aiming to reduce adenotonsillar hypertrophy, and thus treat OSA in children.
Support (optional): Children's Foundation Trust for Sleep and Neurobiology Research

0258

PARENTAL REPORT OF SLEEP PROBLEMS IN DOWN SYNDROME

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Introduction: Sleep problems are frequently reported by the parents of children with Down Syndrome (DS). These include sleep maintenance problems, as well as snoring, and other symptoms of sleep disordered breathing. Laboratory polysomnographic (PSG) studies have reported the presence of obstructive sleep apnea syndrome (OSAS) in this population to be between 30 and 79%. As part of a larger project investigating the relationship between sleep and cognition in DS, we administered a questionnaire to parents as a subjective measure of their child's sleep.
Methods: Twenty four parents of children with DS (age range: 7-18 years, mean age = 13.35; 12 girls) completed the 33-item Child Sleep Habits Questionnaire (CHSQ), a screening instrument for school-aged children based on common clinical symptom presentations of prevalent

sleep disorders. The CHSQ yields symptoms on 8 subscales, including Parasomnias, Sleep Disordered Breathing, Daytime Sleepiness, as well as a total sleep disturbance score.
Results: We found that 91.7 percent of our sample had sleep disturbance scores in the clinical range, that is, greater than 41 (M = 48.63, SD = 6.21, range = 36-62). Compared to published data for typically developing children in a community sample aged 4-10 years, our sample had significantly elevated scores on the Parasomnias ($t(23)= 3.06$, $p = 0.005$), Sleep Disordered Breathing ($t(23) = 2.23$, $p = 0.036$), and Daytime Sleepiness ($t(23) = 7.53$, $p < 0.001$) subscales. Over half of our sample endorsed at least one symptom of sleep disordered breathing, including loud snoring, cessation of breathing, and snorting and gasping during the night. Importantly, each daytime sleepiness item was endorsed by at least 29% of our sample.
Conclusion: These findings are consistent with prior literature that has reported that children with DS are at a greater risk for developing symptoms of sleep disordered breathing and OSAS.
Support (optional): Down Syndrome Research and Treatment Foundation, Arizona Alzheimer's Research Consortium

0259

EFFECTS OF POSITIVE AIRWAY PRESSURE (PAP) ON NEUROBEHAVIORAL FUNCTION IN CHILDREN

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Introduction: PAP is an effective treatment for obstructive sleep apnea (OSA) in children, but it is unclear what effects PAP has on neurobehavioral function. The purpose of this study was to evaluate the effect of PAP use on neurobehavioral function. We hypothesized that regular PAP use would improve polysomnographic parameters, daytime sleepiness, quality of life, attention, and internalizing symptoms in children with OSA.
Methods: 21 children (6-16 years of age) and their parents completed a series of neurobehavioral measures prior to PAP initiation and after three months of PAP use. Objective adherence data were obtained for three consecutive months.
Results: Children were 71% African American, 57% obese, 62% boys and 24% developmentally delayed. As anticipated, the apnea hypopnea index and oxygen saturation improved on PAP (both $p<0.001$). After three months of PAP use, there were significant improvements from baseline in measures of quality of life (PedsQL, $p=0.049$), OSA-specific quality of life (OSA18, $p<0.001$), sleepiness (Epworth sleepiness scale, $p<0.001$), symptoms of attention deficit/hyperactivity (Conners scale, $p<0.001$) and internalizing symptoms (Child Behavior Checklist, $p=0.001$). There was no worsening of nasal symptoms (NOSE scale). PAP was used for 56 +/-36 (mean+/-SD) percent of nights. PAP use correlated with improvements in PedsQL ($r=0.58$, $p=0.006$), Conners ($r=0.48$, $p=.034$), Epworth ($r=0.58$, $p=.006$), and OSA 18 ($r=0.48$, $p=.028$).
Conclusion: These results indicate that, despite suboptimal PAP use, there was significant improvement in neurobehavioral function in children after three months of PAP treatment, even in developmentally delayed children. The implications for improved family, social, and school function are substantial.
Support (optional): Respironics Inc., NHLBI 58585

0260

INFANT SLEEP CHARACTERISTICS IN A NATIONALLY REPRESENTATIVE SAMPLE: CONCURRENT AND PROSPECTIVE RELATIONSHIPS WITH CHILD OUTCOMES

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Introduction: Extant literature suggests that child and parent factors play important roles in the development and maintenance of sleep problems in young children. Data are virtually non-existent regarding the association of infant sleep characteristics and developmental outcomes in large, representative samples.
Methods: Data from the Early Childhood Longitudinal Study - Birth Cohort (ECLS-B) were analyzed to examine whether parents' report of infant night waking and sleep onset difficulties at 9 months are associated with parent and child variables, both concurrently and prospectively at age 2, in a large, nationally representative sample (n = 10,688 at the 9 month assessment). Infants were identified as night wakers if parents reported 3 or more night awakenings and infants were unable to return to sleep most of the time (n = 416, 4%). Sleep onset difficulties were identified if parents reported that infants needed a lot of help to fall asleep most times (n = 1413, 13%) or were put to bed already asleep regularly (n = 3998, 38%).
Results: Night wakers were more likely to (a) be reported as difficult by their parents as both infants and toddlers (9 months: $\chi2=3.61$, $p=.009$; 2 years: $\chi2=3.02$, $p<.02$); (b) have parents who endorse current moderate to severe depressive symptoms (9 months: $\chi2=2.92$, $p=.04$) and (c) currently breastfeed (9 months: $\chi2=3.64$, $p<.0001$). Similar relationships held for infants who needed help falling asleep. Nine-month-olds who needed help falling asleep had higher Bayley Mental subscale scores both concurrently and prospectively (9 months: $t = 2.32$, $p <. 05$; 2 years: $t = 2.21$, $p < .05$), and those who were put to bed asleep had higher concurrent Mental subscale scores ($t = 2.35$, $p < .05$). Nine-month night waking was positively associated with infants' ability to attend during Bayley tasks.
Conclusion: Typically, researchers report negative effects of "poor sleep" on children's cognitive and behavioral functioning. Further analyses will investigate confounding or moderating variables. The data suggest the importance of more careful definitions of "sleep problems" during the first year of life and the need for better measurement of outcomes that may be vulnerable to these "sleep problems." "Sleep problems" may not be as unequivocally detrimental to the infant regulatory system as they have been reported to be in older children.

0261

COMPENSATORY MECHANISMS IN RESPONSE TO CHANGES IN NASAL PRESSURE DURING SLEEP IN CHILDREN WITH THE OBSTRUCTIVE SLEEP APNEA SYNDROME

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Introduction: The response to drops in nasal pressure during sleep in children with the obstructive sleep apnea syndrome (OSAS) is not known. We hypothesized that patients with OSAS would not maintain minute ventilation (V_E) in response to changes in nasal pressure, in contrast to normal controls.
Methods: Fourteen children with OSAS (age 8 ± 2 yr, apnea hypopnea index 15.5 ± 9.1/hr) and 23 normal controls (age 9 ± 2 yr) were studied while breathing at different levels of nasal pressure administered via a mask. During slow wave sleep (SWS) and rapid eye movement (REM) sleep, we measured airflow, inspiratory time (T_I), inspiratory time/total respiratory time (T_I/T_T), respiratory rate (RR), tidal volume (V_T) and V_E

at a holding pressure at which flow limitation occurred, and at 5 cm H_2O below the holding pressure, in both OSAS and controls.
Results: In both sleep states, controls were able to maintain airflow in response to the pressure drop, whereas OSAS preserved airflow in SWS, but had a significant decrease during REM (p = 0.0004). RR increased to a similar extent in OSAS and controls, but the increase was greater in SWS than REM (p = 0.032). OSAS had a greater increase in T_I and T_I/T_T in response to the pressure drop compared to controls, but this did not vary by sleep stage (p = 0.022 and 0.020, respectively). V_T increased in controls in response to the pressure drop, but decreased in OSAS (p = 0.037), particularly during SWS. However, as a result of the respiratory timing compensatory mechanisms, there was no significant change in V_E in response to the pressure drop in either OSAS or controls.
Conclusion: Patients with OSAS, similar to normal controls, can defend V_E in response to mild decreases in nasal pressure. However, compensatory mechanisms differ between OSAS and controls.
Support (optional): This study was supported by NIH grants U54-RR023567, R01-HL58585 and research support from Respironics.

0262
THE EFFICACY AND TOLERABILITY OF RAMELTEON IN A PEDIATRIC POPULATION
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Introduction: Rozerem (ramelteon) is the first melatonin receptor agonist to be FDA approved for the treatment of insomnia characterized by difficulty with sleep onset. Unlike other commonly used hypnotic agents, Ramelteon is not associated with withdrawal symptoms, rebound insomnia or abuse potential making it an attractive choice for use in children. However, there is a paucity of data on its efficacy and tolerability in the pediatric population.
Methods: A retrospective chart review was performed of all children who attended the Pediatric Sleep Disorders Clinic at St Christopher's Hospital for Children and who were prescribed Ramelteon for treatment of either insomnia or DSPS from the period 2006-2008
Results: A total of 15 children were identified who were prescribed Ramelteon.; of these 8 had DSPS and 5 had insomnia. All 13 children had a trial of either melatonin or clonazepam without benefit prior to starting Ramelteon. Ages ranged from 5 years to 19 years with a mean age of 14.3. Ramelteon was prescribed in doses of 4 mg to 8 children and 8 mg to 7 children. Duration of treatment ranged from 2 months to 2 years. Follow up data was available for 13 children; 9/13 (69%) had clear initial benefit with Ramelteon, 1 child refused to take medication and the remaining 3 had no noticeable benefit. Two of the seven children with an initial good response to Ramelteon however reported that it stopped working after 2 and 6 months respectively. No adverse effects were noted in any patient.
Conclusion: Ramelteon appears to be a safe and effective medication for the treatment of DSPS and insomnia in children and was effective in 69% of our patients with follow up data. In a few children, however, an initial beneficial effect wore off in a few months.

0263
PREDICTORS OF INCIDENCE AND REMISSION OF SLEEP DISORDERED BREATHING IN CHILDREN: THE TUCSON CHILDREN'S ASSESSMENT OF SLEEP APNEA STUDY (TUCASA)
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Introduction: There is little evidence using full polysomnography to predict factors associated with the incidence and remission of sleep disordered breathing in a population based sample of normal adolescent children.
Methods: 322 children completed two home polysomnograms approximately 5 years apart. A parent completed sleep habits questionnaires. Height, weight, blood pressure, and neck circumference were measured. PSGs were scored using standard criteria. Sleep disordered breathing (SDB) was determined to be present if a child had a respiratory disturbance index (RDI) ≥ 1 events per hour associated with a ≥3% oxygen desaturation. The following subjective symptoms were present if they occurred frequently or greater: witnessed apnea (WITAP), excessive daytime sleepiness (EDS), difficulty initiating and maintaining sleep (DIMS), and habitual loud snoring (SN). IncidentSDB=(NoSDB Time1 and SDB Time2); RemissionSDB=(SDB Time1 and NoSDB Time2); PersistentSDB=(SDB Time1 and Time2); PersistentNoSDB=(NoSDB Time1 and Time2); PerIncSDB=(PersistentSDB+Incident SDB). BMI percentiles and z-scores were calculated using CDC childhood growth charts adjusted for gender and age. Logistic regression was used to determine predictors of incidence, remission, and persistence or absence of SDB.
Results: The mean age at assessment was 9.0 years (6-12) and 13.7 years (10-18) at Time1 and Time2 respectively. The mean time between assessments was 4.6 years (2.9-7.3). There were 49% females and 36% Hispanic subjects. Children with IncidentSDB were 3.9 (p<.008) times more likely to be boys. Children with PerIncSDB were 2.5 (p<.006) times more likely to be boys and slightly more likely to have an increase BMI percentile change (p<.04). Children with PerIncSDB had 3.4 greater odds of having a BMI <95 percentile at Time1 and a BMI > 95 percentile Time2 (p<.001). Parent reported symptoms were not predictive of future SDB.
Conclusion: Adolescent boys are more likely to have persistent and incident SDB than girls. Children with persistent and incident SDB are more likely to have developed obesity.
Support (optional): HL 62373

0264
MATERNAL AND INFANT SLEEP FOLLOWING IMMUNIZATION
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Introduction: Mothers often report poor infant sleep following immunization, but few studies have evaluated the effect of immunization on infant and maternal sleep-wake patterns.
Methods: Data were collected from 92 mothers and 71 infants during the 3 days surrounding the infant's 2-month immunizations. Sleep-wake patterns were assessed using wrist actigraphy for mothers and ankle actigraphy for infants. Paired t-tests were used to compare sleep-wake patterns before and after immunization.

Results: Contrary to parent reports, most infants (52%) slept >30 mins more following immunization and 20% slept about the same amount they had the day before. In the 24 hr period after being immunized, infants slept an average of 65 mins (95% CI: 28-101 mins) more than they had the day before (p=.001). Most of the additional sleep was active sleep, while quiet sleep increased only slightly. The additional sleep occurred mainly during the daytime, as sleep between 2100 and 0900 hrs was similar both nights. Following immunization, infants had slightly shorter wake durations. Infants receiving 4-5 injections had fewer nighttime wakes of longer duration than infants receiving 2-3 injections. Infants immunized later in the day slept longer that night (r=.26) and had stronger circadian rhythms over the next 36 hrs (autocorrelation, r=.34) than infants immunized earlier in the day. In contrast to their infants, mothers typically had more disrupted sleep on the night following their infant's immunization compared to the night before. Mothers tended to wake more frequently, spend more time awake between midnight and 0600, and wake later in morning, although their total sleep time was the same both nights and daytime sleep was similar both days.
Conclusion: The infant findings are consistent with previous research linking cytokine and immune activation with increased sleepiness. Further research is needed to determine the cause of maternal sleep disruption following infant immunization.
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0265

BAROREFLEX SENSITIVITY IN OBESE LATINO ADOLESCENT MALES: RELATIONSHIP TO FASTING BLOOD GLUCOSE AND OBSTRUCTIVE SLEEP APNEA (OSA)

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Introduction: In overweight adults with OSA, there appears to be a strong association between autonomic and metabolic dysfunction. We therefore hypothesized that baroreflex sensitivity, an index of autonomic control, would be correlated with indices of glucose metabolism as well as severity of OSA in childhood obesity.
Methods: Ten obese, otherwise healthy Latino males (age 13.45 ± 1.86 years (mean ± SD), BMI > 95% for age) were studied. Exclusion criteria included diabetes and treatment for OSA. Each subject participated in the following protocol: (1) polysomnography; (2) morning fasting blood samples, followed by a frequently-sampled intravenous glucose tolerance test for determination of insulin sensitivity (SI); (3) dual energy x-ray absorptiometry for assessing adiposity; and (4) measurement of respiration, heart rate and pulse transit time (PTT) during supine and standing postures. Spectral analysis was applied to determine indices of heart rate variability (HRV) and PTT variability, such as HRV low-frequency power (LFP_HRV) and PTT low-frequency power (LFP_PTT). Using PTT variability as the surrogate measure of blood pressure variability, we estimated baroreflex sensitivity (BRS_PTT) using the spectral method: BRS_PTT = sqrt(LFP_HRV / LFP_PTT).
Results: BRS_PTT measured during the supine posture was negatively correlated with fasting blood glucose (FBG) after adjusting for total body fat percentage (r = -0.68, p = 0.04). BRS_PTT decreased in all subjects during standing, but the decreases were smaller in subjects with higher FBG, suggesting reduced autonomic reactivity to orthostatic stress with increasing FBG. There were tendencies for baseline BRS_PTT to decrease with apnea-hypopnea index (r = -0.30) and arousal index (r = -0.44), and for log(BRS_PTT) to increase with log(SI)(r = 0.41). However, these correlations did not attain statistical significance.
Conclusion: These preliminary findings suggest that baroreflex sensitivity can be substantially reduced in obese children with high FBG, but contrary to findings in adults, the effects of OSA on autonomic function are more subtle.
Support (optional): This work was supported in part by NIH Grants HL090451 and EB001978, USC Center for Transdisciplinary Research on Energetics and Cancer (TREC U54 CA 116848) and Grant M01 RR00047, Childrens Hospital Los Angeles General Clinical Research Center, with funds provided by the National Center for Research Resources, NIH.

0266

INITIAL ANALYSIS OF SLEEP OUTCOME TOOLS OF THE QUALITY IMPROVEMENT INITIATIVE AT CINCINNATI CHILDREN'S HOSPITAL MEDICAL CENTER

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Introduction: As part of a hospital-wide Quality Improvement Initiative (QI) at Cincinnati Children's Hospital Medical Center (CCHMC), we have utilized several sleep outcome tools to track long-term data in children with obstructive sleep apnea (OSA). These tools include the Michigan pediatric sleep questionnaire (PSQ, Chervin et al 2000), quality of life (QL) questionnaire, and Epworth sleepiness scale. The project began at our sleep center in March 2008.
Methods: We conducted a retrospective review of sleep outcome tools as part of our sleep QI initiative. These questionnaires were done electronically in our sleep clinics prior to a physician's visit. All children subsequently underwent an overnight polysomnographic study. Only children with completed questionnaires during the first visit and sleep study were included in the analysis.
Results: A total of 284 new patients were referred to our sleep clinics from March-October 2008, of which 161 completed sleep questionnaires. The completion rate was 56.7%. The average age was 9.0±5.1 years old. Analysis of the Michigan PSQ (threshold PSG>0.33) and sleep study showed sensitivity of 0.81 (obstructive index (OI)>1), 0.82 (OI>3), and 0.85 (OI>5). However, the specificity was 0.15, 0.17, and 0.18, respectively. The QL questionnaire revealed decreased quality in children with OSA.
Conclusion: Our QI data during this period demonstrate that the Michigan PSQ is sensitive, but not specific. We are currently investigating the cause of this low specificity compared to previous established literature. Children with OSA have decreased overall quality of life. We continue to reassess the sleep outcome tools of our CCHMC QI project.
Support (optional): This study is supported by the Cincinnati Children's Hospital Research Fund.

0267

PARENTING MATTERS: RANDOMIZED CLINICAL TRIAL OF A BRIEF, MINIMAL-CONTACT TREATMENT FOR PRESCHOOL-AGE CHILDREN WITH SLEEP PROBLEMS

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Introduction: Many preschool-age children have sleep problems but few receive treatment. New methods of reaching families who might benefit from treatment are needed.
Methods: Parents with concerns about their 2-to-5 year old's sleep patterns or bedtime behavior were recruited when they visited their family physician at 1 of 24 family medicine practices. After completing base-

line measures by mail, they were randomly assigned to receive usual care or the Parenting Matters treatment along with usual care. Parenting Matters combined a self-help booklet (targeting primarily bedtime resistance and night waking) with two calls from a telephone coach during a 6-week treatment period. The primary outcome was the Children's Sleep Habits Questionnaire (CSHQ) mailed at 7-weeks post-randomization; secondary outcomes included the Parenting Scale and the Child Behavior Checklist (CBCL). 140 parents (94% birth mothers) completed the CSHQ at baseline and post-treatment in relation to their 2- (40%), 3- (35%), 4- (12%) or 5-year old child (13%).
Results: Sleep problems (CSHQ scores) decreased significantly more in the Parenting Matters condition compared to usual care alone, based on a significant time X treatment group effect in intent-to-treat analyses ($p < 0.01$). In the Parenting Matters condition, scores on the Parenting Scale also improved significantly more than in usual care alone ($p < 0.01$). There were no significant group differences on the CBCL.
Conclusion: A brief early intervention combining a self-help booklet and telephone coaching is an effective way to treat common sleep problems among young children, and it has the added benefit of improving parenting practices in general. This minimal-contact approach addresses the need for an intervention that can reach the large number of children with sleep problems, has minimal cost, and is time efficient.
Support (optional): The Canadian Institutes for Health Research

0268

FREQUENCY OF OBSTRUCTIVE SLEEP APNEA IN PAEDIATRIC PATIENTS WITH ADENOTONSILLAR HYPERTROPHY

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Introduction: Adenotonsillar hypertrophy is one of the main causes of Obstructive Sleep Apnea (OSA) in children. The consequences of OSA are particularly severe in children, including failure to thrive, enuresis, attention deficit/ behavioural disorders, and poor academic performance. The aim of this study is to explore to the relationship between large tonsils and OSA in children.
Methods: A retrospective study of 45 children (33 with enlarged tonsils and 12 controls) from the Youthdale Child and Adolescent Sleep Centre was conducted. Tonsil size was rated on a 5-point scale ranging from 0 (tonsillectomy or no enlargement) to 4+ (>75% airway blocked). The children underwent overnight polysomnography and questionnaire assessment of sleepiness and fatigue.
Results: Children with enlarged tonsils had significantly higher total AHIs (3.3±5.5 vs. 0.3±0.3, p=0.004) and AHIs in REM sleep (7.7±17.5 vs. 1.0±1.0, p=0.04) when compared to controls. For those with enlarged tonsils, there was no correlation between tonsil size and AHI. No significant differences were found in daytime sleepiness (2.8±1.6 vs. 3.0±0.6, p=0.43) or fatigue (3.0±1.8 vs. 3.2±1.2, p=0.64) between children with enlarged tonsils and controls. Average PO2 saturation did not differ between study groups (98.0±0.8 vs. 97.9±0.5, p=0.511), but there was a trend for lower minimum PO2 saturation in children with enlarged tonsils (79.3±13.5 vs. 86.9±11.6, p=0.077). Lastly, for children with enlarged tonsils, the incidence of OSA was over forty times greater than for children with normal sized tonsils (OR=40.9, 95%CI: 4.5-372.7).
Conclusion: Adenotonsillar hypertrophy in paediatric patients immensely increases their likelihood of having OSA. These children should be sent for overnight sleep assessment as the degree of tonsillar enlargement did not predict the severity of OSA in those with enlarged tonsils. Further, these children do not exhibit typical daytime symptoms of fatigue or sleepiness as a consequence of disturbed sleep, so their OSA may be masked.
Support (optional): The study was supported by the Youthdale Foundation.

0269

HEART RATE VARIABILITY DURING SLOW WAVE SLEEP IN PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS

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Introduction: Changes in heart rate variability (HRV) analyses have shown to be a good marker of a less favorable healthy life in all age spans. The aim of this protocol was to performed HRV analyses on sleeping pediatric patients with juvenile idiopathic arthritis (JIA).
Methods: We studied 10 patients with JIA (mean age= 12 ± 3.1) compared to 10 healthy subjects (mean of age= 13 ± 2.1), matched for age, gender and Tanner stage. The inclusion criteria in the JIA group were a presence of clinical activity and/or an increased erythrocyte sedimentation rate and/or a reactive C-protein as laboratory evidence of inflammation. The HRV Standard Time and Frequency Domain were calculated for 5-minute periods in all sleep stages. The frequency components were subdivided in low and high frequency, and the time domain analyses were calculated by determination of the ratio of the standard deviation of the RR intervals.
Results: We found changes in our patients compared to healthy controls in the standard deviation of normal-to-normal interval (SDNN) during SWS [47.0 ± 38.5 vs 94.6 ± 75.2] (U-test, p=0.02), and the total power of spectral analyses. The total power in all sleep stages were significantly lower in JIA group compared to controls, respectively: stage 2 [7322.3 ± 4197.1 vs 11703.7 ± 5298.4], SWS [5433.3 ± 2802.2 vs 9108.5 ± 5251.9], and REM sleep [10338 ± 2856.6 vs 12995.2 ± 2920.9] (U-test; $p<0.05$, all). Positive correlations were found between a number of joints with impairment and the proportion of adjacent normal NN intervals (pNN50 parameter) ($rs=0.45$; $p<0.05$), and between increases in inflammation measures and low frequency (LF parameter) ($rs=0.72$; $p<0.05$).
Conclusion: Reduction in parasympathetic tone was found during sleep, particularly in SWS. It may represent an autonomic impairment during sleep in children with IJA. This early autonomic dysfunction might increase the cardiovascular risk in this population.
Support (optional): This study was supported by AFIP.

0270

A NATIONALLY REPRESENTATIVE ANALYSIS OF NAPS IN CHILD CARE

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Introduction: Researchers have experienced a growing recognition of the critical role of nighttime sleep in the development and regulation of attention and affective processes. However, the role that napping might play in variations in developmental outcomes during childhood has not been thoroughly studied.
Methods: The analyses use the 9- and 24-month data from the Early Childhood Longitudinal Study - Birth Cohort (ECLS-B). 2,982 cases were included from the original 10,688. The weighted sample has 53% White, 18% Black, 22% Hispanic, and 2% Asian participants, with 19% below poverty level. Multiple regression analyses were used to examine whether nap duration in child care at 2 years of age is associated with socioeconomic status, birth weight, bedtime sleep behaviors, and cognitive and behavior outcomes.
Results: Children were reported by child care providers to nap for an average of 1.94 hours; 9% of children were reported not to nap. Parents reported that 90% had a regular bedtime routine and 13% needed help to fall asleep most nights. Compared to White children, Black children took longer ($\beta = .22$, $p = .01$) and Hispanic children took shorter naps ($\beta = -.18$, $p = .05$), controlling for other child characteristics and bedtime sleep behaviors. There was a trend for children to take shorter naps at child

care if they had a regular bedtime routine (β = -.21, p =.06). No significant associations were found between nap duration and Bayley mental and motor scores and independent observers' ratings of the child's behavior after controlling for the other variables.
Conclusion: Preliminary analyses reveal interesting racial differences in nap duration at child care and an association between bedtime routines at home and shorter nap durations. We plan to investigate this topic further by examining nap duration with child care provider characteristics and the type, duration, and quality of child care.

0271

A LONGITUDINAL STUDY OF THE RELATIONSHIPS BETWEEN INFANT SLEEP AND MATERNAL VS. PATERNAL INVOLVEMENT IN INFANT CARE

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Introduction: Research focusing on the role of fathers in the development of infant sleep has been very limited. The goals of this longitudinal study were to assess: (a) The differences in nighttime interventions between mothers and fathers. (b) The concomitant and predictive links between infant sleep patterns and paternal vs. maternal involvement in overall infant care during the first year of life.
Methods: Fifty-six couples were recruited during pregnancy and were asked after delivery (1, 6, and 12 months) to complete a questionnaire aimed at assessing the relative involvement of mothers vs. fathers in infant care (e.g. bathing, playing). Infant sleep was assessed at the age of 6 and 12 months using actigraphy and sleep diaries. Parental nighttime soothing was assessed by rating scales included in the sleep diary.
Results: Differences between mothers and fathers in frequency, duration and method of night soothing were found. At 6 months mothers demonstrated longer duration of intervention ($F = 7.99$, $p < .01$) and a higher degree of active nighttime soothing ($F = 6.84$, $p < .05$). The findings demonstrated significant concomitant and predictive links between infant sleep and relative involvement of mothers vs. fathers in infant care. According to the ratings of both parents, higher paternal involvement in infant care predicted and was associated with a lower number of objective (actigraphic) and reported infant night-wakings and with shorter sleep duration. For instance, according to the fathers' ratings, the predictive correlation between paternal involvement at 1 month and actigraphic night-wakings at 6 months was -.35 ($p<.01$) and the concomitant correlation at 6 months was -.38 ($p<.005$).
Conclusion: The results suggest that paternal involvement in infant care may contribute significantly to the development of infant sleep. The findings highlight the importance of including fathers in developmental and clinical sleep research.

0272

OBSTRUCTIVE SLEEP APNEA AND SICKLE CELL DISEASE SEVERITY IN CHILDREN

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Introduction: Obstructive sleep apnea (OSA) causes transient hypoxemia and sympathetic nervous system activation, both associated with inflammation. Hypoxemia and inflammation contribute to vaso-occlusive crises (VOC) in sickle cell disease (SCD). Thus, OSA may increase SCD severity. Adenotonsillar hypertrophy, a common cause of pediatric OSA, is common among children with SCD, increasing their risk of OSA. This study explored the association between OSA and SCD severity among children.
Methods: Data was derived from chart reviews of 19 snoring children with SCD referred to a sleep laboratory for evaluation of OSA. SCD severity was defined as the number of medical visits and days of VOC care during the prior year. OSA was defined as none (obstructive apnea-hypopnea index (OAHI) <1), mild (OAHI 1-4.9), or moderate-severe (OAHI≥5). Analyses consisted of descriptive and nonparametric statistics using SPSS.
Results: Mean (SD) age was 7.6 (4.4) years, range 2.5-17.6. Ten were male. Body mass index (BMI) ranged from 14.0-40.0, 84% had a BMI percentile for age (BMI%) less than 50%, and all children with a BMI% >80 had OSA. OSA was diagnosed in 68% (mild n=7, moderate-severe n=6). Medical visits averaged 2.26 (2.4), range 0-8 and days of care averaged 7.11 (8.4), range 0-31. Mean OAHI was 5.05 (6.1), range 0-19.7. Two of the most severely ill patients had an OAHI of 19. Sleep SpO2 ranged from 84.3-98.9, averaging 94.6 (4.3). Lowest respiratory event-related SpO2 ranged from 54.3-98.4%. Sleep time below SpO2 90% (T90) averaged 13.65% (30.3), with 2 children having T90s above 90%. There were trends toward increased visits with mean SpO2<93% ($p=0.086$) and OSA diagnosis ($p=0.067$), and toward increased days of VOC care with mean SpO2<90% ($p=0.073$).
Conclusion: Preliminary data suggest that OSA may influence disease severity in a subset of children with SCD. Frequent VOC and snoring history should prompt referral for polysomnography.

0273

CIRCADIAN ASSESSMENT WITH URINARY 6-SULFATOXYMELATONIN (AMT6S) SECRETION IN HEALTHY PRESCHOOL CHILDREN

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Introduction: The circadian cycle is an approximately 24-hr biological rhythm that influences the timing of many physiological processes and behavior (e.g., sleep, hormones, attention, and performance). Developmental changes in the circadian system may impact early brain and behavior interactions. The present study provides preliminary data on the assessment of urinary melatonin in the form aMT6s. Although aMT6s analysis is useful in describing melatonin onset, offset, acrophase, and amplitude, normative data with preschoolers has not been published.
Methods: Participants included 6 healthy children (4 females, 42-48 months) with no sleep, emotional, or behavioral problems. Children were monitored for 5 days with actigraphy and sleep diaries while following their typical sleep/wake schedule (3 children regularly napped). Parents then collected urine samples passed by the child for a 48 hour period, beginning the morning of the 6th day and ending the morning of the 8th day (volume and time recorded for each sample). Samples were assayed at Stockgrand Ltd., University of Surrey for information regarding aMT6s concentration (RIA) and acrophase (cosinor analysis).
Results: The mean aMT6s onset was 8:00 PM (± 31 min) with a minimum value of 7:20 AM and a maximum of 8:32 PM. The mean aMT6s offset was 7:59 AM (± 1hr 45min), minimum 5:11 AM and maximum 9:53 AM. Average acrophase was 2:25 AM (± 23min), amplitude was 27.40 ng/min (± 9.69), and mesor was 19.07 ng/min (± 7.84).
Conclusion: These preliminary results suggest significant variation among the aMT6s measures reported, with acrophase being the least variable and amplitude the most variable. An initial comparison between salivary dim light melatonin onset and aMT6s onset for the same children showed aMT6s onset was about 13 min later than salivary DLMO. In adults, the average delayed in aMT6s secretion is about 1 hour. A larger sample size and repeated measures across early development will lead to a comprehensive presentation of intra- and inter-individual differences in urinary aMT6s secretion and corresponding sleep measures.
Support (optional): NIMH; Sepracor, Inc.

0274

SLEEP-RELATED RESPIRATORY ABNORMALITIES AND THEIR EFFECT ON SLEEP ARCHITECTURE IN INFANTS WITH LARYNGOMALACIA

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Introduction: Previous studies have shown that obstructive sleep apnea is common in infants with laryngomalacia. However, there is limited information on other respiratory abnormalities during sleep in infants with laryngomalacia and their effects on sleep architecture.
Methods: A retrospective review of polysomnographic study and medical record was performed in infants with laryngomalacia. Any infants with CNS diseases, neuromuscular disease or metabolic disease were excluded. The aged-matched control (C) was obtained from our previous study.
Results: 32 infants with laryngomalacia (S) met the criteria for entry into analysis. The average age was 3.2 ± 1.7 (SD) months. 27 (84.4%) infants had significant obstructive respiratory events (obstructive index > 1/hr), 15 (46.9%) infants had significant central respiratory events, 9 (28.1%) infants had significant alveolar hypoventilation. SDB in infants with laryngomalacia resulted in a significant decrease in sleep efficiency (71.1±11.1% [S] vs 78.6±5.5% [C]; $P<0.05$), a decrease in REM sleep (33.9±13.0% [S] vs 53.0±8.0% [C]; $P<0.05$), and corresponding increase in NREM sleep (54.1±13.1% [S] vs 43.5±8.2% [C]; $P<0.05$).
Conclusion: Infants with laryngomalacia have significant SDB at the early age. Both central and obstructive sleep apneas are common in infants with larygomalacia. SDB in this population is associated with significant change in sleep architecture. This study emphasizes the important of early assessment of sleep-related respiratory events in this population. It is speculated that changes in sleep architecture may have adverse effect on overall outcome in infants with laryngomalacia.
Support (optional): The Cincinnati Children's Hospital Research Fund.

0275

SHORT SLEEP DURATION IS ASSOCIATED WITH POOR PERFORMANCE ON OBJECTIVE MEASURES OF SUSTAINED ATTENTION IN HEALTHY SCHOOL-AGE CHILDREN

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Introduction: The purpose of this study was to examine whether sleep duration is associated with neurobehavioral functioning measured objectively by performance on the Test of Everyday Attention for Children (TEA-Ch) in healthy school-age children.
Methods: Participants: The study population consisted of 39 children (age range 7-11; mean=8.62, SD=1.28) and their average IQ was 104.49 (SD=16.95). Subjects were excluded if they scored less than 80 on the Wechsler intelligence scale-4th edition (WISC-IV), or if they had any psychiatric or medical diagnosis. Design and Measures: Children were off-medication and were instructed not to consume products containing caffeine for the duration of the study. The subjects' sleep patterns were assessed in the home environments using miniature actigraphs (AW-64 series) for 6 nights, with the data further supplemented by parent completion of nightly sleep logs. On the morning of the seventh day, neurobehavioral functioning was assessed using the Test of Everyday Attention for Children (TEA-CH).
Results: Subjects were divided into 2 groups based on their actual sleep duration score during the 6 nights of the evaluation, with subjects above and below the mean (M=478.2 minutes SD=37.2) placed in the Short Sleep Group (SSP) and Long Sleep Group (LSG), respectively. Principal component analyses with varimax rotation produced a 4-factor solution for the TEA-CH measures. Based on component loadings of 0.5, four factors accounted for 38.9%, 11.15%, 9.9%, and 8.3 respectively, of the variance. Analysis of covariance (ANCOVA) was computed with the Sleep Group (LSG or SSG) taken as the between-subject independent factor, the child's performance on the TEA-Ch as indicated by the Factor Scores as the dependent variables, and the child's age, body mass index, SES and gender as covariates. Significant differences were found between the Sleep Groups in performance on the TEA-Ch`s sustained attention factor, $F(1, 35) = 5.33$, $p < 0.05$. Subjects in the Long Sleep Group performed better on these measures compared to the subjects in the Short Sleep Group.
Conclusion: Our findings suggest that performance on neurobehavioral measures associated with sustained attention is moderated by sleep duration; Children with longer sleepers perform better than children with shorter sleep duration on these measures.
Support (optional): This study was supported by Canadian Institutes of Health Research (CIHR) grant number 153139 and Fonds De La Recherche en sante (FRSQ) grant number 10091.

0276

FREQUENCY OF MACROPHAGE MIGRATION INHIBITORY FACTOR (MIF) SINGLE NUCLEOTIDE POLYMORPHISM -173G/C IN CHILDREN WITH EITHER OBSTRUCTIVE SLEEP APNEA (OSA), OBESITY, OR BOTH

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Introduction: Both obstructive sleep apnea (OSA) and obesity are currently viewed as systemic inflammatory disorders. MIF is a multifaceted pro-inflammatory cytokine that is crucial in regulation of immune responses and has also been associated with cardiovascular disease. However, it remains unknown whether the plasma levels of MIF are modified in the presence of OSA or obesity in children, and whether there is an association between a MIF SNP that predicts higher MIF levels in adults
Methods: Consecutive children (ages 4-10 years) were recruited after NPSG and underwent fasting morning blood draw. Obesity was defined as a BMI z score>1.65. Frequency of MIF genotype was evaluated in 93 subjects (25 obese with OSA (OSAob); 20 obese without OSA (Ob); 17 non-obese with OSA (OSAnob) and 31 non-obese without OSA (nob). Genomic DNA from peripheral blood was extracted and genotyping allele frequencies for MIF SNP -173G/C were determined by using RT-PCR. MIF plasma concentrations were determined as well.
Results: The presence of -173G/C MIF SNP was significantly more frequent among Ob, with. allele CC genotype being overrepresented in OSAob compared to OSAnob. The risk variant (C allele) was associated with significantly higher MIF plasma levels, with OSAob children having the highest plasma concentrations
Conclusion: MIF polymorphism -173 (C/G) is associated with obesity and OSA, and is associated with higher MIF plasma levels. Analysis of MIF genotype-phenotype interaction in obese children, particularly in the concurrent presence of OSA, may assist in categorical risk assessment of end-organ morbidities associated with these 2 conditions.
Support (optional): NIH grant HL-65270, Children's Foundation Endowment for Sleep Research and University of Louisville grant E0606 (AK).

0277

C-REACTIVE PROTEIN (CRP) GENE POLYMORPHISMS IN US AND GREEK CHILDREN WITH SUSPECTED OBSTRUCTIVE SLEEP APNEA (OSA)

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Introduction: Previous studies in US and Greek children with OSA have shown disparate findings in the association between the degree of respiratory disturbance during sleep and morning serum CRP levels. Indeed, US children with OSA have higher CRP concentrations while CRP elevations occur only rarely among Greek children with OSA. We hypothesized that genomic variations in the CRP gene may account for these discrepant findings.
Methods: Four SNPs of the human CRP gene (rs2794521, rs1130864, rs1417938, rs1205), corresponding to several critical regions of the encoding sequence were used to genotype 345 US and 113 Greek habitually snoring children (age 4-10 years) with clinical symptoms suggestive of OSA. Linkage disequilibrium was analyzed for the 4 SNPs. All samples were genotyped using a polymerase chain reaction system with predeveloped TaqMan allelic discrimination assay. The Haploview version 4.0 software was used to analyze the linkage disequilibrium structure, calculating D' to define haplotype blocks and to estimate haplotype frequencies.
Results: Mean age, gender distribution, and obstructive AHI were similar for the Greek and US cohorts. A higher frequency in the CRP gene polymorphisms rs2794521 ($p<0.01$ post Bonferroni correction) and rs1130864 ($p<0.05$ post Bonferroni correction) was identified for the US cohort, with no significant differences emerging in the frequency of rs1417938 and rs1205 CRP SNPs among the 2 groups.
Conclusion: Since CRP polymorphisms rs2794521 and rs1130864 are strongly associated with higher serum CRP levels, we propose that the cohort differences in the frequency of these polymorphisms identified herein among Greek and US children with suspected OSA may account for the discrepant serum CRP findings in the context of pediatric OSA.
Support (optional): NIH grant HL-65270, Children's Foundation Endowment for Sleep Research and University of Louisville grant E0606 (AK).

0278

MAXILLOFACIAL GROWTH IN CHILDREN WITH SLEEP-DISORDERED BREATHING (SBD) BEFORE AND AFTER ADENOTONSILLECTOMY

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Introduction: In Japan, the maxillofacial morphology is one of the factors in adult with obstructive sleep apnea syndrome (OSAS). In children with long-term sleep-disordered breathing (SBD) are supposed to cause undergrowth of the upper and lower jaw. This study is about the maxillofacial growth on cephalometrics in children with SBD before and after adenotonsillectomy.
Methods: The study was conducted and characterized, retrospectively, at Ota general hospital from April.2002 to March.2006. As SBD surgery group; 15 children with SBD who had performed polysomnography (PSG) were underwent adenotonsillectomy and as SBD non-surgery group; 7 children with SBD who had also performed PSG were not underwent surgery. For PSG analysis, we used ICSD-2 criteria and R & K international criteria. And as control, 21 children with otitis media were underwent surgery. All children were examined lateral cephalometric radiographs both before treatment and after two years. Maxillofacial morphology analysis used Ricketts method and Downs-Northwestern method. We compared the maxillofacial growth between each three groups.
Results: On 22 SBD group, SNA and facial axis are smaller than the others who do not have SBD. On SBD surgery group, not only SNA but also facial axis after surgery was significantly improved rather than before ($p<0.05$). However on SBD non-surgery group and control, they did not change significantly.
Conclusion: Adenotonsillectomy was supposed to normalize maxillofacial growth in children with SBD. We expect that the early intervention for the children with SBD can improve their maxillofacial growth and prevent to transmigrate to adult OSAS.

0279

SLEEP QUALITY, SLEEP PREFERENCE AND COGNITIVE PERFORMANCE AMONG HEALTHY YOUNG PUBERTAL FRENCH ADOLESCENTS: A PRELIMINARY REPORT

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Introduction: This study explored relationships between subjective sleep quality and preference schedule, anxiety traits, and cognitive performances related to executive functioning and affects regulation processes in healthy pubertal adolescents.
Methods: Forty-one healthy adolescents (14 girls: 14.1y ± 0.5y (13-15y); 27 boys: 14.2y ± 0.6y (13-15y) participated to this study. They completed sleep questionnaires (Morningness/Eveningness Questionnaire (MEQ), Pittsburgh Sleep Inventory Questionnaire (PISQ), Epworth Sleepiness Scale (ESS) and State-Trait Anxiety Inventory for Young. They had a neuropsychological assessment that included subtests (6) from the WISC-IV, the CANTAB battery (spatial working memory (SWM), Cambridge guessing task (CGT), affective Go/noGo (AGN), and rapid visual processing (RVP)), and the Perdue Pegboard. To assess gender differences, we performed t tests or Mann-Whitney U tests on sleep and cognitive variables. ANCOVAs were used to verify relationships between gender, sleep variables, and cognitive performance.
Results: Compared to boys, girls reported a preference for morningness and had higher PSIQ score. In the CGT, girls had better quality decision-making and were more conservative in their bets than boys. No other significant difference was found on neuropsychological performance between girls and boys. For both genders, higher score in ESS was associated to lower delay in making a decision in the CGT which is the reflection of greater impulsivity. Also, a better performance in the Perdue Pegboard was observed in participants that slept more than 9 hours a day in the past month compared to those who slept lesser. In boys, longer sleep latency was associated with longer response delays in the AGN, both for positive and negative stimuli.
Conclusion: Subjective appreciation of sleep is associated with specific executive functions related to risk-taking and impulsivity in decision making, as well as in emotional information processing biases. However, those patterns seem to be different according to gender. Further studies are recommended to better understand those relationships.
Support (optional): Canadian Research Institutes of Health, Fonds de Recherche en Santé du Québec, European Commission (Consortium IMAGEN project).

0280

PROFILE OF PATIENTS WITH EARLY ONSET SLEEP DISORDERED BREATHING COMPARED TO OLDER CHILDREN

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Introduction: Sleep disordered breathing (SDB) is common in children of all ages. Young children presenting with symptoms of SDB require management of their SDB that does not necessarily involve adenotonsillectomy as with older children. There has been no systematic assessment of why younger children with SDB may require different management of their symptoms compared to older children. Our objective was to compare the profiles of children presenting with early versus later onset SDB.
Methods: A cohort of consecutive children under three years who underwent sleep nasopharyngoscopy with or without bronchoscopy were retrospectively identified at a tertiary care centre. Prospectively, the findings of endoscopic examinations and all relevant diagnoses are recorded. The study group was compared with 2 separate control groups who were assessed consecutively to reduce bias. Distribution of gender, airway lesions, syndromic children and diagnoses associated with pharyngeal hypotonia or dysfunction (PHD) were compared.
Results: 74 patients with SDB, from 2004-2008, were identified (51 boys, mean age 2.5 years, range 1.75-3years). 9 airway abnormalities were recorded (6 with laryngomalacia). 35 children had PHD (22 gastroesophageal reflux disease and 9 swallowing dysfunction). There were 8 named syndromes. In comparison, the 2 control groups (n of 75 and 72 rspectively) demonstrated similar and consistent distribution of gender and pathology. Amongst all the controls (n=147) 8 airway abnormalities were found (5 were laryngomalacia). Eleven syndromic children were also found amongst all the controls. PHD diagnoses (46) were largely asthma and obesity. PHD proportion was significantly different between the study subjects and controls (P=0.016, OR=2.02 95% CI 1.14-3.59).
Conclusion: Early onset SDB is associated with congenital airway abnormalities. Even in neurologically normal children, SDB is associated with specific types of PHD. A systematic inquiry into these diagnoses, and endoscopic evaluation of the airway is advisable in this group.

0281

GENE NETWORKS AND BIOLOGICAL PATHWAYS IN BONE MARROW-DERIVED VERY SMALL EMBRYONIC STEM CELLS (VSEL) FROM MICE FOLLOWING INTERMITTENT HYPOXIA (IH)

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Introduction: A murine BM homogenous population of rare Sca-1+ lin-CD45- cells that express markers of pluripotent stem cells, and highly express Rif-1 telomerase protein was identified. These cell express neural and vascular lineage markers and form neurospheres and endothelium in vitro. VSEL are recruited from BM during IH and may play a role in repair mechanisms following IH-induced end-organ injury.
Methods: Adult CB57BL mice (n=60) were exposed to either IH (cycling of 5.7% or 21% oxygen every 3 min) or to room air for 6 hours. VSELs were extracted and sorted from BM using flow cytometry, and total RNA was isolated from VSELs and hybridized onto mouse whole genome oligonucleotide-microarrays. After filtering and normalization of the microarray data, differentially expressed genes in VSEL during IH relative to RA were identified and mapped to enriched functional categories based on Gene Ontology (GO) classification. Next, we integrated our pathway-focused approach with genetic network analysis to explore the details of putative mechanisms activated by IH in VSELs.
Results: IH induced significant changes in the expression of 637 unique genes (FDR < 0.01) in VSELs. GO analysis revealed that the vast majority of these differentially expressed genes could be incorporated into a selected number of functionally relevant pathways underlying anatomical structure development and morphogenesis, regulation of growth, insulin-like growth factor binding, extracellular matrix, cell differentiation, response to axon injury, glycosaminoglycan and lipoprotein binding, angiogenesis, cell proliferation and nervous system development.
Conclusion: Exposure to IH elicits not only end-organ injury, but can also induce repair mechanisms involving recruitment of pluripotent stem cells such as VSELs from the BM. Using novel computational methods, we show that IH activates critical biological pathways and their respective transcriptional networks in VSELs, supporting the concept that VSELs serve as a reserve mobile pool of stem cells that can be mobilized into peripheral blood, and play an important role in end-organ regeneration during IH.
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0282

SLEEP RESTRICTION (NAP DEPRIVATION) IMPACTS EMOTIONAL RESPONSES IN 2-3 YEAR-OLD CHILDREN

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Introduction: Although inadequate sleep may place children at-risk for emotion regulation problems, current understanding of links between sleep and emotion are based upon correlational reports. This experimental study examined the effects of sleep restriction (nap deprivation) on young children's emotional responses during emotionally eliciting tasks.
Methods: Participants were 11 healthy children (8 females; 30-36 months) with no sleep/emotional/behavioral problems. Children followed a strict sleep/wake schedule (actigraphically verified) that optimized sleep opportunity (>12.5hrs TIB/24hrs) and stabilized the circadian system for >5 days before two emotion assessments occurring at the same time (1hr post nap wake time) under nap and no-nap conditions. In each condition, children viewed affect-eliciting pictures (6 positive, 3 neutral, 3 negative) and completed puzzles (1 solvable, 1 unsolvable). Children's responses were video-recorded; emotion responses (neutral, positive, interest-excitement, sadness, confused, worry-anxiety, disgust) were later coded in real-time.
Results: Wilcoxon matched-pairs signed-ranks tests were used to examine emotional responses (% time in seconds) to pictures and puzzles between nap and no-nap conditions. While watching neutral pictures, children exhibited less confusion (Z=-2.39; p=.017) in the no-nap (M=1.5, SD=4.3) than in the nap condition (M=8.4, SD=10.2). When viewing negative pictures, children showed more worry/anxiety (Z=-2.52; p=.012) in the no-nap (M=45.7, SD=30.1) than the nap condition (M=14.6, SD=14.7). Children exhibited more worry/anxiety (Z=-2.40; p=.016) and less confusion (Z=-2.22; p=.026) after sleep restriction (worry/anxiety: M=32.8, SD=19.9; confusion: M=8.3, SD=6.2) than after taking a nap (worry/anxiety: M=15.5, SD=18.8; confusion: M =22.9, SD=15.5) while completing the unsolvable puzzle.
Conclusion: Increased worry/anxiety (e.g., repetitive lip-biting, fist clenching, sucking on fingers) and decreased confusion (e.g., quizzical eye brows) after nap deprivation demonstrate sleepiness is important

for children's emotion regulation. If insufficient or poorly timed sleep consistently "taxes" children's emotion responses, then children may develop a behavioral style that puts them at-risk for emotional dysregulation. Given that early emotion dysregulation is linked to psychopathology during adolescence, early intervention is crucial, including a focus on daytime sleepiness.
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0283

SLEEP DISTURBANCES IN CHILDREN WITH CANCER

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Introduction: Clinicians report that children with cancer experience sleep disturbances, however, empirical data is scarce. Optimal sleep is crucial for normal growth and development and emotional and physical health. Therefore, an understanding of the sleep patterns and disturbances experienced by this population as compared to the general pediatric population is necessary.
Methods: A convenience sample of parents of children with cancer ages 2-18 years-old being cared for at The Children's Hospital of Philadelphia completed the Children's Sleep Habits Questionnaire (CSHQ), a 33-item questionnaire that assesses age-relevant sleep patterns and disturbances. Information was also collected about the child's usual bedtime, wake time, and total amount of sleep over a 24-hour period.
Results: The sample of children included 25 males and 25 females with a mean age of 9.25 years (± 4.5, range 2.5-18). Most of the sample had acute lymphoblastic leukemia (ALL) (68%) with sarcomas (26%) and acute myelogenous leukemia (6%) reported less frequently. Subjects were an average of 13.5 months post diagnosis (± 12, range 1-50). Nighttime sleep disturbances such as needing a parent to fall asleep (40%), restless sleep (42%), and failing to fall asleep in own bed (42%) occurred frequently. Daytime sleep disturbances such as difficulty getting out of bed (42%), waking in a negative mood (44%), and others needing to wake child (48%) were also common.
Conclusion: In comparison to the average pediatric population sleep disturbance rate of 25%, these results suggest that children with cancer may be at higher risk than the general population for certain nighttime sleep disturbances, especially specific measures of bedtime resistance and parasomnias, as well as certain daytime sleep disturbances, especially signs of daytime sleepiness. Because compromised sleep has the potential to adversely affect a variety of health outcomes, further research designed to study the sleep of children with cancer is warranted.
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0284

SLEEP DISORDERED BREATHING (SDB) IN CHILDREN WITH DUCHENNE MUSCULAR DYSTROPHY (DMD)

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Introduction: Previous studies have shown relatively common occurrence of SDB in patients with DMD. However, those studies were focused on older DMD patient with more advance diseases. There is limited information on early manifestation of SDB in children with DMD.
Methods: A retrospective review of sleep study and lung function test was performed in children with DMD. Most children in our comprehensive neuromuscular program have baseline polysomnographic evaluation when they reach age 10 years or exhibit signs of SBD. Only children with complete records were included into the study. Children with other co-existing conditions such as cardiomyopathy were excluded from the study.
Results: A total of 64 children met criteria for entry into analysis. The average age was 10.9±2.4 years old. 43.8% (28/64) of children with DMD had abnormalities from polysomnographic assessment. 26.6% (17/64) of them had obstructive sleep apnea; 15.6% (10/64) of them had central sleep apnea; 9.5 % (7/64) of them had significant hypoventilation (EtCO2>50 mmHg, >25%TST). There was a significant correlation between forced vital capacity (FVC) and the degree of hypoventilation ($r = -0.43$, $P<0.05$), but no correlation between FVC and obstructive or central index was observed. There was no significant correlation between MIP or MEP and any of SDB parameters.
Conclusion: Sleep disordered breathing including obstructive apnea, central apnea and nocturnal alveolar hypoventilation is common in children with DMD even at the early age. The degree of hypoventilation is directly related with changes in the lung function. This study emphasizes the need for early detection and early intervention.
Support (optional): The study is supported by the Cincinnati Children's Hospital Research Fund.

0285

IMPROVING THE ANALYSIS OF HOME OXIMETRY IN CHILDREN WITH SUSPECTED OBSTRUCTIVE SLEEP APNEA

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Introduction: Overnight oximetry has been proposed as a screening tool for obstructive sleep apnea (OSA). However only about 20% of snoring children have an abnormal oximetry, with false negative results in those with OSA without desaturation. We hypothesized that pulse rate (PR) indices and pulse rate standard deviation (PR-SD) would reflect sleep fragmentation, and together with removing periods of wakefulness and poor signal quality, would improve the ability of oximetry to detect OSA.
Methods: Oximetry (Masimo Radical, 2s averaging time) recorded during polysomnography (PSG) in 5 children (mean age 8.8y) was analyzed using Download 2001 (Stowood Scientific) software. The PR increases/h (PRI) chosen were based on previously reported data: PR change from wake to sleep of 10bpm (PRI-10), wake to REM of 8bpm (PRI-8) and sleep to arousal of 15bpm (PRI-15). The entire recording was analyzed with and without automatic removal of periods of poor signal quality. Recordings were then trimmed by PSG-defined sleep onset and offset, and analyzed in the same way. Analysis methods were compared using 1-way ANOVA. Pearson correlations were performed between PRIs and the obstructive apnea hypopnea index (OAHI) and total arousal index (ArI).
Results: Trimming the oximetry lead to significantly lower PR-SD ($p<0.05$). Dips in SpO2 >=3%, PRI-15 and PR-SD were higher and SpO2 nadir was lower if poor signal was not removed ($p<0.05$). Analysis method did not affect mean SpO2, PRI-8 or PRI-10 (NS). None of the PRI correlated significantly with OAHI or ArI (best values, for PRI-15 and ArI: $r=0.62$, $p=0.26$). PR-SD was significantly correlated with OAHI (trim/auto analysis $r=0.97$, $p<0.05$) and ArI ($r=0.95$, $p<0.05$).
Conclusion: Trimming oximetry records to remove awake data and removing periods of poor signal quality affects SpO2, PRI-15 and PR-SD results. PRI-15 and PR-SD hold the most promise for identifying OSA and will be the focus of further studies.
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0286

REDUCED QUALITY OF LIFE IN PRESCHOOL CHILDREN WITH SLEEP-DISORDERED BREATHING

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Introduction: Sleep-disordered breathing (SDB) affects over 30% of children and is most common between 2 and 8 years of age. While reduced quality of life is commonly reported in school-aged children with SDB, preschool-aged children represent a significant proportion of pediatric SDB patients and specific investigation of quality of life in this population is warranted.
Methods: The sample to date consists of 18 children (6F/12M; 3-5y) referred for clinical assessment of SDB. Standard overnight polysomnography (PSG) was performed and parents completed the Pediatric Quality of Life Inventory, Version 4.0 (PedsQL™ 4.0), on which items are combined into four subscales (Physical Functioning, Emotional Functioning, Social Functioning, and School Functioning) and two summary scores (Psychosocial Health Summary and Total). Scores were linearly transformed to a scale of 0-100 with higher scores indicating better quality of life. Published data from healthy age-matched children were used for comparison.
Results: One-sample t-tests showed significantly reduced scores ($p<0.05$) in the children with SDB compared to normative means in the Physical Functioning subscale (mean difference ± SD 6.2±11.7; mean z-score ± SD -0.4±0.7), Emotional Functioning subscale (20.3±15.2; -1.4±1.1), Psychosocial Health Summary score (11.6±11.7; -0.9±1.0), and Total score (9.8±10.1; -0.8±0.8). Following PSG 7 children were diagnosed with primary snoring (PS) and 11 with obstructive sleep apnea syndrome (OSAS). There was no indication that children with OSAS (Total score ± SD 78.1±11.2) were affected to a greater degree than children with PS (73.3±6.2).
Conclusion: Preschool-aged children with SDB had reduced scores on measures of quality of life compared to healthy peers. These results are consistent with reports of reduced quality of life in older children with SDB and underline the importance of early intervention.
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0287

SCREENING AND MANAGEMENT OF OBSTRUCTIVE SLEEP APNEA IN CHILDREN: RESULTS OF A COMMUNITY SURVEY

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Introduction: Obstructive sleep apnea (OSA) is a common medical condition in children with serious adverse consequences including neurocognitive deficits and behavioral problems. In 2002, the American Academy of Pediatrics (AAP) issued a Clinical Practice Guideline on Diagnosis and Management of OSA. The purpose of this study was to assess community pediatricians' awareness of the guidelines and their screening and management practices for OSA in 4 age groups: infant, toddler & preschool, school aged and adolescent.
Methods: The Pediatric Sleep Survey, a validated sleep questionnaire, was used. To assess screening, respondents were asked to select specific sleep history items that they routinely included more than 75% of the time during a well child visit. Practitioners were asked to select items pertaining to evaluation & treatment of a patient with suspected OSA. Approximately 500 AAP members were contacted by email. A web based survey engine (www.surveymonkey.com) was used to collect responses and analyze results.
Results: Response rate was 22%. 58% (63/111) of respondents were not aware that these Guidelines had been issued. 75% (80/111) of respondents were not aware of the guidelines specific recommendations for screening, evaluation and treatment of OSA. In our sample, 40% of practitioners (36/111) did not screen for sleep apnea at all. The most common reasons for not screening were the belief that parents would indicate if there was a problem (34%) and that screening takes time away from inquiring about other health problems (27%). However, 93% of respondents (71/111) screened high risk school aged children for snoring and 75% (57/111) screened adolescents for snoring. For evaluation, only 7.5% of respondents always ordered an overnight polysomnogram (PSG). For treatment, 48% would often or always refer to an otolaryngologist for adenotonsillectomy for suspected OSA.
Conclusion: Despite poor awareness of the guidelines and their recommendations, practitioners are screening high risk school aged and adolescent children for snoring as recommended. However, few pediatricians use PSG to evaluate for OSA as is ideal. The majority of pediatricians refer children for adenotonsillectomy on clinical suspicion of OSA. Our findings emphasize the importance of educating primary care physicians to appropriately screen, evaluate and treat children with suspected OSA.

0288

THE EFFECT OF STIMULANTS ON PERIODIC LIMB MOVEMENTS IN PEDIATRIC ATTENTION-DEFICIT HYPERACTIVE DISORDER PATIENTS

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Introduction: It is unclear if the dopamine effects of a stimulant medication have an altering effect on PLMs during sleep. We have hypothesize that children taking stimulants for ADHD will have lower PLM indices compared to those not taking stimulant therapy, and that there is no significant difference between Amphetamine based or Methylphenidate based medications.
Methods: A retrospective review of all pediatric patients with ADHD and available PSG reports was performed. The database was reviewed for demographics, medical history, medications and PSG variables. PLM indices were compared among three groups (A: Amphetamine-based stimulants; B: Methylphenidate-based stimulants, and C: Patients not on stimulants (controls)). Unifactorial ANOVA and pairwise comparisons were conducted.
Results: 56 patients were included, 13 females and 43 males. Mean age/SD 11/3.4 years, mean PDSS 17/6.47, mean BMI 23.4/7.33. Four (7.1%) patients had the diagnosis of Restless Leg Syndrome. 35 (62.5%) subjects were on stimulants (16 from group A and 19 from group B). There were no significant differences found between the three groups or within the groups in regards to demographics, medical history or PSG findings. When comparing PLMI and PLMAI between and within the three groups we noted a trend for higher but non-significant indices in groups A and B when compared to results of group C (2.04/ 2.81/ 0.84 p= 0.218), (0.29/0.41/0.2, p=0.685). When controlling for other variables known to affect PLMIs (Age, BMI and AHI) the correlation within the stimulant groups continued to be non-significant.
Conclusion: In our pediatric patient population with ADHD undergoing PSG evaluations, we found no significant effect of stimulants medications on periodic limb movements indices during sleep nor did we see significant differences between the two families of stimulants with regard to these indices. Larger studies need to be conducted to confirm these findings.
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0289

RESTLESS LEGS SYNDROME IN CHILDREN: PRESENTING SYMPTOMS

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Introduction: For the diagnosis of RLS in children guidelines have been formulated. The diagnosis remains difficult, because the child gives no clear description of symptoms which may point to RLS. The study aims at the description of these presenting symptoms in a group of young children and teenagers.
Methods: From the records of two centers with special interest in pediatric sleep, 31 patients were identified. (25 boys; age range: 4-16 yrs; median: 10 yrs). All children finally met the ICSD 2 criteria for pediatric RLS and underwent a full polysomnography including recording of periodic leg movements (PLMS).
Results: The first symptoms occurred at a median age of 8 yrs, range: 4-12 yrs. At the first visit to the sleep center all children were tired during daytime. Eight of them had excessive daytime sleepiness. Difficulties in initiating or maintaining sleep during the night were reported in all cases. Twelve children complained about feelings in the legs which were initially diagnosed as so called growing pains. Clear RLS symptoms (the so called 4 criteria) were present in 30% of the children. Deep sleep related parasomnias occurred in 3 children. The main co-morbidities were epilepsy in 8 (possibly a selection bias as SEIN is a center specialised in epilepsy as well) and ADHD in 14 cases. At least for 10 children the family history was positive for RLS, but this data was not present for all patients included in the study. The PSGs revealed that sleep architecture was normal in 90% of the cases. Leg movements occurred with a mean of 61/hr of sleep (range: 40-250). The PLM Index had a mean value of 13/hr of sleep (range: 7-50).
Conclusion: The study gives guidelines for what to ask and look for when RLS is suspected in a child.

0290

PRENATAL ORIGINS OF POOR SLEEP IN CHILDREN

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Introduction: We examined whether small body size at birth and prenatal tobacco or alcohol exposure predict poorer sleep and more sleep disturbances in children.
Methods: An epidemiological cohort study of 289 eight-year-old children born at term gestation. Sleep characteristics (sleep duration, latency, efficiency) were measured by actigraphs for seven consecutive nights (M = 7.1, SD = 1.2). We used both continuous measures of poor sleep and binary variables of short sleep, low sleep efficiency (< 10th percentiles) and long sleep latency (> 90th percentile). Parents filled in the Sleep Disturbance Scale for Children (SDSC).
Results: Lower birth weight and shorter length at birth were associated with longer sleep latency, and lower sleep efficiency. The odds to being in the long sleep latency or low sleep efficiency category increased by 1.7- (95% confidence interval [95% CI] 1.1 to 2.7) and 2.0-fold (95% CI, 1.2 to 3.2) for every 1-standard deviation decrease in birth weight and length at birth, respectively. For every 1-standard deviation decrease in ponderal index at birth the risk of parent-reported sleep disorders increased by 1.4-fold (95% CI 1.0 to 2.0). The odds to being in the short sleep or low sleep efficiency category increased by 2.9- (95% CI 1.1 to 7.6) and 3.6-fold (95% CI, 1.3 to 10.0) among children prenatally exposed to alcohol.
Conclusion: Poorer sleep in children may have prenatal origins. Alcohol consumption during pregnancy may pose a risk for poorer sleep

0291

DO CHILDREN WITH IDIOPATHIC NARCOLEPSY HAVE A LONG SLEEP TIME?

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Introduction: Background and objective: Several investigators emphasize that children with narcolepsy may exhibit more severe daytime sleepiness than adult narcoleptics, with a trend for a less optimal response to stimulants. Studies evaluating the total sleep duration during long term polysomnography in children with narcolepsy are however lacking. We measured the sleep duration during long term monitoring of narcoleptic children at the time of the diagnosis and compared it with historical normative data for children (Ohayon Sleep 2004).
Methods: We retrospectively reviewed the medical files of all children with idiopathic narcolepsy referred to the Lyon children sleep disorder unit from 1991 to 2008. They had completed questionnaires, and undergone a 24-hour ad libitum sleep monitoring, followed by an overnight polysomnography, multiple sleep latency test and human leukocyte antigen genotype (HLA).
Results: 18 children (10 male) were included. Their median age at diagnosis was 13.5 years (7-18). The children did not receive any medication at time of diagnosis and sleep monitoring. 77% had cataplexy, and 88.8% were HLA DR 15 or DQB1*0602 positive. The median sleep time was 487 min (300-718) during the night and 88.5 min (32-175) during the day. The median total sleep time during long term monitoring was 588 min (404-880), or 9.8 hours (6.7-14.6). All children had naps (median 2, range 1 to 7 naps). Seven out of 18 narcoleptic children (38%) had longer sleep duration on a 24h basis than healthy children (normative data, + 2 DS). Respectively 77%, 38% and 22% narcoleptic children slept more than 9, 10 and 11 hours per 24-hour. An overnight polysomnography was performed in 15 patients. No sleep apnea syndrome or periodic leg movement syndrome were found in these patients. No differences were found between short and long sleepers concerning HLA typing or the presence of cataplexy. The children who slept < 7 hours during night-time tended to be more resistant to drug therapy.
Conclusion: Two third of narcoleptic children sleep longer than 9 hours per 24h. Some children have a narcolepsy with long sleep time. Short night sleepers however could be at risk of drug resistance.24-hour ad libitum sleep monitoring could be useful to characterize these patients and give potential information on the severity of the disease

0292

THE PRACTICE OF PEDIATRIC SLEEP MEDICINE: RESULTS OF A COMMUNITY SURVEY

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Introduction: Objective: To assess knowledge, attitudes and practices regarding sleep disorders in pediatrics in a sample of community-based family practitioners in Savoie (alpine area of France).
Methods: Participants: Family practitioners from Savoie. Instrument: A questionnaire containing 21 questions about the most frequent pediatric sleep problems. Statistical significance was performed with the use of an analysis of variance (ANOVA) with the SPSS program for Windows.

Results: From the mailing list of family practitioners that covered Savoie containing 394 physicians, 199 have been contacted by phone (50%). 107 doctors (53,8%) answered the questionnaire. The average physician's age was 51 years old. 59,8% were men and 40,2% were women. The mean of the correct answers has been of 59,6%. The family practitioners knew well the normal development of sleep (77%) and the relation with sleep disturbances and school difficulties or hyperactivity (respectively 95,3% and 72,8%). But only 63,5% advised properly the parents of children with behavioural sleep disorders. Only about respectively half and one quarter of the respondents screen toddlers and school-aged children for hypersomnia and chronic snoring. The advices to give in case of parasomnia were only known by 24,8% of the practitioners and those they should give to prevent the sudden infant death syndrome only by 2,3% of them. Only 25,5% knew the physiology of sleep in adolescence. 40,3% of the responders gave sedative medications for sleep disturbances in children. From this survey, practices were better than attitudes and knowledge about pediatric sleep disorders. 85% of the family practitioners complained about absence of education during their training about children's sleep problems, and 76,6% would like to be trained on the subject.
Conclusion: Knowledge about pediatric sleep problems is poor in family practitioners. It reflects the absence of education in medical school, postgraduate training and continuing medical education in France. Educational effort regarding pediatric sleep issues are warranted in particular regarding the prevention of Sudden Infant Death Syndrome.

0293

SLEEP DISORDERED BREATHING IN CHILDREN: THE RELATIONSHIP BETWEEN SLEEP TIME AND BODY WEIGHT DURING DEVELOPMENT

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Introduction: Sleep disordered breathing (SDB) and shortened sleep time have both been independently associated with overweight/obesity in children. However, it is unclear whether the association between sleep time and increased body weight varies amongst children with SDB, as compared to matched, non-snoring controls.
Methods: Thirty children with SDB (6.7 ± 2.9 yr; 19 males) were recruited from a hospital waiting list for adenotonsillectomy. Forty non-snoring controls (7.4 ± 2.6 yr; 18 males) were recruited from the general community. All subjects (or a parent) completed one-week sleep diaries prior to attending a single overnight polysomnography.
Results: Groups were matched for age, gender and BMI z-score. SDB children displayed greater obstructive apnea and hypopnea index (OAHI), respiratory arousals and hypoxia when compared to controls. There were no group differences in mean sleep diary measures, including time in bed, total sleep time and sleep onset latency. After controlling for age, socioeconomic status and OAHI, sleep time was only mildly predictive of BMI z-score across the total group; $R=0.26$, $p<0.05$. Analyzed independently however, only children with SDB showed a significant association with sleep time; explaining 11.5% of the variance in BMI z-score, $R=0.34$, $p<0.05$, compared to only 5.3% for controls, $R=0.23$, ns. OAHI did not interact with this association.
Conclusion: To our knowledge the association between sleep time and body weight has not previously been compared between children with SDB and healthy controls. Consistent with previous reports, across the total group shorter sleep time was mildly associated with increased body weight. However when analysed separately, the association was much stronger amongst SDB children and absent altogether amongst controls. The difference between groups was not attributable to OAHI severity. Given a large community prevalence of snoring amongst children, these results suggest that the influence of sleep time on body weight during development should be carefully reviewed.

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0294

SLEEP ITEMS IN THE CHILD BEHAVIOR CHECKLIST: A COMPARISON WITH SLEEP DIARIES, ACTIGRAPHY AND POLYSOMNOGRAPHY IN A SAMPLE OF ANXIOUS, DEPRESSED, AND CONTROL YOUTH

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Introduction: There is a paucity of sleep measures in large-scale longitudinal studies of child development. The Child Behavior Checklist (CBCL) is a widely used parent-report measure of behavioral difficulties in children. This measure contains items assessing aspects of sleep (e.g. length and quality). To tap into rich datasets, researchers have used the CBCL sleep items to investigate links between sleep and other variables. Although this approach could provide valuable contributions to understanding the role of sleep in normal and abnormal development; the CBCL was not designed to assess sleep and there is some skepticism about what exactly these measures are assessing. To address these controversies we examined a data set that included CBCL, polysomnography, actigraphy and sleep diaries in children and adolescents.
Methods: 122 youth (59% female, ages 7-17 years) with anxiety disorders (19%), major depressive disorder (8%), both anxiety and depression (25%), or without a history of psychiatric disorder (47%) participated. Parents completed the CBCL and children wore actiwatches for multiple nights; spent two consecutive nights in a sleep laboratory; and completed a sleep diary.
Results: Analyses demonstrate links between some CBCL sleep items and more established sleep measures. For example, there was a positive association between parent reported 'trouble sleeping' and actigraphy-assessed sleep-onset-latency (trouble sleeping: not true: $M = 18.38$ minutes [$SD = 9.38$]; somewhat: $M = 20.31$ minutes [$SD = 7.72$]; often true: $M = 25.52$ [$SD = 12.32$]; $F(2, 96) = 3.11$, $p = .049$). However, the associations between 'sleeps less' than others and objective measures of sleep length were not significant.
Conclusion: These data suggest that some (but not all) CBCL sleep items may be associated with alternative measures of sleep. This information may allow sleep researchers to ask questions of rich datasets which do not include more thorough assessments of sleep.
Support (optional): This study was supported by the National Institute of Mental Health (P01 MH41712); Alice M. Gregory is currently supported by a Leverhulme Research Fellowship.

0295

MYELOID RELATED PROTEIN-8/14 LEVELS IN CHILDREN WITH OBSTRUCTIVE SLEEP APNEA

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Introduction: Similar to adult patients with OSA, pediatric OSA has been recently associated with a higher risk of cardiovascular (CVD) morbidities and metabolic dysfunction, particularly among obese children. The family of myeloid related proteins (MRP) includes calcium binding proteins expressed in circulating phagocytic cells. MRP 8/14 proteins play an important role in the process of atherosclerosis and closely correlate with inflammatory processes in the endothelial wall. Therefore, we hypothesized that plasma MRP 8/14 levels would be elevated in children with OSA.

Methods: A case-control study among children enrolled in a prospective research. All participants underwent polysomnography and a fasting blood draw next morning. Children were divided into 4 groups based on the presence of OSA and obesity (BMI z score>1.65). Plasma levels of MRP 8/14 were assayed using commercial ELISA kits.
Results: Non-obese and obese children with OSA had significantly higher MRP 8/14 levels compared to corresponding controls ($p<0.05$). In addition, MRP 8/14 levels were significantly correlated with both BMI z score and obstructive AHI in univariate analysis. Furthermore, MRP 8/14 levels were independently associated with obstructive AHI after controlling for BMI z score ($r=0.28$, $P<0.05$).
Conclusion: Plasma MRP 8/14 levels are associated with obesity and OSA in children. MRP 8/14 levels may play an important role in modulating phagocytosis and inflammatory responses in children with OSA, and promote atherogenesis.
Support (optional): NIH grant HL-65270 and Children's Foundation for Sleep and Neurobiology Research.

0296

INTERDISCIPLINARY PEDIATRIC SLEEP DISORDERS CLINIC: APPROACH TO TREATMENT AND OUTCOMES

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Introduction: Pediatric sleep medicine has evolved into an interdisciplinary specialty. Our team includes pediatric sleep specialists, a nurse practitioner, and psychologists; and uses an interdisciplinary (medical/psychological) approach, including cognitive behavioral therapies. We evaluated patient demographic/interventions and time from initial visit to improvement/resolution of symptoms for a sample of children in our clinic. Information will be used to refine processes for future completion of all case reviews.
Methods: A retrospective study of 20% (n=75) of 381 children seen between July 2007 and June 2008 who had a behavioral or non-respiratory component to their sleep disorder. Records were randomly selected for review. Statistical analysis was performed using SAS v9.2.
Results: There were seventy-five children (39 boys) including infants through adolescents (13% <2 yrs, 22% 2-5 yrs, 41% 6-12 yrs, 23% 13-18 yrs) and three races (68% White, 24% Black, 8% Hispanic). 75% had at least one employed parent. Insurance included commercial (53%) and HMO-AFDC or Medicaid (41%). Primary sleep diagnoses included: psychophysiologic insomnia (43%), behavioral insomnia of childhood (36%), hypersomnia (8%), obstructive sleep apnea plus an additional sleep diagnosis (7%), delayed sleep phase syndrome (4%). Half of the children had >1 sleep disorder; 37% had a co-morbid psychiatric diagnosis. One-third of children had sleep environments not conducive to good sleep (e.g., television, videogames, lights on). All children were instructed in cognitive behavioral therapy (e.g., bedtime routine, sleep restriction, stimulus control, graduated extinction, positive rewards, and/or relaxation techniques). 57% of children were prescribed medication (usually melatonin). Half were referred for sleep study as part of the evaluation. Follow-up occurred by additional clinic visits, telephone, or email. Of children who had follow-up (n=56), 55% reported improvement/resolution of symptoms. Median time from initial clinic visit to improvement/resolution of symptoms was 2.8 months.
Conclusion: Children experience a broad range of sleep disorders, many of them behavioral or non-respiratory in origin. Often there is more than one sleep disorder. An interdisciplinary approach to treatment is highly effective, with a relatively short time span to improvement/resolution of symptoms.

0297

SUFFICIENT SLEEP MAY BE MORE COMMON AMONG OVERWEIGHT THAN NON-OVERWEIGHT ASTHMATIC CHILDREN

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Introduction: Asthma in adults is associated with overweight and poor quality sleep, but these relationships have scarcely been studied in children. We used a nationally representative U.S. survey data to examine retrospectively whether caregiver-defined "sufficient" sleep differed between asthmatic children with higher or lower body mass index (BMI), after adjusting for sociodemographic variables and asthma severity.
Methods: The 2003 National Survey of Children's Health included question-items on demographics, height and weight, doctor-diagnosed asthma and number of nights of sufficient sleep (0-3, 4-7) obtained in the past week as perceived by a caregiver. Subjects were divided into 2 subgroups by BMI z-scores (adjusted for age and gender). Normal weight was defined as 5th-84th percentile; at risk or overweight as a BMI $\geq$ 85th percentile.
Results: In 2003 among 6,908 asthmatics aged 6-17 years, unadjusted bivariate logistic regression showed that overweight or at risk children in comparison to those of normal weight had higher odds of having 4-7 nights per week of sufficient sleep (OR=19.6, 95% CI: 4.0-98.0). In a logistic regression model that adjusted for race, gender, income, household education and asthma severity, the association persisted (OR=6.0, 95% CI: 1.1-35.3).
Conclusion: Data from this nationally representative dataset indicate that asthmatic children who are overweight or at risk may obtain more rather than less sleep than their counterparts who have normal BMI. These surprising results highlight the importance of developing a better understanding of complex and probably bidirectional relationships between asthma, sleep and overweight.

0298

SIGMA BAND INTERHEMISPHERIC COHERENCE DISTINGUISHES CHILDREN WITH AND WITHOUT OBSTRUCTIVE SLEEP APNEA

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Introduction: Significant sigma band interhemispheric EEG coherence, thought to reflect functional connectivity within the brain, has been observed in healthy adults during the progression from wake to sleep [Achermann and Borbely, Neuroscience, 1998:85(4):1195-1208]. We examined interhemispheric coherence in children and its relationship to obstructive sleep apnea (OSA).
Methods: Polysomnographic data from the Washtenaw County Adenotonsillectomy Cohort were analyzed retrospectively for 48 subjects aged 5-12 years with OSA (AHI$\geq$1.5) and scheduled for adenotonsillectomy, and 20 controls without OSA. Subjects were studied at enrollment, and again one year later in almost all cases. For each subject, the interhemispheric EEG spectral coherence between C3-A2 and C4-A1 at 1-30 Hz was computed over 30 sec epochs throughout the night and averaged over specific sleep stages. Sleep spindle density was computed by identifying time intervals where spindle frequency EEG power exceeded a threshold (10μV).
Results: At baseline, only interhemispheric coherence in the lower sigma band (12-13 Hz) during stage 2 differentiated OSA subjects and controls (0.33±0.11 (sd) vs. 0.38±0.09, Wilcoxon rank sum test, $p=0.01$). Stage 2 sigma interhemispheric coherence varied inversely with AHI (Spearman Rho=-0.41, $p=0.0004$) and directly with minimum oxygen saturation (Rho=0.38, $p=0.002$). Stage 2 spindle density also distinguished OSA

subjects and controls (p=0.05), and varied inversely with AHI (Rho=-0.26, p=0.03), but the association between coherence and AHI retained significance after correcting for spindle density (Rho=-0.31, p=0.01). At follow-up, stage 2 interhemispheric coherence (12-13 Hz) showed little change in the control group (0.37±0.07), increased in the OSA group (0.34±0.09), and no longer distinguished the two groups (p=0.26).
Conclusion: Interhemispheric sigma frequency EEG coherence appears to be diminished in children with OSA, and may improve to some extent with treatment. This metric potentially could serve as a useful biomarker, or shed light on brain dysfunction that underlies neurobehavioral morbidity in pediatric OSA.
Support (optional): This work was supported NIH grants HD038461, RR000042, and HL080941.

0299

CHILDREN WITH OSA EXHIBIT DIFFUSE, INCREASED-AMPLITUDE EVENT-RELATED POTENTIALS ON SPEECH DISCRIMINATION TASK

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Introduction: OSA is estimated to affect approximately 3% of children and has been implicated in neurobehavioral dysfunction, with >250,000 children undergoing adenotonsillectomy (AT) for OSA yearly in the US. More objective and reliable measures of efficacy for AT are needed. This report is from an ongoing study measuring electrophysiological changes in children with OSA before and after AT using event-related potentials (ERP).
Methods: Participants included 16 children: 8 undergoing polysomnography (NPSG) for OSA and 8 matched controls (mean 6.1 years, 10 females). Children participated in a neurocognitive battery while parents completed questionnaires on sleep habits and daytime functioning. Children performed 3 tasks in a 128-electrode net. ERP data were analyzed using temporal principal components analysis (PCA) to identify regions of variability in the waveform, providing dependent variables for mixed-factorial analysis of variance. Time-locked waveforms were used to form spatial models localizing activity in the brain. ERP results from the speech discrimination task were then related to neurocognitive outcomes.
Results: Temporal PCA produced 5 factors accounting for almost 87% of the variance in the model. Factor 4 (peak at 124 ms, 12.674% of the variance) exhibited a main effect of group ($F=10.358$, $p<0.006$) and a significant electrode*group ($F=6.928$, $p<0.005$) interaction. Post hoc corrected t-tests revealed significantly greater activation in all electrode regions for children in the OSA group versus age- and sex-matched control participants. Post AT analyses are currently being completed.
Conclusion: Preliminary analyses indicate altered neural functioning in children with OSA at approximately 124 ms post-stimulus onset. Increased amplitude of potentials in the OSA group reflects more effortful phonological processing and an increase in cognitive resources required to complete the task. This could underlie components of the previously observed neurobehavioral deficits in OSA, with significant implications for post-surgical outcomes of these children.
Support (optional): American Psychological Association grant and a MD/PhD predoctoral fellowship from the National Institute of Mental Health (F30MH79531).

0300

SLEEP MEDICATION PRESCRIPTIONS IN OUTPATIENT PEDIATRIC PRACTICE

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Introduction: Sleep disturbances are common in children and adolescents; however, little is known about the use of medications in this population. The current study is a retrospective electronic medical record review of well-child visits to: 1) determine the percent of children prescribed a sleep-related medication in a primary care setting and 2) determine the most common medications prescribed.children prescribed a sleep-related medication and 2) determine the most common medications prescribed.
Methods: A chart review was conducted of all well-child visits in 2007 across 32 pediatric practices affiliated with the Children's Hospital of Philadelphia (154,957 patients; 51% male, 57% Caucasian, and 26% African American). Eight classes of medications (including 22 medications) were identified as potential sleep medications based on previous studies. Note that each of these medications could potentially have been prescribed for other reasons.
Results: Overall, 0.55% (n=938) of children were prescribed a potentially sleep-related medication. Older children were more likely to receive sleep-related medications with 0.74% (n=239) of adolescents (13-18 years) and 0.79% (n=466) of school-aged children (6-12 years) receiving prescriptions compared to 0.47% (n=112) of preschoolers (4-5 years), 0.24% (n=76) of toddlers (1-3 years), and 0.11% (n=26) of infants (0-12 months). Of these, antihistamines were the most commonly prescribed medications across all age groups (54%, n=490), followed by antipsychotic agents (19%, n=173), alpha-agonists (12%, n=111), benzodiazepines (9%, n=79), SSRIs (4%, n=36), melatonin (2%, n=18), and non-SSRI anti-depressants (1%, n=9). Notably, only 3 patients in the entire sample were prescribed a sedative-hypnotic (0.33%).
Conclusion: Contrary to previous self-report studies, this large population based chart review shows that pediatricians rarely prescribe medications for sleep in children and adolescents. Not surprising, older children were more likely than younger children to be prescribed sleep-related medication, with antihistamines, antipsychotics, and alpha-agonists the most commonly prescribed medications potentially used for sleep. The notable absence of sedative-hypnotic use suggests the need for clinical trials to determine the safety and efficacy of these medications in pediatric populations.

0301

CHINESE VERSION OF THE PEDIATRIC SLEEP QUESTIONNAIRE CHINESE VERSION OF THE PEDIATRIC SLEEP QUESTIONNAIRE

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Introduction: Validation of the Pediatric Sleep Questionnaire (PSQ) in Chinese
Methods: I-PSQ for parents: 1) Translation from English into Mandarin Chinese and translation back into English until versions were completely interchangeable conceptually and linguistically. 2) 50 PSQ obtained on obstructive sleep apnea children (14.37 + 2.9 years, and AHI>5), and completed by parents, with parental test-retest at 1 month interval.
Results: Cronbach'alpha were snoring: 0.766; mouth breathing: 0.811; daytime sleepiness: 0.692; nasal allergy: 0.811; behavior scale (including hyperactivity and inattention): 0.851; sleep related breathing disorder (SRBD) scale: 0.886. At the test- re-test, Spearman correlation coef-

ficients were: snoring 0.867; SRBD 0.786; daytime sleepiness 0.760; behavior scale 0.864; breathing problems 0.623. II-PSQ for children (self-report questionnaire): questions were modified from "your child" to "you". 1) Internal consistency and test-retest reliability were studied on 46 randomly selected high school students (15.53+2.23 years), with test re-administration 4 weeks later. Results: Cronbach's alpha were snoring scale: 0.660; nasal allergy: 0.708; daytime sleepiness: 0.655; behavior scale: 0.875; SRBD: 0.751. test- retest Spearman correlation coefficients were: snoring 0.660; SRBD 0.873; daytime sleepiness 0.715; nasal allergy 0.737; other symptoms 0.994. 2) A second validation on 38 OSA teen-agers (14.07+1.98 years) investigated the parent-child agreement with completion of PSQ by both parents and children separately. Results: Pearson correlation coefficient showed a high correlation between parents and children with snoring: 0.833; breathing problem: 0.888; daytime sleepiness: 0.502; SRBD: 0.718, other symptoms: 0.765; nocturnal enuresis: 0.707; insomnia: 0.655; bruxism: 0.741 and behavior problems (including hyperactivity and inattention): 0.802.

Conclusion: the Chinese version PSQ for children is a reliable and valid instrument to measure snoring, SRBD, daytime sleepiness, and other symptoms (including: morning headache, delay growth, obesity and nocturnal enuresis)

0302

COEXISTENCE OF SLEEP AND FEEDING DISTURBANCES IN YOUNG CHILDREN

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Introduction: Behavioral insomnia of childhood and feeding problems are two prevalent conditions affecting up to 25% of 6-36 month-old children. Although there are many similarities in the nature, etiology, frequency and age distribution of both conditions, no study has examined the co-existence of these disorders. Our objective was to investigate the prevalence of feeding difficulties among children with childhood insomnia and the prevalence of sleep disturbances among children with feeding disorders.

Methods: Parents to children 6-36 month-old referred to either the sleep clinic due to behavioral insomnia of childhood (group 1) or the clinic of feeding disorders (group 2) completed one of two detailed questionnaires about feeding habits and parental concern of their child's feeding (group 1) or about the child's sleep habits (group 2). In addition, parents to children who attended the mother and child clinics for periodic medical examination served as controls and completed both questionnaires.

Results: 381 children (51% male) were recruited: 43 group 1, 40 group 2, 298 controls. Mean age was 16.5±9.2 months. Parents to children with childhood insomnia were significantly more concerned about their child's feeding and growth compared with controls (24% vs. 9%, p=0.005 and 12.5% vs. 5%, p=0.05, respectively) and were more busy with their child's feeding (45% vs. 28%, p=0.03). Compared to controls, parents to children with feeding problems reported decreased night sleep time (520±94 min. vs. 578±80 min., p=0.001), increased number of awakenings (2.0 vs. 1.5, p=0.03) and a higher rate of prolonged sleep latency (30.6% vs.13.9%, p=0.01). In addition, more parents reported bed-time resistance and that their child's sleep was "too short" compared to controls (17.5% vs. 7.4%, p=0.03 and 23.8% vs. 8.3%, p=0.03, respectively).

Conclusion: Young children with behavioral insomnia have increased rate of co-existing feeding disturbances and vice versa. We hypothesize that each of these disorders predisposes for the development of the other.

0303

THE ASSOCIATION BETWEEN PSYCHIATRIC COMORBIDITIES AND SLEEP DISTURBANCES IN CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER

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Introduction: Sleep disorders are common in children, but up to twice as likely in children with developmental disabilities compared with typically developing peers. Children with attention-deficit/hyperactivity disorder (ADHD) have higher rates of psychiatric comorbidity than their typically developing peers. Conditions such as depression and anxiety disorders may affect sleep. We hypothesized that children with ADHD and psychiatric comorbidities would have higher overall sleep disturbance scores on a pediatric sleep questionnaire than children with ADHD without comorbidities. Further, subscales reflecting specific categories of sleep problems would drive differences between subjects with and without comorbidities.

Methods: Cross-sectional analysis of subjects with ADHD aged 6-18 years, enrolled in a prospective genetics study. Parents and children completed the Schedule for Affective Disorder and Schizophrenia for School-Age Children-P-IVR, a semi-structured interview that identifies psychiatric disorders. Parents completed the Children's Sleep Habits Questionnaire (CSHQ).

Results: 325 subjects (76% of 428 subjects) completed CSHQs. Mean age [SD] was 9.9 [3.1] years; 76% male. Median (range) Total Sleep Disturbance Score (TSDS) on CSHQ for all subjects was 45 (33-72). Median TSDS for subjects with no comorbidities was 44 (33-63); for subjects with anxiety, 47 (35-65); and subjects with depression, 46 (34-72). TSDS in subjects with anxiety was greater than subjects without comorbidities (p-value = 0.007). TSDS in subjects with depression was not different than subjects without comorbidities (p = 0.15). Sleep onset delay and night wakings subscales were elevated in subjects with anxiety (p-values 0.005 & 0.01). Daytime sleepiness subscale was elevated in subjects with depression (p-value 0.04).

Conclusion: Anxiety in children with ADHD contributed to higher TSDS scores on CSHQ beyond what could be accounted for by ADHD alone. Further study of the impact of treatment of psychiatric comorbidity on sleep and quality of life for both children and families is warranted.

Support (optional): NIH T32 HL007713-14; HL 58585

0304

NAPPING AND PSYCHOSOCIAL FUNCTIONING IN PRESCHOOL CHILDREN

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Introduction: Research has established the relationship between sleep and daytime functioning (e.g., behavioral, emotional) in children. However, the current literature has focused almost exclusively on relationships with nocturnal sleep, with little attention given to the importance of napping. Increasing social and educational demands frequently reduce opportunities for napping, but little is known about the impact this may have on children. The purpose of the present study was to examine the relationship between napping and psychosocial functioning in preschool children.

Methods: Data were collected from a sample of 62 children (55% White-non Hispanic; 53% male) aged 4-5 years. Caretakers reported

their child's typical weekday and weekend bedtime/rise time, napping patterns, family demographics, and completed the Behavioral Assessment System for Children, Second Edition (BASC-II). Actigraphy data for each child were collected continuously for 7-14 days to provide an objective measure of diurnal and nocturnal sleep.
Results: Children were classified as either napping (77%) or non-napping (23%) based on actigraphy data. Napping children napped an average of 3.4 days per week. Total sleep time (diurnal+nocturnal) did not differ significantly based on caregiver-report or actigraphy. Non-napping children were reported by their caregivers to have significantly higher scores (increased clinical symptomatology) on the Hyperactivity ($p = .02$; $\eta 2 = .09$), Anxiety ($p = .01$; $\eta 2 = .10$), and Depression ($p = .01$; $\eta 2 = .10$) subscales of the BASC-II. Non-napping children were much more likely to have Anxiety (Wald $\chi 2 = 9.8$, $p < .01$; OR = 8.7) and Depression (Wald $\chi 2 = 4.3$, $p < .05$; OR = 3.8) subscale scores within the 'At-Risk' or 'Clinically Significant' range on the BASC-II.
Conclusion: The findings of this study indicate that significant relationships exist between napping and indicators of psychosocial functioning; however, the correlational nature of these data do not allow for causal conclusions. Additional research is needed to understand the impact of napping on the individual child's developmental trajectory (e.g., development of psychopathology). Better understanding of the importance of napping would likely be of interest to parents, educators, and clinicians.

0305

'NORMATIVE' POSTPARTUM MATERNAL SLEEP

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Introduction: Advice to new mothers is usually focused on making up for sleep loss due to caring for an infant. However, little is known about the normative course of maternal sleep during the first postpartum months. As part of a longitudinal study of maternal postpartum sleep and affect, actigraphy measures were used to evaluate 'normative' postpartum sleep compared to nulliparous controls.
Methods: Fifty-four postpartum mothers contributed continuous wrist actigraphy and electronic sleep diaries during their normal routine. Thirty participated during postpartum Week one through thirteen, another 24 participated during postpartum Week eight through sixteen. A group of 14 nulliparous controls participated for one week. For all participants, nocturnal actigraphy measures were averaged within each week.
Results: Postpartum mothers' total sleep time increased from 7.0 (SD±.98) hours during postpartum Week one to 7.5 (SD±.86) hours during Week sixteen. Sleep efficiency also increased from 79.8% (SD±7.1) during Week one to 90.0% (SD±3.4) during Week sixteen. Sleep fragmentation index decreased from 21.6 (SD±6.6) during postpartum Week one to 13.1 (SD±3.4) during Week sixteen. Compared to controls: a) total sleep time did not differ during postpartum Weeks one through eight; but was higher among postpartum mothers from postpartum Week nine ($p=0.006$) through sixteen ($p=0.002$), b) sleep efficiency was lower among postpartum mothers during Weeks one ($p<0.001$) through Week ten ($p=0.024$) after which it did not differ and c) sleep fragmentation was higher among postpartum mothers during Weeks one ($p<0.001$) through Week twelve ($p=0.024$), after which it did not differ.
Conclusion: Postpartum mothers' total sleep time was higher than expected and higher than control participants during the third and fourth postnatal months. However, maternal sleep efficiency was lower than controls due to higher sleep fragmentation through the first three postpartum months. Though mothers appear to obtain 'enough' sleep overall, postpartum sleep is highly interrupted, similar to fragmenting sleep disorders. The larger study is designed to determine whether this fragmentation accounts for deleterious affect and daytime performance.
Support (optional): NIH grant R21HD053836(HMD

0306

DIFFERENCES IN OVERNIGHT POLYSOMNOGRAPHY SCORES USING THE ADULT AND PEDIATRIC CRITERIA FOR RESPIRATORY EVENTS IN ADOLESCENTS

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Introduction: Pediatric criteria are used to score polysomnography in children < 12 yr. However, the impact of pediatric vs. adult criteria on apnea hypopnea index (AHI, events/hr) in adolescents has not been assessed. Our objective was to compare pediatric and adult criteria in adolescents referred for obstructive sleep apnea (OSA). We hypothesized that pediatric respiratory criteria would capture more respiratory events than adult criteria.
Methods: Retrospective cross-sectional analysis of overnight polysomnography events scored using pediatric and adult criteria in 100 adolescents (67% male), 13-18 yr of age. We used AASM adult hypopnea definition VII.4.B, > 3% desaturation or association with arousal.
Results: Median (range) AHI by adult (aAHI) and pediatric (pAHI) criteria were 1.5 (0-97) and 1.8 (0-168), respectively. Median difference (pAHI-aAHI) was 0.2 (0-71). Higher pAHI was associated with greater differences between aAHI and pAHI ($R = 0.94$, $p< 0.0001$). Both aAHI and pAHI were positively associated with respiratory rate (RR) in slow wave sleep ($R = 0.63$-0.65, $p < 0.0001$). Differences between aAHI and pAHI were greater in subjects with greater RR ($p < 0.02$) when adjusted for aAHI, but not when adjusted for pAHI. Differences between scores were not associated with BMI Z-score independent of aAHI or pAHI. Using AHI > 1.5 as the criterion for OSA, 50 subjects were classified as OSA using adult criteria and 54 using pediatric criteria. Using AHI > 5 events/hour as the criterion for OSA, 28 subjects were classified as OSA using adult criteria and 30 using pediatric criteria. In neither case was the rate of discordant classification statistically significant.
Conclusion: Either adult or pediatric respiratory scoring rules can be used in adolescents as results are similar and few subjects change diagnostic category using aAHI versus pAHI. Further research into the clinical relevance of the scoring metric in adolescents is warranted.
Support (optional): NIH T32 HL007713-14; HL 58585

0307

POLYSOMNOGRAPHY AND SELF-REPORT SLEEP IN CHILDREN WITH OLIGOARTICULAR AND POLYARTICULAR JUVENILE IDIOPATHIC ARTHRITIS (JIA)

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Introduction: Approximately 30-60% of children are diagnosed with oligoarticular and polyarticular Juvenile Idiopathic Arthritis (JIA). Children with JIA experience sleep disturbances but few studies have examined polysomnographic sleep in children with JIA subtypes. The purpose of this study was to examine PSG and self-report sleep variables in children with oligoarticular and polyarticular JIA.
Methods: Sixty-six children 6-to-11 years of age (mean 8.5 ±1.9 years) with oligoarticular (n=26) and pauciarticular (n=40) JIA (85% female) participated in the study. Polysomnography (PSG) and self-report measures of sleep were obtained for 2 consecutive nights in a sleep laboratory. Bedtime and rise time was based on the usual home schedule, and remained consistent for both study nights.
Results: During the first night, PSG and self-report sleep variables did not differ in children with oligoarticular and polyarticular JIA. During the second night, PSG mean sleep onset latency was longer in children with polyarticular JIA (22 + 19 minutes) compared to those with oli-

goarticular JIA (14 + 8 minutes). Mean minutes of wake (34 + 11 and of snoring (242 + 121) were longer in children with oligoarticular JIA compared to polyarticular JIA (wake 28 + 11 min: snoring 180 +118 min). Self-report measures of sleep did not differ by disease type on the second study night.
Conclusion: These findings suggest that children with oligoarticular JIA are at risk for sleep disordered breathing. Further research is warranted to better understand the underlying mechanisms of sleep disturbances in children with oligoarticular and polyarticular JIA.
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0308

CYCLIC ALTERNATING PATTERN IN LACTATING CHILDREN

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Introduction: The Cyclic Alternating Pattern (CAP) are neurophysiological features that have been recently described. Pioneering studies suggest a relationship between CAP and estability of sleep. In addition, CAP have been found both in children and adults. In some sleep disorders as apnea a claer relationship have been reported. the influence of CAP in sleep physiology has attracted the attention of several scientific groups. However, it is still unknown when CAP appear in humane. In this study, a polysomnographic analysis was done in lactating children looking for the presence and characteristics of CAP.
Methods: Lactating children (N = 14) of both sexes (age range: 14 days-24 months old), without any illness, were polygraphically recorded for two hours. After an early wake up, recordings were done in the morning immediately after breakfast. Thus, at least two sleep cycles were obtained. Sleep scoring was performed following the criteria of Rechstschaffen and Kales with the adjustement reported for this age. Phase A of CAP were identified following the criteria already published by Terzano and cols. Concerning the phase B of the CAP, particular software especially designed for this task (Somnium) was used. Statistical analysis was done using a linear regression analysis and the Pearson correlation analysis.
Results: The presence of CAP in this group of age was found. In addition, a clear correlation both with age and respiratory events was detected. Phase A showed a peculiar distribution. Furthermore, the presence of central apneas was detected as well as a negative and significant correlation with the age.
Conclusion: Although the presence of CAP in this group of age was detected, the peculiar features of phase A and phase B are still not completely defined. Therefore, it is necessary to increase the sample to further define the presence, characteristics and relationship of CAP with brain development.

0309

MATERNAL DEPRESSION AND CHILD SLEEP OUTCOMES

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Introduction: Few studies have examined the relationship between maternal depression and sleep in offspring beyond very early childhood. In a study of mothers of children 4-7 years old, women at risk for major depressive disorder (MDD) completed measures designed to assess relationships between maternal depression and their child's sleep.
Methods: Mothers at risk for MDD (N = 118) who had previously completed a series of mood assessments (prenatally through 6 months postpartum) were re-contacted 4-7 years after their last assessment to complete the study. MDD was assessed at index pregnancy visit using structured interview. At the recent follow-up, these measures were completed by 85 women (72% of those contacted): Beck Depression Inventory-II (BDI-II), Child Behavior Checklist-Sleep Problems subscale (CBC-SP), and BEARS pediatric sleep screen. T-tests and regression analyses assessed relationships between maternal mood and child's sleep.
Results: Sixteen women (5%) met criteria for MDD at the time of study (BDI-II ≥20), and 39 (46%) reported symptoms consistent with current or past MDD. As compared to mothers without current MDD, children of women with current MDD had greater total BEARS scores (1.4 versus 2.12, p = .003) and CBC-SP subscale scores (2.94 versus 5, p = .02). Across the sample, BEARS snoring and napping items accounted for 17% of the variance in BDI-II score (p = .03), and awakening and snoring items accounted for 14% of the variance in past MDD history (p = .002). For women with current MDD, CBC-SP subscale score accounted for 53% of the variance in BDI-II score (p=.005).
Conclusion: Children of mothers with MDD have more sleep difficulties as compared to women without MDD. Disruption on several child sleep variables was associated with greater maternal BDI-II scores. These results are consistent with previous findings and further confirm the relationship between maternal depression and child sleep problems.

0310

SLEEP QUALITY AND DAYTIME ACTIVITY AS A FUNCTION OF CORTISONE ADMINISTRATION IN CHILDREN WITH ADRENAL HYPERPLASIA

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Introduction: In the treatment of congenital adrenal hyperplasia (CAH), some attempt to improve early morning ACTH suppression and endocrine control by a high bedtime hydrocortisone (HC) dose, while others simulate diurnal variation, expecting the HPA axis to play a role in sleep quality and daytime activity. We Hypotheses that higher morning HC dose simulates physiological pattern of HPA function and allows better sleep and activity pattern. Higher night dose effectively suppresses early morning ACTH peak levels and improves disease control.
Methods: A cross-over study of 15 CAH patients, age 7-18 y, received their regular HC dose of 11-17 mg/sqm, and were randomized to receive for 2 weeks either higher morning dose - 50%, with 25% at noon and 25% at evening or morning, followed by 2 weeks of the reciprocal regimen. During the second week of each treatment schedule sleep and daytime activity were monitored by a 7-day Actigraph, and on the last day of each treatment regimen 8 a.m. levels of 17OHprog, testosterone, Androstendione and DHEA-S, were measured.
Results: Total sleep time was 463 ± 50 and 466 ± 52 min. (NS) in the morning and evening regimens, resp. The number of arousals was 4.7±2.8 vs 4.4±1.7, resp. (NS). Sleep efficiency was 86 ± 8 vs 87 ± 6 %, resp. (NS). Daytime activity index was 60 ± 12 vs 59 ± 8 (NS). 17OHprogesterone was 22.7 ± 25.1 vs 23.8 ± 27.6 nmol/l (NS), testosterone 2.8 ±v5.1 vs 2.3 ±3.0 nmol/l (NS), DHEAS 2.4 ± 4.6 vs 1.8 +/-3.6 µmol/l (NS), androstendione 2.2 ±1.6 vs 4.2± 4.3 pmol/l, (NS).
Conclusion: Both hypotheses were rejected; Sleep quality and day time activity were not affected by treatment schedules. We recommend higher morning HC dose regimen to simulate the physiological diurnal rhythms of the HPA axis.

0311

FIBRIN GLUE DECREASES POST TONSILLECTOMY SYSTEMIC INFLAMMATION IN CHILDREN WITH OBSTRUCTIVE SLEEP APNEA

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Introduction: Fibrin glue applied to the tonsillar bed can reduce post-tonsillectomy bleeding and pain. Post-tonsillectomy anti inflammatory therapy decreases residual obstructive Sleep Apnea, suggesting post tonsillectomy inflammation may be involved in the persistence of the disease. The objective of this study was to evaluate the effect of fibrin glue on systemic inflammation after tonsillectomy.
Methods: A prospective randomized controlled trial was performed on 40 consecutive children undergoing tonsillectomy for obstructive sleep apnea. Patients were randomly assigned to the treatment protocol. In the study group, the tonsillar beds were coated with fibrin glue (Quixil, OMRIX biopharmaceuticals) at the end of the procedure. Children in the control group underwent tonsillectomy without the use of fibrin glue. Complete blood count and circulating pro inflammatory cytokines (assayed by specific EIA) were assessed in serum samples obtained pre and 24 hours post tonsillectomy.
Results: 40 children (age 5.8±2.4y, 72% boys, BMI 16.3±2.1, AHI 5±3.2) were consecutively enrolled. 18 (45%) children were treated with fibrin glue and 22 (55%) were not. Compared to controls, Quixil treatment resulted in a reduction in 24 hours % increment in circulating leukocytes (29.2 % vs. 45.4% ,$p<0.05$), neutrophiles (28.3% vs. 42.1% ,$p<0.05$), IL-6 (1% vs. 42% ,$p<0.05$) and TNF alpha (8% vs 26% ,$p<0.05$). IL-1 beta was further reduced in treated patients (56% vs. 11%, $p<0.05$).
Conclusion: Intra operative fibrin glue therapy is associated with immediate decreased inflammatory response. Long term evaluation is needed to assess persistence of OSA.
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0312

THE RELATIONSHIP OF WEEKDAY AND WEEKEND SLEEP ON ACADEMIC PERFORMANCE IN ADOLESCENTS

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Introduction: Previous studies have demonstrated that insufficient sleep negatively impacts school performance in adolescents. The current analyses examined the relationship between sleep, both weekday and weekend and specific domains of learning and overall academic performance.
Methods: Participants were 56 adolescents (34 female) ages 14 to 18 (M = 16.46) who had complaints of daytime sleepiness and/or insufficient sleep at night. The participants reported their subject grades and overall academic standing on the Youth Self Report (YSR). The sleep measures were one week of daily sleep diaries and night time actigraphy. Linear and binary logistic regressions, controlling for sex and age, were conducted.
Results: Better overall academic scores were related to, less TIB and TST as measured by actigraphy; and less TIB, less awakenings, higher sleep quality, as measured by sleep diaries during weekdays (all $p < .05$). The specific domains of learning and weekday sleep diaries showed that higher Math scores were related to less awakenings, lower TIB, higher SE and greater sleep quality (all $p < .05$); there was a trend for increased SOL, ($p < .07$). Higher English scores were associated with fewer awakenings. Increased SOL during the weekend, as measured by actigraphy, was related to worse academic performance ($p < 05$). The weekend sleep diaries revealed higher Math scores were related to greater sleep quality ($p < .05$) and a trend for increased sleep efficiency ($p < .08$). Higher English and History scores were associated with less difficulty awakening (all $p < .05$).
Conclusion: These results suggest that aspects of sleep are associated with various domains of academic achievement that are critical to overall academic success. Interestingly not all associations were in the expected directions, suggesting the importance of further research. Furthermore, reports of better sleep across both the weekdays and the weekend appear to be positively associated with educational success.

0313

SLEEP ARCHITECTURE IN CHILDREN WITH SICKLE CELL DISEASE WITH AND WITHOUT OBSTRUCTIVE SLEEP APNEA

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Introduction: The prevalence of obstructive sleep apnea (OSA) in children with Sickle Cell Disease (SCD) is higher than normal population data. However, sleep architecture is poorly quantified in children with SCD, and is evaluated in this current research.
Methods: We retrospectively reviewed polysomnography (PSG) data in patients with SCD.
Results: 41 patients (24 females) were referred with history of snoring. 18/41 (44%) patients had OSA (mean AHI 18.4) and 23/41 patients had no OSA (mean AHI 0.4). The OSA group was younger than the no OSA group, with a mean age of 6.4 years and 10.7 years respectively. ($p<0.01$) The OSA group had a significantly better mean sleep efficiency of 91.5% compared to 85.3% in the no OSA group ($p=0.02$) but a higher mean arousal index of 14.4 compared with 6.7 respectively ($p<0.001$). In the OSA group compared with the no OSA group, the mean sleep latency was 17.8 and 20.4 minutes respectively, the mean REM latency was 124.8 and 139.2 minutes respectively, the mean Stage 1 % of total sleep time (TST) was 5.1 % and 4.9% respectively, the mean Stage 2 % TST was 53.4% and 52.5% respectively, the mean Stage 3 % TST was 4.3% and 4.6% respectively, the mean Stage 4 %TST was 15.8% and 19.2% respectively and the mean REM % TST was 21.1% and 18.9% (p=NS for all).
Conclusion: Children with SCD with OSA were younger with improved sleep efficiency but had a significantly higher arousal index than SCD children with no OSA. The higher arousal index may be a better marker for future studies to evaluate the impact of OSA on this population. Further, young children with SCD with a history of snoring should be screened with full PSG to rule out OSA.

0314

SLEEP RELATED DISORDERED BREATHING IN CHILDREN WITH SICKLE CELL DISEASE

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Introduction: Sickle Cell Disease (SCD) is a group of inherited hemoglobinopathies associated with vasoocclusive disease, cardiovascular and neurovascular complications. It is hypothesized that sleep related disordered breathing (SRDB) specifically obstructive sleep apnea (OSA) may exacerbate these complications due to the chronic intermittent nocturnal hypoxia associated with OSA. However despite this, the

prevalence and severity of OSA in SCD is undetermined. OSA has been described in children with SCD in case reports and series but the role of Polysomnography (PSG) in assessing these patients has not been fully explored. The aim of this research is to evaluate the prevalence and severity of SRDB in children with SCD referred for polysomnography (PSG) for suspected OSA.
Methods: At the Hospital for Sick Children, Toronto, we reviewed patients with SCD who underwent formal PSG in 2007 and 2008. Full PSGs were performed on all patients and were scored and reported according to pediatric guidelines.
Results: 41 patients (24 females) were evaluated. Specific diagnoses were Hb SS (28), Hb SC (10), and Hb S/β Thal (3). 35/41 (85%) patients had history of snoring. The mean age was 8.8 years and the mean body mass index (BMI) was 17.9 kg/m2. 18/41 patients (44%) had evidence of SRDB. (Mean AHI 18.4). 12/18 (67%) patients with abnormal PSG had severe OSA (AHI>10/hour). The mean SaO2 ranged between 86-99% and the minimum SaO2 ranged between 34-96%. The highest Co2 ranged between 40.9-62.6 mmHg.
Conclusion: This retrospective review confirms a high prevalence of severe OSA in this population. History of snoring can not predict presence or severity of OSA. Therefore all children with SCD with history of snoring should be referred for PSG to evaluate for OSA in order to prevent exacerbation of co-morbidities associated with SCD.

0315

EXAMINING IMPLICIT ATTITUDES TOWARDS SLEEP IN SCHOOL-AGE CHILDREN USING AN IMPLICIT ASSOCIATION TASK (IAT)

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Introduction: Studies have shown associations between sleep problems and explicit negative/dysfunctional attitudes towards sleep in adults and more recently in children, yet research on implicit attitudes towards sleep is scarce. The aim of the study was to develop a measure to investigate possible implicit negative attitudes towards sleep in children.
Methods: Implicit attitudes of eighty primary-school children aged 8-10 were measured using an Implicit Association Task (IAT) for sleep. In critical trials, "sleep pictures" (target stimuli) and "bad words" (attribute stimuli) were allocated to different and same sides and reaction time was measured to examine the associations. The assumption is that if the children associate sleep and bad together, they will be quicker and make fewer errors in the trials in which sleep and bad are paired together. The child's sleep quality was established with the Child Sleep Habit Questionnaire (CSHQ) and the Sleep Self Report (SSR), administered to the parent and child respectively, which enabled an examination of associations with sleep quality. A simple attitude survey was utilised to determine explicit attitudes towards sleep.
Results: Results showed that the children were faster in trials where "sleep" and "bad" were allocated to the same side (mean RT = 1009ms, SD = 263) than to different sides (Mean RT = 1166ms, SD = 355), $t(75) = 3.8$, $p<0.001$. No associations were found between sleep quality and performance on the IAT. There was a non-significant trend for negative explicit attitudes towards sleep.
Conclusion: Findings are consistent with the possibility that children have negative implicit attitudes towards sleep. Further research is needed to establish whether children have implicit negative associations with sleep per se versus the act of going to bed. This research raises the question of whether targeting these general attitudes might further our understanding of the development of sleep disturbances in children.
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0316

MATERNAL PERCEPTIONS OF THEIR PREMATURE INFANT'S SLEEP

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Introduction: Approximately 13% of infants born in the United States each year are delivered prematurely (before 37 weeks gestation). Premature infants born between 33 and 35 weeks gestational age and <1500 grams have more irregular sleep/wake patterns than those born full-term. Mothers of premature infants view their child as more vulnerable (i.e., more susceptible to health problems) than do mothers of full-term infants. The purpose of the current study was to investigate sleep-related cognitions and perceptions of mothers of prematurely born infants.
Methods: Maternal cognitions and perceptions of premature infant sleep were assessed using two measures: the Maternal Cognitions about Infant Sleep Questionnaire (MCISQ) and the Vulnerable Child Scale (VCS). Lower scores on the VCS reflect greater maternal belief of infant vulnerability. The MCISQ doubt subscale score was used, with higher scores representing more negative maternal concerns and doubts about infant sleep. Infant birth and medical history data were also collected.
Results: The sample consisted of 19 infants born at 29.3 (SD+8.5) weeks with birth weight of 3.1 (SD+2.1) pounds. The infants spent 35.9 (SD+ 40.7) days on oxygen and 16.5 (SD+15.1) days on mechanical ventilation. VCS scores were negatively correlated with MCISQ doubt subscale ($r=-.47$, $p<0.05$). VCS scores were also significantly different between infants who had never had reflux compared to those who had a history of or concurrent reflux ($t(17) = -16.3$, $p<0.01$).
Conclusion: Mothers who viewed their infant as vulnerable were more likely to doubt their parental competency relating to their infant's sleep. Mothers viewed premature infants who had a persistent case of reflux as more vulnerable. Premature infants presenting with reflux tend to have less gastro-motility than other infants, making them fussier during the day and more restless during sleep. Thus, reflux may contribute to both poor infant sleep and maternal perception that the infant is more vulnerable.

0317

A RETROSPECTIVE LOOK AT RELATIONSHIPS AMONG SLEEP VARIABLES AND BODY MASS INDEX IN CHILDREN AND ADOLESCENTS

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Introduction: Obesity continues to be a major health concern because of increasing prevalence in all age groups and relation to medical co-morbidities. Studies have shown that sleep duration, a potentially modifiable risk-factor, is inversely associated with body mass index (BMI). The purpose of the study was to explore whether BMI was associated with polysomnographic sleep measures (total sleep time [TST]) and respiratory indicators (respiratory disturbance index [RDI], RDI/REM, and oxygenation saturation) in children and adolescents.
Methods: As part of an ongoing study, a retrospective chart review was conducted of children and adolescents ages 6 - 18 years evaluated with a laboratory-based polysomnogram at a hospital sleep center from 2001-2007. Demographic, height, and weight data were obtained via medical record. Exclusion criteria included diagnosis of narcolepsy, severe medical or psychological disease, and taking medication that adversely affects sleep. Overweight was defined as BMI (kg/m^2) > 85th percentile-for-age and gender. For this analysis, the sample was categorized into two age groups (children [6-12 years] and adolescents [13-18 years]).

Results: The sample included 60 subjects (33 boys) with a mean age of 10.8 ± 3.4 years (56.7% were 6-12 years); 68.3% were Caucasian, 13.3% were Asian, 11.7% were African-American, and 6.7% were Hispanic. Of the total sample nearly two-thirds of the sample was overweight (63.3%). Mean BMI for the two age groups was 20.6 ± 7.6 and 35.4 ± 14.8 kg/m^2, respectively. Controlling for age and gender, BMI was significantly associated with RDI (r = .50, p = .003), RDI/REM (supine position; r = .64, p = .001), and oxygen saturation nadir (r = -.73, p < .001) in the children group. BMI was associated with oxygen saturation nadir in the adolescent group (r = .56, p = .006). There was no association between TST and BMI in either age group.
Conclusion: Nearly two-thirds of this sample with sleep complaints was overweight. In addition, these findings suggest that respiratory disturbances are associated with obesity and age. Although no relationships were observed between TST and BMI, further study of sleep in a larger sample over a longer time span is warranted.

0318

SLEEP SPINDLES AND LEARNING: NEW INSIGHTS FROM DYSLEXIA

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Introduction: Dyslexia is a learning disability that manifests primarily as a difficulty with written language and particularly with reading and spelling. In literature only one study evaluated the sleep parameters in children with learning disabilities showing an increase of stage 4 and a decrease of REM1. The aims of our study was to evaluate sleep architecture based on conventional parameters and by means of spectral analysis.
Methods: For the purpose of the study, we recruited 16 subjects with developmental dyslexia (mean age: 10.8) and 11 normal readers children (mean age: 10.1). The clinical diagnosis of dyslexia was made according to standard exclusionary criteria defined by DSM- IV. Reading abilities were evaluate using MT, Word and Non-Word Reading Test. All the subjects underwent a PSG overnight recording after one adaptation night to avoid the first-night effect. Power spectral (FFT) analysis of the EEG based on the Cz derivation was computed and spindle density was calculated in stage N2 and in N3.
Results: FFT analysis revealed several differences between the two groups, and specifically dyslexic children showed an increase of power in frequency bands between 0.5-3 Hz and 11-12 Hz in stage N2 and between 0.5-1 Hz in stage N3. Dyslexic children showed also a significant increase on spindle density in N2 (6.2 vs. 3.5; p<0.0001). Sigma band in N2 was positively correlated with Word reading test (r= 0.63; p= 0.02) and MT reading test (r = 0.55; p = 0.03), and spindle density with Word reading test (r= 0.66; p= 0.01).
Conclusion: The main result is the clear increase of spindling activity and of sigma power in dyslexic subjects; this increase is strictly related to the degree of dyslexic impairment. These findings, never reported in literature, seem to be consistent with the most recent reports on the role of sleep and of specific phasic events during NREM sleep on learning and memory

0319

PASSIVE FOOT MOVEMENT IN CONGENITAL CENTRAL HYPOVENTILATION SYNDROME INCREASES RESPIRATORY RATE

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Introduction: Congenital central hypoventilation syndrome (CCHS) is characterized by reduced drive to breathe during sleep and minimal sensitivity to CO_2 and O_2. However, CCHS subjects increase ventilation to passive leg movement during sleep through processes that remain unclear; earlier studies involved cyclic leg motion, incorporating both circulatory and extensive proprioceptive stimulation. A lesser proprioceptive stimulation alone may enhance breathing; therefore, we assessed the impact on respiration of passive foot movement in CCHS and healthy controls.
Methods: Passive motion of the left and right feet was performed in 15 CCHS and 30 healthy control subjects (age in years: CCHS = 15.1 ± 0.6, control = 15.3 ± 0.4; female:male ratio CCHS 7:8, control 13:17). One foot was dorso-flexed by an investigator at 1-Hz for three 40 s periods with 40 recovery periods, and an initial 80s baseline; the procedure was repeated on the opposite foot after 3 min. Breathing rates were derived from abdominal respiratory movements recorded via a pressure transducer. We used repeated measures ANOVA to determine salient between- and within-group responses differences.
Results: Baseline breathing rates were similar between groups (difference 0.7 br/min, ns). Respiratory rates increased to foot movement in both groups, but to a greater and more sustained extent in CCHS subjects. Rates increased by approximately 10% (2 br/min) 7 s after movement onset in CCHS, and remained elevated until 20 s. From 20 to 33 s, rates declined slightly, and remained steady until task completion, when rates declined to baseline after 4 s. Control subjects showed smaller rate increases, with a transient peak of 1 br/min from baseline at 10 s. Control increases were not sustained, and rates did not significantly differ from baseline after 32 s.
Conclusion: Passive motion of the foot increases respiratory rate in CCHS subjects more than controls, demonstrating intact, and more-influential proprioceptive effects on ventilation in the condition.
Support (optional): National Institutes of Health HD-62295

0320

ASSOCIATIONS BETWEEN SLEEP, AND DIETARY, EXERCISE AND ELECTRONIC SCREEN HABITS OF ADOLESCENTS IN THE TUCSON CHILDREN'S ASSESSMENT OF SLEEP APNEA (TUCASA) STUDY

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Introduction: The associations between sleep, and diet, exercise and electronic screen habits (television, internet, computer and video games) have not been extensively studied in adolescents. The aim of this study was to investigate the relationship between sleep, and diet and screen time in adolescent children enrolled in the TuCASA study.
Methods: 320 children enrolled in the TuCASA study completed detailed dietary and physical activity questionnaires during the 2nd examination of the cohort. Correlation and regression analysis were used to study the relationships among diet (Rocket Youth Adolescent Ques-

tionnaire), physical activity (Block Pediatric Physical Activity Questionnaire), self-reported sleep duration and screen time.
Results: Mean age was 13.3 years (sd 1.8, range 10-18) with 51.8% males, 65% were Caucasian and 35% were Hispanic. Correlation analyses showed that children who slept less consumed more caffeine ($r = -0.28$, $p<0.0001$) and had more hours of screen time ($r =-0.16$, $p< 0.005$). More hours of screen time also were associated with higher caffeine consumption ($r=0.14$, $p=0.01$). Consistent with previous studies, our regression models showed that having a higher BMI was associated with shorter sleep duration ($B=-0.18$, $p=0.018$) This finding persisted after adjusting for age, sex, amount of kilocalories consumed and moderate or vigorous exercise.
Conclusion: These findings suggest that adolescent obesity is associated with reductions in sleep time that are mediated by caffeine use and screen time. This may have negative health implications as well as potential psychosocial and academic impact. Future research efforts in this population should include measures of caffeine intake and screen time.
Support (optional): HL 62373

0321

CHANGES IN SLEEP TIMING AND DURATION AS CHILDREN TRANSITION FROM PRESCHOOL INTO KINDERGARTEN

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Introduction: Little is known of the factors influencing changes in sleep duration and timing during early childhood. Kindergarten is the first major life transition for many children due to parental separation, increases in academic and social demands, and perhaps changes in nocturnal and diurnal sleep. The following are the results of a study of children tracked from the summer prior to preschool, and into and beyond their transition to kindergarten.
Methods: Caretakers of 5-year-old children ($n = 11$) were recruited from local preschools and/or daycares. A caretaker-reported sleep diary was among measures used to record the child's sleep/wake behavior for 7 to 10 days at three time points: the summer prior to kindergarten (Time 1), following the first week of the transition to kindergarten (Time 2), and following the first month of the transition to kindergarten (Time 3). Participants were excluded if they did not complete all three time points.
Results: The transition to kindergarten was associated with a reduction in total time in bed (naps + nocturnal) of 30 minutes at Time 2 ($p = .04$) and 52 minutes at Time 3 ($p = .001$). Weekday (WD) scheduled nap duration was reduced at Time 2 ($p = .031$), as was weekend (WE) unscheduled nap duration ($p = .015$). The transition was also associated with an advance of the phase of the WD nocturnal sleep period. An advance of approximately 60 minutes was found at Time 2 and Time 3 in both WD bedtimes ($p < .001$) and rise times ($p < .001$). Weekend bedtimes showed a trend of advancement (Δ 31 minutes; $p = .069$), and WE rise times advanced by nearly one hour at Time 3 ($p < .001$). Reduction in WD and WE nocturnal time in bed approached significance (Δ of 21 minutes; $p = .082$ and Δ 27 minutes; $p = .186$).
Conclusion: Time in bed was reduced for children as they transitioned to kindergarten. This reduction may be partially due to earlier rise times in kindergarten and reduced opportunity to nap during weekdays. It is unclear how reduced time in bed is related to actual sleep time. For example, children could be sleeping more during bed hours or have increased sleep efficiency. Caretakers advanced the timing of the WD nocturnal sleep period presumably to prevent sleep loss as children transitioned to kindergarten. Earlier WE rise times in kindergarten may indicate an advance in the circadian period. Further research is warranted to better understand the effect of sleep loss and changes in circadian processes on behavioral and physiological functioning.
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0322

NREM SLEEP ALTERATIONS IN CHILDREN WITH DYSLEXIA

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Introduction: Developmental dyslexia reflects an unexpected difficulty in reading in children and adults who appear to have all the factors present (intelligence, motivation, exposure to reasonable reading instruction) that are necessary to turn print into meaning. There is only one study that evaluated sleep architecture in children with learning disabilities and no studies attempted to analyze sleep microstructure. The aim of our study was to evaluate sleep the sleep macrostructure and microstructure in children with dyslexia
Methods: Sixteen subjects with developmental dyslexia (mean age: 10.8) and 11 normal readers children (mean age: 10.1) were enrolled and underwent standard polysomnographic recording. Sleep microstructure was evaluated through the analysis of the cyclic alternating pattern (CAP).
Results: CAP analysis showed mainly a reduction of CAP rate in N2 (12.2 vs. 25.39, $p <0.001$) and an increased CAP rate in N3 (76.46 vs. 49.59 $p <0.001$) in dyslexics compared to controls. Moreover, children with dyslexia showed a reduction of A1 index in N2 (21.4 vs. 37.6, $p <0.001$) and an increase of A1 index in N3 (109.7 vs 69.9, $p <0.001$).
Conclusion: The reduction of CAP rate in N2 was already found by our group in children with ADHD that have a high comorbidity with learning disorders (Miano et al., 2006). and support the hypothesis of the role played by NREM and in particular by the slow oscillations (A1) in learning processes and memory (Ferri et al., 2008).

0323

BODY MASS INDEX PREDICTS SLEEP PROBLEMS AND DAYTIME IMPAIRMENT IN AT-RISK ADOLESCENTS

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Introduction: Shorter sleep duration associated with higher body mass index (BMI) has empirical support for children, adolescents, and adults, but the role of BMI in sleep and corresponding wake problems in adolescence remains unclear. This study investigates whether BMI predicts poor sleep and daytime impairment in a sample of at-risk adolescents.
Methods: 32 adolescents participating in the Providence, RI cohort of the Maternal Lifestyle multisite study, aged 13-14 years (54.5 % female, 53 % minority, 42.4 % below poverty line, 72.7 % with prenatal drug exposure), wore actigraphs and kept sleep logs for 8 days and completed a sleep questionnaire. Wake time (total time spent awake during the night) as well as time in bed and time asleep (used to compute percentage of time in bed spent asleep) were derived from actigraphy and sleep logs. BMI was calculated from height and weight taken during clinic visits. Self-report measures included grades (What are your grades in school mostly?) and daytime sleepiness (degree of difficulty staying awake in various situations).
Results: Linear regressions showed that higher BMI predicted 1) lower percentages of time in bed spent asleep ($R2 = .19$, $\beta = -.355$, $p = .016$), 2) more wake time during the night ($R2 = .14$, $\beta = .054$, $p = .039$), and 3) more daytime sleepiness ($R2 = .16$, $\beta = .3$, $p = .039$), which predicted worse grades ($R2 = .32$, $\beta = .275$, $p = .002$). In boys only, higher

BMI also predicted less sleep during the night (R2 = .33, β = -6.98, p = .039).
Conclusion: These findings suggest that the relationships between sleep and weight differ for boys and girls, but for both genders sleep and weight problems may impact daytime performance. A larger sample size by meeting date will yield a more thorough investigation of these preliminary findings.
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0324

PREVALENCE OF SLEEP-RELATED DISORDERS IN CHILDREN WITH SICKLE CELL DISEASE

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Introduction: Children with Sickle Cell Disease (SCD) may have a higher prevalence of sleep disordered breathing. Anemia found in this population, places them at risk for Restless Legs Syndrome. They are also at risk for sleep-onset and maintenance insomnia. Sleep related disorders (SRD) decreases cognitive daytime performance which is frequently seen in SCD. With the goal of exploring the prevalence and types of SRD in children with SCD, we conducted a survey of a pediatric population.
Methods: A questionnaire inquiring about sleep disordered breathing (SDB), restless legs syndrome (RLS), insomnia, parasomnias, and daytime effects of disrupted sleep was offered to 100 patients between the ages of 6 and 18 years. The 28-item survey comprised of questions chosen from validated questionnaires using established diagnostic criteria.
Results: All 100 approached patients completed the survey. 54 (54%) of subjects stated awakening unrefreshed, 41 (41%) of children had short term insomnia (<1 month), and 30 (30%) had sleep maintenance insomnia (waking up >2 times per night). 21 (21%) had chronic sleep onset insomnia (>6 months), and this finding was significantly associated with higher hemoglobin values (.04 p-value). 54 (54%) patients had chronic snoring, 16 (16%) heavy breathing, and 5 (5%) witnessed apneas. 22 (22%) had leg discomfort improved with movement and the estimate of RLS was 11 (11%). Sleepiness, inattentiveness and hyperactivity were common, but not statistically associated with SDB, RLS or insomnia.
Conclusion: Our study revealed a very high prevalence of SRD among children with SCD. Further investigation of SCD-associated factors contributing to this high prevalence is warranted. Higher hemoglobin was found among patients with chronic sleep insomnia. This finding deserves further investigation for possible SCD-associated factors such as treatment of underlying disease (e.g.: hydroxyurea). SRD, RLS and insomnia should be appropriately managed in children with SCD and subsequent testing carried out.

0325

POLYSOMNOGRAPHIC RESULTS BEFORE AND AFTER ADENOTONSILLECTOMY IN CHILDREN WITH OSA

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Introduction: Adenotonsilectomy(AT) is the treatment of choice in children with Obstructive Sleep Apnea (OSA). AIM: To study children's polyssomnography (PSG) before and after AT.
Methods: Thirty children aged four to twelve years were included. PSG data were (AHI,medium saturation) were compared before and after surgery for different groups (aged 4 to 6; 7 to 9; 10 to 12).
Results: Out of 30 children only two (6%) did not improve after AT, only 26% had AHI, 1 (considered normal) after AT. AHI medium changed from 5,31 before to 1,83 after AT.
Conclusion: Adenotonsilectomy improves OSA in children,but only few normalize AHI. Co-morbidities must be investigated.

0326

CONDUCTING HOME-BASED SLEEP RESEARCH ON CHILDREN EXPOSED TO VIOLENCE: LESSONS LEARNED

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Introduction: Astounding numbers of children are exposed to violence, and many of them develop sleep disturbances. However, few investigations have objectively measured in the home setting sleep parameters of children exposed to violence. Conducting home-based research on these children provides needed data about sleep in their "natural environment."
Methods: We are conducting a longitudinal study (baseline, 3-month and 6-month follow-ups) of 60 children 8-16 years of age who have been exposed to family and community violence. Participants are recruited from a social-service agency providing counseling to children who witness violence and who are referred by police. Home-based methods include: (1) 7-day actigraphy; (2) a battery of standardized questionnaires to caregivers and children involving sleep behavior and problems, traumatic stress, behavior problems, physical and psychosocial functioning, home environment; (3) observation of the sleep environment; (4) biological measures.
Results: Of 28 children recruited thus far, we have obtained actigraphic data on 28 and have directly observed the sleep environment of 27. Study implementation has raised both foreseen and unforeseen issues in several critical areas, including confidentiality, harm, safety, inter-agency relations, and logistics. Based on our experience, recommendations are provided for investigators considering conducting home-based sleep research on children exposed to violence.
Conclusion: Home-based research on the sleep behavior and the sleep environment is feasible in this population but requires flexibility and sensitivity to a variety of issues.
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0327

PERIODIC LIMB MOVEMENTS OF SLEEP (PLMS) IN CHILDREN WITH NARCOLEPSY

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Introduction: Sleep in patients with narcolepsy has been described as unstable with frequent stage shifts, arousals and increased motor activity. PLMS occur in a wide range of sleep disorders such as restless leg syndrome, REM sleep behavior disorder, obstructive sleep apnea syndrome, insomnia, and hypersomnia. To our knowledge, there are no published data on the prevalence and sleep associations of PLMS in children with narcolepsy. This study was done to determine the frequency of occurrence of PLMS in a sleep clinic cohort of children with narcolepsy, and to assess the functional impact of PLMS on nocturnal sleep and daytime functioning in these children.
Methods: We identified children (6-21 years) diagnosed with narcolepsy and followed in our sleep disorders center. We collected demographic information, PSG reports and Mean Sleep Latency Test reports by reviewing medical records. We compared the sleep characteristics and daytime sleepiness indices in children with narcolepsy and PLMS to those with narcolepsy and no PLMS.
Results: 28 children with mean age 13 years (SD 3.57) were identified. 18 (64.2%) were male; 9 (32%) Caucasian, 19 (68%) African- American.

Their mean BMI was 25.03 (SD 7.6). 12 (42.8%) had cataplexy, 6 (21%) had hallucinations, 8 (28.5%) had sleep paralysis. Their mean PLM index (PLMI) was 1.3 (SD 2.5); 9 (32%) patients had any PLMS(range 0.9-11.6). 2 (22%) Caucasian and 7 (36.8%) African American children with Narcolepsy had PLMS. This is increased as compared to previously reported numbers of 16.5% in Caucasians and 7% in AA. Only 1 patient had PLMI > 5/ hour. Children with narcolepsy and PLMI> 1/ hour (n=8) had a greater number of total sleep stage shifts (p 0.02), greater number of stage shifts into stage 1 (p=0.01), more spontaneous arousals (p=0.05), and shorter daytime mean sleep latency (p=0.012) than those with PLMI< 1/ hr. There was no difference in the sleep efficiency, the wakefulness after sleep onset time, night time REM latency, and the apnea hypopnea index between the two groups. There was no correlation between presence of PLMS and occurrence of cataplexy, sleep paralysis or hallucinations.

Conclusion: PLMS may occur commonly in children with narcolepsy, however a PLMI above the current threshold for normal PLMI is uncommon. Preliminary results suggest that children with narcolepsy who have any PLMS have increased sleep disruption and increased daytime sleepiness. The adult threshold of >5 PLMS/hour may not apply to children.

0328

LOCOMOTOR DEVELOPMENT, USE OF WALKERS AND SLEEP IN THE FIRST YEAR OF LIFE

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Introduction: Sleep problems are very common in the second half of the first year of life. At the same time this period involves neuromotor milestones which could be responsible for many changes in bio-behavioral regulation. The objective of this study was to examine the association between motor development and sleep patterns in infancy.

Methods: Mothers of 84 healthy infants between 7 and 12 months of age (Mean=9.3 months, SD=1.1)completed a Sleep Questionnaire and a Motor Development and Activities Checklist.

Results: Age correlated with crawling (r=.31, p<.005) but not with any of the night sleep measures. When we compared sleep characteristics of crawlers with pre-locomotor infants, controlling for age, no significant difference was found. However when separated into groups according to experience of crawling a significant contrast was found: new crawlers had shorter night duration compared to non-crawlers (t=1.94, p<.05), but not compared to experienced crawlers. Most interestingly, infants who used walkers had longer night duration (t=2.29, p<.05) and less time awake at night (t=1.97, p<.05) than infants who never used walkers. Moreover, the longer was the experience of using a walker the longer was sleep duration (r=.55, p<.005). There was no difference in crawling between these infants and no correlation between use of walker and crawling onset. Walker users were slightly older than non-users, however when entered into a regression after age, use of walkers still added significantly to the explained variability in sleep duration (F=4.41, p<.05).

Conclusion: Crawling status seems to explain sleep problems better than a chronological age. Contrary to expectation, walker use was associated with a better sleep. Caution should be taken since the data can not suggest a causal relationship and the effect of walkers should be studied further.

0329

PARENTING EFFECTS ON SLEEP PATTERNS OF AT-RISK ADOLESCENTS

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Introduction: Previous studies of the effects of parenting on children's sleep habits are equivocal. This study examines associations between parenting and adolescent sleep in a sample of at-risk families.

Methods: 32 adolescents participating in the Providence, RI cohort of the Maternal Lifestyle multisite study, aged 13-14 years (54.5% female, 53% minority, 42.4% below poverty line, 72.7% with prenatal drug exposure), wore actigraphs and kept sleep logs for 8 days yielding sleep measures such as sleep and wake time. Parents completed a questionnaire that included items comprising the Rules Scale (range 0-9) and the Change Scale (range 0-28). Higher scores indicated more rules and more change in the home environment, respectively. The Rules Scale inquired about rules regarding television, whereabouts, homework, bedtime, chores, caffeine, and candy. The Change Scale inquired about changes in the following environmental factors: bed, bed/sleep room, house, room where eating dinner, occupants of house, parents bed/sleep room, and roommates.

Results: Linear regressions revealed two significant predictors of sleep time during the night: the Change Scale and the rule about drinking caffeinated beverages. More change predicted less nighttime sleep ($R2 = .2$, $\beta = -.05$, $p = .013$) whereas setting a caffeine rule predicted more nighttime sleep ($R2 = .221$, $\beta = .003$, $p = .008$). Results may change by meeting date due to an expected increase in sample size.

Conclusion: Change in the adolescent's home environment was the best predictor of sleep with more change predicting less sleep. Although the Rule Scale did not predict sleep patterns, adolescents with rules about caffeinated beverages obtained more sleep than adolescents without caffeine rules. These findings suggest that a predictable home environment for teens may positively impact their sleep and that establishing rules about caffeine may be particularly helpful in increasing sleep duration.

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0330

IS THERE A CHANGE IN BMI IN CHILDREN TREATED WITH CPAP?

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Introduction: Obstructive sleep apnea syndrome (OSAS) in children has an estimated prevalence of 2-4 percent. Obesity is a common comorbidity in many of these children, particularly those failing surgical intervention. Continuous positive airway therapy (CPAP) has been shown to be an effective therapy for OSAS in children who have either failed surgical intervention or are not good surgical candidates. As a large number of children (87%) in our Positive Airway Pressure (PAP) Clinic are obese we examined our data to determine if CPAP therapy was associated with significant changes in weight.

Methods: 72 otherwise healthy children between the ages of 2-18years (64%male) followed in our PAP clinic were identified as eligible for the study. Height and weight were measured at each visit. Patients were seen 5 times with an average of 90 days between visits. Body mass index (BMI)% for age and z-scores were determined using CDC growth charts. Using mixed models repeated measures analysis changes in growth parameters between visits were examined.

Results: Compliance with CPAP therapy as measured by smart card technology was approximately 65%. BMI at the time CPAP therapy was initiated was 33.7 (93.8% for age, z-score of 2.33). BMI at subsequent visits were 36.3 (90.8% for age, z-score of 2.27), 36.5 (94.2% for age,

z-score of 2.40), 37.0 (92.0% for age, z-score of 2.47) and 34.5 (95.4% for age, z-score of 2.30). There were no significant differences in mean z-scores regardless of whether visits 1-2 (p>0.42), 1-3 (p>0.44), 1-4 (p>0.50), or 1-5 (p>0.45) were compared.
Conclusion: CPAP therapy in children with OSAS is not associated with significant changes in weight or BMI.

0331

INSOMNIA LIKE SYMPTOMS AND MEDICAL COMPLAINTS IN A COMMUNITY SAMPLE OF YOUNG SCHOOL AGED CHILDREN: A PRELIMINARY STUDY

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Introduction: Substantial literature in adults documents significant association between sleep disturbances and various medical symptoms/disorders. However, there is paucity of studies exploring this complex association between sleep and medical symptoms/disorders in children. In this study we examined the prevalence of medical complaints in children with insomnia like symptoms in a community sample of young school aged children.
Methods: A screening questionnaire was sent to parents of every student in 3 local school(K-5) districts(n=7,312) with a 78.5% response rate. Randomly selected children from this sample participated in Phase-II of the study, which consisted of comprehensive history, physical examination, several questionnaires, and 9-hour overnight polysomnogram.
Results: The final sample of 699 was divided into two groups based on parents' response to sleep related items(1.Trouble falling asleep?; 2.Restless during sleep?). 202(29%) of these children "often" or "very often" had either or both of these sleep disturbances[SD(sleep disturbance)group] and 497(71%) "never" or "sometimes" had either or both of these sleep disturbances(NON-SD group). Subjects in the two groups did not differ in gender, percentile for BMI-for-age, apnea-hypopnea index or arousal index. The SD group was older than NON-SD group. Significantly more children in the SD group had parent reported complaints of allergies or hypersensitivity to medications, chronic cough, gastrointestinal pain/colic, gastrointestinal vomiting, joint pains, and headaches. On performing a binary logistic regression analysis while controlling for demographic variables, apnea hypopnea index, current psychiatric/behavioral/learning disorder, socioeconomic status and minority status, sleep disturbance was significantly associated with gastrointestinal vomiting and headaches. Children with gastrointestinal vomiting were 3.7 time more likely to suffer from sleep disturbances and children with headaches were 1.8 times more likely to suffer from sleep disturbances.
Conclusion: These preliminary data indicate significant association of gastrointestinal vomiting and headaches to sleep disturbances in these children despite controlling for all the other possible factors which could affect sleep.
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0332

PILOT DATA ON A COMPREHENSIVE BEHAVIORAL MANAGEMENT CLINIC FOR POSITIVE AIRWAY PRESSURE (PAP) FOR OSA IN CHILDREN

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Introduction: Many children with OSA require treatment with PAP (CPAP/ BiPAP). Limited evidence regarding pediatric compliance with PAP treatment or successful interventions that improve pediatric adherence is available. A clinical program for pediatric PAP users was created involving intensive assessment and behavioral programming by psychologists and a respiratory therapist. Here we report our experience with the first 10 patients seen in this program.
Methods: The CPAP/BiPAP Adherence Program ("Ad Program") sees children prescribed PAP for OSA. Children are seen every two weeks until they show consistent PAP use, defined as usage for more than 4 hrs/night for more than 80% of the nights. They are then followed monthly until they show consistent use for 3 months. We reviewed medical charts of the first 10 patients followed in this clinic.
Results: The first 10 patients have a mean age of 10.6 years (SD 5.86), 60% are boys, 60% are obese and 10% (n=1) overweight; mean AHI was 30.94 (SD 28.91), mean REM sleep related AHI was 62.4 (SD 43.69). 50 % of the patients were seen in the program before their first experience with equipment. Both newly diagnosed patients and previous PAP users are showing improvements in this clinic. One has been discharged from the clinic with consistent use. 80% are still being followed in clinic. 6 (75%) of them show consistent improvement in PAP use from initial visit to most recent visit (from 1.2% average nights use of more than 4 hours on visit 1 among those who were using it at the first visit to 48% average night use of more than 4 hours at the most recent visit).
Conclusion: Preliminary Ad program results suggest significant short term improvements (several weeks to 3 months) in consistent usage among both newly diagnosed children with OSA and previous pediatric users of PAP following initial intensive behavioral programming.

0333

FINDING THE "IMPORTANT" STRUCTURE IN A CORPUS OF SLEEP HABIT QUESTIONNAIRES

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Introduction: Pediatric obesity is a rising problem in the US. Studies have shown that short sleep duration is associated with high body mass index in adults and probably in children. We would like to develop screening questions to determine which children would benefit from more complete evaluation with validated sleep survey instruments. We also want to evaluate the survey instrument to determine the associations among sleep parameters and to identify the useful indicators of sleep duration and quality.
Methods: We obtained a convenience sample of 77 children referred to a dietician after visiting a pediatric clinic. Subjects (or their parents) completed standard sleep questionnaires, including Pediatric Sleep Questionnaires 1 & 2, Pediatric Daytime Sleepiness Scale, and supplemental questions about how they feel upon waking, their napping habits, and sleepiness in school. We used descriptive statistics and t-tests to characterize our population; classification and regression trees and other variable selection techniques were used to isolate which questionnaires provided the most useful information.
Results: The median age was 10.4 years (range: 2.7 to 16.8). Our sample is 23.4% African-American, 55.8% Hispanic, and 19.5% Caucasian with 48 females and 29 males. The median sleep time was 9.0 hours (6.0 to 12.5). Males slept longer than females (9.5 vs. 8.8; $p = 0.04$), but females woke up later on the weekends (9:10am vs. 10:15am; $p = 0.03$). Those who felt "still tired" upon waking had higher PSQ1, PSQ2, and PDSS scores vs. those who felt "rested" ($p < 0.001$, $= 0.09$, <0.001). Children who slept in school had higher PSQ1 and PDSS scores ($p = 0.027$, 0.007) but similar PSQ2 scores ($p = 0.74$). When predicting whether children would feel "rested" or "still tired", PSQ1, PSQ2, and PDSS were selected as useful variables. Children with a PDSS < 15.5 and a PSQ2 < 0.5 were always identified as "rested"; children with a

PDSS > 15.5 and a PSQ1 > 4.5 were always identified as "still tired". Other multivariate results showed being male, sleep duration, and feeling rested as significant predictors of PSQ1. However, when predicting PDSS, when you wake up on a weekend, feeling rested, and PSQ2 were more important.
Conclusion: In these children, three screening questions can identify children with abnormal scores on standard questionnaires (how long you sleep, tired in the morning, and sleep in school). These children may need more formal evaluation with respect to sleep hygiene and behavioral counseling.

0334

COMPLIANCE WITH PAP IN PEDIATRIC PATIENTS WITH DOWNS SYNDROME AND OSA

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Introduction: Obstructive sleep apnea syndrome (OSAS) is a common problem in children with Downs Syndrome (DS) with estimates of up to 60% of children with DS having a diagnosis of OSAS. Children with developmental disabilities often have difficulty tolerating new and/or uncomfortable medical procedures and regimens, such as positive airway pressure (PAP). However data suggests that when presented in a gradual manner, PAP is tolerated by children with Downs Syndrome. As part of our clinic protocol children with DS undergo an individualized desensitization process at the initiation of PAP therapy. As part of a larger study investigating pediatric compliance to PAP therapy we examined the compliance data on children with DS to determine whether this therapy can be effectively utilized in this patient population.
Methods: 13 children (69% males) with DS and OSAS requiring PAP therapy were identified as eligible for evaluation. All subjects had previously undergone surgical intervention for OSAS. Ages ranged from 1 to 23 with a mean age of 14.2. Average AHI on the diagnostic NPSG was 20.2. Average PAP therapy prescribed was 8.2. Five subjects used a full face interface and 8 used a nasal interface. Compliance, using Smart Card technology, was calculated by dividing the # of nights with > than 4 hours of use by the total # of nights studied.
Results: Overall compliance data for these 13 children with OSAS and DS was 74.6%. Over the time interval examined patients were seen 5 times with a mean interval of days between visits. Compliance at visits 2-5 were 47.7%, 56.1%, 59.0%, 55.0%, and 76.5%. This trend indicates that PAP usage improves over time. Children with DS had a statistically better rate of compliance ($p<0.05$) than that of the general pediatric population followed in our clinic (overall clinic compliance 63%). Children with DS have better compliance rates with PAP therapy than the general pediatric PAP therapy clinic population.
Conclusion: Children with DS can be successfully treated with PAP for OSAS. In addition, these children tend to be the most compliant over time once PAP is successfully built into their daily life and routine.

0335

SELF-REPORTED SLEEP HABITS IN MIDDLE SCHOOL GIRLS: THE GIRLS' MIDDLE SCHOOL LONGITUDINAL SLEEP SURVEY

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Introduction: Adolescence is a period of great change in physical, emotional and social development and is also associated with changes in sleep and circadian rhythms. Few studies have focused on sleep habits in middle school children, particularly in girls, and most data have been cross-sectional. We have established the Girls' Middle School Longitudinal Sleep Survey to evaluate changes of girls' sleep habits, at six month intervals, as they progress through adolescence and puberty. Results presented here are cross-sectional data from the first data collection towards the end of a school year.
Methods: One hundred-fifteen girls in grades 6, 7, and 8 (mean ages 12.1, 13.1, and 14.0 years, respectively) from The Girls' Middle School, Mountain View, CA (60% Caucasian) completed a modified version of the School Sleep Habits survey and the Rosenberg Self Esteem Scale. Surveys were administered electronically via independent laptops on a closed network at the school.
Results: Total Sleep Time on school nights (TST) decreased (9.2±1.0, 8.6±1.1, 8.1±.9 hours) and average sleepiness increased (2.1±2.3, 2.2±1.7, 3.9±3.4) across grades 6, 7, and 8. Age was significantly correlated with sleepiness ($r = .3$, $p = .001$), TST on school nights ($r = -.44$, $p < .001$), sleep satisfaction ($r = -.16$, $p < .05$), depression ($r = .24$, $p < .01$) and self-esteem ($r = -.35$, $p < .001$), but not with school grades ($p > .5$). School grades were however correlated with sleepiness ($r = -.27$, $p < .01$) and sleep satisfaction ($r = .21$, $p < .05$) as well as with depression ($r = -.30$, $p < .01$) and self-esteem ($r = .21$, $p < .05$).
Conclusion: The results validate the data collection technique and provide initial indications of important relationships between sleep measures and school performance, and the impact of age on sleep and mood in middle school adolescent girls.
Support (optional): A017320 from the National Institute on Alcoholism and Alcohol Abuse.

0336

SLEEP AND ACADEMIC PERFORMANCE IN HIGH SCHOOL STUDENTS

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Introduction: Sleep is important for learning. However, there is little research on sleep and learning in adolescents. We investigated the association of sleep and academic performance in high school students. We hypothesized that reduced sleep duration and quality would be associated with poor academic performance.
Methods: Students at San Diego Adventist Academy were administered the Pittsburgh Sleep Quality Index (PSQI), the Epworth Sleepiness Scale (ESS) and demographic data were collected. De-identified grade point averages (GPA) were obtained from the registrar.
Results: The entire student body participated (N = 88, 50% girls). Age was 15.6±1.3 years and body mass index (BMI) was normal (22.6±4.5). Total sleep time (TST) was low at 6.74±1.32 hours and students were sleepy (ESS 9.2±4.1). The PSQI global score (6.2±2.8) suggested poor sleep quality. Freshmen had the highest TST as compared to upper classmen (7.25±1.3 vs. 6.44±1.3 hours, $p = 0.006$), and the lowest GPA (2.5±0.85 vs. 3.22±0.73, $p < 0.001$). There was no significant correlation between GPA and PSQI, ESS or TST. GPA was correlated only with age ($r = 0.237$, $p = 0.031$). Linear regression with PSQI, ESS and TST as independent variables showed that TST was an independent negative predictor of GPA ($\beta = -0.187$, $p = 0.029$). Logistic regression categorizing GPA into high and low grades (GPA > 3.0 and GPA < 3.0) and controlling for BMI, age and gender, showed that TST was the only significant negative predictor of GPA ($\beta = -0.594$, $p = 0.02$).
Conclusion: High school students reported sleeping less than recommended for age, had poor sleep quality, and were sleepy. Our data suggest that shorter sleep and greater age are associated with better academic performance. Short sleep duration might be a marker of student academic dedication in this population.

0337

ACTIGRAPHY-BASED ASSESSMENT OF SLEEP IN CHILDREN WITH OBSESSIVE COMPULSIVE DISORDER

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Introduction: The sleep of children with obsessive compulsive disorder (OCD) has rarely been investigated but preliminary evidence suggests the presence of significant sleep disruption. The current study used actigraphy and parent and child reports to examine sleep parameters in youth with OCD. Sleep variables also were examined in association with OCD symptomatology and children's functioning.
Methods: N=7 non-medicated children with primary OCD (ages 7-12; M = 9.0, SD = 1.9 years; 71% male) presenting to an anxiety specialty clinic were assessed based on structured clinical interviews and clinician-reports. Children wore wrist actigraphs for 7 consecutive nights and parents and children completed validated measures of sleep, daytime sleepiness, pre-sleep arousal, anxiety and functioning.
Results: Actigraphy data revealed an average total sleep time (TST) of 6.5 hrs. (+/- 33 min.), sleep onset latency (SOL) of 39.8 min. (+/- 35 min), 22 (+/- 4) nighttime awakenings, wake time after sleep onset (WASO) of 3.3 hrs (+/- 40 min) and sleep efficiency (SE) of 66 % (+/-5.4). OCD symptoms (based on the YBOCS-C) were positively associated with daytime sleepiness ($r=.86$, $p<.05$) and pre-sleep cognitive arousal ($r=.87$, $p<.05$). SE was positively associated with school performance and peer relationships.
Conclusion: Consistent with previous reports, results indicate the presence of significant sleep fragmentation among children with OCD. Comparison with population-based norms indicates that children with OCD obtain significantly less nighttime sleep ($z = -2.4$, $p < .01$). Sleep disruption was associated with more severe OCD symptoms, greater pre-sleep arousal and impairments in functioning. Future research is needed examining whether sleep improves with treatment for OCD or, conversely, whether unresolved sleep problems interfere with effective treatment.

0338

2- TO 6-YEAR-OLD NAPPERS HAVE DIFFERENT SLEEP PERIOD DURATION AND SLEEP QUALITY THAN NON-NAPPERS

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Introduction: A survey of pre-kindergarten and kindergarten napping policy in the United States showed only 28% of 50 states had policies regarding naptime, and three states (6%) restrict naptime or discourage napping without knowing the implication of napping in children. Therefore, there is a need to know about napping. In this study, we address the differences in sleep duration and sleep quality of napping and non-napping.
Methods: Data were collected from a community sample of 866 children (54.0% male; 70.1% White non-Hispanic) aged 2 to 6 years from southern Mississippi. Caretakers reported their child's typical weekday and weekend bedtime/rise time, napping patterns, and family demographics. They also completed the Children's Sleep Wake Scale, a measure of behavioral sleep quality. Children taking > 1 nap a week were considered nappers.
Results: In analyses controlling for age, different sleep period distribution patterns were found for napping vs. non-napping children. Napping children averaged 8 hours and 11 minutes in bed per week during their scheduled nap periods and averaged 6 hours and 44 minutes more total (diurnal plus nocturnal) time in bed per week ($p<.01$). Napping children spent less nocturnal time in bed on weekdays (mean weekly total = 1 hour and 12 minutes; $p<.01$) but not weekends. Compared to non-napping children, napping children had more difficulty falling asleep at night ($p<.05$) and waking in the morning ($p<.01$).
Conclusion: Napping children may spend more time in bed because they need more sleep, spend less time in bed on weekday nights, and/or because they have poorer sleep quality. However, the present findings do not permit strong causal conclusions and other explanations of these data are possible. Further study is needed to identify the determinants of napping and to clarify the interplay between nocturnal and diurnal sleep.

0339

SLEEP DURING PEDIATRIC HOSPITALIZATION

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Introduction: Many health care professionals believe children's sleep is affected by hospitalization; however, there have been no objective determinations of sleep for children in critical care or general medicine units.
Methods: Baseline demographic data and information about the current hospital stay and illness, and usual sleep habits (Children's Sleep Habits Questionnaire, Owens et al, 2000) were collected. Children wore an actigraph for 1-3 days and nights and completed a sleep diary. Sound and light meters were placed at the child's bedside. Sleep variables were averaged over the nights recorded.
Results: From Oct 2007-July 2008, 124 eligible children were approached and 69 consented (84% general medical unit, 16% critical care unit; 51% male; 29% age 1-3, 14% age 4-7, 25% age 8-12, 32% age 13-18). Reason for admission included chronic illness (49%), acute illness/trauma (47%) and planned surgery (4%). Mean nocturnal sleep time (19h30-07h29) was 444 minutes (95%CI 137-600) for ages 1-3; 475 minutes (95%CI 357-662) for ages 4-7; 436 minutes (95%CI 238-595) for ages 8-12; and 384 minutes (95%CI 217-512) for ages 13-18. Mean number of night awakenings was 14 (95%CI 8-21) for ages 1-3; 18 (95%CI 12-23) for ages 4-7; 14 (95%CI 5-24) for ages 8-12; and 12 (95%CI 1-18) for ages 13-18. There was no relationship between usual sleep habits and sleep time or awakenings. Light and sound levels were high at night; mean minutes of light >150 lux ranged from 44 - 99 minutes, mean minutes of sound >46 dB ranged from 84-116, mean minutes >80 dB ranged from 32-47 across the four age groups. Relationships between sound and light and other environmental (e.g. single versus shared room; parental presence; type of unit) and medical (e.g. pain scores; medications) variables and sleep outcomes will be presented.
Conclusion: During hospitalization children experience significant nighttime sleep restriction and frequent awakenings at a time when they most need the benefits of sleep.
Support (optional): Dr. Stremler received the J. Christian Gillin, MD Research Award from the Sleep Research Society Foundation in support of this project. Dr. Stremler's work is also supported by a New Investigator Award from the Canadian Institutes of Health Research. Dr. Parshuram is recipient of a Career Scientist Award from the Ontario Ministry of Health and Long Term Care.

0340

SLEEP CHARACTERISTICS OF PREPUBESCENT CHILDREN WITH PRADER-WILLI SYNDROME BEFORE AND AFTER GROWTH HORMONE TREATMENT

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Introduction: Prader-Willi syndrome (PWS) is a rare genetic disorder arising from the loss of expression of paternal genes within chromosome 15q11-q13, and is characterized by mental retardation, behavioral problems, hyperphagia, and obesity. Severe growth hormone (GH) deficiency is a common feature of PWS. Sleep-disordered breathing and hypersomnia are well-documented. Less is known about sleep in prepubescent PWS children. In this study, we aim to describe the sleep physiology of children with PWS at baseline and after treatment with GH.
Methods: In a retrospective chart review, we identified 23 PWS children (52% male; mean age 3.7 yrs ± 2.9, range from 0.5 - 10.8 yrs) who had baseline overnight polysomnography (PSG). Of these, 12 were treated with GH and had repeat sleep studies within one year. Sleep architecture, arousals and sleep-disordered breathing data were compared before and after GH (paired-sample t-test).
Results: Sleep in children with PWS was notable for obstructive sleep apnea (OSA): 17/23 (74%) had apnea-hypopnea indices (AHI) greater than 1.5 events/hr (median 3.6, range 1.5-97.4), with median REM-related AHI of 21 events/hr (range 2.3-75). As a group, sleep architecture was within normal limits, including slow wave sleep (SWS; 20.0% ±9.4), REM (22.0% ±7.9), with a median REM latency of 72.8 minutes (range 0-279). In the 12 children with pre- and post-GH PSG data, there were no overall changes in sleep architecture or respiratory events after treatment, with a pre-GH median AHI of 0.95/hr (range 0-7) and post-GH median AHI of 2.5/hr (0.1-10). However, in 3/12 (25%) children, the REM-AHI worsened markedly from <2/hr to 11,12, and 51/hr.
Conclusion: Sleep in prepubescent PWS children is notable for significant REM-related OSA that did not appear to be affected by GH treatment in the majority of children. There were a small proportion of children who were significantly worse after GH therapy. Future studies should attempt to identify factors predictive of sleep effects of GH treatment.

0341

CHARACTERIZATION OF SLEEP PROBLEMS IN AN OBESE PEDIATRIC POPULATION

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Introduction: Obese adults are known to have both subjective and objective sleep problems including poor sleep quality and excessive daytime sleepiness. There is scarce information about the quality of sleep in obese pediatric population, and to our knowledge, no literature addressing whether the degree of obesity correlates with increased sleep problems. The aim of this study was to identify parental- report of sleep problems in pediatric obese population and to investigate whether the degree of obesity correlates with increased sleep problems.
Methods: An observational cross-sectional study conducted in a pediatric multi disciplinary obesity management clinic by utilizing the childhood sleep habits questionnaire with concurrently collected data of demographics and BMI percentiles. The means, standard deviations of the scores and demographics compared to to the data published by Owens, et al. in non-obese school aged children.
Results: There were 152 patients with mean age of 9.36 (±1.9), 53 males, 99 females with BMI percentile of 99.1 % (±1.04). First and second grade obese children had greater bedtime resistance, daytime sleepiness, sleep anxiety, sleep duration, and total sleep disturbance scores as compared to historical standards. Third and fourth graders had greater daytime sleepiness, sleep disordered breathing (SDB), sleep duration, sleep onset delay, and total sleep disturbance score. There was significant correlation between sleep anxiety, SDB, and bed-time resistance and BMI z scores.
Conclusion: Preliminary results suggest that obese children have poorer sleep quality than non-obese counterparts regardless of age, sex, and race. Day time sleepiness was common in our obese children probably due to poor sleep quality, regardless of having symptoms suggestive of SDB. Children with SDB mostly do not display daytime sleepiness. The results of this study suggest that there is a significant correlation between daytime sleepiness and poor sleep quality but not necessarily with day time sleepiness and symptoms of SDB.

0342

ADENOIDAL RE-GROWTH: A POTENTIAL FACTOR IN SLEEP RELATED BREATHING DISORDER

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Introduction: Obstructive Sleep Apnea is a common condition in children.This is commonly caused by enlarged adenoids and tonsils and adenotonsillectomy is regarded as the treatment option. Some of these children have recurrance of the Sleep Related Breathing Disorder. Adenoidal re-growth is noted in some children.
Methods: A retrospective chart review of all overnight pediatric polysomnograms (PSG) performed in the University sleep laboratory along with history and physical examination and diagnostic tests including the X ray of the nasopharynx were reviewed from January 2007 until October 2008. History of adenoidectomy ot adenotonsillectomy was obtained from the patient questionnaire and the clinical examination.
Results: 900+ Polysomnography records were reviewed, and the following data was extracted: Apnea Index (AI), Apnea- Hypopnea Index (AHI), patient demographics (age, sex, comorbidities), Physical examination including ear, nose and throat examination and diagnostic radiology studies if available with a focus on adenoids and tonsils. A significant number of children with Sleep complaints had Adenoidal re-growth, but only a small fraction of them fit the criteria for Sleep Related Breathing Disorder. We observed a significantly increase in sleep complaints and distress with breathing at night with adenoidal re-growth. The apnea hypopnea index (AHI): AHI >or=1; AHI >or=3; and AHI >or=5 showed significant relationship with the size of the adenoidal re-growth.
Conclusion: Adenoidal re-growth is not rare. Re-growth of adenoids causing significant sleep related breathing disorder is noted in a small percentage of patients who may benefit from revision adenoidectomy.

0343

SLEEP QUALITY AND QUANTITY PREDICT BRAIN ACTIVATION DURING VERBAL LEARNING IN OLDER ADULTS

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Introduction: Disrupted sleep is more common in older adults than younger adults, often co-morbid with other conditions. How these sleep disturbances affect cognitive performance is an area of active study. Here, we examine whether brain activation during a Verbal Learning (VL) task correlates with sleep quantity and quality the night before testing in a group of older adults.
Methods: Twenty-six older adults ages 59-82 (mean: 67.8 ±6.0) underwent one night of standard PSG recording. Twelve hours post-awakening, subjects performed VL while undergoing functional MRI. Regression models examined the association between PSG measured Total Sleep Time (TST) (mean: 394.1±47.5min) and Sleep Efficiency (SE) (mean: 85.2±8.2%) and cerebral activation during VL, controlling for performance. For comparison, we ran the same regression models on a group of 27 young adults (ages 24.3±5.3; mean TST 445.3±31.8min; mean SE 91.7±4.9%) performing VL. Whole brain alpha was set at p=0.05.
Results: Independent of behavioral performance, TST and SE were negatively correlated with activation in the left inferior frontal gyrus, and positively correlated with activation in bilateral hippocampal formation in the older adults. No relationship between prior sleep and cerebral activation was found in the young adults.
Conclusion: Acutely disrupted sleep affects brain activation during VL in older adults but not young adults. The increased activation seen in the inferior frontal gyrus after disrupted sleep is similar to the changes seen in young adults after acute, total sleep deprivation (TSD) and suggests compensatory recruitment of frontal cortical regions in response to impaired hippocampal function. The appearance of such cerebral activation changes after relatively minor sleep disruption in older adults suggests increased cerebral vulnerability to sleep disturbances. These activation changes are particularly interesting given that studies of behavioral performance in older adults find little decline after TSD relative to young adults, suggesting compensatory recruitment may be more effective in older adults.
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0344

ACTIGRAPHIC MEASURES OF SLEEP DURATION AND RISK OF MORTALITY IN OLDER MEN AND WOMEN

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Introduction: Epidemiologic studies have reported associations between self-reported long sleep duration (e.g. > 8 hours per night) and greater risk of mortality, whereas the relationship between short sleep and mortality has been inconsistent. We examined the association between actigraphic estimates of sleep duration and risk of all-cause mortality among 6,107 community-dwelling older women and men participating in the Study of Osteoporotic Fractures, and the Outcomes of Sleep Disorders in Older Men Study (MrOS Sleep), respectively.
Methods: Sleep duration was assessed using wrist actigraphy (Sleep-Watch-O, Ambulatory Monitoring, Inc.) for a minimum of three 24-hour periods (mean=4.1 and 5.2 nights in women and men, respectively). Deaths were confirmed using death certificates. We tested the association between sleep duration and mortality, after controlling for age, clinic site, race, body mass index, physical activity, smoking status, functional status, comorbidities, depression, and anti-depressant use.
Results: 3,052 women (mean age=83.6) and 3,055 men (mean age 76.4) completed actigraphy measures. Among these, 542 (17.8%) women and 251 (8.3%) men died during 4.1 and 3.5 years of follow-up, respectively. Among women, compared to those who slept 7-8 hours per night, those who slept < 5 hours experienced a 1.8-fold increase in risk of death (relative hazard[RH]=1.8; 95% confidence interval[CI] 1.3 - 2.5). There was no significant relationship between short sleep duration and mortality among men (RH=1.2; 95% CI 0.8 - 1.8). Long sleep duration (≥ 8 hours per night) was not associated with risk of death in women or in men.
Conclusion: Our findings suggest that actigraphic measures of short sleep are associated with increased risk of all-cause mortality among women, but not men. We found no significant increase in risk of mortality associated with long sleep duration in either gender. Further research is needed to explore associations with cause-specific mortality, and to elucidate mechanisms for the associations among women.
Support (optional): The Osteoporotic Fractures in Men (MrOS) Study is supported by National Institutes of Health funding. The following institutes provide support: the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), the National Institute on Aging (NIA), the National Center for Research Resources (NCRR), and NIH Roadmap for Medical Research under the following grant numbers: U01 AR45580, U01 AR45614, U01 AR45632, U01 AR45647, U01 AR45654, U01 AR45583, U01 AG18197, U01-AG027810, and UL1 RR024140. The National Heart, Lung, and Blood Institute (NHLBI) provides funding for the MrOS Sleep ancillary study "Outcomes of Sleep Disorders in Older Men" under the following grant numbers: R01 HL071194, R01 HL070848, R01 HL070847, R01 HL070842, R01 HL070841, R01 HL070837, R01 HL070838, and R01 HL070839. The Study of Osteoporotic Fractures (SOF) is supported by National Institutes of Health funding. The National Institute on Aging (NIA) provides support under the following grant numbers: AG05407, AR35582, AG05394, AR35584, AR35583, R01 AG005407, R01 AG027576-22, 2 R01 AG005394-22A1, and 2 R01 AG027574-22A1.

0345

SLEEP DISTURBANCE PREDICTS DEPRESSIVE SYMPTOMS AND FUNCTIONAL DECLINE AMONG OLDER RESIDENTS IN ASSISTED LIVING FACILITIES

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Introduction: Older adults in assisted living facilities (ALFs) are at high risk for functional decline and future nursing home placement. We investigated whether subjective and objective sleep measures predict change in functional outcomes over 6 months in a prospective descriptive study of older ALF residents.
Methods: We enrolled 121 participants (mean age 85.3 years, 85.6% female; 87.6% non-Hispanic white) residing in 18 ALFs in the Los An-

geles area. Key baseline sleep measures included the Pittsburgh Sleep Quality Index (PSQI) and 72-hour wrist actigraphy. Functional outcomes measured at baseline and 6-months follow-up included health-related quality of life (Medical Outcomes Study, Short-form-12, SF-12), functional status (Activities of Daily Living, ADL and Instrumental Activities of Daily Living, IADL), and the 5-item Geriatrics Depression Scale (GDS). Baseline sleep variables were correlated with change scores in functional outcomes (SF-12, ADL, IADL and GDS) from baseline to 6-months, and regression analyses were used to adjust for other important predictors of these functional outcomes.
Results: Baseline ADL, IADL and GDS scores were 6.31 (SD=0.75), 5.3 (SD=1.46) and 1.12 (SD=1.21), respectively. In regression analyses, more baseline actigraphic nighttime awakenings predicted greater decline in ADLs from baseline to 6-months (model $F(2,108= 6.78$, $p=.002$). Lower baseline actigraphic nighttime sleep percent predicted greater increase in depressive symptoms over 6-months (model $F(2,108)=6.64$, $p=.002$). Worse baseline sleep efficiency (by PSQI) predicted greater decline in IADL over from baseline to 6-months (model $F(2,109)=4.90$, $p=.009$). Sleep measures were not associated with change in SF-12 scores.
Conclusion: These findings suggest that sleep disturbance is an important predictor of adverse outcomes among older ALF residents, including worsening functional status and increased depressive symptoms. Future research is needed to test whether interventions to improve sleep in this setting will delay adverse functional outcomes among these vulnerable older adults.
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0346

EFFECTS OF AGING AND SLEEP EXTENSION ON SLEEP MAINTENANCE QUANTIFIED USING SURVIVAL ANALYSES OF SLEEP AND WAKE BOUTS

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Introduction: Slow Wave Sleep and EEG Slow Wave Activity during NREM sleep are two validated markers of sleep homeostasis. We performed survival analyses of sleep and wake bout lengths as a potential alternate measure of sleep homeostasis for quantifying changes with aging and sleep extension.
Methods: After a baseline night of habitual duration, 18 healthy older and 35 younger subjects were scheduled to sleep for 12 hours at night and 4 hours in the afternoon for the next 3 days in an inpatient protocol. Two consecutive 30-second epochs of NREM sleep, REM sleep, Sleep (NREM or REM), or Wake, were required to initiate a "bout" of that state; this bout lasted until a bout of another state began. Kaplan-Meier survival analyses were performed using SAS PROC LIFETEST with age as a strata variable. Analyses were performed for Sleep-Wake or NREM sleep-REM sleep-Wake transitions. These analyses were performed on the first sleep episode (habitual length) and the 1st and 3rd 12-hour nocturnal sleep episodes, representing expected progressive decline in sleep homeostatic pressure with sleep extension.
Results: Older subjects had significantly shorter "survival" in Sleep, NREM sleep and REM sleep, and longer survival in Wake than younger subjects. Sleep extension was associated with shorter Sleep bouts and longer Wake bouts within a sleep episode in both younger and older subjects. Younger, but not older subjects, had a decline in NREM sleep "survival" across the period of sleep extension. Neither age group had a change in REM sleep bout survival across these sleep episodes.
Conclusion: The observed changes in bout survival are consistent with a deterioration of sleep maintenance with aging and reduced homeostatic sleep pressure. These analyses and its application to other conditions such as insomnia or post-intervention, may aid our understanding of sleep maintenance and its disruption.
Support (optional): NIH P01-AG09975 (EBK, REK, WW), K02-HD045459 (EBK) and NCRR-GCRC M01 RR02635 (to the BWH GCRC). BBSRC (DJD).

0347

FEASIBILITY AND EFFICACY OF A SLEEP EDUCATION PROGRAM TARGETING PERSONS WITH DEMENTIA LIVING IN ADULT FAMILY HOMES

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Introduction: Adult family homes (AFHs) are private residences that provide room and board, 24-hour supervision, and assistance with personal care for 2-6 residents. Identification of behavioral strategies to help staff manage sleep and nighttime behavior problems could enable residents to remain in a less restrictive environment for a longer time, and enhance resident quality of life.
Methods: Randomized controlled trial with blind assessments of residents and staff to evaluate the efficacy of a 4-session Sleep Education Program (SEP) for demented AFH residents with sleep disturbances. To date, 42 residents in 34 adult family homes have been randomized into SEP or usual care control.
Results: Residents were 41% male, 97% Caucasian, with a mean MMSE=7.6 (range 0-23), and mean age of 85.8 years (range 64-101). Caregivers were 97% female, 34% Caucasian, with a mean age of 47.4 years (range 25-66). Total resident sleep in the SEP condition as measured by wrist actigraphy increased from 8.1 hours/night at baseline to 9.0 hours at post-test and 9.9 hours at 6-month follow-up. For control subjects, total night sleep increased slightly at post-test from 8.0 hours/night to 8.3 hours/night, but declined at 6-month follow-up to 6.5 hours/night. SEP subjects also had improvements over the study period in depression (Cornell scores: 10.0, 6.6, and 5.1, respectively, at baseline, post-, and follow-up) and daytime sleepiness (ESS scores: 13.0, 11.6, and 10.7), compared to controls (Cornell scores: 11.9, 13.7, and 10.9, respectively; ESS scores: 10.9, 10.3, and 15.0). Actigraphic estimates of daytime sleep/inactivity showed little change over time in SEP subjects (5.2, 4.9, and 5.6 hours/day) but inactivity periods for control subjects substantially increased (4.6, 5.3, and 8.2 hours/day, respectively).
Conclusion: Preliminary data indicate that a minimal program of 4 sessions of staff education can improve the sleep and daytime inactivity of AFH residents with dementia.
Support (optional): This study was supported in part by grants from the University of Washington (RIFP McCurryS 04 WI), the Alzheimer's Association (IIRG-05-13293), and the National Institute of Mental Health (R01-MH072736).

0348

EFFECTS OF A 2H CHANGE IN BEDTIME ON THE SLEEP OF HEALTHY SENIORS

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Introduction: Some of the sleep disruption seen in seniors (>60y) may be due to circadian pacemaker phase in relation to sleep timing. It is possible that the sleep of seniors is more sensitive to changes in bedtime than that of younger adults. In earlier work we have shown that later bedtimes in seniors are associated with decreased sleep time. The purpose of this study was to determine the effects of imposed 2 hour advances and delays of bedtime, on the sleep of seniors under conditions of ad-lib sleep under temporal isolation.
Methods: Ten healthy seniors (9f, 1m, age 70y - 82y) were each studied individually in three 120h sessions in a time isolation laboratory (separated by >2weeks). For each session, on nights 1 & 2 bedtime and rise-

time occurred at subjects' habitual times; on nights 3, 4 & 5 bedtime was specified by the experiment, but rise-time was at subjects' discretion (without knowledge of clock time). Under the *control* condition subjects went to bed at their habitual bedtime (HBT); under *advance* 2h before HBT, under *delay* 2h after HBT. Sleep was polysomnographically recorded, and subjective ratings collected.
Results: Although total sleep time increased in the *advance* compared to the *delay* condition ($p<0.01$), sleep efficiency decreased and wake after sleep onset increased ($p<0.01$). Subjective ratings of sleep were also worse under *advance* than under *delay* ($p<0.05$). Performance tests showed no difference between *advance* and *delay* conditions.
Conclusion: Advancing bedtime led to more, but less efficient sleep; delaying bedtime led to less, but more efficient sleep, as well as better sleep ratings. The relative benefits of longer sleep vs. more efficient sleep in older adults require further investigation.
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0349

PATTERNS AND CORRELATES OF SLEEP MISPERCEPTION IN OLDER ADULTS

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Introduction: Late-life insomnia is a prevalent and serious health problem. Sleep misperception (SM), overestimating wake time while trying to sleep, predicts insomnia onset and maintenance. Like insomnia, sleep misperception increases with age. However, research on longitudinal patterns and correlates of SM among older adults is needed. We posit SM results from perceptual areas of the brain remaining awake during global sleep, reflecting a form of localized sleep deprivation. Thus, SM patterns may predict homeostatic sleep dysregulation, (e.g., sleep rebound). This study aims to-1) describe the longitudinal pattern of SM among older adults by contrasting the amounts of within- to between-person variability in SM; 2) compare SM that occurs during sleep onset latency (SOL) to SM that occurs during wake after sleep onset (WASO); and 3) determine if SM predicts longer total sleep time ($TST_{objective}$) as a marker of homeostatic rebound.
Methods: 103 community dwelling older adults (M_{age})=72.81,SD=7.12) wore an Actiwatch-L®(24hrs/day/2weeks) and concurrently completed sleep diaries. Daily values for actigraphically-measured SOL and WASO were subtracted from respective diary reports to calculate daily SM for SOL and WASO.
Results: Intraindividual variability analyses (IIV) and multilevel modeling (MLM) revealed-1) 50-85% of total variance in SM was within-persons, suggesting SM is an occasional event; 2) within-person, nights that SOL_{sm} was greater than usual, $WASO_{sm}$ was less than usual [β=-.10,t(87.59)=-2.01,p<.05]. Interestingly, between-persons, those with greater SOL_{sm} had greater $WASO_{sm}$ [β=.21,t(98.91)=3.98,p<.001]; 3) within-persons, nights with increased SOL_{sm} were related to longer $TST_{objective}$ [β=32,t(67.74)=5.02,p<.001].
Conclusion: SM is ubiquitous but highly variable among older adults. Individuals with higher average SOL_{sm} had higher average $WASO_{sm}$; however, days individuals had higher $WASO_{sm}$ predicted lower SOL_{sm}. Finally, a homeostatic sleep rebound may explain the finding that increased $TST_{objective}$ occurred on days that SOL_{sm} was greater than usual. Understanding the variable but predictive patterns of SM may lead to new preventative and therapeutic insomnia interventions.
Support (optional): Intramural grants from the College of Liberal Arts and Sciences and the College of Nursing, University of Florida.

0350

ACUTE EFFECT OF THE RESISTANCE EXERCISE ON THE SLEEP OF MEN ABOVE 65 YEARS OF AGE

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Introduction: The physical exercise has shown beneficial in the improvement of the pattern of sleep of the aged people. The aim of our study was to evaluate the acute effect of the resistance exercise of moderate intensity (60% of 1 repetition maximum) in the sleep pattern of men above of 65 years of age.
Methods: The sample was composed for 30 healthful men aging between 65 and 80 years. The volunteers had carried through the test of 1 repetition maximum (1 RM) to quantify the load of the session of physical exercise and had been submitted to the examination of polysomnograph in the basal condition (without exercise) and acute (after a session of resistance exercise) to 60% of 1 RM.
Results: Our results had shown that the acute physical exercise modified some variables of the sleep in a significant form. There was an increase in the total sleep time ($p=0.02$) and of the REM sleep ($p=0.05$) and a reduction of the wake after sleep onset ($p=0.03$). There were not demonstrated statistically significant modifications in the sleep efficiency, stage 2, stage 4 and slow wave sleep.
Conclusion: The presented results demonstrated that a session of resistance exercise to 60% of 1 RM increased the total sleep time and period of REM sleep and decreased the wake after sleep onset in men above 65 years of age, showing that beyond sleeping for more time, the volunteers had also had a more consolidated sleep suggesting that the physical exercise can act positively in the sleep of this population.
Support (optional): AFIP, CEPE, FAPESP, CEPID, FADA, CNPq and CAPES.

0351

INFLUENCE OF MENOPAUSE ON OBJECTIVE AND SUBJECTIVE SLEEP PARAMETERS

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Introduction: Disturbed sleep is a common complaint of midlife women often attributed to menopause. Few studies have examined the direct effect of menopause on objective measures of sleep and whether the phases of menopause (i.e. perimenopause and age since menopause) influence these measures. Our objective was to investigate the influence of menopausal status on sleep patterns in a representative sample of women in the city of Sao Paulo, Brazil
Methods: A population based survey adopting a probabilistic three-stage cluster sample of the City of Sao Paulo was used to represent the local population according to gender, age (20-80 years), and socio-economic status. All participants answered a sleep questionnaire, underwent polysomnographic recording (PSG) and had hormonal measures taken. They also filled out a gynecological questionnaire in order to be classified as premenopause, perimenopause, early postmenopause (less than 5 years of postmenopause), late postmenopause (more than 5 years of postmenopause).
Results: A total of 1042 volunteers underwent PSG, of which 575 were women: 383 were in premenopause, 11 were in perimenopause, 48 were in early postmenopause (less than five years post menopause), and 133 were in late postmenopause (more than five years of menopause), only 25 of which were under hormone therapy/isoflavone. Our main findings were that despite higher daytime somnolence as measures by ratings in the Epworth scale, women in premenopause had higher sleep efficiency and %REM sleep than the group of women after the menopause, which also had higher sleep and REM sleep latency, arousal index, apnea-hipopnea index (AHI), and periodic leg movements. Interestingly, some of

these sleep parameters differed only between women in premenopause and in late postmenopause, while others were evident in early menopause.
Conclusion: Menopause status exerts a marked influence on objective parameters of sleep which vary depending on the number of years since menopause.
Support (optional): AFIP and FAPESP (CEPID 98/14303-3) and CNPq.

0352

SELF-REPORTED NIGHT-TIME AWAKENING ACROSS THE MENOPAUSAL TRANSITION AND EARLY POSTMENOPAUSE: OBSERVATIONS FROM THE SEATTLE MIDLIFE WOMEN'S HEALTH STUDY

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Introduction: The purpose was to describe changes in night-time awakening across the menopausal transition (MT) and early postmenopause (PM), including effects of age, MT-related factors, symptoms (hot flashes, mood), and stress-related factors in a cohort of midlife women.
Methods: A subset of Seattle Midlife Women's Health Study participants (N=286) provided annual menstrual calendars for staging the MT and symptom diaries and morning urine samples assayed for estrone glucuronide (E1G), testosterone (T), follicle stimulating hormone (FSH), and cortisol on multiple occasions per year between 1990 and 2007. Multilevel modeling using the R program was used to assess the relationship of night-time awakening and age, MT-related factors, symptoms, and stress factors with as many as 6542 observations.
Results: Women experienced increased severity of night-time awakening as they aged (beta=0.028, p< .0001) and experienced the late MT stage (beta= 0.154, p< .0001) and early PM (beta=.272, p< .0001). Women with lower urinary E1G and higher FSH levels reported significantly more severe night-time awakening (betas=-.076 and .073; p=.026, p<.0001 respectively); T effects were not significant. Women reporting higher perceived stress reported more severe night-time awakening (beta=.051, p<.0001), but effects of cortisol were not significant. Women with the most severe hot flashes (beta=.198, p< .0001), anxiety (beta=.105, p < .0001), and depressed mood (beta=.144, p<.0001) reported the most severe night-time awakening. The best multivariate model included age, late MT and early PM stages, hot flashes, depressed mood, anxiety, and perceived stress, but did not include E1G or FSH.
Conclusion: Women who are progressing through the MT are vulnerable to perceived night-time awakening that they perceive as more severe as they age and enter the late MT and early PM, experience lower E1G and higher FSH levels, are troubled by more severe symptoms (hot flashes and mood changes), and experience a stressful social milieu.
Support (optional): Support: NINR R01-NR 04141; NINR P30 NR 04001.

0353

EFFECTS OF AGING AND DAYTIME RECOVERY SLEEP ON N-REM SLOW OSCILLATIONS

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Introduction: The hypothesis that aging is associated with alterations in the build-up function of the homeostatic process is still a matter of debate. Most knowledge on how age modulates the effects of sleep deprivation on NREM sleep synchronization comes from visual scoring of sleep stages and quantitative sleep EEG (e.g. spectral analyses). Spectral analysis provides important indices on sleep EEG synchronization but it does not allow identifying N-REM sleep EEG oscillations per se.
Methods: We used an automatic algorithm to assess the effects of age, sleep loss and topography on N-REM sleep slow oscillations (SO; >75 μm). Twenty-four healthy volunteers with no sleep disorders were separated in two groups: Young (6W, 6M; 24.2y ± 3.3), and Middle-aged (6W, 6M; 53.8y ± 3.7). Each subject participated in a baseline nocturnal sleep and a daytime recovery sleep (after 25-hour of wakefulness). SO detection was performed on artefact-free sections of NREM sleep for Fp1, F3, C3, P3, and O1 (linked-ears), with an automatic algorithm. Three-way ANOVAs (Factors: Age group, Sleep condition, Derivation) were performed on SO amplitude and density (nb/min).
Results: Compared to baseline sleep, SO amplitude increased during daytime recovery sleep and this effect was more prominent in young compared to older subjects in Fp1. SO density was higher during daytime recovery sleep compared to baseline sleep in both age groups and this effect was stronger in Fp1 and F3.
Conclusion: Results are in line with the notion that older subjects have a reduced ability to increase sleep synchronisation following sleep deprivation, particularly in anterior derivations. Interestingly, the age-related difference in the effects of the sleep deprivation was observed on SO amplitude only, and not on SO density. This may be explained by age-related decline in the capacity to synchronize larger neuronal populations after sleep deprivation.

0354

WARM FOOTBATH BEFORE SLEEP INCREASED FOOT TEMPERATURE BUT NOT ALTERED SLEEP IN OLDER ADULTS WITH AND WITHOUT SLEEP COMPLAINS

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Introduction: The fall in core body temperature before sleep onset and during sleep is associated with dilation of peripheral blood vessels that permits heat dissipation from the body core to the periphery. Observational studies have shown that a lower core (rectal) temperature coupled with a higher distal (hands and feet) temperature before sleep are associated with short sleep latency and better sleep quality. A warm foot bath was thought to facilitate heat dissipation to lower core (rectal) body and raise foot temperatures to improve sleep outcomes.
Methods: This study used a randomized crossover design to examine the effect of a warm footbath with 40°C water temperature, 20 minute duration on body temperatures and sleep in older adults (>=55 years) with and without self-reported sleep disturbances.
Results: Forty-three subjects responded to our flyer and 25 participants (with sleep complain=17, without sleep complain = 8) completed this study. Footbath before sleep did not increase core temperature but significantly increased foot temperature (complainer vs non-complainer = 6.0°C vs. 5.6°C) and retained during sleeping in both sleep complainers and non-complainers. However, there were no significant sleep changes in polysomnography, actigraphy-estimated sleep, and perceived sleep quality between non-bathing and bathing nights in both groups.
Conclusion: Footbath of 40°C water temperature, 20 minute duration before sleep onset does not increase core temperature to provide heat load but elevates foot temperature to facilitate vessel dilatation. However, this footbath does not alter sleep in older adults with and without sleep complain.
Support (optional): This study was supported by the National Scientific Council, Taiwan, NSC 94-2314-B-040-029, NSC 95-2314-B-040-026.

0355

SLEEP QUALITY, WORRY, AND IMPAIRMENT AMONG OLDER ADULTS

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Introduction: Older insomniacs report more worry than older good sleepers. The aim of this study was to explore the relation between sleep quality and worry and the extent to which sleep quality influences interference in one's life due to worry in a community-dwelling sample of older adults.
Methods: Forty-nine older adults (77.9 [SD±7.6] years, 64.2% female) completed questionnaires as part of a larger study. Sleep quality was measured by the Pittsburgh Sleep Quality Index (PSQI) with good sleepers identified as <5 on the PSQI. Worry was measured using the Penn State Worry Questionnaire (PSWQ), on which higher scores indicate more worry. Interference in one's life due to worry in each of six domains (daily routine, job, social activities, relationships with others, health, and overall interference in one's life) was assessed using a nine-point scale (0 = none to 8 = very severe).
Results: Good sleepers had significantly less worry than poor sleepers, t(47)=-2.4, p=.02. A stepwise regression was conducted to determine which PSQI components were significant predictors of PSWQ. Component 1, subjective sleep quality, was the only statistically significant predictor, accounting for 27.9% of PSWQ variance, F(1,46) = 18.8, p<.001. Poor sleepers reported more interference in several domains due to worry: social activities (t(48)= -2.17, p=0.04), relationships with others(t(43)=-3.1, p=0.004, and health (t(47.9)=-3.0, p=0.01).
Conclusion: Older adults with more sleep problems had greater worry. Subjective sleep quality was the most important aspects of sleep related to worry. Further, impairment due to worry was worse among poor sleepers. Specifically, impairment was greater in three areas: social activities, relationships with others, and health. Future research should examine the possible bidirectional relation between worry and sleep quality among older adults.
Support (optional): West Virginia University Alumni Fund

0356

EFFECTS OF A MONTH-LONG NAP REGIMEN ON WAKING FUNCTION IN OLDER INDIVIDUALS

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Introduction: We have previously shown that, relative to a comparable rest/no-nap interval, a single 2-hr daytime nap did not substantially affect nighttime sleep in older individuals, and improved waking function on several cognitive tasks both in the evening post-nap, and throughout the next day. We are now investigating whether similar results are observed when older individuals take daily naps at home for a month.
Methods: Twenty-one healthy older subjects were studied in 3 laboratory sessions - Baseline, Mid, and End. Nighttime sleep and scheduled naps were recorded polygraphically, and waking function was assessed throughout the day using 4 computerized tasks. For 2 weeks between lab sessions, subjects were instructed to nap daily between 1000h and 1800h for either 45 min (short; n=11) or 2 hours (long; n=10); nap length condition assignment was random. Continuous actigraphy, combined with a detailed log, was used to assess nighttime and nap sleep at home.
Results: Compared to Baseline, waking performance was significantly higher at Mid and End sessions on 3 of 4 tasks. Mean improvements in performance ranged from 10.8±12.4% on Logical Relations (LOG) to 12.2±12.6% on Memory Search between Baseline and End. No correlations were found between the frequency or the average duration of naps at home and performance improvements measured in the lab. There was a significant positive relationship between nap sleep efficiency (SE) and throughput on the LOG task (r=0.45, p=0.05). There were no differences in performance between short and long nap conditions, despite the 2-hr group obtaining significantly more daytime sleep than the 45-min group (short-60± 42min, long-106±42 min; t<cub>19=2.55, p=.02).
Conclusion: These preliminary results indicate that taking daily naps significantly improves waking function on several cognitive tasks in older individuals. Nap duration and frequency were not significantly correlated with improvements. However, nap SE did predict greater improvement on the LOG task, suggesting that it is not the quantity of naps, but the quality, that improves performance. Nonetheless, a learning effect can not be ruled out at this point. The influence of in-lab naps on performance and more broadly, the feasibility of a daily in-home nap regimen for older individuals, are the focuses of continuing investigation.
Support (optional): Research support provided by NIH grant R01 AG12112.

0357

COMPLIANCE WITH SAMPLING PROCEDURES IMPACTS ASSESSMENT OF THE CORTISOL AWAKENING RESPONSE (CAR)

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Introduction: The CAR is a burst of cortisol upon awakening from sleep which increases up to 2x in the first 30 minutes after awakening. The timing of saliva sampling is important: A delay between waking and collection of the first sample may affect the CAR and explain contradictory findings reported in the literature. We evaluated the impact of delays between wake time and collection of wake time cortisol samples on CAR values.
Methods: Participants (total n = 207, mean age 74.0 ± 7.2 yrs) included bereaved elders (n = 35), caregivers (n =50), patients with insomnia and co-morbid medical disorders (n = 68), and the healthy "Old, Old" (n = 54). Two methods were used to identify wake time: polysomnography (PSG) and self-report (S-R). Saliva samples were collected over 2 consecutive days using Salivettes. Wake and wake+30 cortisol values are reported here.
Results: Mean wake time defined by PSG (6:26AM ± 1:11h) did not differ significantly from S-R wake time (6:22AM ± 1:18h). Large delays were observed between both PSG and S-R wake time and collection of the waking cortisol sample (24.8 ± 32.2 min for PSG and 28.3 ± 49.2 min for S-R). These delays significantly affected CAR values. Mean CAR values for delays of <1 min, 1-15 min, and >15 min between PSG-assessed wake time and S-R assessed wake time and cortisol sampling differed significantly (F(2,204) = 7.18, p = .001) and (F(2,197) = 5.5, p = .005) respectively.
Conclusion: These findings have several important implications on the assessment of the CAR. A delay of > 15 minutes between awakening and collection of the wake time cortisol sample significantly blunts CAR levels, which confounds the interpretation of study results. In addition, self-report assessments of wake time perform equally well to PSG for evaluating compliance with CAR sampling procedures.

0358

COMPLIANCE WITH A MONTH-LONG NAP REGIMEN IN OLDER INDIVIDUALS

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Introduction: We have previously shown that older individuals who took a scheduled afternoon nap exhibited improved waking function after the nap and throughout the next day. The current protocol examines the potential benefits of a longer-term 'nap regimen', wherein individuals with age-related sleep disturbance were instructed to nap every day

for a month. Here we examine the compliance with such a nap regimen.
Methods: Healthy subjects ≥60 years (n=21), who self-reported insufficient nighttime sleep duration and/or quality, have completed the study. Subjects were randomly assigned to a 45min (short, S; n=11) or 2hr (long, L; n=10) nap condition. They were instructed to nap between 10h-18h for the assigned duration every day for a month. Compliance was based on analysis of each nap detected by continuously recorded actigraphy, confirmed by a daily log detailing each nap. Three criteria were assessed: timing-nap initiated 1000h-1715h; duration-nap within 15min of prescribed length; and frequency-minimum of 5 naps/week. Data are presented as % of subjects meeting each compliance criterion.
Results: Subjects in S were more likely to take a nap ≥5 times per week (S: 81%, L: 60%). However, more subjects in L were compliant for nap duration (S: 9%, L: 40%) and timing (S: 55%, L: 70%). Non-compliance for duration in S was primarily due to subjects sleeping "too long" (mean duration = 60±42min). By contrast, naps taken in L were more often "too short" (mean duration = 106±42 min). Only 4/21 participants (1S, 3L) met all 3 compliance criteria.
Conclusion: Many older individuals express interest in finding a non-drug treatment for their sleep problems. Data from our lab and others supports the idea that scheduled daily naps may be an effective means of supplementing nighttime sleep amounts and improving waking function. These preliminary results indicate that while subjects assigned to S were more likely to take a daily nap than subjects in L, they were less compliant for nap duration and timing, and less likely to be "super compliant". Low compliance rates for nap duration for both groups suggest that neither 45 minutes nor 2 hours is a widely accepted duration. In combination with the significant improvements in cognitive function observed in this study regardless of nap condition (see accompanying abstract by Stanchina et al.), these results suggest that an hour may be a more optimal nap length for a nap therapy approach to age-related sleep disturbance.
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0359

SLEEP DISTURBANCE AMONG OLDER ADULTS RESIDING IN ASSISTED LIVING FACILITIES

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Introduction: Sleep problems have not been adequately described among residents of assisted living facilities (ALFs), who generally cannot live independently, but do not yet require nursing home care. We studied a sample of residents in 18 ALFs to describe their sleep patterns and identify factors associated with disturbed sleep.
Methods: 121 participants (mean age 85.3 years, 85.6% female; 87.6% non-Hispanic white) were assessed using the Pittsburgh Sleep Quality Index (PSQI; total score and 3-factor scoring method), Berlin Sleep Apnea scale (high vs. low risk), Restless Legs Syndrome scale (RLS) and 72-hour wrist actigraphy. Mini-mental State Examination (MMSE), 5-item Geriatric Depression Scale (GDS), sedating medication use, comorbidity, body mass index (BMI) and other measures were also collected.
Results: Sixty-five percent reported PSQI total score> 5; 59.5% reported problems falling asleep and 60.3% reported nighttime or early morning awakenings. Thirty-two percent were at high risk for sleep apnea and 11.6% reported RLS symptoms. Based on actigraphy, mean nighttime total sleep was 6.3 hours (SD=1.67) and mean nighttime percent sleep was 77.2% (SD=17.42). Thirty-four percent took nighttime sedating medications. In regression analyses, significant independent predictors of worse PSQI score included more depressive symptoms and use of nighttime sedating medications (model $F(2,118)=10.40, p<.0005$). Significant predictors of worse PSQI 3-factor perceived sleep quality included being male, having RLS symptoms and use of nighttime sedating medications (model $F(3,116)=11.30, p<.0005$). Significant predictors of worse PSQI 3-factor daily disturbances included RLS symptoms and more depressive symptoms (model $F(3,114)=7.33, p<.0005$). Significant predictors of shorter actigraphic nighttime total sleep included higher comorbidity scores and higher BMI (model $F(2,113)=6.540, p=.002$). Significant predictors of less actigraphic nighttime sleep percent included higher BMI and worse MMSE (model $F(2,112)=4.463, p=.014$).
Conclusion: Sleep disturbance is common among ALF residents, with evidence that sleep apnea, RLS, depression and other comorbidities play an important role. Interventions to improve sleep of ALF residents should address these conditions.
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0360

SLEEP DISORDERED BREATHING IS PREVALENT IN ELDERLY COMPLAINING OF POOR SLEEP

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Introduction: Deterioration in sleep quality, efficiency and increased sleep disordered breathing (SDB) occurs with ageing. Moreover respiratory events cause arousals that have additional adverse effects on sleep quality and daytime function. Our goal was the evaluation of SDB in an elderly population complaining of poor sleep/insomnia.
Methods: Active subjects over 60 years old complaining of poor night time sleep were recruited for a yoga treatment study for insomnia. Prior to enrollment, they were interviewed and examined by an experienced sleep physician. Subjects with proved or suspected SDB were excluded. 77 subjects enrolled, age 74.2+/-7.0 years, 80.6% females, BMI 25.9+/-3.8. Sixty seven subjects had at least one home sleep study, and 51 had two studies, performed using ECG, oxygen saturation, pulse wave recordings and ECG derived respiration. Automatic scoring based on HC1000P software yielded sleep architecture information, arousals, sleep efficiency and AHI (respiratory events per hour of sleep). Diagnosis was based on clinical information obtained at enrollment and test results.
Results: 13% had no SDB; 22% had AHI between 5 and 10; 39% between 10 and 20; 13% between 20 and 30; and 12% had AHI above 30. Total sleep time 357min+/-71; Sleep efficiency 84.8%+/-4.2; REM% 17.5+/-6; NREM% 69.3+/-14.2; arousals index 18.3+/-20.3. Similar results were obtained during a second study (51 subjects).
Conclusion: We found that a majority (65%) of elderly active people complaining of poor sleep quality has undiagnosed obstructive sleep apnea that cannot be predicted by clinical findings or questionnaires. This high incidence occurs in a woman predominant population with a multitude of medical problems (hypertension, heart disease, diabetes) and use of various sleep promoting medications. Efficient treatment of the SDB in these patients should have positive impact on their general health and function and improve sleep quality. Since clinical evaluation is unreliable at this age, elderly should have simple, cost effective home diagnosis of their disorder, allowing for treatment, when needed.

0361

EFFECT OF EVENING LIGHT EXPOSURE ON SUBJECTIVE ALERTNESS IN HEALTHY OLDER SUBJECTS

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Introduction: Older adults frequently report early morning awakenings and sleep-maintenance insomnia, which can result in sleepiness in the early evening. Bright light exposure has been reported to have an acute alerting effect, in addition to effects on the timing of circadian rhythms. The aim of this study was to examine the effects of evening bright light exposure on subjective alertness in older adults with complaints of early morning awakenings.
Methods: Ten volunteers (56-79 years; mean=63.3±8.08; 6F) with a complaint of sleep-maintenance insomnia participated in a semi-ambulatory sleep-circadian rhythm study. After 3 baseline nights and a 1-day constant posture to assess melatonin phase, the next 4 days included evening light exposure (LE) for 2h per evening beginning 3h before bedtime. Subjects were allowed to leave the laboratory during the day and returned 6h before bedtime. Subjects were randomized to one of two lighting conditions with an equal photon density, standard polychromatic white (4100K, ~1200 lux, 370μW/m2) or blue-enriched polychromatic white (~500 lux, 320μW/m2) light. The Karolinska Sleepiness Scale (KSS) and a Visual Analog Scale (VAS; sleepy-alert) were administered every half hour for the 4h before bedtime, which included the 2h LE. We compared these subjective alertness measures between baseline (evenings 2, 3) and LE (evenings 6, 7, 8) using the mean KSS and VAS results for each subject.
Results: Subjective sleepiness (KSS) was significantly reduced on LE evenings when compared to baseline ($p<0.05$). Similarly, subjective alertness (VAS) was significantly greater on LE evenings when compared to baseline ($p<0.05$). Subject groups were too small to compare the change in alertness between the two light exposure groups.
Conclusion: Our findings reveal that a brief course of evening light increased alertness in this group of older adults with complaints of sleep-maintenance insomnia. Further analysis is needed to determine whether the light treatment resulted in differences in alertness in the morning, and additional subjects are needed to determine whether there were differences in the acute alerting effects of the two light sources.
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0362

ASSOCIATION BETWEEN NIGHTTIME SLEEP AND DAYTIME ACTIVITY IN MEMORY-IMPAIRED INDIVIDUALS AND THEIR CAREGIVERS

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Introduction: Poor sleep quality in aging is often exacerbated in older individuals with neurodegenerative disorders. Sleep disruption may impair daytime function and reduce life quality. We examined relations between nighttime sleep and daytime activity in older individuals with memory impairments and their caregivers.
Methods: 53 caregiver/care recipient dyads completed seven days of wrist actigraphy and recorded in/out of bed times. Sleep was scored for standard parameters. The daily mean, median, and within and between-day variation of actigraphically-determined activity (arbitrary units) was also determined.
Results: Care recipients were older than caregivers (77.9±8.0 vs 69.2±12.3 years, $p<0.001$), more likely male (56‰ vs 43‰, $p<0.05$), and had lower Mini-Mental State Exam scores (22.0±4.9 vs 29.1±1.1, $p<0.001$). Sleep efficiency (SE) did not differ between care recipients (72.9±17.4‰) and caregivers (77.5±15.5‰), compared as unpaired groups ($p=0.16$) or paired dyads ($p=0.14$). However, the daytime activity mean (188±25.3 vs 171±32.7) and median (209±34.5 vs 182±50.2) were both higher in caregivers than in care recipients, analyzed either as groups or dyads (p's<0.01). The intradaily variation of daytime activity (85.0±8.2 vs 90.8±10.8) was lower in caregivers than in care recipients, treated either as groups or dyads (p's<0.01), while the interdaily variation of daytime activity (16.3±9.1 vs 16.8±8.0) was similar ($p=0.73$, group; $p=0.75$, dyad). In caregivers, nightly SE was not associated with mean daytime activity ($r=0.03$, $p=0.54$) nor was mean daytime activity associated with subsequent night SE ($r=-0.02$, $p=0.74$). In care recipients, mean daytime activity was not associated with subsequent night SE ($r=0.09$, $p=0.15$), but nightly SE was associated with mean daytime activity ($r=0.13$, $p<0.05$) the following day.
Conclusion: Our data confirm both individuals with impaired memory and their caregivers have poor sleep. But they also suggest the possibility that improving nighttime sleep in those with memory impairment might increase daytime activity, which in turn might reduce apathy and improve quality of life.
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0363

SLEEP FRAGMENTATION PREDICTS ALL-CAUSE MORTALITY IN A COHORT OF MIDDLE AGED AND OLDER ADULTS

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Introduction: Sleep-disordered breathing, a major cause of sleep fragmentation, has recently been linked to increased risk for all-cause mortality. Most of the available studies have not directly measured fragmentation; factors other than sleep fragmentation may explain the observed association. Using direct measures of sleep fragmentation, the relation between fragmentation and mortality was quantified.
Methods: Sleep Heart Health Study participants underwent overnight polysomnography to characterize sleep and were followed for health outcomes over eight years. Sleep fragmentation was defined using an index of the number of sleep stage transitions/hour of sleep. In addition to a composite transition index, indexes for each of the six types of transitions (wake-to-NREM, wake-to-REM, NREM-to-wake, NREM-to-REM, REM-to-NREM, and REM-to-wake) were constructed. The odds of death as a function of each transition index were modeled using multivariable logistic regression adjusting for age, gender, race, hypertension, smoking status, respiratory disturbance index, and arousal index.
Results: Over the average follow-up of eight years, 854 of the 5,614 participants with reliable sleep-stage data died. Modeled as a function of overall transition index the odds of death increased 5% (OR: 1.05, 95% CI: 1.02, 1.07) among participants less than 60 years of age. When each transition type was considered separately, two transition types were associated with higher mortality risk (Wake-to-NREM and NREM-to-Wake). Other transition types decreased the odds of death; however, the decrease was observed only when the number of transitions was < 1 per hour of sleep.

Conclusion: The overall transition index showed a detrimental effect of transitions on death even though individual sleep stage specific transition indexes both increased risk of death (NREM-to-wake, wake-to-NREM) and protected against mortality (NREM-to-REM, REM-to-NREM, REM-to-wake). As consensus on the importance of good quality sleep to maintaining health continues to build, research should investigate the role of sleep stage transitions.
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0364

RELATIONSHIP BETWEEN COGNITIVE STATUS AND SLEEP PARAMETERS IN ELDERS WITH COGNITIVE IMPAIRMENT

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Introduction: Nocturnal sleep in people with cognitive impairment (CI) is light and fragmented with frequent awakenings; however, we have little understanding of how sleep quantity, quality, fragmentation, and common sleep disorders may be related to cognitive status in this population. The purpose of this study was to explore the relationship between sleep parameters and cognitive status.
Methods: 173 residents of 9 nursing homes and 5 assisted living centers (mean age, 81.87 years; 116 women) underwent two nights of polysomnography. We averaged the sleep parameters for the two nights. In addition, cognitive status was assessed using the Mini-Mental State Examination (MMSE). Age, education, total sleep time, sleep efficiency, minutes of non-rapid eye movement sleep, minutes of rapid eye movement sleep, apnea hypopnea index, oxygen saturation nadir, number of respiratory awakenings (NRA), number of stages shifts, and periodic limb movement index were potential predictors of MMSE. Multiple regression procedures, including stepwise selection and all subsets regressions in Stata were used to determine the most parsimonious model in which each predictor made a significant contribution.
Results: The mean MMSE score was 20.35 (SD=7.38). Education and NRA uniquely and significantly predicted MMSE (F=22.13; R2=.203; p=.0000).
Conclusion: More education and a greater frequency of awakenings following apneas and hypopneas were predictive of cognitive status in persons with dementia. Reducing the frequency of respiratory awakenings during sleep in persons with CI may improve their cognitive status.
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0365

AGE-RELATED CHANGES IN SLEEP MAINTENANCE QUANTIFIED USING SURVIVAL ANALYSES OF SLEEP AND WAKE BOUTS

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Introduction: A common complaint of older persons is disturbed sleep. We used survival analyses of sleep and wake bout lengths to quantify age-related changes in sleep maintenance, controlling for circadian phase and length of time within a sleep episode.
Methods: 13 older and 11 younger healthy subjects participated in an inpatient forced desynchrony protocol with a 28-hour activity/rest cycle and a 2:1 ratio of activity/rest, with polysomnographic recordings during scheduled sleep. Two consecutive 30-second epochs of NREM sleep, REM sleep, Sleep (NREM or REM), or Wake, were required to initiate a "bout" of that state; this bout lasted until a bout of another state began. Kaplan-Meier survival analyses were performed using SAS PROC LIFETEST with age as a strata variable. Analyses were performed for Sleep-Wake or NREM sleep-REM sleep-Wake transitions. Circadian phase was defined using plasma melatonin.
Results: Older subjects had significantly shorter "survival" in Sleep and NREM sleep than younger subjects; smaller changes with age were observed for REM sleep and Wake bouts. The changes were unrelated to the amount of Slow Wave Sleep at baseline. The survival characteristics for NREM-to-REM were similar to NREM-to-Wake; REM-to-NREM bout survival was similar to REM-to-Wake. There was significant variation in younger participants in the rate of transitioning to another state by circadian phase and length of time within a sleep episode.
Conclusion: Age-related changes in bout duration indicate that a primary disturbance is due to altered NREM sleep maintenance, rather than REM sleep or Wake. Since the relative distribution of Wake bout lengths is unchanged with healthy aging, the increased Wake within a sleep episode reported by older people is due to more frequent Wake bouts. These results are consistent with our previous reports, in which the frequency and duration of awakenings and inter-state transition rates were analyzed in these participants. Based on these data, therapies that increase NREM sleep bout duration will likely reduce sleep disruption in older people.
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0366

DOES POOR SLEEP AMONG OLDER ADULTS DURING INPATIENT POST-ACUTE REHABILITATION PREDICT PERSISTENT SLEEP DISTURBANCE?

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Introduction: Acute illness or injury leading to hospitalization may precipitate sleep disturbance in older adults. Little is known about the persistence of sleep problems that begin in these circumstances. To address this questions, we examined this using data from a descriptive study of sleep among older people receiving inpatient post-acute rehabilitation (PAR) after acute hospitalization, with 12-months follow-up.
Methods: 245 patients (mean age=80 years, 38% female) completed the Pittsburgh Sleep Quality Index (PSQI) on 5 occasions: PAR admission (querying "premorbid" sleep quality prior to the acute hospitalization), 7 days after admission to PAR (querying sleep quality during PAR), and 3, 6, 9 and 12 months after PAR discharge. During PAR, participants also completed the Mini-Mental State Examination (MMSE). Comorbidities were assessed with the Cumulative Illness Rating Scale-geriatrics (CIRS). Regression models were used to test whether premorbid PSQI and PSQI during PAR were significant independent predictors of PSQI scores at follow-up time points, adjusting for age, gender, MMSE and CIRS.
Results: Mean PSQI scores were 5.2 (premorbid), 8.3 (7-day), 7.3 (3-month), 6.9 (6-month), 6.6 (9-month), and 6.0 (12-month). Higher premorbid PSQI predicted higher follow-up PSQI at all time points (p's<.003). Higher 7-day PSQI predicted higher follow-up PSQI scores at 3 and 6 months (p's<.040). Older age (6 and 9 month) and male gender (6 and 12 month) were significant predictors (p's<.033) at some time points. MMSE and CIRS were not significant at any time point.
Conclusion: Among older adults, reported sleep disturbance during PAR predicted continued sleep problems for 6 months after PAR; however, self-reported sleep problems prior to the medical event precipitating PAR predicted poor sleep for up to 1 year. Findings suggest patients in PAR should be screened for sleep disturbance and that treatment of sleep disturbance during PAR may prevent continued poor sleep after discharge.
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0367

GENDER DIFFERENCES IN SLEEP DISTURBANCE PATTERNS ASSOCIATED WITH AGING

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Introduction: Recent evidence suggests that the commonly-accepted axiom of worse sleep in older age groups is more complicated than once thought- many older adults report few sleep problems. This study, utilizing data from the Centers for Disease Control Behavioral Risk Factor Surveillance System (BRFSS), examined sleep disturbance across age groups, differentiated by gender.
Methods: The BRFSS is a survey conducted by the CDC (http://www.cdc.gov/brfss). The present data includes n=159,856 participants who provided complete data. Sleep disturbance (SLEEPDIS) was measured with the item, "Over the last 2 weeks, how many days have you had trouble falling asleep or staying asleep or sleeping too much?" Responses were dichotomized as percentage who reported ≥7 days disturbance. Gender and age (5-year groups) were explored.
Results: All omnibus tests were significant. 18.8% of Americans reported SLEEPDIS. Overall, women reported more SLEEPDIS than men (21.7% vs. 15.8%). The distribution of SLEEPDIS in women and men was as follows: 18-24 (total=22.3%;women=23.7%;men=20.4%) , 25-29 (total=20.2%;women=21.8%;men=16.5%), 30-34 (total=18.5% ;women=19.5%;men=14.8%), 35-39 (total=18.5%;women=19.8%;me n=14.3%), 40-44 (total=19.1%;women=21.0%;men=14.5%), 45-49 (t otal=20.8%;women=23.6%;men=15.5%), 50-54 (total=21.0%;women =24.6%;men=15.5%), 55-59 (total=21.3%;women=23.8%;men=18.5 %), 60-64 (total=18.8%;women=21.4%;men=14.6%), 65-69 (total=17 .4%;women=19.4%;men=14.4%), 70-74 (total=16.8%;women=17.2%; men=14.9%), 75-79 (total=17.3%;women= 17.9%;men= 14.9%), 80+ (total=16.9%;women=17.6%;men= 14.0%).
Conclusion: These results, from the largest sample to date investigating sleep quality, suggest that perceived SLEEPDIS does not worsen with age in a linear fashion. On the contrary, the worst SLEEPDIS was reported in the youngest age group and the best in those over 65. Middle-age (45-64) was characterized by increased SLEEPDIS in women, and this effect, while still present, was attenuated in men. The more prominent age effects in women may be due to menopause. The reduced rates of SLEEPDIS in older adults despite the presence of data from other studies showing higher rates of objectively impaired sleep efficiency in older adults suggests that habituation or adaptation may be playing a significant role. This area warrants further research.
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0368

DAYTIME SLEEPINESS AND FUNCTIONAL OUTCOMES IN MIDDLE-AGED WOMEN: RESULTS FROM THE 2007 SLEEP IN AMERICA POLL

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Introduction: This study evaluated the association between sleep disturbances, daytime sleepiness and functional outcomes in a national sample of middle-aged women.
Methods: We conducted a secondary analysis of 399 community-dwelling women (ages 40-65 years, mean age = 56.42 ± 4.55 years) selected from the of the 2007 *Sleep in America* poll (N= 1003). Daytime sleepiness was evaluated by the question "how often do you have sleepiness during the day so badly that it interferes with you daily activity" with a 5-point Likert scale from "everyday" to "never." The sample was dichotomized as either "sleepy" (daily/ frequently) or "non-sleepy" (never/ rarely). Other variables evaluated included mood (feeling sad/depressed, hopeless, nervous, or anxious), symptoms of sleep disorders (insomnia, restless leg syndrome [RLS], and sleep apnea [SA]), and the effect of sleepiness on functional outcomes (relationships with significant others, work, driving and health behaviors). Descriptive and inferential statistics were computed using SPSS 15.0, with significance set at $p<.05$.
Results: The majority of respondents were post menopausal (84%), overweight (mean BMI = 27.77± 6.07), married or living with someone (70%), and had good or excellent health (77%); only 18% (n=72) were classified as "sleepy." There was no significant difference in age, BMI or sleep duration between sleepy and non-sleepy respondents. Sleepy women had more symptoms of insomnia, RLS, and SA than non-sleepy women, lower self-rated health and higher scores on feelings of depression, hopelessness, nervousness, worry and anxiety ($p <.001$). Sleepiness significantly interfered with job performance, household duties and relationships with family and friends ($p<.001$)). Functional outcomes affected by being "sleepy" included reporting more frequent driving while drowsy, being too tired to exercise, eat right or cook a healthy meal and decreased engagement in leisure activities or sex ($p <.01$)
Conclusion: Sleep disorders and excessive daytime sleepiness can negatively effect daily life of middle-aged women.

0369

REVERSE SLEEP STATE MISPERCEPTION IN THE ELDERLY: A DISCRETE FORM OF AGNOSIA FOR NIGHTTIME WAKEFULNESS

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Introduction: We report a series of elderly patients who demonstrated marked lack of awareness of sleeplessness at night that was dissociated from awareness of daytime impairments. Until recently, there have been few reports of this type of sleep misperception and no reports have focused on this condition in the elderly.
Methods: Clinical description of 3 elderly patients studied with standard polysomnography, including recordings of nasal pressure and end tidal C02, scored according to AASM 2007 criteria.
Results: The 3 patients (2 male, 1 female) had an average age over 80 years. All had daytime impairment (excessive napping, fatigue, and daytime sleepiness) but reported sleeping well at home. Laboratory evaluation revealed markedly reduced sleep efficiency (22%, 55%, and 56%), and average sleep onset latency greater than 100 minutes. Despite polysomnographic evidence of strikingly impaired nighttime sleep with prolonged periods of wakefulness, all patients reported falling asleep within 30 minutes and having their typical quality sleep. 2 of 3 patients had severe periodic limb movements of sleep, primarily without arousals (indexes of 111, 176), and 1 patient had mild obstructive and central sleep apnea syndrome. All patients were aware of daytime symptoms.
Conclusion: Elderly patients with daytime symptoms of fatigue, sleepiness, and excessive napping, may suffer from severely impaired nighttime sleep wihout being aware of it. This may represent a discrete from of agnosia for a particular body state, in this case wakefulness at night, which may be distinct from awareness of other states such as sleepiness during the day. In contrast to paradoxical insomnia, patients with reverse sleep state misperception fail to report a problem and therefore are more likely to receive inadequate diagnostic evaluation. The consequences of a missed diagnosis can be greater in the elderly and consideration of this possibility may lead to improved care.

0370

ELDERLY SLEEP QUALITY AND MENTAL HEALTH

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Introduction: Sleep quality tends to decrease as we age, mainly due to typical sleep architecture modifications, sometimes complicated by more physiological conditions, like primary insomnia. Sleep quality also tends to decrease with mental health, and the goal of this study was to establish if the presence of a mental health condition could influence the evolution of sleep quality during a one-year period in elderly subjects.
Methods: Participants were 1008 subjects (mean age=74,2 years) selected from a probabilistic sample composed of ageing individuals living at home in three different areas of the province of Québec. The inclusion criteria's were: being older than 65 years old, understanding and speaking French and having no diagnostic of cognitive disorders. The interview was held at the residence of the participants and had an average length of 90 minutes. The DIS (Diagnostic Interview Schedule) was used to evaluate the presence of depression or anxiety symptoms in the last 12 months whereas the PSQI was used to measure sleep quality (Buysse, 1989). Data were collected twice, with an interval of one year.
Results: The mental health status examination revealed that 14.7% of the participants had at least 1 diagnostic on the DIS. Of these, more than 2.3 % of respondents presented a dependence on benzodiazepines according to the criteria's of the DSM IV. A cut-off score of 5 on the PSQI score yield to a significant difference between the participants with no diagnostic (17%) compared to those having at least one diagnostic (29.7%) ($p < .05$). Of participants initially having no sleep issues, 16.4% reported a sleep problem after one year. Paradoxically, for subjects initially reporting sleep issues and having at least one mental health condition, we observed after a year an increase in sleep quality for 40.7% of them, while only 5.7% did continue to deteriorate.
Conclusion: This study suggest that the prevalence of affective disorders, anxiety and dependence on benzodiazepines in our population is similar to results from other epidemiological study. However, while aging and mental health problems are associated to a decrease in sleep quality, the co-occurrence of both is not to be readily interpreted as having a long lasting synergistic effect.
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0371

N-REM SLEEP SLOW OSCILLATIONS AMPLITUDE AND DENSITY IN THE YOUNG AND MIDDLE-AGED MEN AND WOMEN

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Introduction: High level of neural synchronisation in N-REM sleep is detectable with the EEG as large amplitude slow-waves (SO). Aging is associated with lower slow-wave activity (SWA; spectral power between 0.5-4.5 Hz). Compared to men, women show higher SWA. However, it is still unknown whether age/sex-related differences in SWA are associated to changes in SO density, SO amplitude or both. We used an automatic detector to assess age and sex differences in SO.
Methods: Eighty-seven healthy volunteers with no sleep disorders were separated in two groups: Young (22W, 26M; 23.3y ±2.4), and Middle-aged (21W, 18M; 51.9y ±4.6). SO on Fp1, F3, C3, P3 and O1 were automatically detected during N-REM using published criteria (Massimini et al. 2004). ANOVAs were performed on SO density (nb/min) and amplitude.
Results: Compared to young subjects, middle-aged subjects showed lower SO density in all derivations but this effect was less prominent in FP1. Age-related decrease in SO density was more prominent at beginning of the night. For SO amplitude, middle-aged men showed lower SO amplitude than young men in all derivations but this effect was less prominent in O1. Middle-aged women showed lower SO amplitude than young women and this effect did not differ between derivations. Men showed lower SO amplitude than women in the frontal derivation only.
Conclusion: In conclusion, effects of aging and sex differed on SO amplitude and density. While age-related decrease in SO density was less prominent in anterior area, age-related decrease in SO amplitude was less pronounced in posterior area (O1) in middle-aged men. Age effects on SO density were more prominent early in the night while age effects on SO amplitude were constant across the night. Sex differences were only observed on SO amplitude and constant across the night. These results suggest different neurophysiological mechanisms underlying age and sex effects on SO.
Support (optional): This research was supported by scholarships and grants from the Canadian Institutes of Health Research (CIHR), the Fonds de Recherche en Santé du Québec (FRSQ) and the Natural Sciences and Engineering Research Council of Canada (NSERC).

0372

FACTORS ASSOCIATED WITH SLEEP DISRUPTION IN THE HEALTH AND RETIREMENT STUDY

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Introduction: The purpose of this study is to examine outcomes of sleep disruption in aging Americans using data from the 2004 wave of the longitudinal Health and Retirement Study (HRS). It was hypothesized that sleep disruption is associated with behavioral/attitudinal traits (cynical hostility, optimism, pessimism and social participation) in a population-based sample.
Methods: The 2004 HRS data (N=20,129) represents a cross-sectional analysis of US community-dwelling adults born 1923 through 1953. Data are stratified by median age (67y) to compare younger and older participants, and date of birth to provide five cohorts of aging Americans. The HRS Psychosocial Leave-Behind Questionnaire (PLBQ) was given to a random sample of participants (N=2,786, 42% male, 58% female, 80% Caucasian, 15% African American, Other 4.2%) who independently completed the 2004 HRS wave. A sleep disruption score (SDS) was computed using 4 items from the dataset, with higher scores representing more sleep disruption. The SDS was compared to behaviors/attitudes that were hypothesized as "sleep disruption sensitive" (cynical hostility, optimism, pessimism and social participation).
Results: A majority (57%) of participants reported that they did not "feel rested after a night's sleep". Significant positive associations ($p<.0001$) were found when comparing the SDS and pessimism ($r=0.19$), cynical hostility ($r=0.14$), social participation ($r=.16$,), and negatively associated with optimism ($r= -0.16$). T-tests revealed no gender differences in SDS or sleep sensitive behaviors when comparing the total sample, age cohorts, or younger versus older subjects. ANOVA revealed no differences in sleep disruption or behaviors across the five age cohorts.
Conclusion: Although a majority of this random sample of aging Americans does not report restful sleep, sleep disruption has a weak effect on behavioral/attitudinal outcomes. Pending regression analyses to examine the predictive effects of sleep disruption on behavioral outcomes will include pertinent demographic variables (age, gender, education, race, marital status, socioeconomic status).

0373

PREVALENCE OF SLEEP DISTURBANCES AND RELATED SYMPTOMS IN A NATIONAL, COMMUNITY SAMPLE OF OLDER ADULTS

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Introduction: Data from the 2005 - 06 National Health and Nutrition Examination Survey (NHANES) were used to explore the descriptive sleep characteristics of persons age 60 years or older, along with their respective reports of sleep disturbances.
Methods: 1570 persons age 60 years or older completed telephone or in-home surveys. We analyzed general sleep habits and the 8 questions of the NHANES sleep module that comprise the "general productivity" subscale of the Functional Outcomes of Sleep Questionnaire (FOS-Q), to explore the relationships between scores on this scale and other functional outcomes.
Results: 51% of the study sample was male with a mean age of 71.9 years (SD 8.17). The sample consisted of 61% Non-Hispanic White; 20.4% Non-Hispanic Black; and 15% Mexican American older adults. Over 55% of the sample reported that they had slept on average for 7 hours or less per night over the past month; with 61% of reporting sleep onset latency of 15 minutes or less. Frequent snoring was reported by 33% of the sample; 78.3% reported that they never snorted or stopped breathing while sleeping; 5.4% of the sample reported that they had a diagnosis of sleep apnea and 18% reported feeling "unrested during the day" as "often," or "almost always." Eleven percent reported frequent use of sleeping pills. Scores on the FOS-Q general productivity subscale were significantly ($p<.00$) correlated with feeling depressed ($r = .29$); poorer mental health ($r = .21$); poorer general health ($r=.10$); and worsened physical health ($r=.09$). Negative correlations were found between FOS-Q scores and memory problems (-.10, $p<.00$) and emotional health (-.14; $p<.00$).
Conclusion: Findings from this national sample of older Americans show that less than half get the recommended 8 hours of sleep each night. The strongest relationships with scores on the FOS-Q subscale were found with the presence of depressive symptoms and poorer mental health.
Support (optional): John A. Hartford Foundation/Atlantic Philanthropies Claire M. Fagin Fellowship (K Rose); University of Virginia Institute on Aging (K Rose, D Landers).

0374

VARIABILITY IN NAP LENGTH PREDICTS HEALTH STATUS IN A SAMPLE OF COMMUNITY-DWELLING OLDER ADULTS

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Introduction: Napping is related to a myriad of mental and physical health morbidities. The precise nature of the relationship between napping and health, however, remains unclear. Day-to-day variability in napping length has not been investigated in relationship to physical health comorbidities. Analyzing variability within individuals enables the examination of fluctuations in behavior that previously may have wrongly been dismissed as random error. This study aims to examine the association between variability in nap length and health comorbidities (number of health conditions).
Methods: 103 community-dwelling older adults (Mage=72.81, SD=7.12) completed daily sleep diaries for 14 days and a Demographics and Health Survey (indicating number of health conditions). All variables were detrended prior to calculating indices of within and between-persons variability. Linear regressions were calculated for all variables with time as the independent variable, and nap variables as the dependent variables. The resulting unstandardized residuals were then used as time-independent values. Two indices were calculated: 1)NAPmean-an index of between-person variability and 2)NAPvariability-an index of within-person variability.
Results: NAPmean and NAPvariability were significantly correlated with number of health conditions (comorbidities; $r=.24, p<.05$, $r=0.32, p<.01$, respectively). A two-step hierarchical multiple regression analysis was run to predict comorbidities. Step one included the predictor variables NAPmean, NAPvariability, and age which accounted for 15% of the variance in comorbidities. Age[$t(100)=2.50$, $p<.05$] and N APvariability[$t(100)=2.38, p<.05$] were significant predictors. Step two excluded NAPmean and still accounted for 15% of the variance in comorbidities. Both age[$t(100)=2.50, p<.05$] and NAPvariability[$t(100)=2.71, p<.05$] remained significant predictors.
Conclusion: Investigating the individual impact of variability in nap duration and average nap behavior on comorbidities is the novel contribution of the study. Initially both mean nap duration and nap variability appeared linked to comorbidities. Hierarchical regression, however, distinguished the contributions of the two nap variables indicating variability, not mean nap duration, significantly predicts health status. The results suggest interventions aimed at stabilizing nap behavior may be warranted.

0375

IMPAIRMENT OF WAKEFULNESS WITH AGING

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Introduction: Daytime sleepiness and impaired nighttime sleep develop with advanced age in the majority of adults. Daytime sleepiness impairs quality of life and cognition and has been shown to contribute significantly to motor vehicle accidents. We have identified impaired function of the catecholaminergic wake neurons in aged mice in association with impaired ER protein folding homeostasis. The dopaminergic and noradrenergic wake neurons, in contrast to other wake-active neuronal groups including orexinergic neurons, contain NADPH oxidase that is distributed in subcellular regions of the neurons that are rich with endoplasmic reticulum: the perinuclear envelope and proximal dendrites. In this study we describe the impairment of wakefulness that occurs with age. We used c-fos staining as a read-out of functional activity.
Methods: 10 Young (2 month old) and 10 aged (18-20 month old) mice under went electroencephalographic/electromyographic recordings to measure wakefulness bout length distribution and average sleep latency in the active period. Brains were then procured for functional assays of wake neurons (c-fos response) during wake.
Results: Aged mice display impaired wakefulness with significantly more sleep to wake transitions with 209+37 bouts compared to 105+47 in the young mice during the lights off period ($n=9$/age group, $p=0.0001$). In addition wake bout durations are significantly shorter in the aged mice compared to the young mice (2.2+0.5 vs 6.2+3.7 min, $p=0.006$). While the total minutes of wake are less in the aged mice during the lights off period it is not significantly different from that in the young mice. Young mice show c-fos activation in 60% of dopaminergic neurons in the VPAG and 80% c-fos activation in orexin neurons. Older mice show rare c-fos activation in VPAG (3%), while orexinergic neurons have 50% activation.
Conclusion: Aged mice display wake fragmentation with shorter wake bout durations and many more sleep to wake transitions. This may be due to impaired function of the catecholaminergic wake neurons.

0376

SLEEP, DEPRESSION, STRESS AND IMMUNITY IN DEMENTIA CAREGIVERS: A SEVEN DAY STUDY

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Introduction: Caregivers of dementia patients report significant sleep disruption. This exploratory study examined relationships between subjective reports of sleep and actigraphy, stress, mood, and a panel of endocrine and immune markers in 30 caregivers.
Methods: The participants were recruited from an Alzheimer's clinic and collected saliva 4 times/day for 2 days, and a venipuncture was done at a home visit. They wore actigraphy watches for 7 days and completed questionnaires about stress, mood and sleep. Saliva samples were analyzed (ELISA) for cortisol. Serum samples were multiplexed using a kit from Millipore for a cross section of 13 cytokines and analyzed by Luminex. Serum norepinephrine and CRP were analyzed by ELISA. Not all data have been analyzed, but several findings can be reported.
Results: Mean age was 65.4 years (22 women, 8 men). Several cytokines (IL-10, IL-13, IL-4, TNF-α and IL-6) were high in comparison to reported age-adjusted norms. The CES-D mean was 33, indicating severe depression. Depression was correlated with lower awakening salivary cortisol levels. The Perceived Stress Mean was 40, indicating extreme stress. Ratings of sleep quality as poor were associated with higher CES-D scores, poorer general health and higher serum TNF-α level. Actigraphy data indicating reduced and interrupted sleep.
Conclusion: This study will provide information about relationships between variables to support a larger study on an intervention to improve endocrine and immune function in caregivers.
Support (optional): Sigma Theta Tau Delta Beta Chapter-at-Large Maureen Groer, RN, PhD for monetary support and use of USF College of Nursing Biobehavioral Laboratory

0377

A PILOT STUDY OF GENTLE YOGA FOR INSOMNIA IN OLDER WOMEN WITH OSTEOARTHRITIS

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Introduction: Osteoarthritis (OA) affects 27 million adults and is the leading cause of disability in the United States. Over 50% of persons with arthritis report difficulty sleeping. Both OA and sleep disturbance are more prevalent in older women than men. Yoga is a multimodal practice that may reduce OA-related insomnia in older women. Study aims are (1) to test the feasibility and acceptability of yoga for older women with OA and insomnia, and (2) to gather preliminary evidence on the effects of the intervention on sleep outcomes.
Methods: The study design is one-group, quasi-experimental with pre- and post-intervention outcome assessment. Sixteen older women with OA and insomnia symptoms will attend 8 weekly 75-minute yoga classes and practice a 20-minute yoga routine nightly at bedtime. The yoga practice includes gentle stretching, strengthening, and relaxing poses and breathing techniques. Sleep is assessed before and after the intervention by one week of sleep diaries and wrist actigraphy (Actiwatch-64).
Results: Eight older women (mean age 67.2±6.9 years) with OA have been recruited. Baseline diary outcomes: sleep onset latency (SOL), 31.1±20.5 min; wake after sleep onset (WASO), 64.6±46.7 min; total sleep time (TST), 344.5±58.1 min; sleep efficiency (%SE), 80.0±14.4%, and VAS sleep quality, 40.8±8.8. Actigraphic findings were similar: SOL, 22.0±18.8; WASO, 59.9±29.2; TST, 375.4±62.4; %SE, 77.7±7.2. The mean PSQI score was 11.13±2.9.
Conclusion: Baseline sleep data are consistent with other studies of persons with OA, showing difficulty with sleep maintenance and quality more than sleep initiation. The first cohort completed the 8-week yoga program in December 2008 and data are currently being analyzed. A second cohort will complete the study in spring 2009. The data from this study will inform an R21 grant proposal of a randomized clinical trial (RCT) of gentle yoga for insomnia in older persons with OA.
Support (optional): This study is supported by a Pilot Project Grant from the UW Center for Interdisciplinary Geriatric Research (funded by the RAND Corporation and the John A. Hartford Foundation).

0378

SLEEP/WAKE PATTERNS IN A NOVEL ENVIRONMENT: THE EFFECTS OF AGE AND STRAIN IN RATS

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Introduction: Novel environments (NE) are known to affect the sleep/wake patterns of humans and rodents. In this study, we investigated the influence of aging on the NE effects and compared them to the differences across 2 strains of rats.
Methods: Three groups of rats were used: young F344 (YF, 3 mo, n=10), old F344 (OF, 24 mo, n=8) and young Wistar (YW, 3 mo, n=10). Rats were implanted with EEG and EMG electrodes using standard methods and allowed to recover for 3 wks. Following a 24 h baseline recording, rats experienced NE (clean cage) and a control condition (CN, picking up and placing back in to the home cage) 2 h into the light period (ZT2). W, NR and REM was scored in 10 s epochs. The data was analyzed with 2-way repeated measures ANOVA within a group and 2-way completely random ANOVA was used to compare OF vs. YF and YF vs. YW. Where indicated, t-tests were used for post-hoc analysis.
Results: Significant age and strain differences were found for both baseline and NE conditions. During the baseline dark period, OF had less W (66.6% vs. 73.3%) and more NR (28.2% vs. 22.9%) compared to YF. W and NR were not different between OF and YF during the baseline light period (38.7% vs. 40.8% and 51.7% vs. 49.4% respectively). REM was not different for either the light or dark periods. In contrast, differences during baseline between YF and YW were found primarily in the light period. YF had more W (40.8% vs. 26.4%), less NR (49.4% vs. 61.3%) and less REM (9.7% vs. 12.3%) than YW whereas no differences were found in the dark period. NE had little effect on OF but had a strong wake-promoting effect on both YF and YW. For the 2 h following NE exposure, W was increased compared to CN in YF (75.8% vs. 44.3%) and YW (80.6% vs. 46.0%) but not in OF. NR was decreased in YF (21.7% vs. 47.7%) and YW (18.8% vs. 47.3%) but not in OF. REM, however, was significantly decreased in all 3 groups (2.4% vs. 7.9% in YF, 0.9% vs. 8.1% in YW, 3.9% vs. 7.2% in OF) when exposed to NE. No rebound in sleep was evident in any of the 3 groups.
Conclusion: During baseline, there were larger differences in sleep/wake parameters between strains than between young and old rats within a strain. However, following NE, age was a more important factor than strain. These and other published studies show that while there may be small differences found in sleep parameters during baseline conditions, important changes can be found in aged rats by testing with challenging experimental designs.
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0379

SLEEP REFRESHES HUMAN EMOTIONAL BRAIN REACTIVITY

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Introduction: While numerous studies have investigated the impact of sleep loss on cognition, few have examined the pro-active benefit of sleep, and specific stages of sleep, on human emotional brain function. Here we demonstrate the benefit of a daytime nap in regulating affective brain reactivity.
Methods: Participants rated four different affective face categories: Fear, Sad, Angry and Happy; with each stimulus category ranging in a gradient from neutral to emotional. Subjects performed the emotional face-rating task twice; once at 12 PM (Test1) and again later that same day at 5PM (Test2). However, half of the subjects undertook a 60-90 min PSG monitored sleep opportunity between Test1 and Test2 (nap group, n=18, 11 males), while the remaining subjects stayed awake (no-nap group, n=18, 7 males).
Results: Relative to Test1 baseline, the no-nap group displayed an amplified reaction to Anger ($p < 0.008$) and Fear ($p < 0.05$) facial expressions at later Test2, later that following day. In contrast, those in the nap group demonstrated no such increase in emotional sensitivity to these emotions (both $p > 0.23$). Moreover, the nap group displayed an increased receptiveness to Happy facial expressions following sleep ($p \leq 0.05$). Most interestingly, only those subjects who achieved rapid eye movement (REM) sleep during the nap exhibited this beneficial amelioration of negative and potentiation of positive emotional reactivity.
Conclusion: Together, these results suggest that the balance of affective human brain reactivity is markedly altered across the day, showing a progressively stronger sensitivity to negative emotion. In contrast, sleep, particularly REM, can reverse this negative bias while restoring responsivity to positive affect. Therefore, sleep, and the unique neurobiology of REM, may enhance the brain's empathetic capacity towards positive emotions, while palliatively redressing the balance towards negative emotions.
Support (optional): NIH

0380

IMMUNE ALTERATIONS AFTER SLEEP DEPRIVATION IN HEALTHY MALE VOLUNTEERS

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Introduction: It is clear that sleep deprivation (SD) affects the immune system however, the consequences of the lack of sleep on immune function remains to be fully comprehended. PURPOSE: To determine the impact of 2 nights of total SD and 4 nights of REM SD on immunological parameters. Secondly, we also examined whether recovery sleep would revert possible alterations.
Methods: Thirty male volunteers ranging from 19-29 years were randomized in three protocols (control, total SD, and REM SD; N=10/group). Both SD protocols were followed by three nights of recovery sleep. We assessed circulating white blood cells, T (CD4/CD8) and B lymphocytes, Ig classes and complement. Daily blood collections were performed.
Results: Monocytes, eosinophils and basophils did not present alterations. 48h of total SD increased the number of total leucocytes and neutrophils compared with baseline and these levels returned to basal at 24 hours of recovery. In this period, the total SD group exhibited a marked increased in slow wave sleep. The most prominent alteration was the increase of CD4 T cells after 24 and 48h of total SD. CD4 T cell count did not return to basal levels after one night of recovery. In relation to REM SD, IgA decreased from 24 to 96h of REM SD.
Conclusion: Our results indicate that T CD4 cells were particularly affected by total sleep loss. Indeed, the adaptive immune response may be more influenced by SD because subsequent to the recovery period the T CD4 levels were not re-established, differently from alterations related to innate immune response. Moreover, we point to the possibility that the reduction of IgA that was observed in REM SD is associated to an increase in the susceptibility to invasion of pathogens through the mucosa.
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0381

SLEEP RESTRICTION CAN COMPROMISE THE BENEFICIAL EFFECT OF DIET-INDUCED WEIGHT LOSS ON TOTAL BODY ADIPOSITY

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Introduction: Short sleep is associated with obesity and changes in human fuel metabolism. We examined whether recurrent sleep restriction can: 1) interfere with the beneficial effects of a reduced-calorie diet on excess body weight and adiposity; and 2) in this setting, modify the circulating concentrations of the orexigenic hormone, ghrelin, and the anorexigenic hormone, leptin.
Methods: Nine healthy, overweight volunteers (2/7 F/M; mean [SD] age 40 [5] y; BMI 27.5 [2.0] kg/m2) each completed two 14-day studies in random order at least 3 months apart. Studies were carried out in the laboratory with 5.5-hour or 8.5-hour bedtimes and nutritionally balanced caloric intake equal to 90% of the subjects' resting metabolic rate. Sleep was monitored by polysomnography. We measured body weight (scale) and composition (DXA), and collected serum samples for leptin and ghrelin (Linco) every 30 min for 24 hours before and after each study.
Results: Subjects slept 314 [6] and 444 [34] min during the 5.5-hour vs. 8.5-hour bedtime condition ($P<0.001$). The amount of weight loss during each treatment remained similar (3.0 [1.1] vs. 2.9 [1.4] kg; $P=0.89$), however, its composition was markedly different. While fat represented only 26% of the weight loss during sleep restriction, it constituted 57% of the weight loss during the 8.5-hour bedtime condition ($P=0.031$). Leptin concentrations decreased during the period of caloric restriction and, when the amount of body fat was controlled for, comparable 24-hour leptin levels were observed both in the presence and absence of sleep restriction (9.2 [9.7] vs. 9.2 [7.4] ng/ml; $P=0.39$). In contrast, body weight adjusted 24-hour ghrelin concentrations (1225 [212] vs. 1112 [238] pg/ml; $P=0.017$), and the ratio of ghrelin to leptin in the circulation (247 [174] vs. 206 [172]; $P=0.036$) were significantly increased at the end of the 5.5-hour compared to the 8.5-hour bedtime condition.
Conclusion: Our results indicate that recurrent sleep restriction can: 1) compromise the beneficial effects of reduced-calorie diet on total body adiposity; 2) cause increased loss of lean body mass; and 3) amplify the human neuroendocrine response to the reduced supply of energy. These findings raise the possibility that the lack of sufficient sleep may interfere with the effective use of key behavioral strategies for metabolic risk reduction.
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0382

ONE NIGHT OF RECOVERY FROM SUSTAINED SLEEP RESTRICTION: A DOSE-RESPONSE STUDY OF NEUROBEHAVIORAL FUNCTIONS

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Introduction: Individuals commonly attempt to recover from sleep loss by extending sleep durations on weekends and days off, but how much

sleep is actually needed to recover? We conducted the first systematic sleep dose-response experiment to determine the nature of recovery in one night following 5 days of sustained sleep restriction.
Methods: N=159 healthy adults (22-45y; 78f) underwent 2 baseline nights with 10h TIB (B1-2); 5 nights of sleep restriction to 4h TIB (SR1-5); and 1 night of recovery sleep (R1) with TIB randomized to 0h, 2h, 4h, 6h, 8h or 10h. A control group (N=17) received 10h TIB each night. Subjects completed a Psychomotor Vigilance Test (PVT), Karolinska Sleepiness Scale (KSS) and Digit Symbol Substitution Task (DSST) every 2h during wakefulness on all days, and a modified maintenance of wakefulness test (MWT) at B2, SR5 and R1. ANCOVA was used to model data across recovery sleep dose (controlling for age, sex, baseline differences, and individual differences in the effects of sleep restriction). The recovery sleep-dose response curve fitted with linear, exponential and sigmoidal models, and the best fit was selected with Akaike's Information Criterion. Full recovery was estimated TIB durations that intersected the control group data.
Results: Exponential models most accurately described the sleep-dose response functions for PVT lapses, KSS and DSST correct, while a linear model best fit MWT data. Recovery to the level of controls was projected to occur at 10.7h (95% CI: 8.0-13.3h) for PVT; 10.6h (95% CI: 7.8-13.4h) for KSS; 8.1h (95% CI: 6.0-10.2h) for DSST; and 15.2h (95% CI: 10.4-19.9h) for the MWT.
Conclusion: The results indicate that to fully recover neurobehavioral functions following 5 nights of sleep restricted to 4h TIB, more than a single 10h TIB is needed. However the large confidence intervals suggest that recovery may be achievable for some individuals.
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0383

THE EFFECTS OF 24 HOURS OF SLEEP DEPRIVATION ON ENDOGENOUS AND EXOGENOUS ATTENTIONAL NETWORKS

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Introduction: The process of attention may be divided into endogenous and exogenous components, which are subserved by partially dissociable brain regions. While it is established that sleep deprivation (SD) has a profound behavioral impact on attention generally, less is known about the neural basis of the separate effects it has on endogenous and exogenous subprocesses.
Methods: 24 healthy adults completed two functional magnetic resonance imaging scans each, during rested wakefulness (RW) and after 24 hours of total SD. During these scans, they were administered an oddball paradigm designed to engage both endogenous and exogenous attention. Faces and houses were used as oddball stimuli such that activation in the fusiform face area (FFA) and parahippocampal place area (PPA) could serve as markers of the integrity of stimulus representation.
Results: After 24h SD, subjects detected significantly fewer targets on the oddball paradigm. When compared with blocks of passive observation, performing the oddball task activated regions of a known frontoparietal network associated with endogenous attention. SD significantly reduced levels of activity in these regions ($p < .01$). In contrast, brain activation to oddballs in areas associated with exogenous attention (e.g. inferior frontal gyrus) and the thalamus, were not significantly affected by SD. In both states, these regions were selectively responsive to relevant vs. irrelevant oddballs. Finally, during RW, we observed enhanced activation in the PPA and FFA to relevant vs. irrelevant oddballs ($p < .01$); this effect was significantly attenuated in the sleep deprived state.
Conclusion: Although stimulus-driven areas of attention have relatively intact functioning following SD, lowered activation of top-down control areas could contribute to the attenuation of attention driven differential activation of functionally distinct ventral visual regions. Diminished response enhancement within ventral visual areas in response to relevant stimuli may be a more nuanced way of accounting for the worsening of selective attention following SD.
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0384

PER3 POLYMORPHISM IS ASSOCIATED WITH SLEEP HOMEOSTATIC RESPONSE TO SUSTAINED SLEEP RESTRICTION BUT NOT TO NEUROBEHAVIORAL RESPONSES

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Introduction: The variable number tandem repeat (VNTR) polymorphism 5-repeat allele of the circadian gene PERIOD3 ($PER3^{5/5}$) has been associated with greater cognitive decline during a night of acute total sleep deprivation (TSD), as well as greater sleep homeostasis. We evaluated whether the PER3 VNTR polymorphism was associated with cumulative neurobehavioral deficits and sleep responses during sustained sleep restriction (SR).
Methods: 52 $PER3^{4/4}$, 63 $PER3^{4/5}$ and 14 $PER3^{5/5}$ healthy adults (aged 22-45 y) completed 2 baseline 10h TIB nights, followed by 5 SR nights at 4h TIB in an experiment that involved assessments on a series of neurobehavioral measures (cognitive performance and executive function tests, subjective sleepiness, MWT), and physiological sleep responses. Comparisons were made among genotypes. There were no significant differences in genotypic or allelic frequencies between Caucasians and African Americans.
Results: There were large phenotypic differences in SR response in $PER3^{5/5}$, $PER3^{4/5}$ and $PER3^{4/4}$ genotypes, and all 3 groups demonstrated equivalent cumulative decreases to SR in cognitive performance (e.g., PVT, Digit Span), executive function (e.g., Hayling, COWAT) and alertness (e.g., MWT, KSS). $PER3^{5/5}$ participants had a greater sleep homeostatic response to restriction (as measured by NREM SWA and SWE) than $PER3^{4/4}$ subjects. PER3 homozygotes did not differ at baseline in habitual sleep, physiological sleep structure, circadian phase, physiological sleepiness, cognitive performance, or subjective sleepiness.
Conclusion: The PER3 VNTR polymorphism was not associated with individual differences in neurobehavioral responses to sleep restriction in a large cohort of healthy adults. It was, however, related to sleep homoeostatic responses during sleep restriction. This suggests the $PER3^{5/5}$ genotype may contribute to differential neurobehavioral vulnerability to sleep loss that involves wakefulness at a specific circadian time in the early morning hours. The comparability of PER3 genotypes at baseline and their equivalent inter-individual vulnerability to sleep restriction indicate other genes contribute to the behavioral effects of chronic sleep loss.
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0385

SUSTAINED SLEEP RESTRICTION IN HEALTHY ADULTS WITH AD LIBITUM ACCESS TO FOOD RESULTS IN WEIGHT GAIN WITHOUT INCREASED APPETITE OR FOOD CRAVINGS

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Introduction: In recent years a number of studies have found an association between short sleep duration and increased BMI, however only a few experimental, laboratory controlled studies have investigated the possible link between sleep loss and weight gain. This study examined the effect of sleep restriction on weight, food cravings and appetite.
Methods: N=92 healthy subjects (22-45yrs; 52 males) participated in a laboratory-controlled sleep restriction protocol. Subjects underwent 2 nights of baseline sleep (10h TIB/night), 5 nights of sleep restriction (SR1-5; 4h TIB/night) and varying recovery for 4 nights. N=9 served as a 10h TIB per night control group. Food consumption was ad libitum such that subjects had 3 regular meals a day and access to healthy snacks, and during nights of sleep restriction (SR) subjects were given a sandwich at 1am. Height and weight measurements were taken at baseline and on the last day of the protocol. The validated food cravings inventory (subscales were high fats, sweets, carbohydrates, fast foods) and questionnaires about appetite and food consumption were completed nightly.
Results: SR subjects experienced a weight gain of 1.31 kilograms over the 11 days of the protocol ($p<0.0001$) while the 10h TIB control subjects did not ($p>0.05$). BMI increased from 24.81±3.64 at baseline to 25.08±3.71 ($p<0.0001$) in the SR group. Controls' BMIs did not change reliably (25.26±3.56 to 25.30±3.85, $p>0.05$). Self reported food cravings decreased during the study ($p<0.0001$). Of those subjects in the SR group who reported a change in their appetite and food consumption >70% said that it decreased by SR5.
Conclusion: In the presence of ab libitum food intake, SR subjects reported decreases in appetite, food cravings and food consumption; however, they gained weight over the course of the study, suggesting that energy intake still exceeded energy expenditure during sleep restriction.
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0386

VERBAL LEARNING ABILITY MEDIATES COGNITIVE PERFORMANCE AND BRAIN ACTIVATION IN OLD AND YOUNG ADULTS AFTER TOTAL SLEEP DEPRIVATION

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Introduction: Prior studies document large inter-individual differences in the response to sleep deprivation. It is uncertain to what extent prior ability mediates these differences. Here, we used age-normed t-scores from the California Verbal Learning Test (CVLT) to determine whether a global index of baseline verbal learning can predict cognitive performance or brain function on a verbal learning memory task (VL) after total sleep deprivation (TSD).
Methods: Thirty-three older (OA; F=25, age=68.3±5.9) and 28 younger adults (YA, F=16, age=28.3±4.9) completed the VL task during fMRI after normal sleep and 36-hours TSD. After the task, subjects immediately recalled a list of words. During a separate appointment participants were given the CVLT. Regression analyses examined if CVLT t-scores could predict cognitive performance or brain function on VL. Whole-brain alpha was p=.05.
Results: Behaviorally, there was a main effect of CVLT scores (positive correlation) and age (YA>OA) on VL performance during TSD. The CVLTxGroup interaction was not significant. Imaging data showed a significant CVLTxGroup interaction in several brain regions, including bilateral anterior frontal regions and temporal lobes, left inferior frontal gyrus, and right fusiform gyrus. For all but right temporal lobe, OA had a significant positive correlation, and YA had a significant negative or no correlation, between CVLT and cerebral responses.
Conclusion: YA performed better after TSD than OA. In all subjects, better basal memory performance (i.e., greater CVLT scores) predicted better VL performance after TSD. Associated cerebral responses, however, varied with the CVLTxGroup interaction. OA with better basal memory seemed to recruit cognitive resources outside typical verbal memory networks following TSD, consistent with CVLT predicting a compensatory recruitment response. In contrast, YA with better basal memory did not require such recruitment to maintain good performance. This pattern suggests different cerebral mechanisms may account for resiliency to TSD in OA vs YA.
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0387

SLEEP DEPRIVATION HEIGHTENS EMOTIONAL REACTIVITY IN ANTICIPATION OF AND IN RESPONSE TO NEGATIVE STIMULI IN HEALTHY YOUNG ADULTS

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Introduction: Many studies have documented sleep deprivation-induced subjective mood impairments. Few studies have employed objective measures, and therefore little is known about the specific emotional processes that are affected by sleep deprivation. We used pupil dilation as an objective, physiological indicator to examine emotional reactivity while anticipating and viewing negative emotional information.
Methods: Using a within-subjects crossover design, 9 young adults 18-25 years old without psychiatric, medical, or sleep disorders were tested under two experimental conditions separated by one week: sleep deprivation (SD; following one night of total SD) and rested wakefulness (RW; following one night of normal sleep). Negative and neutral pictures (24 each) from the International Affective Picture System were randomly presented. Trials consisted of a 6-second cue, a 2-second picture presentation, and an 8-second inter-stimulus interval. Half of the cues indicated the valence of the upcoming stimulus, while the other half did not indicate whether the upcoming picture was negative or neutral.
Results: Across all trials, viewing negative pictures during SD resulted in a sustained and exaggerated pupil dilation response compared to neutral pictures ($F(1,8)=21.049$, $p=0.002$) and compared to responses to negative pictures during RW ($F(1,8)=11.571$, $p=0.009$), whereas pupillary responses did not differ between negative and neutral pictures during RW. While anticipating an upcoming negative picture, a pupil dilation response began 0.5 seconds after onset of the cue during SD, whereas it was delayed by 4 seconds during RW. This response increased throughout the cue during SD, and was significantly larger compared to anticipatory responses to the other cue types ($F(1,8)=13.596$, $p=0.006$).
Conclusion: Sleep deprived individuals displayed significantly larger pupil dilation responses while anticipating and viewing negative picture stimuli. These findings suggest that acute sleep loss specifically impairs the central processing of negative emotion, and may have implications for the link between sleep disturbances and mood disorders.
Support (optional): MH077106, RR024153, and the National Sleep Foundation

0388

PSYCHOMOTOR VIGILANCE TASK PERFORMANCE DURING SLEEP DEPRIVATION IN TWINS: EVIDENCE FOR HERITABILITY OF SLEEP HOMEOSTASIS

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Introduction: Sleep homeostasis is the rate of accumulation of the pressure for sleep during wakefulness. Sleepiness can be quantified by the number of lapses on a reaction time test, the Psychomotor Vigilance Task (PVT). During sleep deprivation there are large and highly reproducible interindividual differences in rates of performance deficit accumulation as determined by multiple PVT trials. We studied monozygotic (MZ) and dizygotic (DZ) twins to determine if these differences arise from a heritable trait.
Methods: Subjects maintained normal sleep/wake patterns in the week prior to testing as confirmed by actigraphy. 58 MZ and 40 DZ twin pairs with a normal overnight polysomnogram underwent 38 hrs of monitored, continuous sleep deprivation during which they performed the 10-min PVT every 2 hrs. Zygosity was determined by DNA analysis. The primary outcome was change from baseline in (transformed) total lapses (response time>500ms) per trial. Subject specific (linear) rates of performance deficit accumulations were separated from circadian effects using multiple linear regression. Heritability was assessed through alternative statistical approaches and implemented using TWINAN92 and SAS.
Results: 30% of pairs were female (mean age 27, range 18-40) and 70% were male (mean age 29, range 18-53). Assessment of assumptions required by alternative analysis approaches is necessary for complete interpretation but critical assumptions required for interpretation of the following were tenable. Intraclass correlation coefficients were 0.562 and 0.171 among MZ and DZ pairs implying a classical heritability of 0.781. The mean of within-pair and among-pair heritability estimates determined from ANOVA-based methods was 0.672, similar to the classical estimate. One variance components model that adequately fit the data implied 40.2% of variance in accumulating deficits was explained by additive genetic variance and 10.9% by dominance genetic variance.
Conclusion: Genetic factors explain an important fraction of variance among rates of performance deficit accumulations on PVT during sleep deprivation. Future studies are needed to determine heritability of sleep homeostasis based on EEG spectral analysis and elucidate the gene variants responsible for variations in this response to sleep deprivation.
Support (optional): NIH P50 HL060287

0389

EFFECT OF SLEEP ON VISFATIN LEVELS

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Introduction: Both sleep deprivation and sleep apnea have been identified as risk factors for insulin resistance though the mechanism is unclear. Elevated levels of visfatin, a hormone secreted by visceral fat, have been associated with insulin resistance. The purpose of this study is to assess the relationship between visfatin and sleep-related exposures.
Methods: After in-laboratory polysomnography, a morning fasting blood sample was assayed for visfatin using a commercial ELISA in 489 adult subjects from the Cleveland Family Study. Apnea hypopnea index (AHI), arousal index (AI), and total sleep time (TST) were assessed in a standardized fashion. Due to its highly skewed distribution, visfatin was categorized into quartiles. The association between sleep exposures and visfatin quartiles was modeled using a cumulative logit model with a random family effect incorporated to account for intrafamilial correlation.
Results: The study population was 42.5% male, 16.6% type II diabetics, had a mean age of 44.7 ± 17.6 years, and a mean body mass index of 32.6 ± 8.2 kg/m2. No association was found between visfatin levels and AHI or AI. However, there was an inverse correlation between visfatin levels and TST. The mean visfatin level in those with a TST of ≤6 h, 6-7 h, and >7 h were 0.94 ± 1.54 ng/mL, 0.77 ± 1.24 ng/mL, and 0.64 ± 0.93 ng/mL respectively (p=0.02). After adjusting for age, sex, and race, every hour decrease in TST was associated with a 32% greater odds of having a visfatin level above the 25th percentile (p=0.02). This association persisted after additional adjustment for waist circumference and diabetes status.
Conclusion: Reduced sleep duration is associated with elevated visfatin levels. This may represent one mechanism by which sleep deprivation predisposes to insulin resistance.
Support (optional): This work was supported by NIH HL081385, RR00080, and RR024989.

0390

EVALUATION OF SLEEPINESS: IS STANDARD MAINTENANCE OF WAKEFULNESS TEST THE RIGHT TOOL?

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Introduction: Drowsiness is a contributing factor in 22-24% of crashes or near crashes. Objective assessment of sleepiness on task becomes an imperative. There is no consensus on detection of the tendency to fall asleep, or if and how to monitor sleepiness while driving. Our aim was to characterize sleepiness and to develop a simple tool to monitor sleepiness while driving.
Methods: Ten healthy volunteers with regular sleep enrolled in the study that included a regular night sleep in the lab followed by 36 hours of sleep deprivation during which subjects performed 2 alternate tasks every 2 hours: (1) Maintenance of Wakefulness Test (MWT) standard conditions for 45 minutes; (2) Driving simulation (90Km on a monotonous road using STISIM Drive simulator). Two occipital, two central EEG, chin EMG, eye movement and ECG were monitored and recorded continuously while audio-video was collected. MWT was interrupted if 2 minutes of any sleep stage intervened. Micro sleeps (3-15 seconds) were manually detected, crashes and driving errors were detected from the simulator.
Results: Sleep latency during MWT decreased and the frequency of micro sleeps increased with increasing sleep deprivation. A circadian modulation of this tendency caused accentuation of sleepiness during late night hours. A striking finding, in all subjects, indicates large amounts of alpha activity with open eyes on MWT when sleep debt accumulates. This is overwhelming after 24 hours. Driving simulations around the same time indicate a large amount of crashes, accompanied by theta EEG activity.
Conclusion: Standard MWT evaluation based on sleep latency is insufficient. The presence of alpha activity with open eyes raises questions regarding scoring and interpretation of MWT. The fact that the presence of alpha on MWT correlates well with low performance on simulator indicates that alpha intrusion, even in the absence of sleep onset or closed eyes, may be an important factor when evaluating drowsy drivers.
Support (optional): This research project is supported by a grant in the memory of Dr. Mona Bogokovski.

0391

REPEATED SLEEP RESTRICTION INDUCES MORPHOLOGICAL CHANGES IN INTERNAL ORGANS IN THE RAT

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Introduction: The purpose of the present experiment was to investigate changes to internal organs of rats after a 10-week period of inadequate sleep, previously shown to produce dramatic increases in food and water intake, loss of body weight, and mortality without pathogenic foci. The purpose behind studying chronic insufficiency of sleep is to understand the adaptive responses that would provide survival benefit, but which also may produce detrimental components and medical implications.
Methods: Cycles of 10 days of sleep restriction and 2 days of sleep ad libitum were repeated in rats 6 times during 10.3 weeks. Sleep restriction (N=8) was produced by applying a 6-sec ambulatory requirement according to a schedule previously shown to heavily fragment and reduce sleep by nearly 40% under the Bergmann-Rechtschaffen disk paradigm. Control rats (N=10) received the same ambulatory requirement of 26% of time, only consolidated into periods that permitted uninterrupted sleep. Both groups were fed an atherogenic diet. Organs were collected for study at the end of the 6th cycle per rat. Statistical comparisons of organ measurements were made by means of Student's t tests and $P<0.05$ significance level.
Results: The most striking changes to internal organs in sleep-restricted rats were a lengthening of the small intestine by 30% ($t16=3.3$, $P<0.002$); decreased adipocyte size by 27 to 45% in 5 of 6 depots (omentum, retroperitoneal, epididymal, and mesenteric and popliteal lymph node sites, $P<0.02$ or better); and, increased incidence of multilocular adipocytes in 4 of 6 depots (perirenal, omentum, mesenteric and popliteal lymph node sites, $P<0.04$ or better), compared to ambulation controls. Also, hearts and livers were heavier in sleep-restricted rats than in controls (each $t16=2.5$, $P<0.01$).
Conclusion: Sleep restriction produces a negative energy balance in both humans and laboratory rats, indicated in one way by decreased leptin, a reliable marker produced by body fat. The present results in rats show that repeated sleep restriction produced adaptive changes to the internal organs. Increases in multilocular adipocytes, known to be rich with mitochondria, reflect high energy production. Shrinkage of adipocytes suggests heavy use of lipid. Increased surface area of the intestine indicates increased need to absorb fats and fluids. Multiple changes in body composition and the underlying altered mechanisms appear adaptive, but also may confer risk and medical complications in susceptible individuals.
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0392

EXPERIMENTAL REDUCTION OF SLEEP DURATION OR QUALITY IS ASSOCIATED WITH IMPAIRED INSULIN SIGNALING IN THE ADIPOCYTE

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Introduction: Accumulating evidence from epidemiologic and laboratory studies suggests that reduced sleep duration or quality may be novel risk factors for obesity, insulin resistance and type 2 diabetes. Previously, we have shown that in normal adults, sleep restriction and slow-wave sleep (SWS) suppression both result in decreased whole body insulin sensitivity and glucose intolerance. Examination of insulin resistance at the cellular level is necessary to begin to understand the underlying molecular mechanisms of decreased glucose tolerance and insulin sensitivity following sleep alterations. Presented here is the first evidence of decreased insulin sensitivity in adipocytes in vitro from healthy young adults in whom sleep was experimentally perturbed.
Methods: Seven healthy young volunteers (mean BMI: 22.3±1.7 kg/m2) were studied under three conditions (baseline, sleep restriction and SWS suppression) with controlled caloric intake and energy expenditure in randomized order. The baseline and SWS suppression conditions involved 4 consecutive 8.5-hour nights. SWS suppression was achieved by delivering acoustic stimuli during NREM sleep. Sleep restriction involved 4 consecutive 4.5-h nights. At the end of each condition, subcutaneous biopsies of abdominal fat were collected. The fat samples were collagenased, washed and stimulated in vitro with increasing concentrations of insulin (0/0.1/0.25/ 0.5/0.75/1.0/5.0/10.0 nM). Adipocyte lysates were resolved by SDS-PAGE and immunoblotted with antibodies specific to AKT phosphorylated on Serine 473 as well as to total AKT, a central protein activated in the insulin signaling cascade.
Results: In all 7 subjects, immunoblots showed a consistent and marked right-shift of the insulin dose-response curve after sleep perturbation compared to baseline, indicating insulin resistance at the cellular level of the adipocyte.
Conclusion: Impaired insulin signaling in adipocytes may be evidenced in vitro following sleep perturbations in healthy young adults. This is the first demonstration of a molecular basis for decreased insulin sensitivity in response to decreased sleep duration or quality.
Support (optional): The project described was supported by Grant Numbers R01-HL086459, 5T32 HL07909, Pfizer/AASM Scholars Grant, UL1RR024999, P60DK020595-31 & PO1-AG11412.

0393

EXTENDED RECOVERY SLEEP DURING THE WEEKEND AFTER MODEST SLEEP RESTRICTION FOR ONE WORK-WEEK HAS BENEFICIAL EFFECTS ON DAYTIME SLEEPINESS, IL-6 AND CORTISOL LEVELS

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Introduction: One week of modest sleep restriction (from 8 to 6 h of sleep/night for 1 wk) adversely impacts sleepiness, performance and circulating inflammatory cytokines. Many individuals in modern societies try to overcome these adverse effects by extending their sleep during non-work days, usually on weekends. The aim of this study was to objectively assess the effects of this common practice on sleepiness, inflammation and stress hormones.
Methods: Sixteen healthy young men, normal sleepers, mean age ± SD 24.4 ± 3.6 years, were studied in the sleep laboratory for 13 consecutive nights. The first 4 nights served as baseline nights (8h/night), followed by 6 nights of partial sleep restriction (6h/night), followed by 3 recovery nights (10h/night). Daytime sleepiness [Multiple Sleep Latency Test (MSLT)] and serial plasma cytokines and cortisol levels were measured on days 4 (baseline), 10 (after one week of sleep restriction) and 13 (after 2 nights of recovery sleep).
Results: Preliminary analysis showed that average sleep latency was significantly decreased after restriction, compared to baseline ($p<0.0001$), whereas it improved significantly after recovery sleep, compared to restriction ($p<0.0001$). Also, 24-h plasma levels of IL-6 increased significantly during the sleep restriction period and decreased to baseline after two nights of extended recovery sleep. Furthermore, 24-h plasma cortisol levels decreased significantly during the sleep restriction period, compared to baseline, and remained low after recovery sleep in a non-stressful environment.
Conclusion: Extended recovery sleep over the weekend reverses the impact of one work-week of mild sleep restriction on daytime sleepiness, fatigue and IL-6 levels and improves cortisol levels. These data suggest that the interaction of plasma IL-6 and cortisol levels might determine the levels of sleepiness/alertness in humans. The long-term effects of a

repeated sleep restriction/sleep recovery weekly cycle in humans remain unknown.
Support (optional): NIH RO1 HL6-4415

0394

SLEEP CURTAILEMENT IN HEALTHY YOUNG ADULTS IS ASSOCIATED WITH INCREASED AD LIB FOOD INTAKE

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Introduction: There is strong epidemiologic evidence for an association between short sleep duration and obesity. One possible explanation for this link is a dysregulation of the neuroendocrine control of appetite leading to excessive food intake and weight gain. Laboratory studies with controlled caloric intake and activity levels showed that sleep restriction is associated with increased hunger and appetite, suggesting that in the presence of ad libitum food, sleep restriction may result in increased food intake. We thus examined actual food intake after sleep restriction in healthy young subjects.
Methods: Ten young lean subjects were studied under baseline conditions and after sleep restriction in a randomized cross-over design. Caloric intake and energy expenditure were rigorously controlled and body weight did not change over the study period. The two conditions involved 4 consecutive nights of either 4.5 hours (restriction) or 8.5 hours in bed (baseline). At the end of each condition, subjects were presented with the same assortment ad lib food tailored to meet their dietary preferences, including a buffet lunch, a buffet dinner, and unrestricted access to snacks. Caloric intake and nutrient composition were measured.
Results: Average total sleep time was 7.9±0.1 hours under baseline and 4.4±0.0 hours under sleep restriction. Sleep restriction as compared to baseline was associated with an increased total caloric intake by 460±196 Kcal. (3735±331 vs 3275±330 Kcal, p=0.04). Caloric intake was higher for carbohydrate-rich nutrients (1940±159 vs 1748±170 Kcal, p=0.05), but did not differ for nutrients rich in proteins or fat.
Conclusion: These findings provide evidence that sleep restriction in healthy young adults results in increased caloric intake when food is allowed ad libitum. These findings suggest that excessive food intake plays a role in the increased risk of obesity associated with short sleep.

0395

COGNITIVE PERFORMANCE PREDICTIONS FROM A NEW BIOMATHEMATICAL MODEL OF SLEEP/WAKE HOMEOSTASIS

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Introduction: Cognitive performance has been mathematically modeled on the basis of two biological processes: sleep/wake homeostasis and circadian rhythmicity. We showed that published equations for the homeostatic process generalize to a broader class of models formulated as coupled nonhomogeneous first-order ordinary differential equations (McCauley et al., J. Theor. Biol., 2008). We investigated the dynamic properties of this model class.
Methods: Model parameters were estimated using psychomotor vigilance test (PVT) lapse data from a laboratory experiment involving 14 days of sleep restriction (4h, 6h, or 8h TIB/day), or 3 days of total sleep deprivation (N=48). From the generalized model equations, coupled difference equations were derived to predict performance at the onset and end of successive wake periods. Mathematical analysis of these equations revealed that a bifurcation (i.e., qualitative change in model behavior) could occur when a specific amount of daily wakefulness is exceeded.
Results: For the estimated parameter values, the bifurcation was predicted to occur at 20.2h wakefulness (3.8h sleep) per day. For daily wakefulness <20.2h, the model converged to a stable state of (impaired) performance. For daily wakefulness >20.2h, no stable state was achieved, and impairment was predicted to escalate over days. These predictions were confirmed by another laboratory experiment, involving 7 days of sleep restriction (3h, 5h, 7h, or 9h TIB/day; N=56). The model explained 72.2% of the variance, and a disproportionate accumulation of performance deficits was observed in the 3h TIB condition.
Conclusion: Analysis and validation of our generalized model of sleep/wake homeostatic effects on cognitive performance revealed that sleep restriction to below a threshold estimated at 3.8h per day results in a fundamentally different (disproportionately accelerated) build-up of PVT performance impairment across days. Since much slow wave sleep (SWS) normally occurs within the first ~3.8h of nocturnal sleep, this suggests that chronic sleep restriction causes cumulative deficits considerably faster when SWS is curtailed.
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0396

DO EARLY BED/WAKE TIMES IMPROVE HEALTH AND GRADES IN A MILITARY SETTING?

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Introduction: Research at the United States Air Force Academy (USAFA) has shown that the majority of Cadets sleep less than 6 hours nightly (Lindsay, Eatman, Yanagi & Dyche, 2005). Further, adolescents (~13-22 years of age) tend to suffer from greater amounts of sleep deprivation than their younger peers, despite evidence demonstrating similar need (Millman, et al. 2005). This discrepancy may be due to differential impact of early wake times on adolescents caused by a biologically-driven shift in the circadian cycle to later bedtimes (Dement & Vaughan, 1999). An assumption is that early rise times result in early bedtimes, but physiological constraints may delay bedtimes for adolescents. The present study investigates the bed and wake time behavior of USAFA Cadets, and its impact on sick call visits and grade point averages (GPA).
Methods: Bed and wake time and total sleep were collected from the Collegiate Sleep Habits Survey (Carskadon, 1990). Sick call visits and GPA were collected from database sources containing information on 1970 randomly selected cadets. Cadets with early class start times (EST; 7:00 a.m.) were compared to those with later class start times (LST; 7:50 a.m.).
Results: Cadets with EST obtained significantly less weekday sleep than those with LST ($p < .05$). Although Cadets with EST were rising earlier than those with LST, there was no significant difference in bedtimes. ESTs were also correlated with significantly increased sick call visits and lower GPA ($p < .001$).
Conclusion: The lack of significant differences in bedtimes suggests that the later circadian shifts associated with adolescence is difficult to overcome, even when forced to rise early in a hyper-structured military environment. The resultant sleep loss seems to make us less healthy and wise.
Support (optional): Defense Advanced Research Projects Agency (DARPA).

0397

WEIGHT LOSS RATE DURING SLEEP AND AWAKE REST

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Introduction: Weight loss can be caused by a loss of body mass due to metabolism and by water loss as insensible water loss, sweating,

or excretion in feces and urine. Although weight loss during sleep is a well-known phenomenon, it has not yet been studied in relation to sleep structure. Our study is proposed to compare weight loss during sleep and awake rest and to assess the relationship between overnight weight loss and sleep structure.
Methods: Fourteen normal male volunteers, 21-30 yrs old, males, underwent adaptation PSG (polysomnography) followed by full PSG on an accurate continuous weighing bed-scale. After breakfast, volunteers remained resting on the bed-scale for 7hrs. Body composition was measured before and after each experimental period. Diet given before and after PSG was proportional to weight, age and metabolic rate. Volunteers had no solid or liquid losses during sleep and vigil rest. Polysomnograms were scored and weight loss rate was calculated.
Results: Weight loss rate during sleep was higher than during awake rest ($p<0.05$, 1,9±1,9 and 0,6±0,5 gr/hr respective.
Conclusion: Contrary to our expectations, weight loss rate during sleep was higher than during awake rest. Weight loss and fat weight loss rates were dependent on sleep structure.
Support (optional): AFIP FAPESP

0398

FOOD RESTRICTION OR SLEEP DEPRIVATION: WHICH EXERTS A GREATER INFLUENCE ON THE SEXUAL BEHAVIOR OF MALE RATS?

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Introduction: Many studies have shown that a reduction in caloric intake is related to lifespan extension. On the other hand, the loss of sleep that results from our modern lifestyle leads to diverse effects. For instance, sleep deprivation in rodents causes several changes including those under hormonal control, like sexual behavior. Although there is a diverse literature on the behavioral alterations in rats undergoing FR, only a limited number of studies specifically focus on sexual behavior. Some authors reported that food deprivation reduces sexual motivation and delays the onset of puberty in male rats.
Methods: This study was designed to examine the effects of FR and PSD, either alone or in combination, on sexual behaviors (mount, intromission and ejaculation) in adult male rats. Food restriction began at weaning with 6 g/day of food, and food was increased by 1 g/week until reaching 15 g/day by adulthood. At adulthood, rats submitted to FR and those fed ad libitum were distributed into PSD for 96 hours or maintained in home-cage groups.
Results: The results indicated that both FR and ad libitum sleep deprived groups showed a significant decrease in performance and motivation to initiate sexual behavior, reflected by the increase in mount and intromission latencies. FR associated to PSD basically reversed the adverse effects of sleep deprivation per se on the number of ejaculations. Testosterone concentrations were decreased after sleep deprivation regardless of food availability, while progesterone was significantly higher in the FR-PSD group only.
Conclusion: Our data suggest that the sleep loss affects sexual response probably due to alteration in hormonal profile.
Support (optional): AFIP, FAPESP (#06/58274-5 to T.A.A., CEPID #98/14303-3 S.T.) and CNPq.

0399

SLEEP AND PROTEOLYTIC ENZYMES: SLEEP DEPRIVATION AND METALLOPEPTIDASES ACTIVITIES CHANGES IN RAT CENTRAL NERVOUS SYSTEM

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Introduction: Proteolytic activities are essential either for neuropeptides liberation from active or inactive proteic precursors or for their inactivation. Neuropeptides have a fundamental role on sleep-awakeness cycle regulation and their actions are probably also regulated by proteolytic processing. Our objective is to establish a study methodology, using internally quenched fluorogenic substrates, specific proteases inhibitors and RT-PCR, to get evidences of changes in proteolytic activities, mainly metallopeptidases, in animal models of sleep deprivation.
Methods: Rats were distributed in 4 groups (sleep deprivation, 24h and 48h rebound and control). Metallopeptidases activities (ACE, NEP, TOP and Neurolysin) were assayed (37 C, pH 7.4, Tris.HCl 50 mM, NaCl 100mM, Triton X-100 0.1%) on hippocampus, striatum and hypothalamus extracts using internally quenched fluorogenic substrates. Fluorescence was monitored on a plate reader. Hydrolysis products were analyzed by HPLC and MS/MS. ACE RT-PCR primers were designed and validated.
Results: The peptidic substrates Abz-GDSPFRQ-DNP and JA-2 inhibitor or AMCA-FRK(DNP)P-OH and Lysinopril plus JA-2, were able to detect TOP and Neurolysin and distinguish from ACE activities. Abz-FRK(DNP)P-OH was only sensitive to ACE. ACE activity and genic expression (RT-PCR) were significantly reduced in the hypothalamus of sleep deprived animals, without important changes in hippocampus and striatum.
Conclusion: A new substrate, with higher sensitivity (AMCA), specificity and improved catalytic efficiency, allows better discrimination of TOP and Neurolysin activities. ACE reduced activities and genic expression are probably leading to alteration on kinins metabolism in the CNS of sleep deprived animals. Real time PCR is underway to correlate changes on enzyme expression to proteolytic activity to enzymes other than ACE.
Support (optional): This work was supported by the CEPID-FAPESP and AFIP.

0400

ASSOCIATION BETWEEN SLEEP LOSS AND IMMUNE CHALLENGE: BEHAVIORAL ALTERATIONS IN MICE

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Introduction: Lipopolysaccharide (LPS)-induced behavioral alterations may change in intensity or magnitude when associated with disorganization of sleep-wake cycle. We aimed to investigate whether the association of SD and an immune challenge with LPS would change anxiety and depression, locomotor activity and the sleep pattern of mice.
Methods: Male C57BL/6J mice were submitted to 72h of SD whereas the control (CTRL) group was maintained in home-cage. Both groups received injection of LPS (5, 10 or 20 µg/animal-ip) or saline (Sal) and were returned to their cages for 2h prior to the open-field, elevated plus-maze and forced swimming tests. Additional animals were operated for electrodes implantation to acess the sleep pattern during the 48h of recovery period after SD.
Results: The CTRL-LPS presented a significant increase of total sleep time at the doses of 10 and 20 µg, reflected by the increase of NREM sleep time. The SD-Sal group showed an increase of 107% of REM sleep in relation to CTRL-Sal. When compared with SD-Sal group, the mice of SD-LPS groups presented an ablation of REM sleep at all doses. LPS reduced locomotor activity in the CTRL groups only at the doses of 10 and 20 µg, however, in the SD animals, locomotion was decreased

at all doses. In the elevated plus-maze test, SD showed a strong effect on number of entries in the open arms. The sal group was significantly increased when compared to the CTRL-Sal, SD-LPS 5, 10 and 20 µg. No significant differences among groups were found in the forced swimming test.
Conclusion: Sleep loss not only modifies immune response per se, but also modulates the behavioral response to immune activation induced by LPS.
Support (optional): AFIP, CNPq and FAPESP (CEPID #98/14303-3 to S.T., 06/58275-1 to A.Z. and 06/55968-6 to M.M.S.L.).

0401

DOES SLEEP DEPRIVATION ALTERS NEUROCHEMICAL RESPONSE TO LIPOPOLYSACCHARIDE IN MICE?

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Introduction: Lipopolysaccharide (LPS)-induced alterations in central neurotransmission may change in intensity or magnitude when associated with sleep deprivation. We aimed to investigate the effects of sleep deprivation (SD) upon neurochemical alterations induced by LPS administration in mice.
Methods: Male C57BL/6J mice were submitted to 72h of SD whereas the control (CTRL) group was maintained in home-cage. Both groups received injection of saline (Sal) or LPS (5, 10 or 20 µg/animal-ip) and were returned to their cages for 2h prior to euthanasia. The brains were dissected for collection of striatum for monoamines concentration analysis (HPLC) and for cyclooxygenase-2 (COX-2) expression in the cortex and hypothalamus (Western Blott).
Results: Our results shown that norepinephrine (NE) is increased at the group CTRL-LPS 20 µg in comparison to CTRL-Sal, however, at the dose of 10 µg, SD increased the NE release in comparison with your respective CTRL. In the CTRL group, dopamine (DA) was significantly increased only at the dose of 20 µg, however, in the SD animals, DA increased in both 10 and 20 µg/animal. SD also increased DA at the doses of 10 and 20 µg in comparison with their respective controls. DA turnover represented by the HVA/DA ratio were strongly decreased by SD and all doses of LPS. When compared with the SD-Sal, only the SD-LPS 20 µg group decreased DA turnover. Regarding the COX-2 expression in the hypothalamus, neither SD nor LPS administration changed this pro-inflammatory protein expression. In the cortex, an increase in the COX-2 expression were found at all groups that received the LPS injection, both SD and control.
Conclusion: Our results indicate that the alterations caused by SD in the sickness behavior induced by LPS are directly related with alterations in the neurotransmission pathways of NE and DA, and are not affected by the expression of COX-2.
Support (optional): AFIP, CNPq and FAPESP (CEPID #98/14303-3 to S.T., 06/58275-1 to A.Z., 06/55968-6 to M.M.S.L. and 04/02213-2 to R.B.M.).

0402

DOES PARADOXICAL SLEEP DEPRIVATION INFLUENCE SEXUAL BEHAVIOR IN FEMALE RATS

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Introduction: Sleep loss has become increasingly prevalent as societal demands on productivity increase. Among the many comorbidities of sleep disorders, sexual dysfunction remains the least studied. In male rats, selective paradoxical sleep deprivation (PSD) induces an increase in the frequency of erection and ejaculations. To determine whether PSD could affect sexual receptivity (male acceptance) and proceptivity (male solicitation) behaviors in female rats.
Methods: Adult female Wistar rats were distributed into three subgroups according to their phase of the estrous cycle (proestrus, estrus and diestrus) and were subjected to PSD for 96h or maintained as controls (CTRL) in their home-cages. After this period, the estrous phase was determined and the females were placed with a sexually experienced male. In order to investigate the role of hormones in sexual behavior, additional groups were included that were artificially induced to be sexually receptive by the administration of a combination of estradiol and progesterone. Receptivity (lordosis) and the proceptivity (genital sniffing, ear vibration, hopping and darting) were evaluated.
Results: Selective sleep loss caused a significant increase in the proceptivity and receptivity behaviors in females exclusively in the proestrus phase. At diestrus and estrus, PSD increased the rejection responses. As for the hormone profile, PSD produced a reduction of progesterone in proestrus relative to the respective estrus phase of the control group. The PSD-proestrus females that displayed the highest sexual motivation had greater concentrations of corticosterone compared to the PSD-diestrus females with an absence of sexual behaviors.
Conclusion: Although mechanisms were not established, the major findings were that heightened sexual motivation in a sleep-deprived paradigm was confined within the proestrus phase only. PSD might produce a distinct response in the hormonal profile according to the phase of the estrous cycle.
Support (optional): CNPq, FAPESP (CEPID #98/14303-3) and AFIP.

0403

ACUTE SLEEP DEPRIVATION INCREASES BLOOD PRESSURE AND IMPAIR BAROREFLEX CONTROL IN MALE RATS

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Introduction: We aimed to investigate the effects of paradoxical sleep deprivation over 24h (PSD 24h) on blood pressure (BP), heart rate (HR) and renal sympathetic nerve activity (RSNA) in rats. The effects of sleep deprivation on the baroreflex control of blood pressure were also assessed.
Methods: Adult Wistar rats were sleep deprived for 24h. Immediately after the PSD period, the animals were instrumented for BP and HR recordings in conscious, freely moving conditions and evaluation of baroreflex responses were made after phenylephrine and sodium nitroprusside endovenous injections. Additionally, rats submitted to PSD were anesthetized and instrumented for RSNA recordings.
Results: BP was significantly increased in PSD animals compared to control rats (control 108 ± 2; PSD 24h 121 ± 2mmHg) without significant alterations in HR and RSNA. PSD animals presented a significant reduction in the tachycardia reflex in response to a reduction in BP. The impairment of such tachycardia did not allow the compensatory mechanism that restores blood pressure during acute hypotension to act as can be observed in the results of baroreflex gain (control -3.2±0.7; PSD -0.44 ±0.8bat/mmHg).
Conclusion: PSD 24h was able to increase BP and leads to impairment of the baroreflex control of the cardiovascular system.
Support (optional): CNPq, FAPESP (CEPID #98/14303-3) and AFIP.

0404

DOPAMINE TRANSPORTER REGULATION DURING FOUR NIGHTS OF REM SLEEP DEPRIVATION AND RECOVERY - IN VIVO MOLECULAR IMAGING STUDY IN HUMANS

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Introduction: An inherent repercussion to societal development is sleep deprivation (SD) during the week followed by sleep compensation on weekends. Because REM sleep predominates in the latter half of the night, people who sleep less may lose REM sleep.
Methods: We report changes in the polysomnographic pattern of sleep and dopamine transporter (DAT) density after four nights of selective REM SD protocol followed by three nights of sleep recovery compared to a control group and a group who received two nights of total SD. Single positron emission computed tomography and [99mTc]TRODAT-1 were used to assess cerebral DAT density in the striatum at baseline, after REM SD and total SD, and after sleep recovery in healthy volunteers (n=10/group). Blood was collected daily to examine prolactin and estradiol levels and correlate these markers with dopaminergic activity.
Results: The REM SD group had longer lasting effects on the percentage of REM sleep seen during the recovery period. The total SD group exhibited a marked increase in slow wave sleep during the first night of recovery, and regular sleep architecture was restored after the first night. Neither REM nor total SD affected DAT density in the striatum or the levels of cortisol, estradiol, and prolactin during the protocol.
Conclusion: Because DA activity has been related to REM sleep and selective loss of REM sleep creates a greater imbalance in sleep architecture than total SD. Our findings are consistent with recent studies indicating a more prominent participation of D2/D3 receptors rather than a pre-synaptic DAT in regulating REM sleep.
Support (optional): AFIP, CNPq and FAPESP (CEPID #98/14303-3 to S.T. and 06/58276-8 to R.C.M.S.).

0405

PREVALENCE AND IMPACT OF SHORT SLEEP DURATION IN REDEPLOYED SOLDIERS

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Introduction: Short sleep duration (SSD) is defined as less than 7 hours of sleep per night and is associated with impaired cognition, cardiovascular disease, and poor overall health. The Mental Health Advisory Team V reported the average deployed soldier sleeps 5.6 hours per night due to mission requirements. The persistence of SSD following deployment and its association with co-morbid illnesses is unknown.
Methods: A cross-sectional study of 3152 U.S. Army soldiers who completed the Health Risk Assessment II (HRAII) questionnaire 90 days after a 6-15 month deployment in support of Operation Iraqi Freedom. Co-morbid illnesses were defined using previously validated questionnaires integrated into the HRAII. Multivariate logistic regression analysis was used to calculate adjusted odds ratios for common medical conditions following deployment after controlling for key confounding variables.
Results: 2738 (86.9%) soldiers answered both questions regarding their self-perceived sleep and were included in the analysis. Their average sleep duration was 5.8 ± 1.2 hours. 1959 (72%) slept 6 hours or less, but only 16% reported a daytime nap or felt their job performance was affected due to lack of sleep. Soldiers who reported combat exposures had an increased likelihood of SSD compared to soldiers without these experiences ($p<0.001$). Compared to 7 or 8 hours of sleep, ≤6 hours of sleep per night was independently associated with the following outcomes ($p<0.001$ for all): post-traumatic stress disorder (adjusted OR, 7.5 [95% CI, 4.0-13.8]); mild traumatic brain injury (adjusted OR, 1.7 [95% CI, 1.4-2.1]); depression (adjusted OR, 4.5 [95% CI, 2.0-10.5]); obesity (adjusted OR, 3.6 [95% CI 1.3-10.2]); panic syndrome (adjusted OR, 4.5 [95% CI, 2.0-10.5]); significant alcohol use (adjusted OR, 1.6 [95% CI, 1.3-2.0]); tobacco use (adjusted OR, 1.4 [95% CI, 1.2-1.6]); and prior suicide attempt (adjusted OR, 5.3 [95% CI, 1.9-14.8]).
Conclusion: SSD is common and persists in a large percentage of redeployed soldiers at 90 days, especially after combat exposure. SSD was strongly associated with a variety of common medical problems after deployment and may be a contributing factor for these conditions. Possible etiologies include persistence of learned poor sleep behaviors during deployment or insomnia from multiple etiologies. Efforts to reestablish good sleep habits and aggressive evaluation of soldiers with persistent SSD after deployment may aid in the prevention and management of associated medical conditions.

0406

OCULOMETRIC INDICES ASSOCIATED WITH DROWSINESS AND PERFORMANCE VIGILANCE IMPAIRMENT IN SLEEP-DEPRIVED NORMAL, SLEEP APNEA, NARCOLEPSY AND ADD/ADHD SUBJECTS

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Introduction: To validate oculometric indices as reliable measures of operator performance we developed a wearable, wireless electronic wraparound eye-frame (Eye-Com Biosensor Communicator and Controller) to use as a real-time ocular monitoring system. The non-invasive biosensor detects and responds to operator impairment, including loss of sleepiness awareness, lapses in attention, micro-sleeps or loss of consciousness in different operational scenarios and environments.
Methods: In an IRB-approved study, thirty-one subjects (9 Controls, 7 OSH/OSA, 8 Narcolepsy, 7 ADD/ADHD) completed a 36-hour sleep deprivation cycle. Every 6-hours a drive-simulator Session was combined with objective and subjective measures of alertness/performance (Test of Variable Attention-TOVA, Electroencephalography, MWT, SSS).
Results: Repeated-Measures ANOVA revealed significant linear trends for the alertness measures, PERCLOS ($p=0.0001$), Blink-Rate ($p=0.002$) and MWT ($p<0.001$). Drive Simulator and performance measures, including Off-Road Accidents ($p<0.002$), Collisions ($p=0.01$), Road-Edge Excursions ($p=0.001$) and TOVA measures, including Omission Errors ($p=0.001$) and d-Prime ($p<0.0001$), also showed significant trends. We performed regression analysis to predict drive-simulator performance from oculometric measures during each individual session. Session 4 showed significant regressions with PERCLOS and Blink-Rate accounting for 54.2% of the variation in Off-Road Accidents, 52.1% in Road-Edge Excursion, and 32.7% in Collisions. PERCLOS and Blink-Rate remained strong predictors for Off-Road Accidents during Session 5, but accounted for only 17% of the variance in Collisions while Road-Edge Excursions was not significant.
Conclusion: Repeated-Measures ANOVA confirmed the sleep-deprivation effects for all tests throughout all Sessions. Narcoleptic subjects performed significantly worse in the drive-simulator, followed by the ADD/ADHD group. Control and OSH/OSA groups had similar performance. PERCLOS and Blink-Rate were sensitive to sleep-deprivation with predictive circadian effects on the performance/vigilance relationships. These results contribute to an early design of an Eye-Com generated Composite Oculometric Fatigue Index (COFI) and Safety Response Algorithm that can be integrated into different clinical settings including a fitness-for-driving lab or any real-world operator domain.

Support (optional): This research was funded by four grants i) CDC/NIH SBIR Phase I No.:1 R43 CE 00151-01; ii) US ARMY SBIR Phase I and II No.: W81XWH-05-C-0045; iii) US DOD Congressional Research Initiative No.: W81XWH-06-2-0037 and iv) this US DOT Congressional Research Initiative Agreement Award No. DTNH 22-05-H-01424.

0407

TWENTY-FOUR HOURS OF TOTAL SLEEP DEPRIVATION SELECTIVELY IMPAIRS WORKING MEMORY CAPACITY

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Introduction: Sleep deprivation has been shown to impair executive functions, but exactly which of the recently proposed executive domains (inhibition, shifting, updating, planning, access to long-term memory, dual task performance) are affected is unknown. Our objective was to investigate the effects of 24 h of total sleep deprivation and of selective deprivation of REM sleep on measures of executive functions considering distinct executive domains.
Methods: This was a parallel group design study with 39 young, healthy male volunteers with no sleep alterations who were randomly allocated to three groups: total sleep deprivation under supervision(n=11), deprivation of REM sleep (n=15) and normal sleep (n=13). Volunteers in the latter two groups had their sleep monitored by means of polysomnographic recordings. Subjects were tested the morning after deprivation or normal sleep. The test battery included measures of executive functions that are representative of the 6 domains described above. We also evaluated performance on the counting span task, a measure of working memory capacity which involves a dual-task paradigm combining a short-term memory span measure with a concurrent processing (executive) task. In addition, assessment of other working memory components was carried out using tests that assess the articulatory loop, the visuospatial sketchpad and the episodic buffer, as well as episodic memory.
Results: Twenty-four hours of total sleep deprivation only impaired measures of working memory capacity in comparison to the other groups. No task performance impairment was found after selective deprivation of REM.
Conclusion: Twenty-four hours of total sleep deprivation selectively impaired working memory capacity, which is likely to affect performance in a wide range of daily activities since this construct relates to performance in other complex cognitive tasks such as reading comprehension, problem solving, measures of the intelligence quotient, and is found to reflect individual differences in the ability to focus/maintain attention.
Support (optional): AFIP and FAPESP (CEPID no. 98/14303-3)

0408

MANAGERS' PRACTICES RELATED TO WORK-FAMILY BALANCE PREDICT EMPLOYEE CARDIOVASCULAR RISK AND SLEEP DURATION IN EXTENDED CARE WORKPLACES

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Introduction: An increasing percentage of US workers have caregiving responsibilities for children and elders. The purpose of this study was to test the hypothesis that employees whose managers are open and creative about work-family needs, such as flexibility with work hours and days off, will have lower cardiovascular risk and longer duration of sleep than their less supported counterparts.
Methods: Trained interviewers administered surveys to and collected physiologic assessments from 393 employees in four extended care facilities in Massachusetts. Interviews were conducted in English, Spanish, or Haitian Creole. Sleep duration was estimated by wrist actigraphy, and valid data defined as 24-hr recordings with <20 minutes of missing data due to watch off as inferred by visual inspection (mean number of valid days: 6.2; median: 7 days, range: 1-10 days). A Framingham-type cardiovascular disease (CVD) risk assessment used results from fresh or dried blood samples (total cholesterol >200, $HbA1_c \geq 6.0\%$), measured high blood pressure (triplicate mean systolic ≥ 140 mm Hg or diastolic ≥ 90 mm Hg), and self-report (BMI ≥30 kg/m^2, physician diagnosis of CVD, current smoking). Our exposure variable was a score quantifying managers' openness and creativity with respect to employee work-family balance. From independent, semi-structured interviews with managers, a qualitative analysis identified openness and creativity as the two key domains of managers' ability to promote work-family balance among their employees.
Results: Employees whose managers scored in the highest tertile for work-family score slept significantly longer, on average almost 30 minutes per day, than those whose managers were less open and creative. Among employees whose managers scored in the lowest tertile on the work-family balance score, 28.57% had 2 or more CVD risk factors, whereas only 18.49% of employees whose managers scored high did (p=0.02). Employees whose managers scored in the low or middle tertile had an OR of 2.11 (95% CI: 0.91-4.89) and 2.03 (95% CI: 1.02-4.02), respectively, of 2 or more CVD risk factors compared with employees whose managers had high scores on work-family balance. CVD risk was further elevated in employees providing direct patient care and with managers in the lowest tertile (OR=6.34; 95% CI: 1.39-28.83).
Conclusion: The findings suggest that managers' attitudes and practices may have an important effect on the health of employees, including sleep duration and cardiovascular disease risk.
Support (optional): NIA/NICHD grants for the Work, Family and Health Network

0409

RECOVERY PROCESS OF PERFORMANCE AFTER FOUR CONSECUTIVE NIGHTSHIFTS

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Introduction: Some strategies to help shift workers adapt to working at night have been proposed. Rotating shift workers, however, return to the diurnal type of life on their dayshifts and days off, experiencing the problems associated with re-adaptation such as disturbed sleep, elevated sleepiness, and poor productivity. The present simulation study examined the effects of consecutive nightshifts on re-adaptation to a dayshift schedule.
Methods: Ten healthy males (22.9 ± 3.2 yr) participated in the experiment. They were required to attend the laboratory for nine consecutive nights under the following conditions: Adaptation sleep (0:00-7:00), Dayshift-1 (10:00-18:00), and Baseline sleep (0:00-7:00), followed by four nightshifts (22:00-9:00) with subsequent daytime sleep (12:00-18:00), Recovery sleep-1 (0:00-7:00), day off (in lab), Recovery sleep-2 (0:00-7:00), Dayshift-2 (10:00-18:00), Recovery sleep-3 (0:00-7:00), and Dayshift-3 (10:00-18:00). We measured performance of a visual vigilance test (VVT), sleepiness on a visual analogue scale (VAS), and quality of sleep by Actiwatch (AW64). Two-way (Dayshift × Time-of-day) repeated-measures ANOVA was performed for performance and sleepiness data and one-way repeated-measures ANOVA for nighttime sleep data.

Results: VVT reaction times and lapses significantly increased after consecutive nightshifts (Main effect: $F2,18 = 7.16$, $p = 0.022$, and $F2,18 = 3.77$, $p = 0.049$, respectively), while VAS sleepiness improved (Interaction: $F14,126 = 2.86$, $p = 0.007$). Significant difference among 4 nighttime sleeps was observed in sleep efficiency ($F3,27 = 7.12$, $p = 0.026$). Particularly, sleep efficiency in Recovery sleep-1 was low (57.4±31.2%) compared to the other nighttime sleeps.
Conclusion: Our findings suggest that performance and subjective sleepiness might show different recovery process during dayshifts after consecutive nightshifts. It is considered that the dissociation found here might reflect an unstable state that participants can not realize a decline in their performance by themselves.
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0410

THE EFFECTS OF SLEEP DEPRIVATION INTO MICE SURVIVAL RATES INFECTED BY MURINE MALARIA

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Introduction: Sleep is an important physiological event that directly influences health and is related to immune system function. Previous studies with sleep-deprived animals reported decreased immune system responses to challenges with different pathogens. In this study, the immune system of mice was challenged by pathogen infection under sleep deprivation. Our aim is to evaluate the survival rates of sleep deprived animals submitted to different periods of recovery.
Methods: Our survival assay was performed with male Swiss mice (n = 20) subjected to 72 hours of sleep deprivation by multiple platform technique and allowed to sleep for 24 and 48 hours after the deprivation. After recovery periods, each group (recovery and controls; n=10 each) was inoculated intraperitoneally with $1x10^6$ *Plasmodium chabaudi* (murine malaria) infected erythrocytes. Blood was collected from the mice 7 days after infection by incision of the tail. Parasitemia was determined by GIEMSA staining and was examined by light microscopy under an oil-immersion objective at × 1000 magnification. Survival of the mice was followed over 20 days.
Results: The group which was allowed to sleep for 24 hours showed a significant reduction in survival ($P \leq 0.05$), indicating that immune response to infection is not restored by one day of sleep recovery. On the other hand, 48h of sleep recovery was sufficient to bring survival back to the level of the control group, as analyzed by the cumulative survival Kaplan-Meier curve and Log-Rank test.
Conclusion: Together these data are very interesting, as they showed the time required for restoring normal function of the immune system of sleep deprived mice and supported the previously described mechanism of the immunosuppressor effects of sleep loss.
Support (optional): FAPESP (CEPID 98/14303-3), CNPq and AFIP.

0411

LOW SERUM VITAMIN D CONCENTRATION AS A PREDICTOR OF SHORT SLEEP DURATION: A NHANES 2005-2006 ANALYSIS

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Introduction: The daily rhythmic melatonin production from the pineal gland is considered a vital process in the modulation of circadian rhythms. The suprachiastmatic nucleus which is the main input to the pineal gland is shown to be immunoreactive to Vitamin-D dependent calcium binding proteins(Calbindin-D9k, Calbindin-28K). We therefore hypothesized that low serum Vitamin-D would directly affect the synthesis of endogenous melatonin and in turn alter the sleep-wake cycle.
Methods: The National Health and Nutrition Examination Survey (NHANES) 2005-2006 is a cross-sectional multistage survey of the US civilian non-institutionalized population. Participants answered demographic, health, and sleep related questions and serum Vitamin-D levels were measured. The two sleep related questions; "How much sleep do you get (hours)?" and "How long does it take to fall asleep (minutes)?", were analyzed using multivariable logistic regression models, controlling for age, gender, race, overweight, arthritis, cancer, parathyroid levels, night-time leg jerks and daily consumption of milk.
Results: There were 3,028 participants (46% male) with a mean age of 50.1±18.7years who had complete data available. In a multivariate analysis, Vitamin-D level was found to be a significant predictor of sleeping <5 hours ($p<0.0005$). The participants were further categorized by serum vitamin-D quartiles (≤14 ng/ml; 15-20 ng/ml; 21-26 ng/ml; ≥27 ng/ml). Relative to the top three Vitamin-D quartiles, the lowest quartile was significantly more likely to sleep <5 hours (odds ratio [OR] 1.79 [95% Confidence Interval (CI) 1.25-2.57]). Lower Vitamin-D quartiles also showed a trend towards taking >30 minutes to fall asleep (OR 1.20 CI [0.87-1.65]).
Conclusion: Low serum Vitamin-D levels (≤14 ng/ml) are associated with an increased risk of sleeping <5 hours. Our results also show a trend towards difficulty in sleep onset in participants with lower Vitamin-D levels. The role of Vitamin-D in the reduction in total sleep time remains unclear.

0412

OBESITY RESISTANT RATS EXHIBIT INCREASED WAKEFULNESS AND CONSOLIDATED SLEEP COMPARED TO SPRAGUE-DAWLEY RATS

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Introduction: Recent studies provide evidence that obesity is associated with disordered sleep. However, sleep/wake states associated with obesity resistance are not known. Here we used the obesity resistant (OR) rats to study the sleep-obesity relationship, as these rats are obesity resistant despite high energy diet feeding. Earlier work from our laboratory has shown increased orexin sensitivity in the OR rat. The orexin system is implicated in the regulation of energy homeostasis as well as sleep/wake cycle. Thus, we hypothesize that OR rats might exhibit consolidated sleep and increased wakefulness, compared to Sprague-Dawley (SD) rats. Accordingly, the aim of this study was to examine the sleep/wake differences between OR and SD rats.
Methods: OR and SD rats of 3 months age (N = 6/group) were implanted with transmitters (Data Sciences International: TL11M2-F40-EET) for recording electro-myogram and electro-encephalogram via telemetry for sleep/wake analysis. Rats were habituated to a 12-h light-dark cycle in a chamber that allows free movement, followed by 24-h recordings of sleep/wakefulness cycle. Each 24-h recording was scored as rapid eye movement (REM) sleep, non-REM (NREM) sleep, or wakefulness, in 10 second epochs.
Results: The OR rats spent significantly more time in wakefulness ($P<0.001$) and less time in NREM sleep ($P<0.05$) compared to SD rats during the 24-h recording period. The OR rats also spent less time in REM sleep ($P<0.05$) during the dark period. Relative to SD rats, the OR rats showed significantly fewer number of sleep/wake episodes ($P<0.05$ for all three stages), and increased duration of these episodes ($P<0.05$), indicating less sleep fragmentation during the 24-h recording period.

Conclusion: These results are consistent with the hypothesis that obesity resistance is associated with increased wakefulness and consolidated sleep in OR rats. The present study also indicates that the OR rat is a promising animal model to study the neurobiological basis of the relationship between sleep quality and obesity.

0413

A PROSPECTIVE STUDY OF SLEEP DURATION AND PNEUMONIA RISK IN WOMEN

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Introduction: Experimental data suggest that the immune response to vaccination is impaired in the setting of acute sleep deprivation. However, it is unknown, whether chronic partial sleep deprivation is associated with an increased risk of infections. We sought to assess whether habitual sleep duration is related to incident cases of pneumonia using the Nurses Health Study II (NHS2) cohort.
Methods: We studied a cohort of 64,354 female nurses (ages 37 to 54 years old) who responded to a question on average sleep duration contained in the 2001 NHS2 questionnaire, had no prior history of pneumonia, and were free of cardiovascular disease, cancer, diabetes, and asthma. Questionnaires in which a new diagnosis of X-ray confirmed pneumonia was assessed were mailed every two years. Cox proportional hazards models were used to assess the relative risk for incident pneumonia over 4 years.
Results: The distribution of habitual sleep duration was 5.4%, 23.5%, 42.6%, 23.4%, and 5.0% for 5 or fewer, 6, 7, 8, and 9 or more hours respectively. A total of 1673 cases of pneumonia were identified over 263,596 person-years of follow up. Relative to 8 hour sleepers, the age-adjusted hazard ratio (HR) for pneumonia in those sleeping 5 hours or less was 1.49 [1.21-1.83]; 6 hours: 1.22 [1.06-1.41]; 7 hours: 1.09 [0.96-1.25]; and 9 or more hours: 1.44 [1.16-1.80]. After adjusting for smoking, alcohol use, body mass index, depression and snoring, the HRs were 1.32 [1.07-1.62], 1.16 [1.01-1.34], 1.10 [0.96-1.25], and 1.27 [1.02-1.59], respectively.
Conclusion: Reduced and prolonged habitual sleep durations were associated with greater risk of incident pneumonia. Further research is needed to understand how altered sleep habits can influence risk of serious infections.
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0414

POSTPARTUM PARENTS: GUILTY OF RESISTING A REST?

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Introduction: Although both postpartum mothers and fathers report disturbed sleep, little research has examined postpartum fathers' sleep. Additionally, the magnitude of postpartum parents' sleepiness has never been objectively indexed. The purpose of this study is to objectively describe sleep among postpartum fathers and to be the first to objectively index sleepiness among new mothers and fathers during the early postpartum period.
Methods: The current data are preliminary from an ongoing study. Four first-time postpartum mother and father dyads (N=8, 26.4 SD±4.3 years, 75% White, with 14.9 SD±3.4 years of education), all with no/low risk for sleep disorders, completed one continuous week of wrist actigraphy monitoring followed by a standard four-nap Multiple Sleep Latency Test (MSLT) when their infant was 5.3 (SD±1.3) weeks old. For each participant, descriptive statistics were calculated based on their averaged nightly actigraphy values and their averaged MSLT Sleep Onset Latencies (SOL).
Results: Postpartum mothers' average nocturnal sleep time was 7.85 (SD±1.8) hours; sleep efficiency was 78.5% (SD±9.1%). Postpartum mothers' average SOL was 5.6 (SD±4.3) minutes (Range: 2.8-12.0 minutes). Postpartum fathers' average nocturnal sleep time was 6.85 (SD±2.0) hours; sleep efficiency was 80.8% (SD±7.6%). Postpartum fathers' average SOL was 4.1 (SD±.5) minutes (Range: 3.6-4.8 minutes).
Conclusion: Although their total nocturnal sleep times and efficiencies were higher than expected, both postpartum mothers and fathers' MSLT scores indicate that they are experiencing potentially pathological sleepiness. These results should be considered in relation to the expectation that these new parents are responsible for the care of their infant, they drive vehicles, and they are expected to return to work to be productive members of society. Continued data collection is in progress, along with a comparison control group.
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0415

INSUFFICIENT SLEEP SYNDROME AMONG THE MIDDLE-AGE HONG KONG CHINESE

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Introduction: To investigate the insufficient sleep syndrome among the Middle-age Hong Kong Chinese, and evaluate the definition of insufficient sleep syndrome in international classification of sleep disorder - diagnostic and coding manual (ICSD-II).
Methods: Parents of students in 13 primary schools were recruited as our target sample, whose characteristics about sleep and socioeconomic were gathered. According to ICSD, we defined insufficient sleep syndrome by ratio of weekday night versus weekend night differences in time in bed (RTIBdiff) >20% and self-rating insufficient sleep in healthy sleepers. These healthy sleepers would be divided into four groups: subject with both criteria (Genuine Insufficient Sleeper, GIS), subject with RTIBdiff>20% (Objective Insufficient Sleeper, OIS), subject with self-rating insufficient sleep (Subjective Insufficient Sleeper, SIS), and subject without both criteria (Genuine Sufficient Sleeper, GSS).
Results: A total of 9788 subjects comprised noninstitutionalized Chinese middle-aged residents in Hong Kong, and 5362 (54.8%) subjects were healthy sleeper. They were divided into 1109 (20.7%) GIS, 769 (14.3%) OIS, 1058 (19.7%) SIS, and 2426 (45.3%) GSS. Compared to GSS and OIS, GIS and SIS expected longer sleep than their actual sleep, were more prone to complain daytime sleepiness, and had better socioeconomic status.
Conclusion: The prevalence of insufficient sleeper was much higher than other regions, which might due to the sleep habit in Asia. On the other hand, the definition of insufficient sleep syndrome in ICSD-II should be credible, so GSS did sleep sufficiently, and GIS did sleep insufficiently. Although OIS slept insufficiently in weekday, it could be compensated by prolonging his weekend sleep duration. We hypothesized that OIS might have adapted the life style in modern society and become a unique type of sufficient sleeper, while SIS should sleep insufficiently.

0416

BODY OVER MIND: PREDICTORS OF DAYTIME SLEEPINESS AMONG POSTPARTUM MOTHERS

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Introduction: Sleep disturbance and self-reported sleepiness are well documented among postpartum mothers. Yet postpartum women's

sleepiness and its specific associations with subjective/objective sleep measures are relatively unexplored. The purpose of this study was to examine whether a profile of subjective sleep reports or objective sleep recordings account for more variance in postpartum mothers' Epworth Sleepiness Scale (ESS) scores.
Methods: As part of a larger study, 54 postpartum mothers (28.1 [SD±5.0] years, 94.4% white, 16.4 [SD±2.7] years of education) participated during postpartum week 8. Within two hours of awakening each morning, participants used a hand-held computer to report the number of times they awoke during the night, the length of their nocturnal wake time, and their sleep quality (100-point scale). Corresponding objective nocturnal sleep measures (wake bouts, wake time, sleep efficiency, and total sleep time) were calculated from continuous nocturnal wrist actigraphy. Several times daily (3.03 [SE±.15]) participants completed the ESS (M=8.82, SE±.53). Stepwise linear regressions were used to examine ESS variance independently accounted for by either subjective or objective sleep measures.
Results: For the subjective measures, sleepiness was best predicted (R^2=.11, F[1,48]=5.8, p<0.05) by the single item sleep quality β=-.33. For the objective measures, sleepiness was best predicted (R^2=.24, F[2,45]=7.09, p<0.01) by actigraphically-measured sleep efficiency (β=-.39) and nocturnal sleep time (β=-.33). When all subjective and objective measures were entered into the model, sleepiness was predicted (R^2=.34, F[3,44]=7.56, p<0.001) by objective sleep efficiency (β=-.41), subjective sleep quality (β=-.32), and objective nocturnal sleep time (β=-.30).
Conclusion: Greater variance in daytime ESS scores among postpartum mothers is accounted for by objective rather than subjective sleep measures, which may indicate that how new mothers actually slept may have more of an impact on their daytime sleepiness than how they think they slept. Additionally, our results may indicate that new mothers' knowledge of their sleep disturbance is poor.
Support (optional): NIH Grant R21HD053836 (HMD).

0417

SHORT TOTAL SLEEP TIME IN 12-HOUR SHIFT NURSES: SLOW UNWINDING, CIRCADIAN DISRUPTION, OR TIME ALLOCATED TO SLEEP?

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Introduction: Short total sleep time (TST) (< 6 hours) is common in 12-hour shift nurses. Three plausible reasons may account for this. Extended exposure to stressful work may produce slow unwinding, with delayed sleep or poor sleep efficiency (SE). Night nurses' sleep can be disrupted if lights out time is delayed. Insufficient time between shifts may reduce sleep opportunity (shift overruns, parenting, little time allocated to sleep). The aim is to describe the association of job stress, delay to bed, and limited sleep opportunity on sleep. We hypothesized that (1) higher job stress would reduce TST and SE, (2) delaying lights out would increase waking after sleep onset (WASO) after night shift, (3) loss of sleep opportunity would modify the effect of time at home to total sleep time.
Methods: Registered nurses working consecutive 12-hour shifts were studied using accelerometry (TST, SE, WASO), diary (actual hours worked, commute time, home responsibilities), and job stress survey (job demands, satisfaction, performance barriers, frustration) post shift (N=73). Correlations were done to test hypotheses 1-2. Regression was used to test hypothesis 3.
Results: TST averaged 5.5 hours between 12-hour shifts. Correlation between job stress scales and TST/SE was low. Later lights out was associated with increased WASO. Shift overruns were common. Parents showed no relationship of time at home to TST, whereas those without children had longer TST with more time at home. Nurses with two jobs got less sleep with longer time at home.
Conclusion: 12-hour shift nurses have significant partial sleep deprivation. Stronger relationships exist between circadian disruption, lack of sleep opportunity, and achieved sleep between 12-hour shifts than between job stress and sleep. Interventions to improve sleep should focus on creating individual work schedules that allow sufficient time at home for restorative rest.
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0418

INDIVIDUAL DIFFERENCES IN RESPONSE TO SLEEP DEPRIVATION ON 3 DISTINCT COGNITIVE TASKS

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Introduction: Past studies on individual differences in response to sleep deprivation (SD) have suggested that individuals are not wholly vulnerable or resistant to the effects of SD but are differentially affected across cognitive domains. These studies, however, have tended to analyze groups of poor or good performers instead of characterizing each individual's performance. Our study was designed to examine the individual performance of 55 subjects on 3 distinct cognitive tasks to determine whether any individuals showed vulnerability or resilience across cognitive domains after sleep deprivation.
Methods: Fifty-five healthy adults completed Verbal Learning (verbal memory encoding and retrieval), N-Back (working memory maintenance and updating), and Go-NoGo (selective attention) after both 8-12 and 32-36 hours of wakefulness. Subjects were rank ordered based on percent change in performance after SD. We then identified any individuals ranked in the bottom quartile of performers or the top quartile of performers on all 3 tasks. We examined demographics (age, gender, years education), actigraphy (TST and SE), scores on intake questionnaires (ESS, PSQI, MEQ and NAART), and baseline task performance of anyone identified as consistently resilient or vulnerable to examine potential predictors of SD response.
Results: After 32-36 hours SD, 3 individuals were among the quartile with the greatest decline on all three tasks (3/55 "vulnerable") and 3 individuals consistently showed the least decline across all three tasks (3/55 "resilient"). While there were not sufficient numbers of vulnerable and resilient individuals for formal analyses, no obvious group differences in demographics, actigraphy, intake questionnaire scores or baseline task performance emerged.
Conclusion: Contrary to previously published studies, results here suggest some individuals may indeed be vulnerable or resilient to SD across cognitive domains. However, such individuals may make up <10% of the population. Larger studies are needed to test if these individuals show vulnerability/resiliency across a wider variety of cognitive domains and if any baseline characteristics can predict vulnerability/resiliency.
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0419

MAINTENANCE OF EFFICACY, SAFETY AND TOLERABILITY OF ARMODAFINIL: AN OPEN-LABEL EXTENSION STUDY

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Introduction: In previous placebo-controlled, double-blind studies, armodafinil (NUVIGIL®) was found to be generally well tolerated and to improve wakefulness, overall clinical condition, and fatigue in patients with excessive sleepiness associated with obstructive sleep apnea (OSA), shift work sleep disorder (SWD), or narcolepsy.
Methods: This multicenter, open-label, flexible-dose extension study from the previous double-blind armodafinil studies evaluated once daily armodafinil administration (100 to 250 mg) for 12 months followed by an open-ended extension period. For patients with SWD, armodafinil was taken only on nights worked. The primary objective of the study was to evaluate safety and tolerability. Secondary measures of efficacy were, for all patients, the Clinical Global Impression of Change (CGI-C) and the Brief Fatigue Inventory (BFI), and, for patients with OSA or narcolepsy, the Epworth Sleepiness Scale (ESS).
Results: A total of 743 patients (age 18-69 years) enrolled in this study: 474 patients with OSA, 113 patients with SWD, and 156 patients with narcolepsy. Armodafinil was generally well tolerated. Adverse events were mild-moderate, with the most frequently reported being headache (25%), nasopharyngitis (17%), and insomnia (14%). Armodafinil improved patients' overall clinical condition, as evaluated by CGI-C: 80% for OSA (95% CI, 76.0, 83.3), 92% for SWD (95% CI, 87.3, 97.5) and 75% for narcolepsy (95% CI, 68.4, 82.2). Armodafinil improved global BFI scores and BFI worst fatigue scores. Armodafinil improved wakefulness, as measured by ESS for patients with OSA and narcolepsy.
Conclusion: Armodafinil was generally well tolerated. Armodafinil maintained, for 12 months or more, improvements seen in the previous double-blind studies in patients' overall clinical condition, patient's fatigue, and excessive sleepiness (in patients with OSA or narcolepsy). The safety and tolerability profile for armodafinil appeared similar to that reported in the previous double-blind studies.
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0420

OLDER ADULTS ARE LESS VULNERABLE TO SLEEP DEPRIVATION THAN YOUNGER ADULTS DURING COGNITIVE PERFORMANCE

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Introduction: Previous research has shown that younger adults exhibit greater decline in performance after total sleep deprivation (TSD) than older adults. Most of these studies have focused on a single cognitive task. Here, we compare the performance of older and younger adults on 3 distinct cognitive tasks before and after sleep deprivation.
Methods: Older adults (OA: n=33) and younger adults (YA: n=27) completed the NBack, Go-NoGo, and Verbal Learning (VL) tasks after 12 and 36 hours of wakefulness. Group (older vs. younger) by night (well rested vs. TSD) ANOVAs were conducted to examine performance on each task (NBack: 1- and 3-back accuracy, Go-NoGo: d-prime, VL: immediate free recall, delayed recognition). Interactions were followed-up with t-test examining the Night effect in each Group.
Results: Significant interactions were found for VL recognition (p=.001) and NoGo d-prime (p=.034), with a marginally significant interaction for 3-back (p=.053). For all three tasks, YA significantly declined during TSD while OA did not change significantly. For NoGo, both groups showed more inhibition errors during TSD, but only YA showed reduced hits. VL recall showed a significant effect of Night (worse performance after TSD).
Conclusion: OA showed more resiliency to TSD than YA on a range of measures of cognitive performance, including working memory (NBack), selective attention/inhibition (Go-NoGo), and verbal encoding/retrieval (VL). VL data suggest YA show an encoding deficit with TSD while OA show a retrieval deficit. NoGo data argue both groups are vulnerable to disinhibition during TSD, but YA additionally show selective attention deficits. N-back data suggest OA can maintain working memory performance despite TSD, while YA cannot (potentially due to selective attention deficits). Overall, variability in OA was much greater after TSD than in YA. Future research should explore the source of this apparently greater level of inter-individual differences in OAs' response to sleep loss.
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0421

EFFECTS OF SLEEP DEPRIVATION ON ACTUAL AND ESTIMATED PERFORMANCE ON COMPLEX COGNITIVE TASKS

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Introduction: Research indicates that sleep deprivation negatively affects performance; however, little research has investigated performance and self-assessed performance on complex cognitive tasks. The purpose of the current study was to determine the effects of short-term sleep deprivation on performance and self-assessed performance on complex mathematical and spatial processing tasks.
Methods: Twenty-three college students (15 male, 8 female) took part in an acute one-night sleep deprivation study. The participants completed a wide range of tasks during an 18-hour sustained work period from 6 PM on day 1 to noon on Day 2. Each task was completed once during each of four testing sessions. The tasks used in the current study included the quantitative portion of the Gradate Record Exam and the spatial portion of the Dental Admissions Test. After each task, the participants completed a meta-cognition survey to rate the accuracy of their answers. Different versions of the GRE and DAT were administered during each testing session.
Results: A 2x4 ANOVA was completed to compare actual and estimated performance on each task across the four testing sessions. There was no significant difference across testing sessions on either the actual or estimated performance on the GRE Quantitative task; however, the participants significantly over-estimated their performance (p<.001). There was a significant decrease in actual performance on the DAT Spatial task (p=.014) but there was no change in estimated performance on the DAT across the testing sessions. The participants also significantly over-estimated their performance on the DAT (p<.001).
Conclusion: The current results indicate that sleep deprived persons over-estimate their performance levels and do not always accurately recognize a decrease in performance across the night. These findings suggest that persons who are sleep deprived should be cautious when trusting their self-assessment of performance on complex cognitive tasks.
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0422

THE EFFECT OF SLEEP DISTURBANCES ON METABOLISM IN RATS

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Introduction: An increasing number of epidemiological studies show a correlation between short sleep duration and an increased risk for obesity and type 2 diabetes. However, it is unclear whether insufficient sleep plays a causal role in these relationships and, if so, what the underlying mechanisms might be. In this context, we applied an animal model of chronic sleep restriction to investigate the metabolic consequences and mechanisms of sleep restriction in a controlled laboratory setting.
Methods: Rats were equipped with a jugular vein cannula to allow stress free blood sampling. Ten days after surgery, the animals were subjected to a schedule of restricted sleep allowing them 4h of sleep per day for 8 days (SR). Sleep deprivation was achieved by placing the animals in slowly rotating drums. A forced activity group served as control (FA). These animals walked at twice the speed for half the time, allowing them 14h of sleep per day. Body weight and food intake were measured daily. Intravenous glucose tolerance tests (IVGTT) were performed at baseline, after 8d of sleep restriction, and after 5d of recovery. Blood samples were collected for hormone assays.
Results: Eight days of sleep restriction led to a reduction in body weight, while food intake was increased and remained increased during the recovery period. Furthermore, SR led to decreased leptin levels and anhedonia. Both SR and FA showed decreased baseline glucose and insulin levels. This was accompanied by elevated glucose and reduced insulin profiles during the IVGTT.
Conclusion: Eight days of sleep restriction leads to marked alterations in energy metabolism in rats. These changes are comparable to what has been reported for humans and are associated with an increased risk for obesity and type 2 diabetes.

0423

HOMEOSTATIC AND CIRCADIAN CONTRIBUTION TO CHANGES IN PER2 PROTEIN IN WHOLE LIVING MICE

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Introduction: Sleep is regulated by a homeostatic and a circadian process. Both processes are thought to act independently. We have shown, however, that expression of circadian clock genes, in particular Period 2 (Per2), increases during waking and decreases during sleep. Here, we investigate the dynamics of PER2 protein levels as a function of time-of-day and as a function of time-spent-awake in Per2: Luciferase knock-in (Per2Luc) mice.
Methods: Brain mRNA levels for several circadian and 'homeostatic' genes were measured by qPCR in sleep-deprived (6h SD starting at ZT0, -6, -12, or -18) and time-matched C57BL/6J controls. PER2 protein levels were measured in brain, liver, and kidney of Per2Luc mice using a bioluminescence imaging system (Xenogen). PER2 changes were verified by Western analysis. Diurnal changes in PER2 were sampled at 3h intervals. Sleep-wake dependent changes after a 6h SD and after 2h of recovery sleep.
Results: Expression of the activity-induced Homer1a gene and the circadian Per2 gene both followed the diurnal sleep-wake distribution in control conditions. Homer1a expression was high and no longer varied with time-of-day in the SD group. Per2 expression also increased with SD but remained rhythmic due to a time-of-day modulation of the SD-induced increase. PER2 protein equally varied with time-of-day in brain, liver, and kidney. SD increased PER2 protein in all three tissues albeit with different dynamics.
Conclusion: We show that PER2 protein can be followed around the clock in the whole living mice. As mRNA also PER2 protein increased with sleep loss, supporting a role for Per2 in the homeostatic regulation of sleep.
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0424

SLEEP DEPRIVATION AFFECTS LEARNING STRATEGY AND MEMORY FLEXIBILITY

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Introduction: Distinct cognitive strategies can be used for place learning. Spatial strategies rely on the hippocampus, whereas response strategies involve the dorsal striatum. These memory systems can compensate for each other in case of damage. Sleep deprivation (SD) has adverse effects on hippocampal function. However, no studies have determined whether the striatal system can compensate for SD-induced hippocampal impairments. In this study, we examined whether SD affects learning the location of a food reward (training), and learning that a previously non-rewarded location was now rewarded (reversal training).
Methods: Male C57BL mice were trained in a symmetrical T or Y maze. One group served as control and another group was sleep-deprived for 5h immediately after each daily training and/or reversal training session. A home cage control group was added to examine learning strategy specific increases in phosphorylation of cAMP response- element binding protein (CREB), a transcription factor involved in memory formation.
Results: Five hours of SD after each training session did not affect performance during training. However, in contrast to controls, sleep-deprived mice avoided to use a spatial strategy and preferably used a response strategy. In line with this, SD reduced the normal training-induced increases in hippocampal phosphorylation of CREB but enhanced CREB-phosphorylation in the dorsal striatum. Importantly, while sleep-deprived mice performed well during training, performance during reversal training was significantly attenuated. The latter may be a consequence of the known rigidity of the striatal response-based memory system.
Conclusion: These data suggest that the brain may compensate for the negative effects of SD on the spatial memory system by promoting the use of a response memory system. However, effects of SD may still appear later, long after the actual sleep loss, because using the more rigid striatal memory system may result in reduced flexibility under conditions requiring adaptations of existing memories.

0425

EFFECT OF CHRONIC SLEEP RESTRICTION ON RAT PERFORMANCE IN INHIBITORY AVOIDANCE TASK

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Introduction: There are numerous studies suggesting that sleep deprivation induce deleterious effects in the rat performance on memory tasks. However, there are but a few studies on the effects of experimental chronic sleep restriction (CSR) on those tasks. The mechanisms underlying learning and memory deficits following sleep loss are not understood at present. One of the aspects that have been neglected is the role of circadian rhythms. Recently, we observed that rats submitted to a protocol of CSR in which the animals were sleep-deprived for 18h/day

and allowed to sleep (sleep opportunity - SO) for 6h in the light phase, during 21 consecutive days, showed no deficits on memory. Here, we investigated the possibility that CSR would impair the performance on the inhibitory avoidance (IA) task when rats are allowed to sleep in different circadian phases.
Methods: Rats were deprived of sleep using the platform method. Three experiments were held: experiment 1: 6h of SO (light and dark phase) and 18h of sleep restriction for 21 days; experiment 2: 4h of SO (light and dark phase) and 20h of sleep restriction for 14 days and experiment 3: 3 h of SO (light phase) and 21h of sleep restriction for 14 days. At the end of the SO for each experiment, the animals were trained and tested in a step-through IA task. One hour after training, the animals were given a retention test.
Results: Neither 6h SO (light and dark phase) nor 4h SO (light phase) induced impairment on inhibitory avoidance on test session. However, 4h SO (dark phase) and 3h SO (light phase) impaired acquisition/retention in rats on test session.
Conclusion: These results suggest chronic sleep restriction impairs memory, and this is related of sleep opportunity duration and disrupted coincidence between circadian and homeostatic drivers to sleep.
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0426

PATTERN OF SLEEP LOSS USING ACTIGRAPHY OVER FOURTEEN DAYS IN POLICE OFFICERS DOING 12-HOUR ROTATING SHIFTS

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Introduction: The Calgary Police Service Health and Human Performance Research Initiative Phase II, is a pilot study designed to objectively monitor sleep/wake cycles during 12-hour rotating shifts for the purpose of determining critical fatigue factors and to develop fatigue countermeasure strategies.
Methods: Subjects (N=9)were monitored over 14 days of a 12-hour shift rotation (D/D/D/N/N/O/O/O/O/D/D/N/N). Data was collected using Proportional Integrating Measures with actigraphy sensitivity. 01 G at 2.5 Hz, epoch length of 60 seconds, sampling rate 10 Hz. Sleep/wake was manually scored combining University of California San Diego (UCSD) algorithm, sleep log and event marker information. Total sleep time is defined as the number of epochs scored as sleep within 24 hours (06:00-06:00).
Results: Actigraphy data was analyzed for patterns of cumulative sleep loss and sustained wakefulness. Over 14 days of 12-hour rotating shifts, two periods of extended wakefulness (>18 hours, equivalent to BAC of 0.05%) were observed when officers transitioned from dayshift to nightshift. This transition is characterized by termination of nighttime sleep between 05:28-09:24, on average 103.9 minutes of daytime sleep/nap, a 12-hour nightshift and sleep onset between 05:12-10:49. Over 14 days it is estimated that there is an accumulation of 13.66 hours of sleep debt, based on an average sleep requirement of 7.5 hours per day.
Conclusion: This pilot field study reveals a pattern of extended hours of wakefulness specifically associated with the transition from dayshift to nightshift and that officers accumulate approximately 13-14 hours of sleep debt over 14 days. Larger cohorts need to be studied over the full shift rotation to confirm the results. Fatigue countermeasures such as strategic use of caffeine and prophlactic naps are recommended during the transition and sleep recovery strategies need to be developed.
Support (optional): The Calgary Police Service, City of Calgary, Calgary, Alberta, Canada The Centre for Sleep and Human Performance, Calgary, Alberta, Canada

0427

RECOVERY OF SLEEPINESS AND FATIGUE FOLLOWING SUSTAINED SLEEP RESTRICTION

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Introduction: Although a central issue in work-rest scheduling, little is known about the extent to which people recover from a period of sleep restriction. This study sought to explore the extent to which objective and subjective measures of daytime sleepiness returned to normal baseline levels after 1 and 2 nights of recovery sleep following 5 nights of sustained sleep restriction to 4h time in bed (TIB) per night.
Methods: N=27 healthy adults participated in a controlled laboratory experiment. N=18 (M=28.6yr, 8f) were randomized to 2 nights of baseline sleep (TIB=10h) followed by 5 nights of sleep restriction (TIB=4h) and two randomized nights of 8 or 10h TIB recovery sleep (R1, R2). N=13 subjects completed a modified MWT but all 27 subjects completed the Karolinska Sleepiness Scales (KSS), and Profile of Mood States (fatigue subscale = POMSf) on the day after B2, after 5 nights of sleep restriction, and again after R1 and R2. N=9 subjects (M=27.2yr, 6f) of the 27 served as controls who had 10h TIB per night for all 9 nights of the protocol.
Results: Sleep-restricted subjects had KSS scores that increased with sleep restriction ($p<0.001$), then declined on R1 and R2, which did not differ from each other. On both recovery days these scores were significantly above baseline KSS scores (R1 $p=0.02$, R2 $p=0.01$), but not different from control group KSS scores. POMSf increased with sleep restriction ($p=0.007$) and showed a slightly different pattern than KSS in that it was different from baseline at R1 ($p=0.03$) but not at R2 ($p=0.11$). MWT latency at R1 and R2 were not statistically different from baseline latency, but were below the MWT values of the control group (R1 $p=0.054$; R2 $p=0.004$).
Conclusion: One night of recovery sleep limited to 8-10h TIB may not be adequate to normalize sleepiness following 5 nights of sleep restriction.
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0428

DIGIT SPAN PERFORMANCE IN RELATION TO EXECUTIVE FUNCTION RESPONSES TO SUSTAINED SLEEP RESTRICTION

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Introduction: There is uncertainty whether the cognitive effects of sleep restriction (SR) reflect a common or idiosyncratic neurocognitive effect(s). This study sought to address this issue by determining if deficits in working memory capacity induced by SR were correlated with performance on executive function (EF) tasks.
Methods: N=141 healthy adults (29.6 ± 6.7y; 70 females) completed 2 baseline nights (10h TIB/night), followed by 5 nights of SR (4h TIB/night) in a laboratory setting. Digit Span task (DS) forward and backward versions were administered daily every 2h along with other measures. DS total number correct on SR day 5 was the outcome measure. EF tests administered on SR day 5 included: Tower of London (TOL, planning ability), Controlled Oral Word Association Test (COWAT, word production speed), and the Hayling (inhibition) and Brixton (spatial ability) tests. Spearman's rho was used to quantify the relationships on SR5 between DS scores and EF outcomes.
Results: Lower DS scores on SR5 (i.e., a greater effect of SR on working memory performance) were significantly related to lower COWAT word production scores on SR5 ($rho=0.405$, $p<0.001$). Similarly, lower DS scores were associated with fewer correct responses on the TOL ($rho=0.272$, $p=0.001$), as well as more TOL moves ($rho=-0.298$,

p<0.001) and slower TOL execution times (rho=−0.230, p=0.006). Other TOL measures, including time and rule violations, were not significantly related to DS (rho= 0.039-0.158). DS performance was also unrelated to Hayling (rho=0.123, p=0.154) and Brixton (rho=0.119, p=0.160) scaled scores.
Conclusion: Better working memory capacity during sustained sleep restriction was associated with better word fluency and planning abilities as markers of executive function, but unrelated to aspects of rule violation, response inhibition and spatial ability. This finding indicates that sleep restriction has a common effect on aspects of cognitive function involving working memory.
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0429

THE ROLE OF NON-REM SLEEP STAGES 1 AND 2 IN NEUROBEHAVIORAL RESPONSE TO SUSTAINED SLEEP RESTRICTION

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Introduction: We investigated the accumulation of neurobehavioral deficits resulting from daily restricted time in bed (TIB), as a function of deficits in slow wave sleep (SWS), REM, and stages 1 and 2 (S1&2), during 10 days of chronic sleep restriction. We examined if removing S1&2 from a model that included SWS, REM and S1&2 as separate independent variables resulted in a model that was significantly less predictive of performance impairment across days of sleep restriction.
Methods: N=90 healthy adults (aged 21-49y; 39 females) participated in a 10-day sleep restriction protocol involving polysomnographic sleep recordings and measurements of neurobehavioral performance every 2 hours during wakefulness. Models using the cumulative difference between daily sleep durations (i.e., SWS, REM, and S1&2) and the estimated amount of sleep needed to preserve waking function across days were fitted to Psychomotor Vigilance Test (PVT) scores (i.e., change in number of lapses).
Results: The build-up of impairment (i.e., increasing PVT lapses) resulting from sleep restriction was adequately described by a combination of SWS, REM and S1&2 as separate independent variables, with greater restriction of these components of sleep resulting in more PVT lapses (67.2% variance explained). Removing the S1&2 independent variable resulted in a significant loss of information in the model ($\chi 2[1]=18.0$, p<0.001).
Conclusion: In a 10-day laboratory study of chronic sleep restriction, reduced amounts of stage 1 and 2 sleep were associated with greater accumulation of PVT lapses across days. Since stage 2 sleep accounted for the vast majority of S1&2, it is likely responsible for this finding. This suggests that stage 2 sleep, which is often de-emphasized relative to sleep benefits, may be an essential contributor to the maintenance of waking neurobehavioral functions, although this contribution cannot be easily separated from the relationship of S1&2 to total sleep time.
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0430

THE EFFECTS OF SUSTAINED SLEEP RESTRICTION ON SUBJECTIVE SLEEPINESS BEFORE AND AFTER COGNITIVE WORK

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Introduction: Limited data suggests that cognitive work can exacerbate subjective sleepiness during acute total sleep deprivation. We sought to determine if this phenomenon was observed during chronic partial sleep deprivation.
Methods: N = 146 healthy adults (29.9±6.8y; 75 females) participated in a controlled laboratory experiment. N=128 underwent 2 baseline nights (10h TIB/night, 10pm-8am), followed by 5 sleep-restriction nights (4h TIB/night, 4am-8am). N= 18 served as a 10h TIB/night control group. Each day, every 2h from 08:00 to 20:00 subjects completed a 30-min cognitive work bout that included tests known to be sensitive to sleep loss (Digit-Span [3m], DSST [3m], PVT [10m], Visual Search and Tracking Task [3m], N-back [3m], POMS [4m], Symptom Checklist [4m]). The Stanford Sleepiness Scale (SSS) was completed immediately before and after each cognitive work bout. Daily averages were computed for SSS ratings before (pre) and after (post) each cognitive work bout.
Results: A three-way repeated measures ANOVA was conducted on pre-work and post-work SSS scores comparing the sleep restricted and control groups across protocol days. Cognitive work increased SSS scores (main effect, p<0.0001), but did so more for sleep-restricted subjects (2-way interaction, p<0.0001), especially as sleep-restriction continued across days (3-way interaction, p<0.006, Huynh-Feldt).
Conclusion: Cognitive work increased subjective sleepiness during chronic partial sleep restriction. This finding is consistent with studies showing that cognitive work increases sleepiness after total sleep deprivation. Taken together, these results suggest that elevated sleep homeostatic drive interacts with cognitive work demands and the latter potentiate sleepiness. It remains to be determined how specific these effects are for sleepiness relative to the overlapping concepts of fatigue, tiredness, mental exhaustion, and effort. There is also a need to determine whether the magnitude of change in subjective sleepiness produced by cognitive work during sleep loss is correlated with the degree of objective sleepiness and actual cognitive performance.
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0431

AGE DIFFERENCES IN NEURAL ACTIVATION ON A WORKING MEMORY TASK FOLLOWING TOTAL SLEEP DEPRIVATION

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Introduction: Working memory is a temporary storage system for the maintenance and manipulation of information. Older adults (OA) show a failure to activate task-related neural areas as working memory demands increase. The dorsolateral prefrontal cortex (DLPFC) is important in maintaining performance as working memory is taxed. We examined the neural and behavioral changes on an n-back task in OA compared to younger adults (YA) following total sleep deprivation (TSD), specifically focusing on changes in the DLPFC with increasing demands.
Methods: Twenty-three older (age=67.0±5.5yrs) and 23 younger (age=28.3±5.3yrs) subjects performed an n-back task during FMRI after 36 hours TSD. A group (OA vs. YA) by load (1-back vs. 2-back vs.

3-back) ANOVA was conducted in a priori DLPFC regions to determine activation following TSD, as well as on behavioral performance.
Results: Clusters of activation in the DLPFC associated with group-by-load interaction included right Brodmann's Area (BA) 10/9/46, right BA9/46, and left BA9. For both right DLPFC clusters, both groups had similar activation on 1-back and 2-back, but YA showed greater activation than OA on 3-back. For left DLPFC, OA showed greater activation than YA on both 2 and 3-back. Behaviorally, a significant group-by-load interaction was found, with OA showing steeper decline in performance from 1 to 2-back. There was also a main effect of load with decreased performance with increasing task demands in both groups.
Conclusion: Both groups showed increased activation in DLPFC during TSD in response to increased task demands, but recruited different hemispheres to cope with such demands. Behaviorally, sleep deprived OA showed performance decrements secondary to increased task demands earlier than YA, but performed comparably to YA at the hardest condition. Thus, YA may have utilized a more effective neural system than OA after TSD. These findings suggest the cerebral response to increased working memory task demands during TSD varying across age.
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0432

NREM SLOW WAVE ENERGY INCREASES WHEN SLEEP IS RESTRICTED TO 4 HOURS FOR 5 NIGHTS

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Introduction: It is well established that total sleep deprivation results in elevated homeostatic sleep drive as reflected in NREM slow wave energy (SWE). However, it is uncertain whether chronic sleep restriction (SR) results in increased homeostatic sleep drive. We investigated this question using data from an experiment on recovery from sustained SR.
Methods: N=141 healthy adults (31±7y, 69f) underwent baseline sleep (B2: 10h TIB) followed by 5 nights of sleep restriction (SR1-5; 4h TIB). A control group of 17 subjects (31±7y, 9f) underwent 10h TIB every night. PSG was recorded at B2, SR1 and SR5, and NREM SWE was calculated (0.5-4.5Hz from C3 derivation sampled at 128Hz in 5 second bins using FFT after EEG artifact removal). Total SWE was calculated for each 30sec NREM epochs and summed within each night (total SWE); data were then normalized as a percent of baseline (%B2 SWE).
Results: In the sleep-restricted group, SWE at SR1 averaged 64% of B2, and at SR5 SWE averaged 77% of B2. The relative increase in SWE from SR1 to SR5 averaged 13% ($P<0.001$). The control group (10h TIB) averaged 108% SWE of B2 at both SR1 and SR5. SWE was significantly less in the sleep-restricted group relative to the control group at both SR1 ($p<0.001$) and SR5 ($p=0.001$).
Conclusion: Sleep restricted to 4h TIB for 5 nights showed reliable evidence of increased homeostatic drive as measured by NREM slow wave energy—the putative marker of sleep homeostasis. However, SWE deficits on sleep-restricted nights remained below baseline and below SWE from controls (10h TIB). Thus, although SWE showed a clear homeostatic response to sustained nights of 4h sleep restriction, the response was inadequate to normalize SWE. It remains unresolved what limits the SWE response to sleep restriction, and to what extent the response affords protection from further sleep restriction.
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0433

EFFECTS OF SLEEP RESTRICTION ON MORNING ADIPONECTIN LEVELS IN HEALTHY ADULTS

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Introduction: Adiponectin is an anti-inflammatory hormone produced by adipocytes that is thought to play a role in insulin sensitivity in humans. Despite increasing evidence that both obesity and insulin resistance are associated with short sleep durations, no previous studies have examined the effect of sleep restriction on adiponectin levels.
Methods: Eight-five healthy adults (ages 22-45; 28 Caucasian, 57 African-American) underwent two nights of baseline sleep (10 time in bed [TIB]) followed by either five nights of partial sleep restriction (4 hours TIB, N=78) or control sleep (10h TIB, N=7). Blood samples were collected by venipuncture between 0900-1100 in the morning following the second night of baseline sleep and the fifth night of sleep restriction or control sleep. Adiponectin levels were quantified using a standard immunoassay.
Results: Morning adiponectin levels did not change significantly in either the sleep restriction or control group (p-values >0.25). Within the sleep restriction group, there were significant differences in adiponectin levels at baseline between sexes (women had higher adiponectin levels; $Z=-4.97$, $p<.001$), but there were no ethnic differences. Caucasian participants showed a decrease in adiponectin levels following sleep restriction ($Z=-2.06$, $p=.04$), while African-American participants showed an increase ($Z=-3.06$, $p=.002$). These ethnic differences were confined to women, however. Caucasian females had a significant decrease in adiponectin levels in response to sleep restriction ($Z=-2.19$, $p=.028$), while African American females had a significant increase ($Z=-2.73$, $p=.006$). No significant changes in adiponectin were observed for male participants of either ethnicity. Body mass index (BMI) was not correlated with adiponectin levels at baseline within gender/ethnic groups (p-values >.12)
Conclusion: Sleep restriction affected morning adiponectin levels in otherwise healthy women more so than men. Caucasian women, in particular, may be at greater risk for decreased adiponectin in response to sleep curtailment.
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0434

INCREASES IN DELTA AND SIGMA POWER FROM BASELINE TO RECOVERY SLEEP PREDICT INHIBITORY PERFORMANCE RECOVERY AND CONCOMITANT ACTIVATION CHANGES WITHIN PREFRONTAL CORTEX

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Introduction: How the physiology of recovery sleep facilitates performance recovery remains unclear. In the current study, spectral analysis of electroencephalography (EEG) data during sleep was used to examine how changes in sleep physiology from normal sleep (NS) to recovery sleep (RS) were associated with next day brain activity during functional magnetic resonance imaging (fMRI) and performance following NS and RS.
Methods: Nine young (26.0±3.6 years) subjects underwent fMRI scanning at 3T while performing a go/no-go task after 9 hours of NS and after 10 hours of RS following 38 hours awake. Condition order was counterbalanced. Spectral analysis of sleep EEG data was performed in the delta and sigma frequency bands (bands of slow waves and spindles respectively). A multiple regression model was used to examine the re-

lationship between percentage change in spectral data, activation change within right prefrontal regions of interest, and change in the percent of trials successfully inhibited.
Results: Bigger increases in delta and smaller increases in sigma power from NS to SR predicted a smaller inhibitory performance difference (delta, B=-0.101, r^2=0.575, p=0.018; sigma, B=0.434, r^2=0.727, p=0.003). Delta and sigma change predicted 90% of the inhibitory performance variance (r^2=0.901, p=0.001). When prefrontal activation was included in the regression model, delta power was not significant (p=0.818), and sigma and prefrontal effects remained significant (p=0.024 and p=0.040 respectively). Prefrontal activation mediated effects of delta and partially mediated effects of sigma on inhibitory performance (Sobel tests: p=0.002 and p=0.03 respectively).
Conclusion: Changes in prefrontal activation mediated the effects of delta rebound and partially mediated the effects of sigma rebound on performance recovery. Therefore, slow waves may act to restore prefrontal function to facilitate inhibitory performance recovery, while spindles may affect performance through action on additional neural systems.
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0435

MEMORY PERFORMANCE DURING SLEEP RESTRICTION WITH AND WITHOUT PHARMACOLOGICALLY ENHANCED SLOW WAVE SLEEP

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Introduction: Evidence suggests that sleep facilitates memory consolidation, and certain sleep states appear to preferentially facilitate the consolidation of certain types of memory. We examined performance on two memory tasks during a period of sleep restriction to determine: 1) the effect of sleep restriction on encoding and 2) the effect of a 3-hour sleep period, with or without pharmacologically enhanced SWS, on sleep-dependent memory consolidation.
Methods: Following screening and baseline (Day 2) assessments, subjects underwent two consecutive nights without sleep, each followed by a 3-hour daytime (0800-1100) sleep opportunity (Days 3 and 4) with either sodium oxybate 3.5g (SO; n=30; mean age: 27.1) or placebo (PBO; n=28; mean age 27.1). Training and an initial test to measure encoding were conducted on Day 2 at 0830 and on Days 3 and 4 at 0700 (prior to drug administration and sleep) for a declarative word pair task (WPT) and a nondeclarative finger-tapping task (FTT). Retest occurred 5 hours later.
Results: During daytime sleep, the SO group had more SWS (p<0.001), while the PBO group had more REM (p<0.001). Encoding was decreased by sleep loss, compared to baseline (p<0.031 for WPT, p<0.003 for FTT). There were no differences in improvement from encoding to retest between groups on Days 3 and 4 for either task. However, improvement on the FTT was greater for Days 3 and 4, compared to Day 2 (without intervening sleep) in the PBO group (PBO: Day 2=1.4±2.35, Day 3=4.1±3.71, Day 4=3.8±3.45, p<0.01 for both; SO: Day 2=2.9±2.54, Day 3=3.1±3.69, Day 4=2.7±2.97). WPT improvement was similar on all days for both groups (PBO: Day 2=4.5±3.56, Day 3=4.4±5.07, Day 4=4.0±3.91; SO: Day 2=3.9±4.68, Day 3=4.6±3.82, Day 4=3.2±3.66).
Conclusion: Sleep loss impaired encoding on both tasks. A 3-hour sleep period following sleep loss appears to be insufficient to improve memory consolidation for a declarative memory task, even with SWS enhancement. However, 3 hours of sleep following sleep loss appear to facilitate nondeclarative memory consolidation (in the absence of slow wave sleep enhancement), perhaps because of relatively more REM sleep.
Support (optional): Jazz Pharmaceuticals

0436

HOMEOSTATIC AND CIRCADIAN PROCESSES CONTRIBUTE JOINTLY TO THE MAGNITUDE OF SYSTEMATIC INDIVIDUAL DIFFERENCES IN PERFORMANCE IMPAIRMENT DURING SLEEP DEPRIVATION

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Introduction: Studies of trait individual differences in cognitive impairment during sleep deprivation have focused primarily on performance averaged over the circadian cycle, leaving homeostatic and circadian processes intertwined. Here we use mathematical modeling to 1) separate systematic individual differences from noise and 2) examine the contributions of the two processes to the magnitude of individual differences in vulnerability to sleep deprivation.
Methods: As part of a larger laboratory study, 12 healthy young adults (aged 22-37y; 5 females) were sleep-deprived for 62h following two baseline nights (10h TIB each). Performance on a 10-minute psychomotor vigilance test (PVT) was assessed at 2h intervals through most of the sleep deprivation period. Using a standard two stage approach for quantifying individual differences, each subject's time series of PVT lapses (RT>500ms) was fitted with the two-process model of sleep regulation using a linear combination of the homeostatic and circadian equations. The mean and standard deviation over subjects of modeled performance were computed for each measurement time. The standard deviation served as an index of the magnitude of systematic individual differences for each time point.
Results: Across time points, the correlation of the magnitude of individual differences with mean modeled homeostatic pressure was 0.92, while the correlation with mean modeled circadian rhythm was 0.26. The correlation with mean modeled performance was 0.99, exceeding the correlation with either homeostatic pressure or circadian rhythm alone. The correlation of individual differences with mean performance over subjects was still high (0.934) when using mean raw instead of modeled performance, indicating that the modeling results represented the data adequately.
Conclusion: Although individual differences in circadian and homeostatic processes may contribute independently to individual differences in performance impairment during sleep deprivation, the findings suggest that the magnitude of individual differences is predominantly determined by a single performance-degrading force in which the homeostatic and circadian processes are combined.
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0437

SLEEP IMPACT ON MEDICAL RESIDENTS BASED ON PGY LEVEL

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Introduction: Sleep deprivation among medical residents may decrease cognitive performance, impairs decision making and affects patient care. Effects of sleep loss include motor vehicle accidents, depression and somatic complaints. Resident duty hour regulations developed by the ACGME have been regulated and put into effect. We wanted to measure whether these regulations make a difference in sleep quality and whether the year of residency has an impact.
Methods: Twenty medical residents in each year of training were assessed for sleepiness with Stanford Sleepiness Scale (SSS) and the Epworth Sleepiness Scale (ESS). They were also asked about the rotations where they felt well rested and the rotations they felt overworked and

excessively sleepy. They were also inquired about the average Total sleep time during the last six months.
Results: 55% of first year, 25% of second year and 35% of the third year medical residents rated themselves as excessive sleepy based on ESS score > 10 and had mean ESS scores of 11.1+ 4.8 SD (standard deviation), 6.35+3.9 SD and 8+3 SD respectively (p>0.05). The first, second and third year residents had mean SSS scores of 2.6+1.18, 1.95+1 and 1.85+1.13 respectively. There were no significant differences between the 1st, 2nd and 3rd year medical residents in the average hours of sleep (1st year = 6 hours, 2nd year = 6.1 years, 3rd year = 6.15 hours). Medical residents reported excessive sleepiness during the ICU/Floor rotations and well rested during the ambulatory and elective rotations.
Conclusion: Sleep education should be included in medical training so that there is good sleep hygiene such as set bedtime and awakening time, avoiding alcohol and caffeine. The first year residents should be helped by senior residents during their busy rotations. Measures should be taken to see that the residents reliably use time off from work to rest, are well rested after a night call by providing facilities for napping and restricting moonlighting during those rotations.

0438

EFFECTS OF SLEEP DEPRIVATION ON WORKING MEMORY: FIRST VERSUS SECOND LANGUAGE SPEAKERS

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Introduction: Working memory is required for completing many of our daily tasks including communication and language-based tasks. The purpose of the current study was to determine whether acute short-term sleep deprivation had a differential effect on working memory in first and second language speakers of English.
Methods: Participants included 25 native English speaking and 38 non-native English speaking college students. The participants completed three working memory tasks. All tasks were administered in English and were completed four times during 30 hours of acute sleep deprivation and sustained operations. One task was a simple Sternberg memory task (ST6). The second task was a continuous performance task (CPT) that required participants to recognize if the current stimulus matched the last presented stimulus. The last task was a working memory task (AX) that required participants to remember an A-X combination with a series of distracter letters between the stimulus letters.
Results: Three 2x4 ANOVAs were completed to compare performance on the working memory tasks across the four testing sessions for the first and second language speakers. Performance on the ST6 and CPT did not differ by language but decreased significantly across the testing sessions (both tasks at p<.001). Performance on the AX differed by language with the second language speakers performing significantly worse than the first language speakers (p=.023) and with the second language speakers showing a significant decrease in performance across the testing sessions (p=.001).
Conclusion: The current results indicate that the AX, ST6, and CPT are sensitive to the effects of sleep deprivation and that the AX task may be especially useful to assess language-related working memory deficits in second language speakers as a function of sleep deprivation.
Support (optional): This research was funded in part by the Center for Advance Study of Language at the University of Maryland and by the Creative Inquiry Program at Clemson University.

0439

EFFECTS OF DEPRESSION ON PERFORMANCE AND SELF-ASSESSED PERFORMANCE UNDER SLEEP DEPRIVATION CONDITIONS

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Introduction: Sleep deprivation and depression affect many people and often result in serious detrimental effects on performance, health, and well-being. The purpose of the current study was to determine the effects of short-term sleep deprivation on performance and self-assessed performance in depressed and non-depressed people.
Methods: Participants included 26 depressed and 68 non-depressed college students. The students were rated as depressed or non-depressed based on their responses to the Center for Epidemiologic Studies Depression Scale. The participants completed a variety of tasks four times during 30 hours of acute sleep deprivation. The tasks included the Law School Admission Test (LSAT), which measured logical reasoning ability, and a meta-cognition survey that asked participants to rate the accuracy of their answers on the LSAT. Different versions of the LSAT were administered during each testing session.
Results: Two 2x4 ANOVAs were completed to compare performance in the depressed participants to the non-depressed participants across the four testing sessions. Actual performance on the LSAT decreased significantly across the night of sleep deprivation (p<.001) with depressed participants performing significantly worse on the LSAT (p=.033) than non-depressed participants. Self-assessed performance on the LSAT also decreased significantly across the night of sleep deprivation (p<.001). There was a trend for worse self-assessed performance in the depressed participants than the non-depressed participants (p=.074). There was no significant interaction for either actual performance or self-assessed performance.
Conclusion: The current results suggest that depressed persons performed significantly worse under sleep deprivation conditions than non-depressed persons on a logical reasoning task. Furthermore, both depressed and non-depressed participants indicated that their performance decreased across the night of sleep deprivation. The current findings indicate that sleep deprivation may differentially impact performance based on current mood states.
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0440

SLEEP DURATION AND QUALITY IN TYPE 2 DIABETES MELLITUS

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Introduction: Sleep deprivation is considered to be a risk factor for the development of obesity and diabetes type 2 (T2DM). This assumption is mainly based on large epidemiological studies in the normal population. We studied whether short sleep or disturbed nocturnal sleep is more prevalent in a large cohort of patients suffering from T2DM.
Methods: Questionnaires including the Epworth Sleepiness Scale (ESS) and the Pittsburgh Sleep Quality Index (PSQI) were handed out to all diabetes patients visiting the outpatient clinic for diabetes care of the LUMC for a period of 3 months. As controls, acquintances of the patients who were matched for sex and age and not suffering from diabetes were asked to complete the same questionnaire. The data of T2DM

patients were also compared to a group of patients suffering from type 1 diabetes (T1DM).
Results: Questionnaires were returned by 117 T2DM, 123 T1DM patients, and 157 controls. Response rates were 51.17% for the patient group (T1DM and T2DM) and 33.48% for controls. There was a larger proportion of T2DM patients sleeping less than 5 hours compared to T1DM and controls (10.26% vs. 4.10% vs. 3.18%, p=0.02). Disturbed sleep, defined as a score >5 on the PSQI, was also more prevalent in T2DM than in T1DM or controls (42.46% vs. 30.17% vs. 24.36%, p=0.00). Another finding was a high prevalence of Excessive Daytime Sleepiness (EDS) (defined as a score of > 11 on the ESS) in the T2DM group compared to controls (15.38% vs. 4.55% p=0.00).
Conclusion: T2DM patients more often had a short night time sleep and a lower nocturnal sleep quality when compared to T1DM patients and controls. Unexpectedly a higher prevalence of EDS was found in diabetes patients.

0441

DIFFERENTIAL BENEFIT OF RECOVERY SLEEP FOR COGNITIVE PERFORMANCE BASED ON DETERIORATION THROUGHOUT SLEEP DEPRIVATION

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Introduction: Previous studies of individual differences in response to sleep deprivation indicate participants who perform the worst during their sleep deprived condition also show the slowest recovery. Here, we utilized baseline performance and the magnitude of deterioration in performance after two nights TSD to predict recovery status after each of two nights of recovery sleep.
Methods: 40 subjects (age=24.0 +/- 4.9yrs; 18F) completed Arithmetic, Verbal Learning, and Psychomotor Vigilance Tasks (PVT) after normal sleep (baseline), 60 hours total sleep deprivation (TSD), and two nights of recovery sleep. Participants were classified as "recovered" after the first recovery night if their performance returned to baseline levels. Those not recovered after one night were reclassified after the second night. Logistic regression predicted recovery status using baseline performance and deterioration after 60 hours TSD.
Results: Magnitude of deterioration predicted recovery status following one night of recovery sleep for the PVT (number of lapses: p=0.025, Exp(B)=0.926) and accuracy scores on the easier arithmetic task (p=0.03, Exp(B)=0.936). Recovery after the second night was not significantly predicted for any task. Baseline performance did not predict recovery status for any task.
Conclusion: Those individuals more vulnerable to deficits in attention and arithmetic working memory during 60 hours TSD benefited less from one night of recovery sleep. For each additional lapse in attention during TSD, an individual's odds of recovery after the first night change by 0.926. Likewise, for each percentage decrease in arithmetic accuracy, odds of recovery change by 0.936. Conversely, performance deterioration did not predict who would benefit from a second recovery sleep night. These findings suggest rate of recovery from TSD may reflect an underlying trait. In fact, of those not recovered after the first night, relatively few (PVT: 5/18, arithmetic: 9/15) showed performance recovery after the second night, suggesting a subset of individuals require much greater amounts of recovery sleep.

0442

MODELING RECOVERY AFTER CHRONIC SLEEP RESTRICTION: SLEEP EXTENSION CAN PROVIDE RECUPERATION OF PERFORMANCE BUT MAY BE NEITHER NECESSARY NOR SUFFICIENT

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Introduction: Little is known about effective strategies for recuperation from performance impairment due to chronic sleep loss. Mathematical modeling may be used to extrapolate from laboratory data sets to generate targeted hypotheses for experimental investigation of this issue. We consider a recently developed mathematical model of sleep/wake homeostatic effects on cognitive performance that may generate new insights into recuperation following cognitive performance degradation due to chronic sleep restriction.
Methods: We used an extension of the two-process model described in a companion abstract (McCauley and colleagues). The model was calibrated using PVT lapse data from a laboratory study involving 14 days of sleep restriction to 8h, 6h or 4h TIB daily, or 3 days of total sleep deprivation (N=48; 72.4% of variance explained). The model was validated using PVT lapse data from a laboratory study involving 7 days of sleep extension/restriction to 9h, 7h, 5h or 3h TIB per day (N=56; 72.2% of variance explained).
Results: Several predictions were made based on an analysis of the dynamics of the model. First, for chronic sleep restriction to no less than ~4h TIB per day, performance converges to a steady state of impairment over days. Second, from the steady state, performance deficits diminish when daily TIB is increased even if still restricted. Third, if increased TIB occurs only intermittently, then performance deficits subsequently converge back rapidly to a steady state of impairment.
Conclusion: Based on mathematical model predictions that extrapolate from observations (>100 subjects) in chronic sleep restriction experiments, we derive the following hypotheses: 1) It is possible to recuperate from performance impairment after chronic sleep restriction by reverting to a schedule of sustained non-restriction, without requirement for further sleep extension (or making up for "lost" sleep); and 2) Sleep extension ("oversleeping") may accelerate recuperation but is not sufficient to restore performance unless followed by a schedule of sustained non-restriction. Experimental confirmation of these hypotheses will have significant implications for scheduling in operational settings.
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0443

CONCENTRATE: SUBJECTIVE MEASURES PREDICTING COGNITIVE PERFORMANCE OVER THE COURSE OF SLEEP DEPRIVATION

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Introduction: Sleep deprivation reliably affects performance on cognitive tasks, but individuals are often poor at assessing their performance while sleep deprived. This suggests other means of alerting individuals to potential performance deficits during sleep loss are needed. We examined subjective parameters to see if any introspective measure can predict quality of performance during sleep deprivation.
Methods: Forty healthy adults underwent 64 hours of total sleep deprivation. Arithmetic working memory (Math), verbal learning (VL), and psychomotor vigilance tasks (PVT) were administered at 12, 36, and

60 hours awake. Subjects were administered the Karolinska Sleepiness Scale (KSS) and Spielberger's State-Trait Anxiety Inventory (STAI) before each test session, and the subjects rated "difficulty," "motivation," and "concentration" on a 10-point Likert scale after completing each task. Multiple regression analyses were utilized to determine if any of the five subjective measures predicted Math accuracy, total words immediately recalled, or median reaction time on the PVT at each test session.

Results: Concentration was the only subjective measure significantly associated with cognitive performance. Concentration predicted performance on Math ($p<.001$) and PVT ($p=.0032$) at 12 hours, VL ($p=.015$) and PVT ($p=.003$) at 36 hours, and Math ($p=.001$) and VL ($p=.003$) at 60 hours. Effect sizes for concentration in these analyses are small to large: partial R-square values at 12, 36, and 60 hours are sequentially .356, .075, and .275 for Math, .070, .166, and .233 for VL, and .141, .247, and .088 for PVT.

Conclusion: Concentration is a strong predictor of cognitive performance during sleep deprivation, while other subjective measures, including sleepiness, do not reliably predict cognitive performance. Thus, training individuals who must perform while sleep deprived to take corrective action when they recognize a drop in the ability to concentrate may help reduce errors and accidents resulting from sleep deprivation.

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0444

SOUND SLEEP: AROUSAL THRESHOLDS AND SLEEP DISRUPTION FROM COMMON HOSPITAL NOISES

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Introduction: Noise in hospitals is an urgent concern documented through national surveys as having a negative impact on patient satisfaction. For the first time, proposed changes to the Guidelines for the Construction of Healthcare Facilities that become law in most states recognize improved acoustical conditions as vital to the health care environment. There is little evidence to inform recommendations about typical sounds encountered in a hospital and their impact on sleep. The purpose of this study was to test arousal thresholds to specific hospital-based sounds to determine the impact of noise on patient sleep.

Methods: Recordings were captured of hospital sound sources corresponding to specific categories identified as salient in the American Institute of Architects' Draft Interim Guideline on Sound and Vibration in Healthcare Facilities. Fourteen sounds were calibrated for dynamic presentation through a speaker array at the sleep lab with rising 5 decibel step exposures from 40 to 70dB(A). Healthy young adult sleepers were monitored by PSG on three, 8.5 hr nighttime sleep periods for an undisturbed baseline and two noise exposure nights. Noise-related EEG arousals were quantified using current AASM criteria and summed for each sleep stage by sound type and decibel level to calculate arousal probability threshold curves.

Results: The tested stimuli evoked a range of arousal thresholds. At the 50% arousal probability level, stimuli spanned 15 dB(A) Leq in Stage 2 sleep, 17 dB(A) Leq in REM sleep and 30 dB(A)Leq in stage 3. Within-hospital, but exterior-to-room type noises (e.g., ice machine) were arousing for 50% of subjects below 40 dB(A) in stage 2 sleep, between 45 and 50 dB(A) from REM, but exhibited a lower arousal threshold across a broader range of dB in stage 3. Electronic sounds (e.g., phone) intentionally designed to be alerting were very effective in evoking high arousal probabilities, 50% between 40 and 43 dB(A) in REM, above 75% at 40 dB(A) in stage 3 sleep, and 85% at 40 dB(A) in non-REM stage 2. Voices were also highly alerting at above 50% arousal probability in all sleep stages at 40dB(A). Within-room noises (snoring, toilet, towel dispenser) aroused at 50% probability from stage 2 sleep at below 40dB(A,) in 3 between 40 and 50dB(A) and from REM at between 40dB(A) and 55dB(A).

Conclusion: The findings provide evidence that repeated arousals from sleep occur even in healthy young adults when hospital sounds exceed 45dB(A), and responses vary widely by stimulus types.

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0445

SLEEP DEPRIVATION AFFECTS SPATIAL WORKING MEMORY AND REDUCES HIPPOCAMPAL AMPA RECEPTOR PHOSPHORYLATION

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Introduction: Sleep deprivation (SD) before acquisition can affect learning and memory formation. The majority of studies showing this used REM SD over a relative long period of time (1 to 5 days). In the present study we examined the effects of a relatively short 10-12h total SD on spatial working memory. In addition we examined hippocampal AMPA receptor phosphorylation as a possible mediator in the effects of SD.

Methods: The experiments were performed with adult male C57BL mice. One group served as controls and another group was sleep deprived for 10-12h during the light (resting) phase. To assess spatial working memory, animals were subjected to a novel arm recognition test, performed in a Y-maze, immediately after the SD period. Animals were first allowed to explore two arms of the maze for 10 minutes. After an intertrial-interval of 2 minutes, the animals were then allowed to explore all three arms for 5 minutes. To examine changes in molecular correlates after SD, different groups of animals were sacrificed immediately at the end of the 10-12h SD. Brain material was collected and processed for western blotting.

Results: Despite 10-12h SD, experimental mice showed normal activity levels in the Y-maze. The total number of arm entries was similar to that of rested control animals. However, whereas control animals had a preference for the novel arm, SD mice did not differentiate between the old arms and the new one. At the molecular level 10-12h SD significantly reduced hippocampal AMPA receptor phosphorylation at the serine 845 site of the GluR1 subunit.

Conclusion: The data show that SD during the normal resting phase impairs spatial working memory and reduces AMPA receptor phosphorylation at the GluR1 subunit. These findings provide further insight into the possible mechanism of sleep loss-induced hippocampal dysfunction and memory impairment.

0446

INFLUENCE OF SLEEP EXTENSION ON SLOW EYE MOVEMENTS DURING THE SLEEP TRANSITION

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Introduction: Slow eye movements (SEMs) have been reported to be a physiological marker of sleepiness during sleep deprivation and the transition from wakefulness to sleep. SEMs appear prior to sleep onset and decrease after stage 2 onset. We tested the hypothesis that extending sleep would reduce SEMs during the sleep transition.

Methods: Twenty-three subjects (10 women) aged 22.8+4.1(mean+SD) with self-selected habitual short sleep durations of <6.5h during the work/school week participated in a month long protocol. During the first two weeks subjects maintained their habitual short sleep schedules (~6.0h per night). During the second two weeks, subjects were random-

ized to maintain their habitual sleep schedule or extend time in bed by ~2h/night. Sleep was monitored using wrist-actigraphy, diaries, and call-ins to a time-stamped recorder. At the end of each two-week segment, subjects were studied in the laboratory for ~24h and SEMs were assessed during the sleep transition at scheduled bedtime. SEMs were defined as eye movements >1sec in duration with amplitude >50 microvolts. Records were scored in 15sec epochs from lights off until SWS onset. Data were aligned according to stage 2 onset and analyzed using repeated measures ANOVA for the number and occurrence (yes/no) of SEMs.

Results: Latency to stage 2 did not significantly differ between groups either visit ($p=0.17$). Number and occurrence of SEMs decreased across the sleep transition ($p<0.05$) and SEMs were lowest after stage 2 onset. Sleep extension reduced SEMs prior to stage 2 onset ($p<0.05$); whereas SEMs were similar between visits for subjects who maintained short sleep schedules (one epoch had more SEMs on visit 2; $p<0.05$).

Conclusion: Sleep extension reduced the frequency and occurrence of SEMs during the transition to sleep suggesting that increased SEMs during chronic sleep loss may be a physiological marker of sleep debt that can be reduced by extended sleep.

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0447

THE EFFECT OF CAFFEINE AND PHOTOTHERAPY ON VIGILANCE

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Introduction: Sleepiness causes 37% of fatal road accidents in France. Accidents peak between 2am and 7 am with a second peak between 2pm and 4pm, implying that circadian rhythms as well as sleep deprivation are involved. Caffeine and naps have been shown to improve driving performance in sleep deprived subjects in several studies, but the chronobiological effects of intense light in addition to caffeine on driving performance have not been explored. This study explores the effect of caffeine and phototherapy on night-time vigilance in healthy sleep deprived volunteers.

Methods: Each participant spent 4 periods of 30 hours of EEG recording, with psychometric testing (Karolinska, VAS), vigilance testing (PVT) and driving (York driving simulator) from 1.30am to 7am following treatment by caffeine 200mg (C+)/ placebo (C-) and phototherapy 10000 lux (L+)/ placebo (L-). Each participant was treated by C+L+, C+L-, C-L+, C-L-, in random order. The night of sleep deprivation and testing was followed by a night of recovery with PSG.

Results: 12 men participated, mean age 34.5 (range 26-49). Performance on psychometric testing, PVT and driving simulator deteriorated during the night despite treatment. Patients receiving caffeine were less sleepy on the Karolinska (4.75 vs 7.16 $p<0.001$), more confident about their performance and had faster reaction times on the PVT. In the final test patients in the group C+L+ had fewer accidents (4.2 vs 12.8 for C-L- $p=0.006$), and drove straighter (31.38 vs 33.68 for C-L- $p=0.004$). Patients receiving caffeine only were more likely to exceed the speed limit (5.26 for C+L- vs -0.67 C+L+ $p=0.032$) and had as many accidents as patients receiving C-L- (12.25 vs 12.83 NS). Phototherapy alone had no effect on driving performance. Neither caffeine nor phototherapy affected recovery sleep.

Conclusion: Driving performance at the end of the night can be improved by combining caffeine and phototherapy.

0448

EARLY REM ONSET IN A NATURALLY OCCURRING SLEEP DEPRIVED POPULATION

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Introduction: United States Air Force Academy (USAFA) Cadets are a population of late adolescents with naturally occurring sleep deprivation. Due to military and class schedules, Cadets receive approximately 5-6 hours sleep per night, much lower that the recommended 9 hours sleep for this age group (Lindsay, Lee, & Dyche, 2006). In normal nightly sleep cycles, REM onset begins 90 - 120 minutes after sleep onset, and constitutes 20-25% of total sleep time. Early sleep onset (e.g., less than 8 minutes) and early REM onset (e.g., less than 10 minutes after sleep onset) is a characteristic of pathologically sleep deprived populations (e.g., narcoleptics). The present study investigates the effects of natural sleep deprivation on sleep onset and REM onset times measured by Multiple Sleep Latency Tests (MSLT) after a week of partial deprivation (on a Friday) and after two nights of partial sleep recovery on a weekend (on a Sunday).

Methods: Ten USAFA Cadets (nine freshmen, one sophomore) wore an actigraph to measure sleep the week prior to MSLT testing at the Lynn Institute of the Rockies. MSLT testing was conducted on a Friday and Sunday and consisted of four 20 minute naps per day.

Results: Actigraph data indicated that Cadets obtained an average of 5.85 hours sleep per weeknight. MSLT data showed no significant differences in REM sleep behavior from Friday to Sunday, with 7 out of 10 Cadets entering REM sleep during at least one nap. Sleep onset (M = 5.96 minutes, SD =2.69) and REM onset (M = 7.41 minutes, SD = 3.53) were both consistent with sleep disorder patients. Analyses showed that the percentage of REM sleep for an average nap was 38%.

Conclusion: The present data indicate that the level of sleepiness for USAFA Cadets is such that recovery sleep did not significantly alter sleep patterns. Furthermore, most Cadets entered REM-sleep soon after sleep onset, consistent with data for pathologically sleep deprived patients.

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0449

FATIGUE AND COMMUTING IN MINE SHIFTWORKERS

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Introduction: In Queensland, Australia, many mine workers are required to live on site during their roster cycle. For most, the commute distance to return home is long. A challenge facing industry and workers is how best to manage the effects of fatigue during the commute, and reduce prevalence of drowsy driving accidents. Addressing these challenges requires a better understanding of work hours, commute lengths and attitudes towards fatigue management.

Methods: In 2008, a questionnaire was distributed to 17 coal mines in Central Queensland, with n=917 employees responding. Responses were confidential. Employees were asked about their normal roster length, where they lived during the roster cycle, how long their commute was and whether they rested before commencing this commute at the end of a roster cycle.

Results: Employees worked between 8-13.5h shifts, with most working 12-12.5h, and 78% working both day and night shifts. During their roster cycle, most employees resided in a house (64%), 21% in a studio style unit and 10% in a room only. 67% commuted between 1-3h, with 19% traveling 3-5h, and 12% traveling more than 5h. 81% of workers

reported driving alone in a car, while only 12% reported car pooling. Approximately half (46%) do not rest following their last shift, although 33% reported resting between 1-4h before starting home.
Conclusion: The data demonstrates that that many shiftworkers in the Queensland mining industry engage in long drives following the end of roster cycles, with little or no rest or nap breaks between finishing work and driving. These findings highlight the potential fatigue-related risks due to inadequate sleep facing workers who are required to drive long distances home. Additionally, the data suggests that voluntary rest breaks prior to driving are not an effective fatigue management strategy.
Support (optional): Data collection was supported by the CFMEU Mining and Energy, Queensland District.

0450

WORKER VIEWS ON CHANGES IN WORK HOURS AND FATIGUE MANAGEMENT RELATED TO COMMUTING IN THE QUEENSLAND MINING INDUSTRY

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Introduction: In recent years, reforms in OH&S requirements for shiftwork regarding fatigue have prompted considerable changes in fatigue management policies in many industries in Australia. Some reforms are aimed at decreasing fatigue related accidents during the commute to and from work. We examined the views of workers regarding some proposed changes in hours of work that would impact on fatigue management in the coal mining industry.
Methods: In 2008 a questionnaire was distributed to 6 coal mines in Queensland, Australia, with n=98 workers responding. All responses were confidential. Issues addressed included: can a company require 12+h shifts followed by a 2h commute; how safe do you feel working with individuals working 16h consecutive shifts; and what action would workers take to expose changes that appear to negatively affect safety.
Results: Nearly all workers thought it unreasonable for a company to require 12h shifts + 2h commutes, especially given that it is illegal for commercial drivers to work 12h shifts (10h driving + 2h non-driving) within 24h. Approx. 99% of mine workers did not feel safe knowing that individuals had worked more than 4 consecutive 16h shifts when they were working alongside them, were maintaining their machinery or were driving vehicles in the mines. If proposals to extend work and commute times to 15h or more per 24h were put in place, most workers believed these changes would negatively affect mine safety, and were willing to fight against these changes.
Conclusion: There are high levels of awareness in workers regarding fatigue and the impact on safety. Our findings demonstrate that workers appreciate the link between number of hours worked and the effect this may have on fatigue. In addition, the importance of including commute time in hours of work is highlighted as ongoing issue that is currently inadequately addressed.
Support (optional): Data collection was supported by the CFMEU Mining and Energy, Queensland District.

0451

INDEPENDENT DIMENSIONS OF TRAIT INDIVIDUAL DIFFERENCES IN SLEEP ARCHITECTURE

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Introduction: In a recent study of trait individual differences in sleep architecture, PSG-derived sleep variables clustered in three dimensions tentatively interpreted as representing sleep duration, sleep intensity, and sleep discontinuity. Here we investigate the replicability of this finding in a different study of trait individual differences.
Methods: As part of a larger study, 21 healthy subjects (ages 21-38y; 9 women) underwent two 36h total sleep deprivation sessions during separate, strictly controlled laboratory visits. Each sleep deprivation session was preceded by baseline sleep and followed by recovery sleep (12h TIB, 22:00-10:00) in the laboratory. PSG records of the two baseline and the two recovery sleep periods were visually scored by R&K criteria. Standard sleep parameters were extracted, and slow-wave activity (SWA; 0.75-4.5Hz) was computed from the NREM sleep EEG for four derivations (Fz,C3,C4,Oz vs. A1/A2). A total of 13 sleep records was discarded because of equipment failure. For each of the remaining 71 records, 18 sleep variables were entered into principal components analysis (PCA) to determine which variables covaried over subjects and across nights. Sleep variables with absolute factor loadings >0.5 were used for interpretation.
Results: Three factors were retained in the PCA following inspection of the scree plot. The following independent dimensions of sleep architecture emerged after varimax rotation: 1) sleep duration (TST, sleep efficiency, S2, REM, number of sleep cycles, and negative loadings for REM latency and WASO); 2) sleep intensity (SWS, and SWA for the four derivations); and 3) sleep discontinuity (S1, movement time, and stage transitions). Latencies to S1, S2 and SWS did not load >0.5 on these dimensions.
Conclusion: This study yielded converging evidence that there are at least three independent components of systematic individual variability in sleep architecture. The results are congruent with our earlier finding that individual differences in nocturnal PSG-derived sleep variables cluster in three dimensions, which appear to represent sleep duration, sleep intensity, and sleep discontinuity.
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0452

ACCURACY OF SELF-EVALUATION UNDER SLEEP DEPRIVATION AND AFTER DAYTIME RECOVERY SLEEP

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Introduction: The ability to assess the change in one's own performance under sleep deprivation (SD) is crucial to make adaptive behavioural decisions (e.g. drive, nap, or pursue activities). This study aims to evaluate whether subjects are able to assess their performance deterioration under sleep loss as well as their performance improvement after recovery sleep.
Methods: Twenty-four healthy volunteers (13W, 11M; 37.1y ± 1.14) spent one night of sleep deprivation in the laboratory. Daytime recovery sleep (DRS) was initiated one hour after habitual wake time (HWT). Subjects stayed in bed during DRS for their habitual sleep duration. Psychomotor vigilance task (PVT) was performed in the evening before SD (PVT-1; 12 hours before HWT), at the end of the SD in the morning (PVT-2) and in the evening after DRS (PVT-3; 12 hours before HWT). PVT was immediately followed by an analogical subjective performance scale (APS). Differences between PVT-2 and PVT-1 (SD effect) and between PVT-3 and PVT-2 (DRS effect) were calculated on APS and PVT variables (median reaction time-RT, lapses, fastest and slowest RT). Pearson correlation coefficients were used to evaluate relationships between APS and PVT variables for SD and DRS.
Results: In SD, only the fastest RT significantly correlated with the APS ($R = -0.45$, $p = 0.03$) with subjects reporting stronger deterioration of performance showing a stronger increase in fastest RT. After DRS, all PVT variables were strongly correlated with APS (all $R > -0.60$, $p < 0.001$). The subjects who reported stronger improvements of perfor-

mance after DRS showed greater decreases in median RT, lapses, fastest and slowest RT.
Conclusion: These results suggest that subjects were less able to accurately evaluate the decrease of their performance during SD than its increase after DRS. This may be explained by a loss of one's points of reference as a result of higher homeostatic/circadian sleep pressure.

0453

EVOKED HEMODYNAMIC RESPONSES DECREASE FOLLOWING SLEEP DEPRIVATION

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Introduction: In order to study evoked cortical hemodynamic responses following sleep deprivation, we utilized optical imaging techniques to measure responses following auditory stimulation. We have previously shown that evoked electrical response potentials (ERPs) are larger during quiet sleep (QS) compared to wake and REM. Additionally, we found that the evoked hemodynamic response is larger during QS, perhaps due to increased blood vessel compliance. If blood vessels remain in a semi-dilated state during wakefulness and become constricted during QS, we hypothesized that evoked optical response amplitudes after sleep deprivation would be larger since the animal will spend more time asleep; however, we found the opposite result.
Methods: We implanted five Sprague-Dawley rats with EEG electrodes, an LED (660nm) light, and a photodiode over the auditory cortex. In order to probe the cortical state, we delivered a train of five speaker clicks (10Hz) at random intervals from 2-13s while recording the electrical and optical changes. Rats were deprived of sleep for 0, 2, 4, 6, or 8 hours. We continuously recorded throughout the deprivation period a 16 hour recovery period.
Results: During the first recovery sleep hour the ERPs were larger in amplitude for increased prior sleep deprivation. The corresponding cortical hemodynamic response showed decreased peak amplitudes occurring around 1.8s after the stimulus and decreased trough amplitudes occurring around 3.7s after the stimulus.
Conclusion: We found larger ERPs in the first hour of recovery sleep following deprivation as would be expected with longer QS periods; however, the evoked optical response amplitudes were smaller during the first hour of recovery after deprivation. Further analysis of the data are required to confirm the hypothesis that blood vessels become maximally expanded during sleep deprivation and require more time to constrict back to their initial state.
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0454

ELECTROPHYSIOLOGICAL CORRELATES OF DELAYED RESPONDING IN A TASK TAPPING SUSTAINED ATTENTION

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Introduction: Functional brain imaging has shown that response slowing in the context of sleep deprivation (SD) generates signals that can be differentiated from those recorded after a normal night of sleep. Here we evaluate the electrophysiological changes associated with response slowing to provide a complementary view of the neural processes that underlie these transient deficits in attention.
Methods: 32-channel EEG from 15 right-handed healthy participants (9 male, mean age = 22.1years SD = 1.5 years) was recorded while they performed a letter-identification task after a normal night of sleep. The stimuli were 'Navon figures' comprising large global H or S made up of smaller local Hs or Ss. Participants identified global or local letters as quickly as possible.
Results: Correct letter identifications from each subject were ranked by response time (RT). We compared the fastest 20% and the slowest 20% of these responses. Slower responses were associated with reductions in: 1) N1 amplitude at occipital electrodes suggesting reduced top-down biasing of visual sensory processing. 2) Pre-stimulus frontal-occipital gamma phase synchrony suggesting decline in cortical-cortical connectivity between regions mediating attention control and extrastriate cortex. This contrasted with post-stimulus reduction in gamma synchronization for fast responses. The latter may reflect the benefit of disengaging long range cortical connections to enable local processing of the stimulus 3) P3 amplitude in fronto-central electrodes that may be linked to deficits in higher order cognitive processes.
Conclusion: Electrophysiological data collected after a normal night sleep indicates that response delays are associated with multi-faceted electrophysiological changes in frontal cognitive control and visual sensory cortices as well as long-range communications between these areas. It remains to be seen if these changes are compounded by SD.
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0455

DOES PVT PERFORMANCE REFLECT IQ?

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Introduction: In the 19th century, Sir Francis Galton sought to relate intelligence to performance on physical and sensory tasks by quantifying performance in an effort to measure "hereditary talent." Galton particularly took an interest in reaction time as a predictor of intelligence. This study examined the relationship of IQ scores to Psychomotor Vigilance Test (PVT) reaction time (RT) measures to determine the influence of IQ on PVT performance.
Methods: Data from 307 healthy adults (22-45yr) who underwent laboratory-based experimental sleep-deprivation protocols is being used to evaluate the relationship of IQ to RT. Data have thus far been analyzed for N=27 of these adults (M=30y, 12f), all of whom were assessed with a 7-subtest short form of the Weschler Adult Intelligence Scale (WAIS). Subjects completed 10min PVTs in a laboratory setting during 40h without sleep. Average PVT RT (fastest 10% and mean RT) when not sleep deprived (day 1, 13:00-21:00) and when sleep deprived (day 2, 00:00-21:00) were related to WAIS IQ Full Scale scores.
Results: Full Scale WAIS scores were not correlated with either mean PVT RT or mean fastest 10% RT, either before sleep deprivation ($r=-0.14$, $p=0.47$ and $r=-0.10$, $p=0.62$, respectively), or after sleep deprivation ($r=0.03$, $p=0.90$ and $r=-0.12$, $p=0.56$, respectively). Analyses using only the poorest PVT performance at 09:00 after a night without sleep also showed no relationship to IQ ($r=-0.01$, $p=0.96$). All findings were confirmed using nonparametric Spearman rho.
Conclusion: The data analyzed to date show no relationship between WAIS IQ scores and PVT performance. The addition of another 280 subjects will help resolve the certainty of these findings. If they hold up, the independence of PVT performance from IQ in both the alert and sleep-deprived state will further strengthen the uniqueness of the PVT among cognitive measures, most of which (unlike the PVT) are contaminated by aptitude, which includes IQ.
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0456

THE EFFECTS OF EXTENDED SLEEP-DEPRIVATION TO HEART RATE VARIABILITY ON COLLEGIATE FEMALE STUDENTS IN TAIWAN (2005-2008)

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Introduction: To explored the variations of physiological effects by automatic nervous system due to extended sleep-deprivation on collegiate female students in Taiwan.
Methods: There were 409 collegiate female students who were selected as subjects from Chinese Culture University. Subjects were divided into extended sleep-deprivation (ESD) group, sleeping hour less than 6 hours and lasting for 3 months, which had 134 counts and into normal sleeping (NS) group, sleeping hour which between 6 to 9 hours and lasting for 3 months, which had 275 counts. The sleeping quality were collected by Simply Sleep Quality Index and the 5-minutes sitting heart rate variability were monitored by WG-MD-ANSA01.
Results: The activity of index of total power (TP, 0-0.5 Hz), very-low-frequency (VLF, 0.003-0.04Hz), low-frequency power (LF, 0.04-0.15Hz), LF in normalized units (LF%), the ratio of low-frequency to high-frequency (LF/HF) in ESD group were significant lower ($p<.001$) than NS group but the index of HF% in ESD group was significant higher ($p<.001$) than NS group. The results of above were analyzed under the ESD group who had time to go to bed at am 2.34±1.41 which later than NS group for 1.64±.14 hours ($p<.001$) and had 5.30±0.65 sleeping hour which less than NS group by 1.78±0.10 hours ($p<.001$) for lasting 27.26±23.64 months.
Conclusion: It should be concerned to the individual health, family disbursement and social development that the decline of activity of automatic nervous system which due to stay-up and shrink sleeping hour on collegiate female students in Taiwan.

0457

BEHAVIOURALLY INDUCED INSUFFICIENT SLEEP SYNDROME AND ITS BORDERLAND

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Introduction: Behaviourally induced insufficient sleep syndrome (BIISS) occurs when an individual persistently fails to obtain the amount of sleep required to maintain normal levels of alertness and wakefulness.
Methods: This study presents the results of the post hoc evaluation (Clinical evaluation, Sleep questionnaire (SQ), actigraphy, PSG, MSLT, MWT, HLA typing, hypocretin) of 47 consecutive patients who received the diagnosis of BIISS in our Sleep Disorders Center.
Results: Mean age of the BIISS patient was 40±12 years (mean±SD). 70% were males. Patients mostly complain symptoms of hypersomnia with excessive daytime sleepiness, however, many individuals reported other symptoms as sleep attacks without general daytime sleepiness, fatigue, sleep drunkenness, concentration and attention deficits or cognitive impairment. Mean ESS was 14.1±3.6. Time in bed (TIB) estimation based on the SQ revealed TIB of 7:10h±1:03h during weekdays and 8:29h±1:16h on weekend. TIB estimation based on actigraphy recordings revealed significantly shorter TIB on weekdays and on weekends (weekday: 6:25h±0:57h, weekend: 7:56h±1:13h) compared to TIB taken from the SQ. In this population the PSG recording revealed short sleep latency 8.4±7.9 minutes and high sleep efficiency (91.5±16.7%). MSLT mean sleep latency was 5.5±3.3 minutes. Sleep onset REM (SOREM) episodes with 2 and more SOREM were present in 8 patients. MWT mean sleep latency was very variable. A clear reduced ability to maintain wakefulness (sleep latency < 12 min) was present in 34% of patients.
Conclusion: The results of this case series indicate (1) that there are a noticeable large number of patients who were not aware that their sleep duration was insufficient and (2) that there is a substantial clinical overlap between BIISS, narcolepsy without cataplexy and idiopatic hypersomnia without long sleep. A positive response to increased sleep time is diagnostic of BIISS and an important feature to differentiate between these three entities.

0458

EXECUTIVE FUNCTION MEASURES IN RELATION TO PHENOTYPIC PVT PERFORMANCE RESPONSES TO SUSTAINED SLEEP RESTRICTION

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Introduction: Differential vulnerability to the cognitive effects of total sleep loss appears to be phenotypic, based on Psychomotor Vigilance Test (PVT) performance (Van Dongen et al., Sleep 2004), and recent data on nocturnal deficits in executive function tasks (Groeger et al., Sleep, 2008). This study sought to determine if chronic sleep restriction (SR) resulted in PVT phenotypic responses that covaried with measures of executive function performance.
Methods: N = 141 healthy adults (M=29.6y; 50% females) completed 2 baseline nights (10h TIB/night), followed by 5 nights of SR (4h TIB/night) in a controlled laboratory setting. A 10-min PVT was administered every 2h during wakefulness along with other measures. Executive functions (EF) tests administered on the final SR day included: Tower of London (TOL, planning ability), Controlled Oral Word Association Test (COWAT, word production speed), and the Hayling (inhibition) and Brixton (spatial ability) tests. Phenotypic responses to SR were operationalized by the mean difference in PVT lapses (RTs>500ms) per trial between baseline day 2 and all 5 SR days. Spearman's rho was used to quantify the relationships between the PVT response and EF outcomes.
Results: PVT phenotype responses were unrelated to Hayling (rho=0.029, p=0.741) and Brixton (rho=0.143, p=0.091) scaled scores, as well as all seven TOL measures (rho ranged from 0.037 to 0.119, all $p>0.10$). Only the COWAT word production score showed a weak, inverse correlation to the PVT phenotype (rho=−0.199, p=0.027).
Conclusion: Greater increases in PVT lapses during sustained SR were not associated with most performance measures of executive function. The exception was word production speed on the COWAT word fluency test (more PVT lapses correlated with slower COWAT production). Since both measures rely on speed, the classic slowing effects of sleep loss may be the reason the measures were related.
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0459

SLEEP DURATION AND RISK OF DIABETES: ANALYSIS OF THE NATIONAL HEALTH INTERVIEW SURVEY

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Introduction: Clinical and epidemiological evidence suggests that habitual sleep duration is associated with both obesity and diabetes. It is unclear whether these observed associations are independent of each other. The purpose of this study was to determine whether sleep duration has an independent association with diabetes using data from the National Health Interview Survey.
Methods: Participants (n=29,818) in the 2005 National Health Interview Survey provided data for the present analysis. The age range of the sample was: 18-85 years; 85% were white and 15%, black; 56% were women. The NHIS is a cross-sectional household interview survey, which uses a multistage area probability design. Probability samples of the civilian population of all 50 states and DC were obtained. During face-to-face interviews conducted by trained interviewers from the U.S. Census Bureau, respondents provided socio-demographic data and information about physician-diagnosed chronic conditions. They estimated their habitual sleep duration and provided height and weight data.
Results: Prevalence of obesity (BMI ≥30kg/m2) for blacks and whites was 52% and 38%, respectively [p<0.0001]. Prevalence of diabetes for blacks and whites was 12% and 8%, respectively [p<0.0001]. Odds ratios for diabetes associated with short sleep (≤5hrs) and long sleep (≥9hrs) were 1.93 [95% CI: 1.59-2.33, p<0.0001] and 2.21 [95% CI: 1.83-2.63, p<0.0001], respectively. Adjusting for effects of age, sex, ethnicity, obesity, and hypertension reduced OR to 1.24 [95% CI: 1.01-1.54, p<0.05] and to 1.48 [95% CI: 1.21-1.81, p<0.01] among short sleepers and long sleepers respectively.
Conclusion: Both short and long sleepers are at great risk for diabetes, independently of their age, sex, ethnicity, or the presence of obesity and hypertension. Individuals sleeping longer than 8 hours may be particularly vulnerable. Further research is needed to identify the mechanisms by which long sleep duration increases risk of diabetes.
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0460

EXTENDED DRIVING IMPAIRS NIGHT-TIME DRIVING PERFORMANCES

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Introduction: Despite the fact that fatigue and sleepiness at the wheel are well-known risk factors for traffic accidents, many drivers combine extended driving and sleep deprivation. Fatigue-related accidents occur mainly at night but there is no experimental data available to determine if the duration of prior driving affects driving performance at night.
Methods: Participants drove in 3 nocturnal driving sessions (3-5am, 1-5am and 9pm-5am) on open highway. Fourteen young healthy men (mean age [±SD] = 23.4 [±1.7] years) participated Inappropriate line crossings (ILC) in the last hour of driving of each session, sleep variables, self-perceived fatigue and sleepiness were measured.
Results: Compared to the short (3-5am) driving session, the incidence rate ratio of inappropriate line crossings increased by 2.6 (95% CI, 1.1 to 6.0; P<.05) for the intermediate (1-5am) driving session and by 4.0 (CI, 1.7 to 9.4; P<.001) for the long (9pm-5am) driving session. Compared to the reference session (9-10pm), the incidence rate ratio of inappropriate line crossings were 6.0 (95% CI, 2.3 to 15.5; P<.001), 15.4 (CI, 4.6 to 51.5; P<.001) and 24.3 (CI, 7.4 to 79.5; P<.001), respectively, for the three different durations of driving. Self-rated fatigue and sleepiness scores were both positively correlated to driving impairment in the intermediate and long duration sessions (P<.05) and increased significantly during the nocturnal driving sessions compared to the reference session (P<.01).
Conclusion: Extended driving impairs night-time driving performances and therefore should be restricted.

0461

SLOW WAVE SLEEP ENHANCEMENT DURING SLEEP RESTRICTION REDUCES THE HOMEOSTATIC RESPONSE TO SLEEP LOSS

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Introduction: In a companion abstract (Schweitzer et al, this volume) we describe a reduction in the neurobehavioral impact of sleep restriction when SWS is enhanced with sodium oxybate. In the present abstract, the effect of SWS enhancement upon recovery sleep is examined.
Methods: A parallel groups design was used to compare sodium oxybate 3.5 grams (SO) and placebo (PBO). Following screening and baseline assessments, subjects underwent 2 consecutive sleep deprivation nights, each followed by a 3-hour daytime (0800-1100) sleep opportunity, and a 9-hour night of recovery sleep. SO (n=30; mean age 27.1) or PBO (n=28; mean age 27.1) was administered prior to the daytime sleep periods. MSLT, PVT, KSS and other measures were evaluated during all waking hours.
Results: During daytime sleep opportunities TST did not differ between groups (SO=171.8±0.87, PBO=172.8±0.85 min, ns), but the SO group had more SWS than PBO (88.2±2.8 vs 56.8+2.9 min, p<.001) and less REM (12.3±2.2 vs 34.9±2.2 min, p<.001). During recovery sleep the SO group had less TST (521.9±7.7 vs 548.6±7.7 min; p=.016), less SWS (68.7±3.8 vs 81.4±3.9 min; p=.023), less REM (114.4±4.0 vs 133.1±4.0 min; p=.002), and longer latency to persistent sleep (26.8±3.6 vs 16.6±3.6 min, p=.05). The most common adverse events were dizziness, nausea, and vomiting
Conclusion: The PSG differences between groups are consistent with the interpretation that the PBO group was impacted more by sleep restriction compared to the SO group. To our knowledge, this is the first demonstration that SWS enhancement during sleep restriction results in a reduced homeostatic response to sleep loss during recovery sleep.
Support (optional): Jazz Pharmaceuticals

0462

CEREBRAL ACTIVATION IN OLDER ADULTS DURING A VERBAL LEARNING TASK FOLLOWING 36HRS TOTAL SLEEP DEPRIVATION

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Introduction: Memory deficits are often reported with increasing age. Older adults often exhibit increased activation in specific brain regions relative to young adults during learning. Young adults show similar increased brain responses during learning after total sleep deprivation (TSD). Such increased cerebral responses have been interpreted as compensatory in both populations, however it is unclear if the brain can compensate for both age and TSD. Here we used functional neuroimaging (fMRI) to examine the effects of TSD on brain response during verbal encoding in older adults.
Methods: 27 subjects (21F, mean age=67.1yrs ± 5.7) performed a verbal learning task during fMRI both while well-rested (WR) and following 36-hrs TSD. Recognition memory (d') served as the behavioral outcome variable. FMRI analyses focused on task-specific regions of interest and examined BOLD activation during word learning. To assess brain regions underlying successful performance after TSD, BOLD response data were regressed onto performance data.
Results: Performance analyses revealed subjects scored similarly on the recognition memory test on both WR and TSD nights. The right parahippocampal gyrus showed decreased responses to memorization after TSD, while the left inferior parietal lobe showed increased responses to memorization after TSD. Regression analyses showed that those subjects with better recognition memory after TSD had greater activation in bilateral anterior parahippocampal gyri, bilateral inferior frontal gyrus, the left inferior parietal lobe, as well as less activation in the retrosplineal cortex.
Conclusion: Recognition memory remained intact after 36-hours TSD in older adults. FMRI results suggest older adults, on average, compensate for impaired hippocampal function during TSD with increased recruitment of cortical regions. Those older adults least vulnerable to TSD, though, showed a more wide-spread compensatory response in hippocampal, frontal, and parietal regions associated with relatively intact performance. These data suggest older adults show similar compensatory recruitment during learning after TSD as young adults, especially during successful performance.

0463

SHORT SLEEP DURATION AND THE RISK OF OBESITY AMONG BLACK AND WHITE AMERICANS

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Introduction: While the optimal sleep time for wellness and survival has not been systematically examined, evidence suggests that individuals experiencing less than the population modal sleep duration might be at greater risk of becoming obese. The effect of race on the risk of obesity with short sleep duration is largely unknown. This study assessed whether the short sleep-obesity link differentially affects black and white Americans.
Methods: Analysis was based on data obtained from 29,818 Americans (age range: 18-85 years) who participated in the 2005 National Health Interview Survey, a cross-sectional household interview survey, using a multistage area probability design. Probability samples of the civilian population of all 50 states and DC were obtained. During face-to-face interviews conducted by trained interviewers from the U.S. Census Bureau, respondents provided socio-demographic data and information about physician-diagnosed chronic conditions (e.g., hypertension, heart disease, diabetes, and arthritis). Subjective and anthropometric data including mood, habitual sleep duration and height/weight were also collected.
Results: Of the sample, 28.3% reported hypertension; 8.3%, heart disease; 8.4%, diabetes; 23.4%, arthritis; and 26.1%, sadness. Compared with whites, blacks were less likely to report sleeping 7 hours [23% vs. 30%, $p<0.0001$], with characteristically greater prevalence of short sleep (≤5 hrs) [12% vs. 8%, $p<0.0001$]. Blacks had a greater prevalence of obesity (BMI ≥30kg/m2) than did whites [52% vs. 38%, $p<0.0001$]. Short sleep was associated with obesity among both blacks and whites [OR=2.22, 95% CI: 1.68-2.95, $p<0.0001$; and OR= 1.82, 95% CI: 1.60-2.07, $p<0.0001$, respectively]. Multivariate-adjusted ORs for blacks and whites were 1.78 [95% CI: 1.30-2.45, $p<0.0001$] and 1.43 [95% CI: 1.24-1.66, $p<0.0001$], respectively. Demographic and medical risk factors were adjusted.
Conclusion: Race significantly influences the risk of obesity conferred by short sleep duration increased risk among Blacks. An excess of 35% of blacks showed greater obesity risk associated with short sleep. Further research is needed to examine the mediators of excess risk among Black population.
Support (optional): This research was supported by funds from NIH (1R24MD001090 and HL085042).

0464

VIGILANCE PERFORMANCE IS DETERMINED BY AN INTERACTION AMONG ACUTE HOMEOSTATIC, CHRONIC HOMEOSTATIC, AND CIRCADIAN MECHANISMS

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Introduction: Performance is modulated by acute homeostatic (duration of wakefulness), chronic homeostatic (wake-to-sleep ratio over days) and circadian mechanisms. The amplitude of the circadian performance rhythm increases with longer time awake. We tested whether chronic sleep restriction modifies the interaction between the acute homeostatic and circadian processes.
Methods: Nine healthy volunteers participated in an inpatient protocol including 12 forced desynchrony (FD) rest-activity cycles of 42.85 hours, with a 3.3:1 wake-to-sleep ratio causing chronic sleep restriction. These were compared with eight historical controls from a 42.85-hour FD protocol with a 2:1 wake-to-sleep ratio. There were three beat cycles during FD of both studies, with the start of each beat cycle defined by each subjects' habitual waking circadian phase. The circadian amplitude of psychomotor vigilance task median reaction time (RT) was determined at both low and high acute homeostatic sleep pressure (2 versus 26 hours of wakefulness) and early and late into the FD protocol (1st versus 3rd beat cycles).
Results: The circadian amplitude of median RT increased with time awake in both protocols. The amplitude was larger at all time points in the sleep restriction protocol than in the non-sleep restricted, with ratios between the two protocols in Beat 1 at 2 hours of wake =1.7; Beat 1 at 26 hours =7.0; Beat 3 at 2 hours = 2.14, and Beat 3 at 26 hours =15.5. The

increase in amplitude primarily reflected a greater deterioration of performance at the circadian nadir. In contrast, even after 26 hours awake in Beat 3 of the sleep restriction protocol, median RT was only 280 ms at the circadian phase of peak performance.
Conclusion: Vigilance depends on an interaction among acute homeostatic, chronic homeostatic, and circadian mechanisms. The increase in the circadian amplitude of performance under high acute and chronic homeostatic pressure primarily reflects deterioration of performance at adverse circadian phases. Despite high homeostatic pressure, performance can be remarkably preserved during the biological day.
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0465

PREVALENCE OF SLEEPINESS AT THE WHEEL AND SLEEP RELATED ACCIDENTS AMONG A REPRESENTATIVE POPULATION OF FRENCH DRIVERS

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Introduction: Sleepiness at the wheel has been identified as a major risk factor for traffic accidents, but the prevalence of sleepiness-related accidents has never been clearly investigated in France.
Methods: An epidemiological survey (ASFA) based on telephone interview has been conducted in 2007 on 5000 subjects representative of the french drivers (response rate: 80%).
Results: 12.7% of the population was aged from 18 to 30 years (n=597), 43.6% from 31 to 50 years (n=2046), 27.6% from 51 to 65 years (n=1297) and 16.1% was over 65 years old (n=755). The population was composed of 45% of males and 55% of females. 72% of drivers never experienced sleepiness at the wheel, 24% report at least one severe episode of sleepiness at the wheel in the past year (i.e. requiring to stop driving), 3% at least once per month and 1% at least once per week. In the past year, 10% of drivers reported at least one near-miss accident (i.e. inappropriate line crossings) and 45% of these near-miss accidents were sleep-related. In the past year, 5.6% of drivers reported at least one accident and 4.6% of these accidents were sleep-related. Accidents concerned 12.4% of young drivers (18 to 30 years) and 3.3% of mature drivers (51 to 65 years old). Sleep related accidents represent 2.7% of accidents in young drivers and 9.3% in mature drivers.
Conclusion: Our survey shows a high prevalence of traffic accidents possibly of moderate severity (none of the responders were hospitalized). Sleep related accidents represent 2.7 to 9.3% of the accidents on our drivers according to age groups and interestingly, mature subjects seem highly vulnerable to these types of accidents.

0466

ENHANCING SLOW WAVE SLEEP WITH SODIUM OXYBATE REDUCES THE BEHAVIORAL AND PHYSIOLOGICAL IMPACT OF SLEEP LOSS

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Introduction: Prior investigations demonstrated reduced sleep restriction-induced deficits when SWS was pharmacologically enhanced. We examined whether enhancement of SWS with sodium oxybate reduced the impact of sleep deprivation.
Methods: A parallel groups design compared sodium oxybate 3.5 grams (SO) and placebo (PBO). Following screening and baseline assessments, subjects underwent two consecutive sleep deprivation nights, each followed by a 3-hour daytime (0800-1100) sleep opportunity with SO (n=30; mean age: 27.1) or PBO (n=28; mean age 27.1). MSLT, PVT, KSS and POMS were evaluated during all waking hours.
Results: During daytime sleep TST did not differ between groups, but the SO group had more SWS (88.2±2.8 vs 56.8±2.9 min, p<.001) and less REM (12.3±2.2 vs 34.9±2.2 min, p<.001). Mean MSLT was longer for SO on the first night following drug administration (SO=5.0±.47 min, PBO=2.1±.49 min, p<.001) and on the second day (SO=6.7±.88 min, PBO=3.3±.89 min, p=.017). On the first day after drug administration mean latencies were in the same direction (SO=7.1±.87 min, PBO=5.4±.89 min, p=.2). Median PVT reaction time was faster in the SO group on the second day (264.7±4.7 vs 280±4.8 msec; p=.041). On the first night following drug administration, the SO group rated themselves as significantly less sleepy than the PBO group (KSS rating = 7.0±0.2 vs 7.5±0.2; p=.047). The SO group had more negative POMS scores on both days, but not at night. The change from baseline in SWS was correlated with the change in daytime MSLT for the entire sample (r=.334, p=.011). The most common adverse events were dizziness, nausea, and vomiting.
Conclusion: These findings indicate that SO reduces the impact of sleep loss on alertness and attention. The most plausible explanation for this finding is enhancement of SWS.
Support (optional): Jazz Pharmaceuticals

0467

DETECTION AND CHARACTERIZATION OF THE COGNITIVE EFFECTS OF 24 HOURS OF SLEEP DEPRIVATION IN SOLDIERS

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Introduction: Health care professionals, emergency responders, and soldiers frequently undergo extended periods of sleep deprivation in the line of duty. Errors of comprehension and decision-making derived from altered cognitive abilities can influence operational success and survival. The current experiment examines the effects of 24 hours of sleep deprivation on cognition and perception.
Methods: To test our hypothesis that brain structure, physiological function, training and experience affect performance during sleep deprivation, four cohorts were selected: cadets from the U.S. Military Academy at West Point, soldiers from Fort Hood-TX, ROTC soldiers, and age- and sex-matched civilians. Structural brain maps were generated using magnetic resonance imaging (MRI) for gray matter anatomy and diffusion tensor imaging (DTI) for white matter tracts. Vigilance abilities were measured during functional (f)MRI with a virtual reality humvee simulation requiring attention to the appearance of visual threats. Complex decision-making was tested with an alternative forced choice task. Electroencephalographic (EEG) measures of alpha wave activity during eyes-open and eyes-shut were used to measure "alpha reactivity" relating to cognitive state. Brain structural correlates of susceptibility to sleep deprivation were measured by comparing MRI and DTI scans of participants exhibiting susceptibility (i.e. significantly decreased performance on Day 2) or resilience (i.e. performance did not decline on Day 2). To examine the effects of extended periods of sleep deprivation, we administered a battery of perceptual tasks to Norwegian cadets undergoing 8 consecutive days of wakeful activity.

Results: Results demonstrate significant changes in vigilance, decision-making, and sensory perception during sleep deprivation with associated altered brain activity. Cohort-related differences in performance and brain activity were detected.
Conclusion: This study shows that training and individual differences contribute to impaired cognition and altered brain activity during sleep deprivation.
Support (optional): Funding was provided by the Office of the Assistant Secretary of the Army for Acquisition, Logistics and Technology [OASA(ALT)] through the Army Research Laboratory Human Research & Engineering Directorate (ARL-HRED).

0468

CAFFEINE EFFECTS ON VIGILANCE, MELATONIN AND CORTISOL UNDER HIGHER AND LOWER SLEEPINESS LEVELS

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Introduction: It is suggested that the initial activation level influences the effects of caffeine but no study has directly compared the effects of similar doses of caffeine in situations of varying sleepiness levels produced by homeostatic/circadian sleep pressure. Also, effects of caffeine on melatonin/cortisol levels are still a matter of debate and it is unknown whether time of caffeine administration influences these results. This study compares the effects of caffeine in two situations of varying levels of sleepiness (i.e. in the evening after a normal day and during a night of sleep deprivation).
Methods: Fifty moderate caffeine consumers (mean age: 38.3) were assigned to an Evening protocol (EP) or a Night protocol (NP). All subjects participated in both caffeine (200 mg) and placebo (lactose) conditions in a double-blind crossover design. In the EP, subjects received 100 mg of caffeine (or placebo) 3 hours and 1 hour before habitual bedtime. In the NP, subjects were sleep deprived for one night and received 100 mg of caffeine (or placebo) 2 hours before and at habitual wake time. All measures were collected between 30 and 45 minutes after the second dose.
Results: Compared to placebo, caffeine increased subjective alertness and decreased median reaction time for psychomotor vigilance measure (PVT) similarly in the EP and NP. However, the effect of caffeine on PVT slowest reaction time was more prominent in the NP than in the EP and caffeine decreased the number of PVT laps in the NP only. Caffeine increased melatonin secretion in both protocols, but increased cortisol secretion in the NP only.
Conclusion: In conclusion, caffeine shows stronger effects on vigilance in high sleepiness conditions induced by enhanced homeostatic/circadian sleep drive. The effects of caffeine on cortisol but not on melatonin are influenced by time of day.

0469

ATHLETIC PERFORMANCE IMPROVEMENTS AND SLEEP EXTENSION IN COLLEGIATE TENNIS PLAYERS

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Introduction: Few previous studies have focused on the impact of extended sleep and the effects over a prolonged period of time. The present study investigated sleep extension over multiple weeks with a specific focus on the relationship between obtaining extra sleep and assessments of athletic performance. These trials were part of an ongoing study examining varsity sport teams at Stanford University.
Methods: Five healthy students (age 18-21) on the Stanford women's tennis team maintained their habitual sleep/wake patterns for a 2-3 week baseline during their regular tennis season. Athletic performance assessments were reported after every practice throughout the study including sprinting and hitting drills. Both deuce and ad sides were conducted for hitting drills which included valid serves and a depth exercise targeting within 3 feet of the tennis court baseline. Athletes then extended their sleep aiming for 10 hours each night for 5-6 weeks. Profile of Mood States (POMS) was conducted weekly to evaluate mood changes and Epworth Sleepiness Scale assessed daytime sleepiness. Daily sleep/wake activity was monitored by actigraphy and participant reported sleep journals.
Results: Sleep extension was associated with significant improvements in measures of athletic performance. Athletes executed a faster sprinting drill (19.12 ± 0.55 seconds at baseline, 17.56 ± 1.23 seconds at end sleep extension, $p<0.05$) and increased hitting accuracy including valid serves (12.60 ± 2.23 serves vs. 15.61 ± 1.48 serves, $p<0.05$) and hitting depth drill (10.85 ± 2.21 hits vs. 15.45 ± 1.97 hits, $p<0.05$). Athletes reported improved ratings during practices (5.80 ± 1.50 vs. 8.41 ± 1.03, $p<0.05$) and Epworth scores decreased (7.60 ± 3.21 vs. 2.40 ± 2.07, $p<0.05$). POMS vigor scores increased (16.12 ± 4.80 vs. 23.40 ± 3.05, $p<0.05$) and POMS fatigue scores decreased (7.75 ± 3.74 vs. 3.70 ± 3.67, $p<0.05$).
Conclusion: Sleep extension significantly improved assessments of athletic performance and mood in collegiate tennis players.

0470

THE EFFECT OF IN-FLIGHT SLEEP ON FATIGUE-RISK IN ULTRA-LONG-RANGE (ULR) FLIGHT - COMPARISON OF 4-PILOT ULR TO 4-PILOT NON-ULR FLIGHTS

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Introduction: Ultra-long range (ULR) flights are flights greater than 16 hours in duration for more than 10% of flights. To reduce the risk of error, incident, and accident from fatigue, ULR flights are required by the Federal Aviation Administration to have 4-pilot crews and the opportunity for in-flight sleep. To evaluate the relative fatigue-risk of ULR vs. non-ULR flights, we used mathematical modeling to predict the performance effectiveness of Captains flying ULR vs. Captains flying non-ULR flights. In this study, we compared predicted effectiveness of ULR 4-pilot crews with non-ULR 4-pilot crews. Each ULR pilot had the opportunity for 6-7.5 hours in-flight sleep. Each non-ULR pilot had the opportunity for 5-7.5 hours in-flight sleep.
Methods: We used the schedules of 114 Boeing 777 Captains flying both ULR and non-ULR flights. There were 252 ULR flights and 385 non-ULR flights. We estimated in-flight, layover, and at home sleep based on rules taking sleep opportunity and circadian factors into account. The resulting sleep/wake histories were inputted into the SAFTE™/FAST™ mathematical model providing a minute-by-minute effectiveness prediction (scaled 0-100) based on sleep/wake history and circadian rhythm. The first and last hours of flight (critical periods of flight) of the 4-pilot ULR flights were compared to those of the 4-pilot non-ULR flights.
Results: There was no significant difference between the predicted performance effectiveness of ULR Captains (88.7±0.2) and non-ULR Captains (88.6±0.1) averaged across both critical periods of flight ($t[635]=1.7$, $P<0.1$). The ULR Captains predicted performance effectiveness (92.0±0.2) over the first hour of flight was significantly better than the non-ULR Captains predicted performance effectiveness (88.6±0.4) ($t[535] = 9.0$, $P<0.001$). For the last hour of flight the reverse was true. The non-ULR Captains predicted performance effectiveness (88.1±0.3) over the last hour was significantly better than the ULR Captains predicted performance effectiveness (85.4±0.2) ($t[632] = -6.7$, $P<0.001$).

Conclusion: During critical periods of flight, the predicted effectiveness scores for Captains flying both ULR and non-ULR flights were satisfactory (SAFTE™/FAST™ predicted performance > 80). Our modeling findings suggest that there is no overall difference between 4-pilot ULR flights and 4-pilot non-ULR flights. Since 4-pilot non-ULR flights are historically safe, it appears as though fatigue risk in ULR flights is effectively mitigated by in-flight sleep.
Support (optional): Continental Airlines funded this study.

0471

WITHIN-SESSION ANALYSIS OF PSYCHOMOTOR VIGILANCE REVEALS CHANGES IN REACTION TIME AS TIME-ON-TASK INCREASES UNDER ACUTE SLEEP DEPRIVATION AND CHRONIC SLEEP RESTRICTION

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Introduction: Mean reaction time (RT) on the psychomotor vigilance task (PVT) increases during acute sleep deprivation and chronic sleep restriction. We examined whether these increases varied within a PVT session as a function of inter-stimulus interval (ISI) and time within the session (i.e., time-on-task).
Methods: Nine healthy subjects participated in an inpatient protocol that included two 24-hour days (14-hour:10-hour activity:rest) followed by 12 cycles of T=42.85-hour forced desynchrony (FD) with a 3.3:1 activity:rest ratio (32.85-hour:10-hour). A 10-minute PVT was administered every 4 hours. Data were analyzed for well-rested (WR, two 24-hour days preceding FD, PVT given 2-h and 6-h after wake), acute sleep deprivation (ASD, first FD cycle, PVT given 26-h and 30-h after wake) and chronic plus acute sleep deprivation (CASD, eighth or ninth FD cycle, PVT given 26-h and 30-h after wake) conditions. ASD and CASD conditions were matched for circadian phase. Mean RT as a function of ISI (binned by 1000 ms) was calculated for the first ("Early") and last ("Late") 2 minutes and full 10-minutes ("All") of each PVT session. A two-way ANOVA was used to test the effect of time-on-task and ISI on mean RT in each sleep condition.
Results: Mean RT and RT variability increased from WR to ASD to CASD. A main effect of time-on-task on mean RT was observed in all 3 conditions (WR p=0.003, ASD p=0.002, CASD p=0.01), with mean RT increasing from "Early" to "Late". No main effect of ISI or interaction of time-on-task and ISI was observed. The increase in mean RT from WR to ASD to CASD was observed in both "Early" and "Late", but increases in variability were observed in "Late" only.
Conclusion: PVT RT mean and variability change with time-on-task even under well-rested conditions. Increases in mean RT and variability as a function of time-on-task suggest reduced ability for subjects to maintain vigilant attention, especially after insufficient sleep (ASD and CASD).
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0472

THE EFFECT OF IN-FLIGHT SLEEP ON ESTIMATED FATIGUE-RISK IN ULTRA-LONG-RANGE (ULR) FLIGHT - COMPARISON OF 4-PILOT ULR WITH 2 TO 3 PILOT NON-ULR FLIGHTS

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Introduction: Ultra-long range (ULR) flights are flights greater than 16 hours in duration for more than 10% of flights. To reduce the risk of error, incident, and accident from fatigue, ULR flights are required by the Federal Aviation Administration to have 4-pilot crews and the opportunity for in-flight sleep. To evaluate the relative fatigue-risk of ULR vs. non-ULR flights, we used mathematical modeling to predict the performance effectiveness of Captains flying ULR flights vs. Captains flying non-ULR flights. In this study, we compared predicted effectiveness of ULR 4-pilot crews with non-ULR 2 to 3-pilot crews. Each ULR pilot had the opportunity for 6-7.5 hours in-flight sleep. For 3-pilot crews each non-ULR pilot had the opportunity for 1.5-3 hours in-flight sleep, while 2-pilot crews had no in-flight sleep opportunity.
Methods: We used the schedules of 114 Boeing 777 Captains flying both ULR and non-ULR flights. There were 252 ULR flights and 264 non-ULR flights. We estimated in-flight, layover, and at home sleep based on rules taking sleep opportunity and circadian factors into account. The resulting sleep/wake histories were inputted into the SAFTE™/FAST™ mathematical model providing a minute-by-minute effectiveness prediction (scaled 0-100) based on sleep/wake history and circadian rhythm. The first and last hours of flight (critical periods of flight) of the 4-pilot ULR flights were compared to those of the 2 to 3-pilot non-ULR flights.
Results: Over the combined critical periods, predicted performance effectiveness was greater for ULR Captains (88.4±0.2) than for non-ULR Captains (83.8±0.2) ($t[514]=20.9$, $P<0.001$). The predicted performance effectiveness of ULR Captains (92.0±0.2) was also significantly better during the first hour of flight compared to that of the non-ULR Captains (88.1±0.5) ($t[315]=7.3$, $P<0.001$). Similarly, during the last hour of flight, the predicted performance effectiveness of ULR Captains (85.4±0.2) was significantly greater than the predicted performance effectiveness of non-ULR Captains (79.5±0.5) ($t[400]=11.7$, $P<0.001$).
Conclusion: During critical periods of flight, Captains flying ULR flights had greater predicted effectiveness than Captains flying 2-3 pilot non-ULR flights. Two to 3-pilot non-ULR flights have historically been safe. Our modeling findings suggest that the augmented 4-pilot crews in ULR flying and associated longer in-flight sleep opportunities effectively mitigate fatigue-risk in ULR flights.
Support (optional): Continental Airlines funded this study.

0473

CAFFEINE PROTECTS AGAINST INCREASED RISK-TAKING BEHAVIOR DURING SEVERE SLEEP DEPRIVATION

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Introduction: Previous research suggests that sleep deprivation increases risky decision-making but may actually have a mitigating effect on a behavioral task of risky behavior that requires the expenditure of effort (i.e., Balloon Analog Risk Task; BART). Furthermore, stimulant medications such as caffeine show no effect on these measures. Here we extend the period of sleep deprivation to 75 hours to assess the effects of continuous wakefulness and repeated doses of caffeine on risk-taking behavior on the BART.
Methods: Twenty-five healthy volunteers (21 men; age range 20-35) were deprived of sleep for three nights. In a double-blind administration, subjects received 200mg caffeine gum (n=12) or identical placebo gum (n=13) bi-hourly from 0100-0700 each morning during the sleep deprivation period (i.e., total 800 mg/session). The BART was administered at 1020 on the first morning following a full night of sleep (8 hours time in bed), again following 51.3 hours of continuous wakefulness, and finally after 75.3 hours of wakefulness. The dependent variable for the BART was the Cost/Benefit Ratio (i.e., percent of all balloons exploded/percent of possible money won). Data were analyzed with a mixed-model analysis of covariance, controlling for education level, handedness, study week, and total BART pumps at baseline.

Results: There was a significant drug x session interaction (p=.023). The placebo group was unchanged from baseline on the Cost/Benefit Ratio at 51 hours of sleep deprivation, but showed a significant increase in risk-taking by 75 hours. In contrast, the caffeine group remained unchanged from baseline at either 51 or 75 hours of wakefulness, and was significantly less risky than the placebo group at 75 hours.
Conclusion: Two nights of sleep loss did not affect risky behavior, consistent with previous findings. However, when extended to three nights, sleep deprivation was associated with greater risk-taking. Overnight caffeine prevented this increase in risky behavior.

0474

CHARACTERISING THE LAPSE DUE TO EYES OPEN, EYES CLOSED OR DISTRACTION: EFFECTS OF SLEEPINESS AND DISTRACTION

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Introduction: To avoid tedium, and remain awake, sleepy people seek alternative stimulation. Little is known about behavioural concomitants of a lapse and whether this changes as a function of sleepiness and/or environment. Here, we identified each PVT lapse as occurring with eyes open, eyes closed, or due to distraction and assessed the change due to sleepiness and/or distractive environment.
Methods: Twenty-four healthy, young adults (23.2±2y), screened good sleepers (8±1h), without daytime sleepiness (<2naps/month and ESS scores <10) underwent two 30 minute psychomotor vigilance task at 22:00h and 04:00h in a repeated measures 2x2 counterbalanced design, with two sleepiness conditions (22:00h vs. 04:00h) and distraction Vs no distraction. Distraction comprised a video in the visual periphery, showing an episode of a popular TV show. Subjects had to ignore this and attend to the PVT. For 'no-distraction', the TV was off. Lapses (responses ≥500msecs) were logged and distractions assessed from a video camera on the subjects' faces. Each lapse was categorized as eyes open (EO), eyes closed (EC), or distraction (D).
Results: EO and EC lapses showed a main effect of sleepiness ($p<0.0005$) but no effect of distraction. D lapses (due to a head turn) increased due to sleepiness ($p<0.01$) and distraction ($p<0.03$), and were exacerbated when sleepy and distracted ($p<0.04$). For lapse duration, there was a significant effect of lapse type ($p<0.0005$): EC-lapses were longer than EO- and D-lapses ($p<0.0005$) and D-lapses were significantly longer than EO-lapses ($p<0.005$).
Conclusion: Individual characterisation of lapses show eyes closed-lapses and distraction-lapses are longer in duration than those occurring with eyes open. Both eyes closed and distraction lapses are sensitive to sleepiness, with distraction-lapses being further exacerbated in a non-sterile environment. Our findings reveal more insight can be gained from the PVT which has important implications on the real world.
Support (optional): This work was financially supported by a UK Economic and Social Research Council (ESRC) grant: RES-000-23-1583.

0475

WITHIN-SESSION ANALYSIS OF PSYCHOMOTOR VIGILANCE REVEALS DEPENDENCE OF ANTICIPATIONS ON INTER-STIMULUS INTERVAL UNDER ACUTE SLEEP DEPRIVATION AND CHRONIC SLEEP RESTRICTION

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Introduction: The number of anticipatory responses (i.e., physiologically impossible response times) on the psychomotor vigilance task (PVT) increases during acute and chronic sleep deprivation. We examined whether these increases varied within a PVT session as a function of inter-stimulus interval (ISI) and time elapsed within the session (i.e., time-on-task).
Methods: PVT data from 9 inpatient subjects scheduled to two 24-hour days (14-hour:10-hour activity:rest) followed by 12 cycles of T=42.85-hour forced desynchrony (FD) with a 3.3:1 activity:rest ratio (32.85-hour:10-hour) were used for this analysis. A 10-minute PVT was administered every 4 hours. Data were analyzed for well-rested (WR, two 24-hour days preceding FD, PVT given 2 hours and 6 hours after wake), acute sleep deprivation (ASD, first FD cycle, PVT given 26 hours and 30 hours after wake) and chronic plus acute sleep deprivation (CASD, eighth or ninth FD cycle, PVT given 26 hours and 30 hours after wake) conditions. ASD and CASD conditions were matched for circadian phase. The number of anticipations (RT<100ms) as a function of ISI (binned by 1000 ms) were calculated for the first ("Early") and last ("Late") 2 minutes and full 10-minutes ("All") of each PVT session. A two-way ANOVA was used to test the effect of time-on-task and ISI on anticipations in each sleep condition.
Results: The number of anticipations increased from WR to ASD to CASD. A positive linear relationship between ISI and anticipations was observed for "All" in each condition (WR: $p=0.001$ slope=0.08; ASD: $p<0.0001$, slope=0.22; CASD: $p=0.02$, slope=0.22). The number of anticipations "Early" and "Late" within a session differed only in WR ($p=0.002$). A significant main effect of ISI in "Early" and "Late" was observed only in ASD ($p=0.002$).
Conclusion: An increase in anticipations as ISI increases during sleep deprivation or sleep restriction suggests altered response to vigilance tasks with insufficient sleep. However, there was only an effect of time-on-task on anticipatory responses during WR.
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0476

COMPENSATORY CHANGES IN NUCLEOSIDE TRANSPORTERS AND SLEEP-WAKE PATTERN IN TYPE 1 EQUILIBRATIVE NUCLEOSIDE TRANSPORTER KNOCKOUT MICE

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Introduction: Adenosine has been suggested to be a sleep inducing factor in homeostatic sleep regulation. The nucleoside transporters are one of the factors that regulate the levels of intra- and extra-cellular adenosine. There are two main classes of nucleoside transporters including equilibrative transporters (ENT) and concentrative symporters (CNT). Previous studies have shown that blocking the ENT1 transporter increased the levels of extracellular adenosine, inducing increased sleep. Sleep deprivation (SD) compromised the adenosine binding function of ENT1, suggesting a decreased transport into the cell may be responsible for the elevated levels of extracellular adenosine during SD. Consequently the effects of ENT1 gene knock out on sleep-wake behavior, SD-induced changes in brain adenosine levels, and compensatory changes in the mRNA expression of other transporters are of interest.
Methods: ENT1-null mice were generated and genotyped using published method (Doo-Sup Choi et al, 2004). In order to assess any compensatory change in other adenosine transports, we performed real-time

polymerase chain reaction (RT-PCR) for relative quantification of the mRNA expression of ENT2, ENT3, ENT4, CNT2, and CNT3. We measured the sleep-wake behavior and nonREM delta activity (1-4Hz) using electroencephalogram during spontaneous sleep-waking cycle, 6h SD and recovery sleep. Microdialysis cannulae were implanted into the cholinergic basal forebrain (BF) for measuring extracellular adenosine levels by microdialysis and high performance liquid chromatography during baseline, 6h SD and recovery sleep.
Results: There were no compensatory changes observed in the mRNA expression of ENT2, ENT3, ENT4, CNT3 and CNT3 between wild type and ENT-null mice. We observed no change in the duration of Wake, nonREM or REM sleep both during baseline and 18h following 6h SD. However, there was a significant difference in the delta activity during the baseline nonREM sleep ($F(5,35)=2.154$, $p<0.001$) between the WT, hetero and KO groups. The SD studies and adenosine measurements are in progress.
Conclusion: Absence of ENT1 expression in knockout mice showed a significant decrease in NREM delta. This effect is presumably due to the changes in extracellular adenosine levels resulting from the absence of ENT1 as there were no compensatory changes observed in the expression of other transporters.
Support (optional): VA Merit Award and NIMH 39683

0477

EXECUTIVE FUNCTIONS PREDICT THE ABILITY TO SUSTAIN PSYCHOMOTOR VIGILANCE DURING SLEEP LOSS

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Introduction: There is considerable variability among individuals in the ability to sustain performance during sleep loss. We tested the hypothesis that individuals with higher trait-like functioning of the prefrontal cortex may be less vulnerable to fatigue.
Methods: Fifty-four healthy volunteers (29 men; mean age = 23.5 years, SD = 4.0) stayed in a sleep laboratory and received a normal night of sleep (8 hrs). While well-rested, participants were administered a battery of neuropsychological tests that included several tasks that measured executive functioning (Letter Fluency; Stroop Color-Word Test; Color Trails Test) and a variety of tasks not specifically designed to measure executive functioning (i.e., demographics, intelligence, perception, handedness, morningness-eveningness, and control portions of the Color Trails and Stroop Tests). Participants completed psychomotor vigilance testing (PVT) bi-hourly while deprived of sleep for 41 hours. Two groups were formed comprising the upper and lower quartiles of performance on the PVT. The top 25% of the sample was classified as "Resistant" to sleep deprivation while the bottom 25% was classified as "Vulnerable" to sleep deprivation. The two groups were compared for performances on baseline testing using t-tests.
Results: Resistant subjects (n = 13) scored significantly higher than Vulnerable subjects (n = 13) on the three baseline tasks designed to assess prefrontal executive function abilities ($p<.05$), whereas groups did not differ on any of the non-executive function tasks (all p-values>.05). Similarly, there were no group differences on demographic variables such as age, education, hand preference, morningness-eveningness, IQ, or sleep history.
Conclusion: Subjects scoring higher on measures of executive functioning at rested baseline were more resistant against one night of sleep loss than subjects with lower baseline executive function abilities. This is consistent with the notion that the ability to sustain alertness during sleep loss is related to the functional capacity of prefrontal brain systems.

0478

IDENTIFYING GENES THAT REGULATE SLEEP HOMEOSTASIS IN *DROSOPHILA*

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Introduction: Sleep homeostasis is a defining feature of sleep in mammals, birds, reptiles and invertebrates yet little is known about the underlying mechanisms. The homeostatic response to sleep loss is exacerbated in some clock mutants suggesting they may be particularly useful in elucidating mechanisms underlying homeostasis. Thus, we conducted gene profiling in flies mutant for the canonical clock gene *timeless* (*tim01*). *tim01* mutants exhibit a specific sleep phenotype that makes them uniquely suited to identify genes involved in sleep homeostasis. Specifically, *timeless* mutants show no homeostatic response to 3 or 6 h of sleep deprivation, whereas 9 or 12 hours of sleep deprivation results in an exaggerated sleep rebound.
Methods: Flies mutant for *timeless* were maintained in constant conditions and sleep deprived for 3, 6, 9 or 12 hours. RNA was extracted from whole heads and converted to cDNA for micro-array analysis and compared to untreated controls. Quantitative RT-PCR was used to validate changes in expression levels.
Results: Approximately 10,000 genes were "present" of which 500 genes were significantly different following post-hoc tests. These genes were fell into gene-ontology categories including chaperones, channels, proteolysis, transcription factors, kinases/phosophotases, and metabolism. Follow up studies have begun to provide genetic evidence for the role of several of these genes in sleep homeostasis.
Conclusion: These results show that genes can be identified that mediate homeostasis using the gene profiling in the canonical clock mutant *timeless*.

0479

METABOLIC DISTURBANCES IN INTERNAL MEDICINE TRAINEES AT THE VACHS

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Introduction: During training, physicians are subject to changes in their sleep pattern. We aim to evaluate the effects in metabolism to a cohort of trainees that recently began their training.
Methods: Cohort ongoing study. Forty two subjects were enrolled. Eleven continue on the study and 31 were excluded from the initial evaluation due to failure to attend for blood samples follow up. Samples for leptin, insulin, fasting blood sugar (FBS) and lipid profile at base line and 3 months follow up were obtained, as well as sleepiness questionnaire
Results: Mean leptin levels at baseline/3months follow up was 9.054,10 respectively. Mean insulin levels were 12.172/10.227 baseline and follow up; Mean FBS were 83.727/81.454 respectively. No statistical difference was seen at baseline and follow up in these variables, as well as in the lipid profile. When comparing groups by sex, women have lower levels of insulin, FBS, cholesterol, TG, LDL and HDL than men, at initial and at follow, but there was no statistical difference. Within the 3 month evaluation, comparing women and men, women had reported higher levels of leptin hormone with a statistical difference ($p= 0.005$). None of our subjects slept less than 4 hrs daily.
Conclusion: These initial findings suggest that the circadian rhythm alterations suffered by trainees that worked prolonged hours did not have an effect on metabolism. The lack of sleep deprivation may be the culprit of our findings, considering that it is documented that the effects in metabolism related to sleep deprivation are expected after at least 6 continuous days with 4 hrs or less of sleep. The study is ongoing.

0480

LEPTIN LEVELS IN YOUNG HEALTHY MEN AND WOMEN ARE INCREASED AFTER ONE NIGHT OF SLEEP LOSS IN A NON-STRESSFUL ENVIRONMENT

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Introduction: Short-term sleep curtailment in healthy men is associated with decreased leptin levels, impaired insulin sensitivity and increased hunger and appetite. The objectives of this study were to assess: 1) the effects of one night of sleep loss in non-stressful environment on leptin, adiponectin and hunger, and 2) whether a 2-hour mid-afternoon nap reverses the changes associated with sleep loss.
Methods: Twenty-one young healthy individuals (10 men, 11 women) participated in a 7-day sleep deprivation experiment (four consecutive nights in the sleep laboratory followed by a night of sleep loss [fifth night] and two recovery nights). Half of the subjects were randomly assigned to take a mid-afternoon nap (1400-1600) the day following the night of total sleep deprivation. Serial 24-hour blood sampling, subjective and objective levels of sleepiness, and performance were obtained on the fourth (pre-deprivation) and sixth days (post-deprivation). Also, during these two days hunger was assessed prior to each meal with the Penn State Hunger/Fullness Scale.
Results: The day after one night of sleep deprivation, there was a significant increase of sleepiness, decrease of performance and no difference in hunger level. Leptin levels were significantly increased on the day after one night of total sleep deprivation (13.92 ± 2.4 vs. 17.35 ± 2.7, P=0.001), however, during the ensuing night there was no difference in leptin levels compared to baseline. Adiponectin levels were not affected by one night of sleep loss. Daytime napping did not influence the effects of sleep loss on leptin, adiponectin or hunger.
Conclusion: Acute sleep loss in a non-stressful environment influences leptin levels in an opposite manner from that associated with short-term sleep curtailment. It appears that high leptin levels during the daytime after one night of total sleep loss may serve to adjust eating behavior in a manner that promotes sleep and sleepiness.
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0481

AMPHETAMINE-INDUCED SLEEP DEPRIVATION DOES NOT IMPAIR PAVLOVIAN FEAR CONDITIONING IN MICE

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Introduction: Inadequate sleep is becoming increasingly common in our 24-hour society. Recent studies suggest sleep is critical to consolidation of hippocampus-dependent memories. The current study aims to use a mouse model to assess the impact of sleep deprivation on Pavlovian fear conditioning.
Methods: Mice were trained on Pavlovian fear conditioning an hour prior to their light/sleep phase. The sleep deprived group were administered 8kg/mg of amphetamine immediately prior to their first light phase and 4 hours later to sustain wakefulness throughout the first 12 hours of the light phase. The control group were administered a vehicle immediately and 4 hours post-training. Following 72 hours after training, both groups were tested for contextual and cued fear.
Results: There were no differences in performance between the sleep deprivation and control groups on either context or cued memory.
Conclusion: This suggests that prior sleep deprivation impairments may be a result of stress-related consequences and not from sleep deprivation itself.

0482

MEASUREMENT AND ESTIMATION OF SLEEP IN RAILROAD WORKERS

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Introduction: Operational fatigue is a constant factor in round-the-clock railroad operations. Fatigue risk management systems (FRMS) often utilize fatigue modeling as a tool to assess fatigue and operational risk. Biomathematical fatigue models generally depend on some method to estimate the amount of sleep associated with a work schedule. From this estimate of sleep, the model then predicts alertness or performance decrements.
Methods: The study to be reported was conducted with a random sample of railroad workers who maintained log books of work, sleep and other activities. These records of sleep were used to characterize the levels of sleep restriction in different work groups and the expected changes in performance based on the Sleep, Activity, Fatigue, and Task Effectiveness (SAFTE) model. We also estimated sleep under the work schedules using an algorithm used in conjunction with SAFTE called AutoSleep. The study evaluated the accuracy of the AutoSleep algorithm and the implication for predictions of performance and fatigue. We randomly sampled dispatchers (N=443), signalmen (N=389), and maintenance of way workers (N=254). Volunteers recorded in a paper log book work, sleep, commuting, and other activities during a 14 day period. The sleep data were used to estimate performance effectiveness from SAFTE and the work schedule data were used to drive the AutoSleep algorithm to estimate sleep patterns. We compared the concordance of the estimated sleep patterns with the log book recorded sleep.
Results: The results showed that the AutoSleep algorithm was highly predictive of sleep patterns in all groups, with the lowest concordance found in night shift dispatchers. The importance of errors in sleep estimation was evaluated by comparing performance predictions using recorded sleep versus estimated sleep.
Conclusion: These results indicate that computer modeling and simulation can be a useful tool for estimating aggregate railroad work group sleep patterns and fatigue based entirely on work schedule information.
Support (optional): Funding for this research was provided by the Federal Railroad Administration.

0483

SLEEP DEPRIVATION AND FRAGMENTATION EFFECTS ON ANTERIOR CINGULATE FUNCTION - A FMRI STUDY

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Introduction: Sleep disorders causing sleep fragmentation have been associated with disorders of attention and mood.
Methods: We studied twelve medication and disease free healthy, non-snoring individuals (age 21-55) with functional MRI (3 Tesla, thirty 3 mm whole brain slices, parallel to the AC-PC line). Participants were initially randomized to one of three conditions: 1) rested, 2) one night of sleep deprivation, or, 3) one night of brief-tone auditory sleep fragmentation. Each participant was studied in all three conditions. Participants performed a performance vigilance task before entering the scanner and a Stroop-like task (Multi Source Interference Task) during functional imaging.
Results: Participants slept an average of 384 minutes (+/-18.6) during the baseline night and 352 minutes (+/-34.2) during the fragmented night. During the baseline night, participants spent 6.0 minutes (+/- 3.3) in stage 1, 22.0 minutes (+/-4.8) in stages III and IV, and 18.7 minutes

(+/- 3.7) in REM, while during the fragmented night, participants spent 14.8 minutes (+/-6.8) in stage 1, 16.0 minutes (+/- 6.6) in stages III and IV, and 15.6 minutes (+/- 3.2) in REM. The arousal index was 8.0 (+/- 2.9) during the baseline night 16.0 (+/- 4.4) during the fragmented night. Fragmentation altered functional activation as follows: Both sleep deprivation and sleep fragmentation reduced activation in the executive network, including in the anterior cingulated cortex. Fragmented sleep resulted in greater activation reductions than sleep deprivation. ANOVA revealed significant effects for baseline non-response, baseline-fast, and task non-response. Contrast analyses revealed that these effects were due to differences between rested and deprived conditions for task non-response and baseline-fast, and between rested and deprived and rested and fragmented for baseline non-response. Performance differences between fragmented and deprived conditions were not significant, while activation was.

Conclusion: Sleep fragmentation and deprivation may have differential effects on components of complex cognitive tasks. The results have implications for sleep apnea and conditions associated with acute sleep fragmentation, such as environmental noise.

Support (optional): Funding: National Institutes of Health

0484

IMPACT OF ACUTE AND CHRONIC SLEEP RESTRICTION ON PVT PERFORMANCE: A STUDY OF MEDICAL RESIDENTS

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Introduction: Under controlled laboratory conditions, chronic sleep restriction of 3 to 6 hrs/night for 7-14 nights gradually degrades Psychomotor Vigilance Task (PVT) performance. Less is known about whether this accumulative decrement occurs outside the laboratory. US medical residents work 24- to 30-hr extended shifts twice per week, resulting in both acute and chronic sleep loss. Here, we address the impact of working repeated extended duration work shifts on PVT performance.

Methods: Seventeen PGY-1 medicine residents (26-32y, 7F) worked 30-hour shifts twice per week in an intensive care unit (ICU) for three weeks, such that they worked at least six extended duration shifts; this followed 3 weeks of non-extended shifts. Subjects completed 10-min PVTs 3-6 times at regular intervals across each extended duration shift. Mean log_reaction time (RT) and transformed lapses greater than 500ms ($\sqrt{n}+\sqrt{(n+1)}$) were assessed for change over time (extended shifts block 1-6). Controlling for time of day, we assessed differences in performance at the start and end of each shift as a function of the number of extended shifts.

Results: Mean RT and lapses worsened with increasing number of extended shifts (one-way repeated measures ANOVA, $p<0.05$, $p<0.02$, respectively), with post hoc comparisons showing performance to be worse during the last two extended shifts as compared to the first two ($p<0.008$). For overnight performance (23:00-08:00h), there was a significant effect of extended shift number for mean RT ($p<0.05$) but not lapses. For day-time performance (7:00h-14:00h), both mean RT and lapses showed a significant worsening with increasing number of extended shifts ($p<0.009$, $p<0.003$, respectively) and time on shift ($p<0.002$, $p<0.0005$, respectively).

Conclusion: Residents working traditional on-call schedules exhibit poorer performance in the second half of each 24-30-hr extended shift as a result of acute sleep deprivation, and show a chronic deterioration in performance with increasing number of extended shifts.

Support (optional): Data collection was supported by grants from NIOSH (RO1 OH07567) and AHRQ (RO1 HS12032) and was conducted in a General Clinical Research Center (NCRR M01 RR02635).

0485

CHRONIC SLEEP RESTRICTION AUGMENTS THE ACQUISITION OF DRUG-SEEKING AND DRUG-TAKING BEHAVIORS IN RATS

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Introduction: Substance abuse is a major concern within the United States, compounded by the propensity of many addicted individuals to relapse. The clinical literature suggests sleep deprivation is a factor that can induce relapse in humans, and, in fact, our society is plagued by chronic sleep deprivation. Previously, our lab demonstrated that acute sleep deprivation reliably increases the rate and efficiency of drug-seeking and drug-taking behaviors in otherwise unresponsive, low drug-taking rats. The current study utilized a chronic sleep restriction model to further elucidate the effects of sleep deprivation on drug addiction in a model more similar to that experienced by the human population.

Methods: Naïve male Sprague-Dawley rats were chronically deprived of approximately 30% of their baseline sleep (CSD; n=20) or served as non-sleep-deprived controls (NSD; n=15). During the same time period, all rats were trained to self-administer cocaine on a fixed ratio (FR) schedule of reinforcement. In addition, progressive ratio (PR) testing was used to assess the willingness of the rats to work for cocaine.

Results: In accordance with our acute sleep deprivation data, CSD rats self-administered more cocaine infusions during FR training, compared to NSD controls. Also, CSD rats exhibited higher break points (i.e., worked harder for cocaine), shorter inter-infusion intervals (i.e., self-administered cocaine more quickly), and more goal-directed behavior (i.e., focused more exclusively on the drug-associated operandum) than NSD controls during PR testing.

Conclusion: These data have profound clinical implications, and highlight the importance of the awareness of potential relapse-inducing factors, such as sleep deprivation, in the treatment of drug addiction.

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0486

GENERAL INTELLECTUAL FUNCTIONING DOES NOT PREDICT PERFORMANCE IMPAIRMENT ON THE PSYCHOMOTOR VIGILANCE TEST DURING TOTAL SLEEP DEPRIVATION

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Introduction: There are substantial, trait-like individual differences in performance impairment on the psychomotor vigilance test (PVT) during total sleep deprivation (TSD). Based on theories of cognitive reserve and compensatory brain mechanisms, we hypothesized that overall cognitive ability might predict individual differences in PVT impairment due to TSD. In the present study, we aimed to test this hypothesis using the Shipley Institute of Living Scale (SILS), a validated measure of general intellectual functioning.

Methods: As part of a larger study, 12 healthy young adults (age 27.4±4.5; years of education 14.3±1.9; 5 females) spent 7 consecutive days in a laboratory. Following two baseline days with 10h time in bed, subjects underwent 62h of TSD. Performance on a 10min PVT was tested at 2h intervals throughout most scheduled wakefulness. PVT number of lapses (RT>500ms) was averaged across a baseline period from 0h to 14h awake; across the 24h TSD period from 14h to 38h awake; and across the subsequent 24h TSD period from 38h to 62h awake. The SILS was administered during baseline. Raw SILS scores were converted to

Wechsler Adult Intelligence Scale (WAIS) estimates of IQ stratified by age using established benchmarks.
Results: SILS scores ranged from 51 to 69, corresponding to IQ estimates ranging from 103 to 119. Substantial individual differences in PVT performance impairment were similar in magnitude to those reported in earlier studies. No significant relationship was found between the SILS scores and average PVT lapses during 14h-38h awake (r=-0.17, P=0.59); during 38h-62h awake (r=0.07, P=0.82); or during the two intervals of TSD combined (r=-0.05, P=0.88). Results were similar when using estimated IQ scores: there was no significant relationship with average PVT lapses during 14h-38h awake (r=-0.13, P=0.68); during 38h-62h awake (r=0.09, P=0.79); or during these intervals of TSD combined (r=-0.02, P=0.95). Correcting for baseline PVT performance did not substantively alter these results.
Conclusion: In our sample of healthy young adults with average to above-average estimated IQ, individual differences in PVT performance impairment during TSD were not predicted by SILS scores, or by estimated IQ scores corrected for age. In this population, vulnerability to PVT performance impairment due to TSD does not appear to be a function of general intellectual functioning.
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0487

ASSESSING FATIGUE USING EEG CLASSIFICATION METRICS DURING NEUROCOGNITIVE TESTING

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Introduction: Fatigue is a primary contributor to transportation and industrial accidents in the US and has been increasingly recognized as a major public health concern. The Alertness and Memory Profiler (AMP) quantifies electroencephalogram (EEG) and performance during vigilance and memory tests to objectively characterize neurocognitive impairments due to fatigue.
Methods: 35 healthy participants (16 male; age=24.5±8.5, apnea-hypopnea-index - AHI≤5 in all) completed two separate 4-hour AMP sessions: one fully rested (FRS) session, followed by one sleep deprived (SDS) session. Participants were allowed to sleep for two hours the night before SDS. Test battery included 3-Choice-Vigilance-Test(3C-VT), Standard Image-Recognition(SIR), Image Recognition with Interference (IIR), Verbal Paired-Associate-Learning(VPA), Number Image Recognition(NIR) and Sternberg-Verbal-Memory-Scan(VMS). AMP quantified performance (reaction times, % correct answers), measured engagement on a 4-category scale (high, low, distracted, drowsy) on the basis of the EEG power spectra, and derived neurocognitive factors(NCF) for Visuospatial Processing speed(VPS), Recognition Memory Accuracy(RMA) and Sustained Attention(SA). Differences in performance-based NCF between FRS and SDS were tested with RMANOVA.
Results: Compared to FRS, SDS showed decreases in EEG high engagement during 3C-VT ($F=50.387$, $p<.05$), SIR2($F=5.964$; $p<.01$), VMS($F=12.63$; $p<.01$), and VPA($F=4.592$; $p<.05$) and increases in EEG-distraction and EEG-drowsiness during 3C-VT($Fs>6.338$, $ps<.01$), NIR($Fs>6.365$,$ps<0.05$), SIR2 ($Fs>9.893$; $p<.01$), and VMS($Fs>5.876$; $ps<.05$). SDS also significantly decreased performance-based NCF: VPS($F=7.242$; $p<.05$), RMA($F=6.672$; $p<.05$), and especially SA ($F=11.111$; $p<.05$), which dropped to 3 SD below normative levels.
Conclusion: Sleep deprivation resulted in decreased visuospatial processing speed, recognition memory accuracy, and sustained attention based on AMP task performance. Performance decreases during sleep deprived sessions were coupled with significant changes in EEG classification metrics. EEG-Engagement decreased while EEG-distraction and EEG-drowsiness increased. Thus, EEG classification metrics proved to be accurate indicators of fatigue-related neurocognitive impairments in healthy participants, allowing for a more comprehensive assessment of fatigue.
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0488

HIGH THROUGHPUT BRAIN-BEHAVIOR ASSAY: QUANTIFICATION OF EEG AND PERFORMANCE IN PATIENTS REFERRED FOR ASSESSMENT OF DAYTIME DROWSINESS

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Introduction: Excessive daytime somnolence (EDS) is currently assessed with the Maintenance of Wakefulness Test (MWT). The Alertness and Memory Profiler (AMP) quantifies EEG/performance during vigilance and memory tests to objectively quantify drowsiness and characterize neurocognitive impairments.
Methods: Patients referred to the NYU Sleep Disorders Center with any diagnosis of a sleep disorder (n=28, 20 males, mean RDI=29.7/hr, SD=20.7, range 2.7-65.3) underwent full polysomonography followed by MWT (four 20-minute sessions, every two hours) scored according to AASM guidelines. Mean Epworth Sleepiness Scale (ESS) was 9.6, SD=4.7, range 0-20). AMP assessments conducted between MWT trials included EEG/performance quantified during: 3-Choice-Vigilance-Test, Recognition-Memory, Verbal/Number-Image Paired-Associate-Learning, and Sternberg-Verbal-Memory-Scan. Four neurocognitve factor scores, Visuospatial-Processing-Speed (VSPS), Sustained Attention (SA), Recognition-Memory-Accuracy & Recognition-Memory-Speed (RMA/RMS) and a global severity level were derived from EEG/performance data.
Results: Mean MWT across all sessions was 16.22 min (SD=5.13, range 2.25-20.0); eleven patients maintained wakefulness during the full 20-minutes for all sessions. Mean MWT was significantly correlated with AMP Sustained-Attention (Pearson $r=0.50$,$p<.001$) confirming previous results showing impaired Sustained Attention in sleep-deprived normals and patients with Sleep Apnea. In comparison to matched healthy controls (n=28), NYU patients evidenced significantly slower VSPS ($F(1,54)=11.90$,$p<.0001$), impaired RMA ($F(1,54)=8.77$,$p<.005$) and higher global severity as measured by an EEG composite evaluation score from a 2-class Linear Discriminant Function Analysis using 60 EEG variables ($F(1,54)=8.20$,$p<.01$).
Conclusion: Patients evidenced varying degrees of EDS as measured objectively by MWT and AMP Sustained Attention scores and subjectively by ESS. In addition to EDS, patients evidenced slower visuospatial processing speed and impaired recognition memory accuracy in comparison to healthy controls and higher levels of an EEG-based measure of global severity previously shown to be elevated in patients with sleep apnea. An assay that quantifies neurocognitive impairments associated with sleep and neurological disorders offers additional information that could improve diagnostic and treatment outcome evaluations.

0489

EEG DYNAMICS DURING REPEATED SLEEP RESTRICTION AND RECOVERY SUPPORT ROBUST HOMEOSTATIC RESPONSES TO LOST SLEEP OVER TIME

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Introduction: The strong reciprocal balance between time awake and slow wave activity (SWA), also called sleep homeostasis, has not been confirmed in studies with chronic sleep loss. The aim of the present study was to investigate which parts of sleep physiology that react in a compensatory manner during repeated sleep restriction and subsequent recovery.
Methods: Nine healthy males (age range 23-28 yrs) went though a laboratory protocol including 2 baseline days (sleep 23-07h), 5 days with sleep restriction (03-07h) and three recovery days (23-07h). Non REM (NREM) -sleep EEG was analyzed with respect to spectral analysis.
Results: Sleep restriction resulted in an acute reduction of all NREM-sleep frequencies (0.50-8.00 Hz constituting the delta and theta frequency bands) if total sleep is considered ($p < .05$). However, if only the first 3.8 hours of sleep are analyzed most sleep frequencies (1.50-8.00 Hz) increased already the first night with restricted sleep and continued to increase in a gradual fashion, leveling off after 3-4 days (p's <05). Although the compensatory increase is most obvious in the lower frequencies (2-4Hz), which is within the traditional SWA-delta band, "all" sleep frequencies (0.75-8.00 Hz) were augmented also during the first recovery night.
Conclusion: SWS and summed power density in a broad low frequency band respond to repeated sleep restriction in a dose-response fashion during the first 4h sleep, apparently reflecting a robust and stable homeostatic response to sleep loss. Thus, the data did not support an allostatic change during chronic sleep restriction that has been reported in rodents. In addition, it seems as if all NREM-sleep frequencies are part of a compensatory response.

0490

SYMPATHETIC ACTIVATION AND CARDIAC RESPONSE TO 88 HOURS OF WAKEFULNESS IN HEALTHY MEN AND WOMEN

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Introduction: Indices of sympathetic and parasympathetic activation such as blood pressure and heart rate have been shown to be affected by sleep deprivation, but patterns of results have been variable, as have the conditions of deprivation such as duration of vigil. We performed a study of sleep deprivation in which food, water intake, light exposure and posture, were carefully controlled, and examined the changes in a number of cardiovascular indices across nights of deprivation and through subsequent recovery sleep.
Methods: Following adaptation and baseline sleep nights, subjects were randomly assigned to sleep (N=9, 6 male) or sleep deprivation (N=15, 10 male) conditions. Subjects were healthy controls (average age 35, SD=7), free of sleep disorders and cardiovascular disease. Subjects assigned to the deprivation condition were kept awake for a total of 88 hours. During the normal sleep period time, participants who were sleep deprived were kept in a semi-recumbent posture with ambient light levels <40Lux. Subjects had normal indoor light exposure and controlled hourly walks outside of the normal sleep period time. Beat to beat blood pressure was measured throughout nights of sleep and/or sleep deprivation using alternating inflation of finger cuffs using a Portapres system. HR (single channel) was recorded using the Embla polysomnographic recording system and exported for off line analysis.
Results: Significant interactions were found for SBP and MAP with elevations in SBP on each night of deprivation ($F(3,57)=4.58$, $p<0.01$; and $F(3,57)=3.65$, $p<0.05$, respectively). SBP reached approximately 16 mmHg on average, over SBP levels in the sleep control group, without any change in baroreflex sensitivity. A significant interaction effect was found for change in HR ($F(3,57)=7.10$, $p<0.01$). During the first two nights of sleep deprivation HR increased slightly (an average of about 2-3 beats per minute). In contrast, increases in sympathetic activity to the vasculature, as indicated by low frequency SBP power, did not occur until the 2nd and then remained elevated on the third night of sleep deprivation ($F(3,57)=4.95$, $p<0.01$).
Conclusion: Initial increases in blood pressure during the first 24 hours of sleep deprivation are associated with small but significant increases in heart rate. In contrast long term deprivation is associated with a persistent increase in sympathetic activity while heart rate returns to baseline levels.
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0491

RESIDENT PERFORMANCE ON A SIMULATED CASE-BASED MEDICAL DECISION MAKING TASK AFTER HEAVY CALL AND ALCOHOL CONSUMPTION

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Introduction: Sleep deprivation during postgraduate medical education is common and associated with deleterious effects on neurobehavioral performance parameters equivalent to low doses of alcohol. We compared residents' actual and self-rated performance on an on-line simulated medical decision making task (MedCases) under four conditions: rested (Light Call; LC), sleep loss (Heavy Call; HC), Rested + Alcohol (LC/Alcohol), and Sleep Loss + Placebo (HC/Placebo).
Methods: Twenty-seven pediatric residents (13 women, 28.7 ± 2.9 years, 10 PL-1, 14 PL-2, 3 PL-3) completed 4 on-line, medical cases in a counterbalanced order after a month of light call (LC and LC/Alcohol) and post-call after a heavy-call (q 4 or q 5) month (HC and HC/Placebo). Subjects were presented with an initial case presentation of a typical outpatient problem and selected appropriate differential diagnoses (DD), laboratory tests (LT), final diagnoses (FD) and treatment plan (TP) from a range of options within 15 minutes. Participants self-rated performance post-test from 1 (extremely good) to 7 (extremely poor) and effort from 1 (very little) to 4 (extreme). Primary outcomes included appropriate selections (%Hits), Omission, and Commission Errors for DD, LT, and TP (%Hits for FD), and self-ratings of performance and effort.
Results: Subjects completed the cases in less time in LC/Alcohol (8.78 ± .4 minutes) and HC/Placebo (9.11 ± .5 minutes) compared with LC (11.01± .5 minutes) and HC (10.89 ± .5 minutes) ($F3,26=14.75$, $p<0.0001$). No differences among the conditions in Hits or Errors of Omission/Commission were found for DD, LT, TP, or FD. Subjects self-rated performance worst in the HC conditions, followed by LC/Alcohol, and LC ($F3,26=4.95$, $p = 0.0075$). No differences in effort ratings were found.
Conclusion: Residents rated their performance worse following heavy call compared to alcohol, but no objective differences in simulated medical decision making were evident.

0492

LOWER NEURAL RESPONSE TO INCREASING WORKING MEMORY DEMAND DURING SLEEP DEPRIVATION

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Introduction: Working memory (WM) is a key component of complex task performance. We have previously identified a network of brain regions that monotonically increased in activation with greater number of items to remember (i.e., WM demand) on a delayed item recognition task in well-rested participants. Here, we forward applied this network to sleep deprivation data within the same participants to see if its expression was still related to WM demand after 48 hours without sleep.
Methods: 18 healthy subjects (aged 20-35y; 17 males) performed a delayed item recognition task during fMRI before and after 48 hours without sleep. Memory sets were 1, 3, or 6 letters, providing 3 levels of demand. Using Ordinal Trend Canonical Variates Analysis (OrT-CVA), a network was previously identified that monotonically changed activation as a function of WM demand during retention ($p < 0.001$). This network was forward applied to the sleep deprivation (SD) data.
Results: The network identified using the well-rested data shared the same linear relationship with WM demand during SD ($p = 0.004$). At the lowest WM demand (one letter), network expression was not significantly different during SD (18.5 ± 22.8 versus 15.6 ± 90.5 at baseline, $p=0.89$). Change in expression of this network with increasing WM memory demand, however, was significantly lower during SD (5.8 ± 7.5 versus 37.2 ± 33.8 at baseline, $p < 0.001$).
Conclusion: A network of brain regions was previously shown to increase in activation with increasing WM demand during information retention in well-rested individuals. Here, we show that during sleep deprivation this network was still significantly responsive to demand during retention, although the magnitude of change was significantly lower. Any functional significance of this lower neural response to WM demand during sleep deprivation remains to be determined.
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0493

COMBINED EFFECTS OF REM SLEEP DEPRIVATION AND HIPPOCAMPAL FIMBRIA-FORNIX TRANSECTIONS OR LESIONS ON ABILITY TO ACQUIRE A SPATIAL LEARNING TASK

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Introduction: The hippocampus has long been implicated in spatial learning and ability to acquire novel information. Animals with either hippocampal lesions or fimbria-fornix transections have delayed acquisition of spatial learning. Similarly, REM sleep deprivation (REMSD) also disrupts the hippocampus-dependent learning process and the ability to acquire spatial memory. In the present study we combined both paradigms to verify the effect of REMSD on hippocampally lesioned rats' spatial memory acquisition.
Methods: 23 male Fisher 344 rats were tested on an 8-box maze track for spatial learning. One group of rats (n=10) underwent fimbria-fornix transections for disruption of hippocampal inputs or excitotoxic lesions (ibotenic acid and NMDA). Sham operations conducted on another group (n=13) served as controls. Following surgical recovery, spatial learning ability was assessed in an 8-box maze for 30 minutes each day for 5 days. Rats were put into 1 of 4 groups such that at the end of each trial they were either REM sleep deprived for 4 hours (1 lesioned and 1 control group) or allowed to sleep in their home cages (1 lesioned and 1 control group). The learning curve was determined by calculating the average number of errors per lap each day.
Results: Previous observations that both hippocampal lesions and fimbria-fornix transactions result in more errors on a spatial task than controls were confirmed. Further, REM sleep deprivation worsened spatial learning abilities. However, those lesioned/transected rats that also underwent REM sleep deprivation did not make significantly more errors per lap than the lesioned rats alone.
Conclusion: REM sleep deprivation did not further reduce the ability of animals with hippocampal lesions to acquire a spatial learning task. Therefore REMSD may normally affect spatial learning through affecting hippocampal function.
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0494

IMPACT OF SHORT-TERM SLEEP RESTRICTION ON GLUCOSE HOMEOSTASIS

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Introduction: Impaired glucose homeostasis and elevated evening levels of the stress hormone cortisol have been reported to be consequences of severe sleep curtailment (bedtimes restricted to 4 hours per night for 6 nights). The aim of the present study was to evaluate glucose tolerance, circulating insulin levels and insulin secretion following a modest degree of sleep restriction.
Methods: Thirteen healthy young men (20-27 years) participated in 4 different studies, in randomized order: 2 sessions with 2 nights of 10 hours in bed, and 2 sessions with 2 nights of 4 hours in bed. On the morning after the second night of each session, an intravenous glucose infusion at a constant rate was initiated and blood was sampled at 20-min intervals for the measurement of glucose, insulin and C-peptide levels. Insulin secretion rate (ISR) were estimated by deconvolution of C-peptide levels using a 2-compartment mathematical model.
Results: Mean sleep duration averaged 8h45min±8min for the long sleep sessions and 3h28min±2min for the short sleep sessions. Considering the period between 8 am (initiation of glucose infusion) and 12 pm (steady glucose levels), short sleep was associated with significantly higher glucose levels (108.5±2.4 vs 114.79±2.1 mg/dl, $p=0.03$) and peak glucose levels attained after initiation of constant glucose infusion were significantly greater after 2 nights of short sleep than after 2 nights of long sleep (127.3±2.5 vs 117.2±2.5 mg/dl, $p=0.006$). Insulin levels and ISR were similar under both sleep conditions (respectively 116.9±17.9 vs 112.5±14.3 µU/ml, $p=0.6$; and 176.2±21 vs 163.9±17.3 µU/min, $p=0.16$). No significant difference in the HOMA index, a measure of insulin resistance, was observed (6.2±1 vs 5.5±0.8, $p=0.18$).
Conclusion: In conclusion, these results confirm and extend the adverse impact of short sleep duration on morning glucose and insulin profiles, which could be mediated by an elevation of cortisol levels the preceding evening.

0495

ASSESS VIGILANCE AMONG NURSES WORKING ON MEDICAL UNIT

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Introduction: A significant prevalence of sleepiness has been described amongst nurses and has been linked to medical errors. Few studies have

attempted to formally study the relationship between chronic sleepiness, and vigilance. We undertook the study to assess vigilance among nurses by using the PVT 192- a validated tool.
Methods: After IRB approval, 12 nurses (eight day shift and 4 night shifts) from medical telemetry unit underwent the study. We measured Epworth sleepiness scale (ESS), Stanford sleepiness scale at the beginning and end of shift, and reaction time measurement by using PVT 192 at the beginning and end of shift.
Results: 33.3% of the nurses were chronically sleepy, as defined as an abnormal Epworth score (10 or greater). Three of them were from day shift. The mean ESS in the abnormal group was 12.25 +/- 2.62, whereas in the group with normal ESS was 4.75 +/- 1.9. There was no difference in the mean, slowest and fastest reaction time between two groups at the beginning and end of shift (table 1). There was no difference in Stanford sleepiness score at the beginning and end of shift between groups. Abnormal ESS Normal ESS P value MRT Pre 322 +/- 71 265 +/- 32 .21 MRT Pos 304 +/- 44 279 +/- 34 .36 SRT Pre 2.22 +/- .6 2.6 +/- .4 .27 SRT Pos 2.1 +/- .36 2.38 +/-.47 .38 FRT Pre 242 +/- 37 201 +/- 23 .11 FRT Pos 220 +/- 28 196 +/- 20 .19 (MRT: Mean Reaction Time, SRT: Slowest reaction time, FRT: Fastest reaction time)
Conclusion: Chronic sleepiness as assessed by Epworth score alone does not seem to be impact vigilance in nurses. Task, interest and environmental factors may play a role in modulating vigilance. Future studies may help to shed more light on these and other mechanistic factors.

0496

DOES THE MODE OF WEANING FROM MECHANICAL VENTILATION ADVERSELY AFFECT SLEEP ARCHITECTURE?

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Introduction: Our understanding of sleep architecture and impact of sleep quality on overall health outcomes in the ICU is not known. Sleep disruption can contribute to outcomes such as delirium which independently increases mortality in this patient population. Patients weaning from mechanical ventilation are a homogenous population in the ICU as they are resolving from an acute illness. This population may be most vulnerable to affects of poor quality of sleep. However, sleep architecture in this group has not been extensively studied. The two common modes of weaning used in our ICU is pressure support ventilation (PSV) and trach mask trials (TMT). However, to what extent these weaning methods contribute to abnormalities in sleep architecture is not known.
Methods: Prospective observational study at London Health Sciences Critical Care Trauma Centre. Patients were included if they were mechanically ventilated for >24 hours and met weaning criteria by the ICU team. Patients recovering from general anesthesia, pregnancy, hemodynamically unstable, have neuromuscular disease, and who have documented brain injury were excluded from the study. Twenty-four hour attended continuous PSG was recorded.
Results: To-date we have recorded 7 patients (age=76 yo; male=5). We report results (n=4) from an ongoing study that shows reduced mean sleep efficiency in patients weaning from mechanical ventilation (PSV= 23%; TMT=48%). REM sleep was recorded in both patient populations (mean % total sleep period PSV= 3.5%; TMT=20%).
Conclusion: Our observational study to-date suggests that sleep architecture is abnormal in this patient population. While REM sleep is reduced in the PSV group, our preliminary assessment suggests that there is adequate REM sleep in the TMT group. Our study will establish baseline data for a population that is not available in the literature.

0497

EFFECT OF SLEEP LOSS ON THE HYPOTHALAMO-PITUITARY-ADRENAL (HPA) AXIS

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Introduction: Hyperactivation of HPA axis may play a role in the development of metabolic abnormalities observed under partial sleep deprivation. We evaluated the effect of 2 days of sleep restriction, compared to 2 days of sleep extension, on the profiles of ACTH and total cortisol in plasma and free cortisol in saliva, as well as on their response to an evening CRH injection.
Methods: Thirteen healthy young lean males participated in four study conditions, in randomized order: 2 sessions of 2 nights of 10 hours in bed, and 2 sessions of 2 nights of 4 hours in bed. On the 2nd day of each session, plasma ACTH and total cortisol profiles were measured for 23 hours (10:00-9:00), while salivary free cortisol profiles were measured for 10 hours (14:00-24:00). At 18:00, an intravenous injection of either CRH (1 μg/kg) or saline was administered.
Results: In the sessions with saline injection, plasma cortisol levels, over the 20:00-24:00 hour period, were higher in the 4-h bedtime than in the 10-h bedtime condition (AUC: 1080.42±80.39 vs 763.81±89.08 ng/ml.min, $p<0.05$). Similar findings were obtained for salivary cortisol (AUC: 127.38±19.85 vs 72.64±15.49 ng/ml.min, $p<0.05$). ACTH levels also tended to be higher but the difference failed to reach statistical significance, most likely because too many concentrations were under the limit of assay detection. In the sleep restriction condition, the onset of the quiescent period of cortisol secretion was delayed (20h16±19 min vs 17h30±38 min, $p < 0.05$) and the duration was shorter than during sleep extension (384±31 min vs 530±58 min, $p < 0.05$). The response of ACTH and cortisol to CRH injection was similar under both sleep conditions.
Conclusion: These results indicate that even a modest degree of sleep restriction results in an elevation of evening cortisol levels which could promote insulin resistance and adversely affect glucose regulation.

0498

THE ASSOCIATION BETWEEN OBSTRUCTIVE SLEEP APNEA AND NEONATAL BIRTHWEIGHT

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Introduction: Obstructive sleep apnea (OSA) has been implicated as a cause of low birthweight. We sought to determine the impact of OSA on neonatal birthweight.
Methods: We performed a retrospective cohort analysis of women delivering between 2000-2008 with polysomnogram confirmed OSA in an academic center. Normal weight and obese controls were randomly selected from a perinatal database at a 1:1 ratio. Charts were reviewed for diagnosis, pregnancy and neonatal data. Maternal and neonatal characteristics were compared between groups. Analyses were performed to evaluate maternal characteristics, neonatal birthweight and prematurity.
Results: The cohorts included 57 women with OSA, 57 normal weight and 57 obese controls. The OSA cohort had a median AHI of 22.7 (IQ range 12- 47) and median lowest oxygen saturation of 86 %(IQ 77-89). Compared to obese controls, the OSA cohort was older (30 vs. 26 yrs, p<0.001), had a higher BMI (49.9 vs. 44.4 kg/m2, p<0.001), more chronic hypertension (51.9 vs. 10.7%, p<0.001) and more diabetes, (24.1 vs. 3%, p<0.001). The OSA cohort had higher rates of very low birthweight (11.1% vs. 1.8%, p=0.04), low birthweight (23.1 vs. 7.1%, p=0.02), prematurity (30.2 vs. 7.1%, p=0.002) and preeclampsia (17.6 vs. 8.9%, p=0.05). Even larger differences were observed when the OSA group was compared to normal weight controls. Among all full term deliveries, there was no difference in very low birthweight and low birthweight. Birthweight was highest in the full term neonates of OSA mothers. Large for gestational age neonates were noted in 20, 12 and 2% of the cohort (for the OSA, obese controls and normal weight controls, respectively).
Conclusion: OSA during pregnancy is associated with a high prevalence of prematurity. The relatively high birthweight of full term offspring of mothers with OSA may also indicate an increased risk of later life health problems for these infants.

0499

SLEEP-DISORDERED BREATHING, BODY MASS INDEX AND C-REACTIVE PROTEIN AMONG OLDER ADULTS

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Introduction: The correlates for and clinical significance of sleep disordered breathing (SDB) among older adults are not well characterized. C-reactive protein has been reported to independently predict future vascular events. In this cross-sectional study, we examine the relationship between high sensitivity-plasma C-reactive protein level (hs-CRP) and SDB among older adults.
Methods: A total of 54 non-smoker, community dwelling older adults were admitted to General Clinical Research Center of Emory University for evaluation of 24-hour blood pressure and SDB. Breathing during sleep was monitored using the Embletta, PDS recorder (Embletta PDS, Medcare, Iceland). Apnea hypopnea index and hypoxic burden (% time spent in oxygen saturation <90%) were used as measures of SDB. Plasma CRP was measured by enzyme-linked immunosorbent assay (ELISA) using a highly sensitive commercially available kit from ALPCO Diagnostics (Salem, NH).
Results: There were 32 (59%) female and 22 male (41%) study participants, and the mean (sd) age was 75.8 (7.9) and 74. 2 (5.2) years for women and men respectively (p=.386). There was a significant positive correlation between CRP level and hypoxic burden (Spearman's correlation .284, p <.047) and CRP level and body mass index (Spearman's correlation .519, p <.001). No significant correlation was observed between CRP level and apnea hypopnea index. Multiple linear regression analysis was performed with CRP level (log-transformed) as the dependent variable, hypoxic burden (log-transformed)and body mass index as independent variables. Age, gender, and comorbidity were included in the model as covariates. There was independent association between CRP level and hypoxic burden and CRP level and body mass index (B =.285,p=.007 and B = .376, p = .009; respectively; R2 = .39). Limitation: Small sample size.
Conclusion: To our knowledge, this is the first report to describe an independent association between a measure of SDB (hypoxic burden) and elevated CRP level among older adults. These results suggest that the severity of oxygen desaturation associated with SDB may be an important factor in the relationship between SDB and elevated CRP level. As expected, stronger association was observed between elevated CRP level and body mass index.
Support (optional): K23-AG-025963

0500

RECIPROCAL INTERACTIONS OF OBSTRUCTIVE SLEEP APNEA AND HYPERTENSION WITH ACE I/D POLYMORPHISM IN MALES

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Introduction: The angiotensin-converting enzyme (ACE) insertion/deletion (I/D) polymorphism gene contributes to the genesis of hypertension (HTN) and may help explain the relationship between obstructive sleep apnea (OSA) and HTN. However, ACE is a pleiotropic gene that has several influences, including skeletal muscle and control of ventilation. We therefore tested the hypothesis that ACE polymorphism influences OSA severity.
Methods: Male OSA patients (apnea-hypopnea index [AHI]>5 events/h) from 2 university sleep centers were evaluated by polysomnography and ACE I/D polymorphism genotyping.
Results: We studied 266 male OSA (age=48±13y, body mass index=29±5kg/m2, AHI=34±25events/h). HTN was present in 114 patients (43%) who were older (p<0.01), heavier (p<0.05) and had more severe OSA (p<0.01). The I allele was associated with HTN in patients with mild to moderate OSA (p<0.01), but not in those with severe OSA. ACE I/D polymorphism was not associated with apnea severity among normotensive patients. In contrast, the only variables independently associated with OSA severity among patients with hypertension in multivariate analysis were BMI (OR = 1.12) and II genotype (OR = 0.27).
Conclusion: Our results suggest reciprocal interactions between OSA and HTN with ACE I/D polymorphism, suggesting that among hypertensive OSA males the homozygous ACE I allele protects from severe OSA.
Support (optional): FAPESP; CEPID/FAPESP; AFIP; CNPq.

0501

ENDOTHELIAL FUNCTION AS A PROGNOSTIC FACTOR OF CARDIOVASCULAR MORBIDITY IN PATIENTS WITH OBSTRUCTIVE SLEEP APNEA SYNDROME

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Introduction: Endothelial dysfunction (ED) has been shown to be abnormal in patients with obstructive sleep apnea (OSA), and to be predictive of ischemic heart disease. Aim: To follow up on patients who underwent endothelial function analysis at the diagnosis of the OSA, and to investigate whether ED is predictive of the development of cardiovascular complications in these patients. We hypothesized that ED will predict cardiovascular deterioration in untreated but no in treated patients.
Methods: Eighty six patients with OSA (66 men) aged 52.5±9.4years, BMI 29.2±4.7Kg/m2 underwent analysis of their endothelial function utilizing the post-obstruction reactive hyperemia test (Endo_PAT, Itamar medical, Caesarea, ISRAEL). Telephone follow up took place on average 51.9±11.8months thereafter. Cardiovascular deterioration was quantified by newly developed hypertension, diabetes, dyslipidemia, angina pectoris, myocardial infarction, stroke and cardiac arrhythmia. Any of these was given a value of 1 and the summation of all resulted in the cardiovascular deterioration quantification.
Results: During the 4.3 years f/u period, 13% stopped smoking, 22% started exercising, but the BMI remained unchanged. Surprisingly, only 17 patients (20%) were treated with CPAP. These patients were older and had more severe OSA than those who were not treated. During the follow up period, 24 patients (28%) developed dyslipidemia, 13 (15%) hypertension, 10 (12%) angina pectoris, 6 (7%) diabetes, 2 (2%) stroke, and 1 patient (1%) had new onset of cardiac arrhythmia. Multiple regression analysis revealed that the most significant factor contributing to cardiovascular deterioration was ED (t=-3.3, p=0.002), followed by BMI (t=3.0, p=0.004), time from PSG (t=2.6, p=0.01) and RDI (t=1.9, p=0.057). Age, total sleep time, and oxygen desaturation did not enter the model, regardless of testing all patients or only those untreated.
Conclusion: Endothelial dysfunction, body mass index, time of follow up and RDI are predictive of cardiovascular complications in patients with OSA.

0502

PREVALENCE OF OBSTRUCTIVE SLEEP APNEA SYNDROME IN SAO PAULO EPIDEMIOLOGICAL SLEEP STUDY

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Introduction: Prevalence of Obstructive Sleep Apnea Syndrome (OSAS) in different studies has varied from 1.2 to 7.5%. Such variations can be attributed to limitations of those epidemiologic investigations. The aim of this study was to estimate OSAS prevalence by age, gender, and nutritional status in an adult population based sample from Sao Paulo city, using up-to-date clinical and epidemiologic techniques and procedures.
Methods: A population based survey adopting a probabilistic three-stage cluster sample of the Sao Paulo city was used to represent the population according to gender, age (20-80 years), and socioeconomic classes. Questionnaires and in lab full night polysomnography, using nasal pressure cannula and thermistor were done. OSAS criteria were of the AASM-ICSD-2.
Results: From 1101 questionnaires, 1042 volunteers underwent to polysomnograph (refusal rate=5.4%). Mean age was 42±14 yrs, 55% were women, and 60% presented BMI>25 kg/m2. AHI<5 was found in 61.8% and AHI>15 in 16.89%. Applying the generated sample weight variable, OSAS was observed in 32.9% [95%CI:29.6-36.3]. Men presented OR=4.11[95%CI:2.9-5.8]; volunteers with BMI>40 kg/m2 had OR=10,55 [95%CI:7.07-15.7] and with 60-80 years old OR=34.48 [95%CI:18.5-64.2]. Low income socioeconomic class was a risk factor for females (OR=1.96). Menopause was an explanatory factor to the increased risk (OR=2.09 95% CI1.39-3.88).
Conclusion: This study shower high OSAS prevalence. This maybe explained by the excellence of epidemiological sampling method with a very low polysomnograph refusal rate, use of nasal cannula, along with the adoption of the most recent AASM criteria for OSAS diagnosis or the high prevalence of overweight subjects in the Sao Paulo population.
Support (optional): AFIP, FAPESP, CNPq

0503

REVERSE CAUSALITY IN THE ASSOCIATION OF SLEEP-DISORDERED BREATHING AND CARDIOVASCULAR DISEASE

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Introduction: Prospective data suggest that sleep-disordered breathing causes incident or recurrent cardiovascular disease; however, a reverse causal pathway whereby incident cardiovascular disease causes or worsens sleep-disordered breathing has not been well studied.
Methods: 2737 Sleep Heart Health Study participants (mean age 61 (SD 10) years, 57% women, 24% ethnic minorities) without cardiovascular disease at baseline underwent two polysomnograms 5 years apart. Incident cardiovascular disease, including myocardial infarction, congestive heart failure and stroke, were prospectively adjudicated. The relation of incident cardiovascular disease to the change in apnea-hypopnea index (AHI) between the two polysomnograms was tested using general linear models, adjusting for age, sex, race, site, change in BMI, change in neck circumference, history of diabetes, baseline waist to hip ratio and the time between the two polysomnograms.
Results: Incident cardiovascular disease occurred in 116 participants between the first and second polysomnograms and was associated with a larger increase in AHI between polysomnograms. The difference in adjusted mean AHI change between subjects with incident cardiovascular disease and subjects without incident cardiovascular disease was 2.23 events per hour (95% CI 0.32-4.17; p=0.02). This association was not driven by the known association of cardiovascular disease and central sleep apnea, as it persisted after excluding subjects with central sleep apnea and subjects whose central apnea index increased more than the obstructive apnea index. Incident cardiovascular disease was associated with a greater mean increase in both obstructive (by 2.08 events per hour; 95% CI 0.83-3.33; p=0.001) and central apnea indices (by 0.84 events per hour; 95% CI 0.31-1.38; p=0.002) compared to subjects without incident cardiovascular disease.
Conclusion: In a diverse, community-based sample of middle-aged and older adults, incident cardiovascular disease was associated with worsening sleep-disordered breathing.
Support (optional): This work was supported by National Heart, Lung, and Blood Institute cooperative agreements U01HL53940 (University of Washington), U01HL53941 (Boston University), U01HL53938 (University of Arizona), U01HL53916 (University of California, Davis), U01HL53934 (University of Minnesota), U01HL53931 (New York University), U01HL53937 and U01HL64360 (Johns Hopkins University), U01HL63463 (Case Western Reserve University), and U01HL63429 (Missouri Breaks Research).

0504

CANDIDATE GENE ANALYSIS FOR OBSTRUCTIVE SLEEP APNEA

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Introduction: Many studies have confirmed the presence of a strong genetic basis for obstructive sleep apnea (OSA). However, no specific susceptibility genes have yet been defined.
Methods: Using the Illumina platform, genotyping of tagging single nucleotide polymorphisms (SNPs) that provided > 80% coverage for SNPs with a minor allele frequency of 5% or more in each of 56 OSA candidate genes was performed in 1480 participants of the Cleveland Family Study. Standardized polysomnography was used to define OSA status using age-specific thresholds. All analyses utilized an additive inheritance model and adjusted for age, sex, and body mass index as well as the correlated family structure of the cohort.
Results: After performing quality control checks, a total of 1040 SNPs were assessed for association with OSA in 683 African-Americans and 513 SNPs in 705 Caucasians. The prevalence of OSA was 27%. Among Caucasians, only 1 SNP was associated with OSA at a false discovery rate (FDR) of 10%. This SNP is located 1 kb 3' to the C-reactive protein (CRP) gene and the major allele increased OSA risk 1.8-fold. Among African-Americans, 27 SNPs were associated with OSA at a 10% FDR. The strongest associations were for intronic SNPs in the lipoprotein lipase (LPL) and serotonin 3B receptor (HTR3B) genes where the major allele was associated with a 2.4-fold and 4.2-fold increased risk respectively.
Conclusion: Specific allelic variants in candidate genes are associated with OSA in both Caucasians and African-Americans. These findings point to the potential importance of pathways influencing inflammation, dyslipidemia and serotonergic signaling on OSA susceptibility and support the need for larger genetic association studies.
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0505

ROLE OF OBESITY ON SLEEP BREATHING DISORDER NOT ASSOCIATED WITH OSA

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Introduction: Sleep breathing disorders currently includes the diagnosis of obstructive sleep apnea and upper airway resistance syndrome. Consequences of these disorders are related to sleep fragmentation and oxygen desaturation. Presence of oxygen desaturation during sleep not associated with OSA has not been investigated in populational based studies. The purpose of this study was to evaluate the prevalence of oxygen desaturation during sleep not associated with OSA.
Methods: A population-based survey adopting a three-stage randomized cluster sampling of Sao Paulo city was used to represent the population according to gender, age (20-80 years), and social class. Questionnaires and in lab full night PSG using nasal pressure cannula and thermistor were done. Statistical analysis was performed with multiple regression analysis.
Results: From 1101 questionnaires, 1042 volunteers underwent to PSG (refusal rate=5.4%). From the total group, 644 (61%) had AHI< 5. From this group, 138 (21,4%) had lowest oxygen saturation < 90%. Mean age: 43,5± 12, 65,7% was women and 62% had BMI > 25. Gender: men (OR:1.96), BMI (OR:2.37) and menopause in women (OR:1.72) was associated with higher risk for dessaturaion during sleep. The chance for desaturation among the group obese + menopause is 22 times higher than in the eutrophic and non-menopause group.
Conclusion: There was a high prevalence of individuals with oxygen desaturation not associated with OSA. Obesity is the most important factor related to non OSA oxygen desaturation during sleep. However there are other factors that can cause this breathing abnormality was associated with gender, BMI and menopause. Oxygen desaturation during sleep not associated with OSA (AHI> 5/h) is usually not recognized as SBD and it may lead to consequences. Studies are necessary to demonstrate the consequences of this abnormality.
Support (optional): Supported by AFIP/FAPESP/CEPID

0506

TREATMENT EFFECT OF CONTINUOUS POSITIVE AIRWAY PRESSURE ON 24 HOURS BLOOD GLUCOSE LEVEL IN PATIENTS WITH TYPE 2 DIABETES AND OBSTRUCTIVE SLEEP APNEA SYNDROME

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Introduction: Obstructive sleep apnea hypopnea syndrome (OSAHS) is associated with insulin resistance and impaired glucose metabolism. However, there are few reports on 24h dynamic change of blood glucose level in patients with OSAHS and DM. The study aimed to assess the effect of short-term CPAP on glucose control both night and in daytime measured with a continuous glucose monitoring system (CGMS)
Methods: Eleven type 2 diabetes patients (56±10 y, M/F 8/3) with OSAHS admitted to the sleep ward was recruited to the study. All patients were under singlet alimentary control, and the five were also treated by oral drugs. All these treatment maintained the same during the study. The mean body mass index was 28.5±5.5 kg/m2; and the mean AHI was 45±23 times/h. Continuous glucose monitoring system (CGMS, MiniMed Inc.) was applied 2 days before and 4 days during the CPAP treatment. The sensor is calibrated by entering the blood glucose measurement obtained from a glucose meter into the monitor. The 24h, night (1am-7am) and daytime (7am-1am) glucose level and glucose variability were analyzed, only the 2nd day data of pre and post treatment were included into the statistical analysis. Insulin resistance was assessed with fasting plasma blood glucose (FBG), plasma insulin (FINS) and homeostatic model assessment of insulin resistance (HOMA-IR) index.
Results: The glucose sensor records interstitial glucose concentration every 10 seconds and stores an average glucose value for each 5-minute period, thus enabling up to 288 measurements to be made per day. Short-term CPAP treatment corrected sleep disordered breathing, and induced significant decreases of 24h (7.97±1.31 Vs 7.52±0.94, p=0.033) and night (7.24±1.51 Vs 6.77±1.65, p=0.017) blood glucose level. Blood glucose level during daytime had the tendency of decline (8.21±1.34 vs 7.77±0.86, p=0.108). 24h glucose variability significantly decreased after CPAP treatment (1.80±0.42 vs.1.26±0.50, p=0.018). FBG (8.13±2.84 vs 6.43±1.15,p=0.096) and FINS (10.43±5.63 vs 9.39±4.77, p=0.418) also had the tendency of decline, but no significant change. Short term treatment also induced, as indicated by a significant decrease of HOMA-IR(3.65±1.93 vs 2.79±1.68,p=0.047).
Conclusion: Short-term CPAP treatment in type 2 diabetes with OSAHS may have an improved effect not only on insulin resistance but also on whole-day's blood glucose and glucose variability.
Support (optional): NSFC 30770938

0507

OBSTRUCTIVE SLEEP APNEA IS INDEPENDENTLY ASSOCIATED WITH IMPAIRED FASTING GLUCOSE: DATA OF SAO PAULO EPIDEMIOLOGICAL STUDY

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Introduction: Epidemiological studies controlling for confounders are necessary to asses the independent relation between OSA with Glucose Intolerance and Insulin Resistance. To evaluate the relation between OSA with Glucose Intolerance and Insulin Resistance in a population based sample of adult inhabitants of São Paulo city.

Methods: A population-based survey of Sao Paulo city. PSG at sleep laboratory and blood samples after 12-h overnight fasting for measurements of plasma glucose, insulin and lipids were done. Impaired fasting glucose was defined as fasting glucose ≥ 100 mg/dl. Hepatic insulin resistance index was assessed by the homeostasis model assessment Program (HOMA-IR) and calculated as fasting serum insulin (U/ mL) x fasting plasma glucose (mmol /L) /22.5.
Results: 1042 volunteers underwent to PSG. OSA was considered if AHI > 5/h. Subjects with mild OSA were 21,2%, with moderate and severe OSA were 16,9%. Age was 37.3 + 12.3, 48.3 +13.6 and 53.3 +13.3 years and BMI was 25.3 + 4.4, 28.3 + 5.2 and 30.3+6.0 Kg/m2 in mild, moderate and severe OSA groups respectively. Severe OSA subjects were older and more obese than the mild and moderate groups (p< 0.001). Fasting glucose and HOMA were higher in severe OSA than mild and moderate groups (p<0.001) as well as in moderate OSA compared to mild OSA (p<0.001). Multivariate regression analyses showed that AHI (OR:1.18; p=0.032) is independently associated with impaired fasting glycemia as well as Sat O2 <90% (OR: 1.44; p= 0.035) with HOMA .
Conclusion: OSA is related with abnormalities in glucose metabolism independent of obesity and age in a sample of the adult population of São Paulo city.
Support (optional): Supported by AFIP, FAPESP_CEPID, CNPq.

0508

TYPE 2 DIABETES IS RELATED TO SEVERITY OF OBSTRUCTIVE SLEEP APNEA IN A POPULATION-BASED SURVEY OF SAO PAULO CITY

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Introduction: Higher prevalence of type 2 Diabetes has been detected among subjects with Obstructive Sleep Apnea however, without adequately adjusting for confounders. To analyze the relationship between the severity of OSA and the prevalence of type 2 diabetes in a population based sample of adult inhabitants of São Paulo city.
Methods: A population-based survey of Sao Paulo city. The diagnosis and severity of Obstructive Sleep Apnea were done by PSG according to ASDA criteria. Blood samples were collected after 12-h overnight fasting for measurements of plasma glucose in 1042 subjects submitted to attended polysomnography in a population-based survey of Sao Paulo city. Type 2 Diabetes was defined as fasting glucose >= 126 mg/dL or use of antidiabetic medication.
Results: 1042 volunteers met the enrollment criteria and classified as Control group (AHI < 5, n=646), Mild OSA (AHI 5-15, n=221) and Moderate plus Severe OSA subgroups (AHI >= 15, n=175). Subjects with moderate and severe OSA have the highest prevalence of diabetes (19.8% vs 8.5 % vs 3.8%) compared to mild OSA and controls subjects respectively. After adjustment for BMI and age, the presence of moderate and severe OSA (AHI >= 15) was associated with a nearly 2-fold higher risk of type 2 diabetes than controls without OSA (p=0.037).
Conclusion: The severity of OSA was a highly significant predictor of type 2 diabetes in a sample of the adult population of São Paulo city.
Support (optional): Supported by AFIP_ FAPESP, CNPq.

0509

SLEEP DURATION AND CARDIOVASCULAR CONSEQUENCES IN PATIENTS WITH OBSTRUCTIVE SLEEP APNEA

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Introduction: Obstructive Sleep Apnea (OSA) is a risk factor for a number of cardiovascular conditions such as arterial hypertension, congestive heart failure, coronary artery disease and increased cardiovascular mortality. On the other hand, it has been reported a strong association between sleep duration obesity and cardiovascular mortality. We hypothesize that short sleep duration could have an association with the cardiovascular consequences of OSA patients. The aim of this study is to evaluate the clinical, polissonographic and laboratorial parameters in OSA patients according to the sleep duration.
Methods: Subjects were consecutively selected from the Sleep Clinic database between September 2007 and March 2008 who have AHI>5/h. All subjects underwent to a blood sample withdraw, physical examination, 12-lead ECG, spirometry, and actigraphy during 7 consecutive days. The study was approved by Ethics Committee and all subjects signed an informed consent form.
Results: One hundred thirty three patients were divided into four groups using cluster analysis: very short sleepers (n=11, total sleep time=3,10±0,75h); short sleepers (n=21, total sleep time=5,13±0,63h); medium sleepers (n=56, total sleep time=6,37±0,40h); long sleepers (n=45, total sleep time=7,72±0,55h). Very short sleepers has higher cervical and abdominal circumference, glycemia, BNP, HDL and more severe OSA when compared to other groups. BNP still predictor of sleep duration after adjusted analysis for all confounder's factors.
Conclusion: OSA and very short sleep duration is associated to OSA severity and increased cardiovascular risk.
Support (optional): AFIP, FAPESP

0510

VENTILATORY CONTROL STABILITY (LOOP GAIN) MEASURED WITH CPAP DIAL-DOWNS

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Introduction: Loop gain, a measure of ventilatory control stability, is an important variable in the pathogenesis of sleep disordered breathing. However, current techniques for measuring it are difficult to interpret and to accomplish technically. We propose a relatively simple method using CPAP dial-downs.
Methods: In 5 OSA patients and 5 non-OSA subjects, the ventilatory control system was disturbed by lowering CPAP to a sub-therapeutic positive level or to a negative airway pressure for 3-minute intervals during sleep. These dial downs in CPAP reduced ventilation and increased PCO2. The ventilatory response to the increase in PCO2 was assessed by turning CPAP back to the optimum pressure, which opened the airway and permitted ventilation to increase. Loop gain was calculated by dividing the ventilatory response (the ventilation increase above eupnea when CPAP was turned back to the optimum pressure) by the ventilatory disturbance (amount by which ventilation was reduced below eupnea during the dial-down). This yielded the steady state loop gain, i.e., the ratio of the ventilatory response to a steady state disturbance in ventilation (this is different from the loop gain at the frequency associated with a 180 degree phase angle, which previous studies have generally reported).
Results: In the non-OSA group, the loop gain values were 1.8, 2.6, 2.9, 4.2, and 4.6 (mean 3.2), and in the OSA group the values were 2.5, 2.6, 3.2, 5.1, and 5.9 (mean 3.9). While there was no significant difference (p = 0.38) the results were quite variable in both groups, suggesting that the propensity to instability may vary considerably in both the normal population and in OSA patients.
Conclusion: We conclude that 1) loop gain can be successfully measured using CPAP dial downs, and 2) there does not appear to be a fundamental difference in loop gain between OSA patients and normals. However, more data are needed to test the latter hypothesis.

0511

THE EFFECT OF POSITIVE AIRWAY PRESSURE THERAPY ON HIGH DENSITY LIPOPROTEIN AND INSULIN RESISTANCE IN PATIENTS WITH SLEEP APNEA

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Introduction: Sleep apnea has been recognized as an independent risk factor for hypertension, insulin resistance and low High Density Lipoprotein (HDL). It has been postulated that sleep fragmentation and decrease in slow wave sleep due to sleep apnea impairs growth hormone surge, resulting in impaired lipolysis and increased levels of cholesterol. Secondly, autonomic dysregulation as a result of hypoxemia, hypercapnia and acidosis results in sympathetic activation leading to release of cytokines which could influence HDL level. The insulin resistance seems to be the global effect of the combination of overproduction of Very Low Density Lipoprotein, Apo B (Apo lipoprotein B- 100) and decreased catabolism of Apo B containing particles; this causes decrease in HDL levels. We hypothesized that positive airway pressure therapy may thus affect the HDL level and insulin resistance.
Methods: Subjects on positive airway pressure (PAP) therapy for obstructive sleep apnea were enrolled in the study. Those with diabetes and/or on any lipid lowering therapy were excluded. Lipid profile (LDL, Triglycerides, HDL and Total cholesterol), glucose and fasting insulin levels were obtained, and homeostasis model assessment insulin resistance index (HOMA-IR) calculated. The values were compared before and after three months of PAP therapy. Compliance was monitored from the compliance card data.
Results: Preliminary results from our study showed that with 3 months of PAP therapy, HDL (n=18) increased from 34.05 ± 4.36 to 37.33 ± 4.49 ($p<0.01$). The HOMA-IR (n=15) decreased from 4.58 ± 2.72 to 4.36 ± 2.53 ($p=0.8069$). Thus the use of PAP improved HDL level; however the change in insulin resistance was not statistically significant.
Conclusion: Improvement in lipid profile with the use of PAP therapy may have an impact in the prevention of cardiovascular complications of sleep apnea even in non-diabetics and in those who are not on any lipid lowering therapy.

0512

THE ROLE OF OBESITY AND SLEEP APNEA SEVERITY IN THE INFLAMMATORY STATE IN OBSTRUCTIVE SLEEP APNEA: THE ISAC STUDY

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Introduction: Obstructive sleep apnea (OSA) and obesity commonly coexist and have many shared pathways such as oxidative stress and inflammation. In this study the relative role of obesity and OSA severity on IL-6 levels in serum was assessed in a large cohort of untreated OSA patients.
Methods: Untreated OSA patients with an apnea-hypopnea index (AHI) ≥15 were invited to participate and were a part of the Icelandic Sleep Apnea Cohort (ISAC) study. The patients underwent abdominal magnetic resonance imaging (MRI) to measure visceral and subcutaneous fat mass (divided by height squared), measurements of body mass index (BMI), waist circumference, waist-to-hip ratio, neck circumference and fasting morning IL-6 levels in serum. Log transformation of IL-6 values produced statistical distributions amenable to parametric analyses. Multiple linear regression analyses were performed in order to examine the relative importance of obesity and OSA severity to expected IL-6 levels.
Results: Altogether, 415 untreated OSA patients were included with a mean age (±SD) of 54.6±10.4 and BMI 32.3±4.9 kg/m^2. The mean AHI severity was 40.8±19.6 and the oxygen desaturation index (ODI) 33.0±18.7. The average IL-6 levels were 2.04±1.89 pg/ml. The correlation between log IL-6 levels and different measures of obesity was highest for BMI and waist circumference ($r=0.32$ and 0.30, respectively, $p<0.0001$). The correlation for visceral and subcutaneous fat and IL-6 levels was similar ($r=0.25$, $p<0.0001$) but lower for neck circumference ($r=0.20$, $p<0.0001$) and waist-to-hip ratio ($r=0.11$, $p=0.03$). A multiple linear regression model showed that BMI accounted for 6% of the variance controlling for ODI. ODI accounted for 1% of the variance controlling for BMI. When assessed with waist instead of BMI, the results were similar but both visceral and subcutaneous fat explained less of the variance in IL-6 levels. Additionally, age, gender, hypertension and coronary artery disease were all independently associated with IL-6 levels.
Conclusion: These results indicate that of the various obesity measurements, BMI and waist circumference best predict IL-6 serum levels. OSA severity has an independent contribution to IL-6 levels, although smaller than the obesity effect.

0513

GENIOGLOSSUS ACTIVITY IN OBESE, NON-SNORING ADOLESCENTS DURING SLEEP

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Introduction: The current obesity epidemic in adolescents is associated with an increased prevalence of obstructive sleep apnea syndrome(OSAS). Obese patients develop OSAS, at least in part due to a narrowing of the upper airway. However, many obese adolescents do not develop OSAS, despite having a presumably narrower upper airway. The reasons for this are unclear. We hypothesized that obese, non-snoring adolescents would have a compensatory neuromuscular response to subatmospheric pressure loads during sleep, that may be protective against airway collapse during sleep.
Methods: Obese, non-snoring adolescents underwent baseline polysomnography. On a separate night, they underwent polysomnography wearing a customized intra-oral mouthpiece with surface electrodes to measure genioglossal EMG (EMGgg). Subjects breathed through a nasal mask. Airflow and EMGgg were measured in response to stepwise decrement in nasal pressure (P_N) during non-rapid eye movement sleep. The area under the curve of the filtered, rectified inspiratory EMGgg moving time average was analyzed.
Results: Eight subjects (age 14 ± 1 [mean ± SD] yr, body mass index z-score 2.5 ± 0.3, apnea hypopnea index 0.6 ± 0.4/hr) were studied. The critical closing pressure was -16.6 ± 9.2 cm H2O, and the slope of the pressure-airflow relationship was 14.5 ± 7.6 ml/s/cm H_2O. There was a strong inverse correlation between P_N and EMGgg, which was significant in all but one subject (p values range from 0.001 to 0.062). The average correlation coefficient between PN and EMGgg was r = -0.73 ± 0.12, range = -0.49 to -0.86.
Conclusion: Obese, non-snoring adolescents have active upper airway neuromuscular reflexes during sleep in response to subatmospheric pressure challenges. We speculate that obese children who lack these compensatory upper airway responses are more likely to develop OSAS.
Support (optional): This study was supported by NIH grants U54-RR023567 and R01-HL58585.

0514

SYMPTOM QUESTIONNAIRES DO NOT PREDICT THE PRESENCE OR SEVERITY OF OBSTRUCTIVE SLEEP APNEA IN OBESE PATIENTS WITH TYPE 2 DIABETES

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Introduction: Sleep AHEAD (Action for Health in Diabetes) is a 4-site ancillary study of the Look AHEAD Study, a multicenter, randomized controlled trial of a weight loss intervention in obese adults with type 2 diabetes. The primary aim of Sleep AHEAD is to determine the effect of weight loss on sleep disordered breathing in a subset of Look AHEAD participants. Symptom questionnaires were administered to Sleep AHEAD participants at baseline to determine if they predicted the presence and severity of obstructive sleep apnea (OSA).
Methods: A home unattended polysomnogram was performed, using a portable monitor (PS2, Compumedics), on 305 participants (mean age 61.3 ± 6.5 [SD] yr; mean BMI 36.5 ± 5.8 kg/m^2) with no previous treatment for sleep apnea. Participants completed the Epworth Sleepiness Scale (ESS) and Functional Outcomes of Sleep Questionnaire (FOSQ). Apnea-hypopnea index (AHI) was used to categorize participants into no OSA (AHI < 5), and mild (5-14.9), moderate (15-29.9) and severe OSA (≥ 30). Differences across the 4 groups were assessed using chi square and t-tests.
Results: Over 86% (n = 264) of participants had OSA based on an AHI ≥ 5 events/hr. Among the participants with OSA, the mean AHI was 23.2 ± 16.5 events/hr and 33.4% had mild OSA, 30.5% moderate OSA, and 22.6% severe OSA. No significant differences were present across the 4 groups (no OSA and mild, moderate and severe OSA) in total scores on the ESS (7.6 ± 4.5, 8.2 ± 5.2, 7.9 ± 4.3, 7.7 ± 4.3 respectively) and FOSQ (17.9 ± 2.1, 17.5 ± 2.6, 17.9 ± 2.0, 18.0 ± 2.2 respectively).
Conclusion: ESS and FOSQ do not predict the presence or severity of OSA in obese patients with type 2 diabetes. Given the high prevalence and severity of OSA in obese patients with type 2 diabetes, the decision to perform sleep testing in these patients should not be based solely on symptom related questionnaires.
Support (optional): NIH HL070301

0515

SLEEP-DISORDERED BREATHING AND WEIGHT GAIN: THE SLEEP HEART HEALTH STUDY

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Introduction: It is well known that obesity is a risk factor for sleep-disordered breathing (SDB). However, whether SDB predicts weight gain is not well defined. Data from the Sleep Heart Health Study (SHHS) were analyzed to determine whether SDB predicts longitudinal weight change, adjusted for confounding factors.
Methods: A full-montage unattended home PSG and body anthropometric measurements were obtained. Complete weight and PSG data were available for 3001 participants. AHI was categorized using clinical thresholds: < 5 (normal), ≥ 5.0 to < 15 (mild sleep apnea), ≥ 15.0 (moderate to severe sleep apnea). Linear regression was used to examine the association between the three AHI groups and the change in BMI over approximately 5 years. The model included age, gender, race, baseline BMI, and change in AHI as covariates.
Results: Among the 3001 subjects in this analysis, mean (SD) age was 62.19 (10.14), 55.2% were female and 76.1% were Caucasian. Five-year change in BMI was modest with a mean (SD) change of 0.53 (2.62) kg/m^2 (p=0.094). A multivariable regression model for the change in BMI as a function of baseline AHI and covariates showed that subjects with a baseline AHI of ≥ 5.0 to < 15 had a mean change in BMI of 0.22 kg/m^2 (p=0.049) and those with baseline AHI ≥ 15 had a BMI change of 0.52 kg/m^2 (p<0.001) compared to those with baseline AHI of < 5.
Conclusion: Our findings suggest that there is a positive association between severity of SDB and subsequent change in BMI over approximately 5 years. This association was significant despite adjustments for key covariates.

0516

DETERMINANTS OF ENDOTHELIAL DYSFUNCTION IN PATIENTS WITH OBSTRUCTIVE SLEEP APNEA

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Introduction: OSA patients free from cardiovascular diseases have apnea severity dependent endothelial dysfunction (ED), an early sign of atherosclerosis. ED is associated with a variety of other conditions such as oxidative stress, hyperlipidemia, smoking, hyperhomocysteinemia, sedentary life style, and obesity, which are also associated with sleep apnea. The aim of the present study was to investigate the determinants of ED in OSA.
Methods: 106 randomly selected patients (82 men and 24 women aged 25-70 yrs) referred to whole night sleep study in the Technion Sleep Medicine Center because of suspected OSA participated. Blood pressure, fasting blood samples and measurement of the reactive hyperemia peripheral arterial tonometric index (RH-PAT), as a measure of endothelial function, were performed after waking up in the sleep laboratory between 6:00 to 7:00 AM. To determine the variables contributing to ED, the RH-PAT index was stratified into quartiles and correlated with age, BMI, AHI, ODI3%, Thiobarbituric Acid Reactive Substances (TBARS) that is a measure of oxidative stress, homocysteine (HC), cholesterol, TG, HDL, LDL, and C-reactive protein (CRP). A Chi square analysis was used for sex, smoking, physical activity, ischemic heart disease (IHD), and hypertension (HT). Multivariate analysis was used to determine the independent predictors of ED.
Results: Significant associations were found for age (p<0.04), AHI (p<0.01), ODI3% (p<0.007), TBARS (p<0.05), HC (p<.07), smoking (p<0.05), physical activity (p<0.02), and IHD (p<0.04). Increasing values of these variables were associated with decreasing RH-PAT index except for physical activity that was associated with higher levels of RH-PAT. Multivariate analysis revealed that AHI (p<0.005), HC (p<0.01), IHD (p<0.05) and physical activity (p<.08) were independent predictors of RH-PAT index, accounting together for 22% of the total variance.
Conclusion: The results of this study suggest that sleep apnea patients should be encouraged to avoid smoking, engage in regular physical activity and monitor their HC and vitamins levels. Possibly, they should use antioxidants to improve endothelial function if needed.

0517

EFFECT OF TREATMENT WITH VITAMINS AND ANTIOXIDANTS ON ENDOTHELIAL FUNCTION IN SLEEP APNEA

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Introduction: Obstructive sleep apnea (OSA) is associated with increased oxidative stress which may mediate the associated cardiovascular complications. The present report describes a preliminary study on the effects of 3-month treatment with vitamins and antioxidants (E, C, Selenium and coQ10-Supraherb) in comparison with placebo on endothelial function in co-morbities free patients with moderate-severe OSA.
Methods: The primary study group consisted of 17 patients (age: 43.5±8.7 years) examined by a whole-night PSG, and found to have AHI>20. Patients who smoked or with chronic diseases (cardiovascular diseases, obstructive lung disease, liver cirrhosis, diabetis mellitus, thyroid dysfunction, rheumatid arthritis, chronic renal failure) and a previous history of treatment for OSA were excluded. Patients were randomized to either vitamins (N=9) or placebo (N=8) conditions. A separate independent group of 10 patients aged 32-69 (mean 48.3±12.8 years) were treated with CPAP as the 'gold standard' treatment therapy. All three study groups were assessed twice - at baseline and after 3 months of treatment. Both assessments included PSG, endothelial function by the peripheral arterial tonometry technique and blood sampling.
Results: Vitamins treatment exerted no effect on OSA severity. Plasma vitamin E increased from baseline levels of 12.1±2.6 to 20.0±4.3 µg/% ($p=0.0007$) but there were no significant changes in the oxidative stress marker, thiobarbituric acid reactive substances (TBARS), with baseline and post-treatment levels of 20.2±9.6 and 20.0±5.8 nmol MDA/mL, respectively ($p=0.96$). FRAP, as a measure of total antioxidants in plasma, tended to increase with vitamin treatment ($p<0.06$) and the index of endothelial function tended to increase from 1.89±0.3 to 2.1±0.4 ($p=0.07$). No changes were recorded in the placebo group. CPAP treatment significantly reduced AHI from 48.2±22.4 to 4.9±3.5 n/hr ($p<0.0001$), TBARS decreased significantly from 23.6±0.4 to 14.1±5.2 nmol MDA/mL ($p=0.027$), and FRAP increased significantly ($p<0.05$). Endothelial function increased significantly from 1.73±0.3 to 2.2±0.2 ($p=0.009$).
Conclusion: The vitamins group exhibited limited improvement in oxidative stress and endothelial function. CPAP treatment has proved more effective in reversing OSA and subsequent sub-clinical markers of atherosclerosis risk.

0518

SLEEP LOSS REDUCES APNEA-INDUCED RESPIRATORY NEUROPLASTICITY

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Introduction: Sleep loss leads to deficits in neuroplasticity that underlie long-term potentiation (LTP) and important physiological functions such as learning and memory. Long-term facilitation (LTF) is a form of respiratory neuroplasticity that serves to enhance airway patency and shares common features with LTP. However, the affect of sleep loss on respiratory neuroplasticity is unknown. We previously showed that repeated airway obstructions, as experienced in obstructive sleep apnea (OSA), trigger LTF of upper airway genioglossus muscle tone in rats. The goal of this study was to determine if short-term sleep loss affects apnea-induced respiratory LTF
Methods: LTF of genioglossus EMG tone was measured in anesthetized (2% Isoflurane), tracheostomized, spontaneously breathing adult male rats. Protocol-1 (n=12), control rats: Respiratory activity was recorded for 60 minutes before and after exposure to ten, 15-second apneas, each separated by one minute. Protocol-2 (n=6), sleep deprived rats: At the onset of the light phase, rats were sleep deprived for 6 hours by gentle handling. They were then anesthetized and the same protocol as the control rats was performed. LTF was quantified as an increase in genioglossus EMG from baseline for at least 60 minutes after repeated apneas
Results: Repeated apneas triggered LTF of genioglossus EMG tone (i.e., respiratory plasticity), increasing it by 61 ± 11% above baseline levels ($p<0.05$, 60-min after apneas) in control rats. Although repeated apneas still elicited a 30 ± 9% increase ($p<0.05$, 60-min after apneas) in genioglossus tone after 6-hours of sleep loss, this intervention significantly reduced ($p<0.05$) the magnitude of genioglossus LTF compared to control rats.
Conclusion: We conclude that repeated obstructive apneas trigger LTF of genioglossus muscle tone, which could help maintain airway patency in OSA. However, sleep loss potently suppresses the potentially beneficial effects of apnea-induced LTF of genioglossus activity. Therefore, the lack of LTF in some OSA patients could be caused by the sleep loss/fragmentation associated with apnea-induced arousals. Triggering LTF by pharmacological mechanisms could be a useful strategy for improving airway patency in OSA patients

0519

EXPIRATORY EMG ACTIVITY IS COMMON IN NON-OBESE FEMALES DURING SLEEP

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Introduction: Expiration is largely expected to be a passive process during sleep. Expiratory effort activity in surface EMGs during polysomnography (PSG) is rarely evaluated; however, our clinical experience suggests such activity is common. Expiratory muscles such as the internal intercostals have a greater fast-twitch aerobic fiber component than the accessory muscles of inspiration. We hypothesized that the expiratory frequency distribution of the surface EMG would effectively differentiate expiratory from inspiratory EMG activity.
Methods: We analyzed 50 consecutive PSGs of females with BMI<30 and a right intercostal EMG (RIC) with a sample rate of 512Hz (low frequency filter (LFF) of 10Hz), between 9/1/2008 and 11/6/2008. Of these, 40 demonstrated inspiratory activity in RIC (mean age=53.2 years; mean BMI=23.7). 11 of these 40 (27.5%) demonstrated expiratory activity during sleep. 10 were further analyzed (1 excluded due to respiratory rate above 20 bpm). One 60-second segment was selected (not encompassing a respiratory event) from each of: a) Relaxed Wakefulness (RW), b) NREM sleep with visible inspiratory activity only (NI), and c) NREM sleep with visible expiratory activity (NE). We performed FFTs (0.5 second non-overlapping windows), on each of these full segments, capturing 1 second during each inspiratory (-Insp) and expiratory (-Exp) phase. Two-tail paired T-tests were performed to compare inspiratory to expiratory phases, and across the 60-second segments.
Results: Significant differences in frequency distribution between Insp and Exp was observed (mean NE-Insp=60.44, NE-Exp=84.61 ($p<0.0005$); 3rd quartile (Q3) NE-Insp=70.53, NE-Exp Q3=107.02 ($p<0.0005$); maximum NE-Insp=105.83, NE-Exp Q3=122.66 ($p<0.0005$). NE-Exp Mean, Q3, and maximum values were higher than NI-Exp values ($p<0.005$, $p<0.001$, $p<0.001$ respectively). NE-E Mean was higher than RW-E Mean ($p<0.005$), and Q3 and Max values trended higher. Insp and Exp activity largely fell below and above 100Hz, respectively. Employing a LFF=100Hz post hoc, 60% of all PSGs (24/40) evidenced expiratory activity during sleep.
Conclusion: Sleep-related expiratory EMG activity may be under-appreciated. Sixty percent of our sample population had expiratory effort evident in the RIC. A LFF of 100Hz aids in distinguishing expiratory from inspiratory activity.

0520

THE EFFECT OF GENIOGLOSSUS MUSCLE STIMULATION ON PHARYNGEAL COLLAPSIBILITY AND SLEEP-RELATED INSPIRATORY FLOW LIMITATION

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Introduction: The genioglossus (GG) is the major pharyngeal dilator muscle. As such decreased GG activity most likely plays an important role in the genesis of upper airway obstruction during sleep in individuals with obstructive sleep apnoea (OSA). Stimulation of the GG via fine wire intramuscular electrodes during sleep may be of therapeutic benefit to individuals with OSA. The aim of the study was to determine the effect of inspiratory-synchronous stimulation of the genioglossus muscle (GG) on pharyngeal collapsibility and the magnitude of inspiratory flow limitation during sleep in individuals with OSA.
Methods: Fine wire electrodes were inserted percutaneously, unilaterally into the GG muscle of 6 volunteers with moderate-severe OSA (AHI, 33±10 (±SD), range 22-51). During sleep, nasal mask pressure was manipulated to induce varying degrees of inspiratory flow limitation. Maximum inspiratory flow was measured with and without inspiratory-synchronous GG stimulation (3.2±0.8 mamps, range 2-4 mamps), provided by an external stimulator (Apnex Medical). The primary site of pharyngeal collapse during obstructed efforts was determined via a multi-sensor pharyngo-esophageal pressure catheter. In one individual, pharyngeal collapsibility (critical closing pressure, Pcrit) was quantified with and without GG stimulation.
Results: Compared to flow-limited breaths, inspiratory-synchronous stimulation of the GG increased maximum inspiratory flow from 0.33±0.24 to 0.46±0.24 L/sec ($p<0.05$). Where measured (in one subject), GG stimulation decreased Pcrit from -2.6 to -10.9 cmH2O. In all subjects the primary site of collapse was the velopharynx and GG stimulation overcame obstruction at this site.
Conclusion: Stimulation of the GG during sleep via intramuscular fine wire electrodes can improve inspiratory airflow and decrease pharyngeal collapsibility during sleep. These effects are evident in individuals in whom the primary site of collapse is at the level of the velopharynx.
Support (optional): Apnex Medical Inc., St. Paul, Minnesota, USA.

0521

THE ROLE OF OBESITY AND SLEEP APNEA SEVERITY IN LEPTIN LEVELS IN OBSTRUCTIVE SLEEP APNEA: THE ISAC STUDY

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Introduction: Leptin is an adipokine, with a regulatory role in body adiposity with high levels acting as a satiety signal. Leptin also has a proinflammatory role. The contribution of obstructive sleep apnea (OSA) to basal leptin levels independent of body adiposity remains unclear. To estimate the relative role of obesity and OSA severity on serum leptin levels, we evaluated different measures of obesity and the severity of sleep apnea in a large cohort of untreated OSA subjects.
Methods: Untreated OSA patients with an apnea-hypopnea index (AHI) ≥15 were invited to participate and were a part of the Icelandic Sleep Apnea Cohort (ISAC) study. The patients underwent an abdominal magnetic resonance imaging (MRI) to measure visceral and subcutaneous fat mass (divided by height squared), measurements of body mass index (BMI), waist circumference, waist-to-hip ratio, neck circumference and fasting morning leptin levels in serum. Log transformation of leptin values produced statistical distributions amenable to parametric analyses. Multiple linear regression analyses were performed in order to examine the relative importance of obesity and OSA severity to expected leptin levels.
Results: Altogether 451 untreated OSA patients were included with a mean age (±SD) of 54.4±10.7 and BMI 32.3±5.0 kg/m^2. The mean AHI severity was 41.6±19.4 and the oxygen desaturation index (ODI) 33.1±18.6. The average leptin levels were 13.9±15.2 ng/ml (2.35±0.71 for log values). The correlation between log leptin levels and different measures of obesity was highest for subcutaneous fat ($r=0.66$, $p<0.0001$) and BMI ($r=0.60$, $p<0.0001$) somewhat less for waist circumference ($r=0.45$, $p<0.0001$), lower for visceral fat ($r=0.30$, $p<0.0001$) and neck circumference ($r=0.13$, $p=0.007$) and nonsignificant for waist-to-hip-ratio. A multiple linear regression model showed that BMI accounted for 36% of the variance controlling for ODI. In contrast, ODI was not a significant predictor controlling for BMI. When BMI was replaced with subcutaneous fat in the model, the results were similar but waist circumference and visceral fat explained less variance in leptin values. In none of the models did ODI have a significant effect on leptin levels. Additionally, age and gender were independently associated with leptin levels.
Conclusion: These results indicate that of the various obesity measurements, subcutaneous fat mass and BMI best predict leptin levels. OSA severity does not independently contribute to leptin levels.

0522

REDUCTION OF C-REACTIVE PROTEIN WITH SURGICAL TREATMENT OF OBSTRUCTIVE SLEEP APNEA/HYPOPNEA SYNDROME

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Introduction: To determine whether surgical treatment of obstructive sleep apnea/hypopnea syndrome (OSAHS) has an impact on C-reactive protein (CRP) level.
Methods: This study is a retrospective case series of at a tertiary care center. All patients undergoing surgical correction of OSAHS had preoperative CRP levels measured in addition to full polysomnography (PSG). Postoperatively, patients had follow-up PSG and CRP testing. 175 patients underwent surgery for moderate to severe OSAHS. 70 patients had elevated preoperative CRP and complete data to be included in the study
Results: Overall the mean CRP level decreased significantly (from 0.33 mg/dL preoperatively to 0.16mg/dL postoperatively). The patients were further subdivided into those who achieved "cure" by PSG criteria and those who failed. Postoperative CRP levels were significantly reduced even in the "PSG failure" group.
Conclusion: Patients with moderate to severe OSAHS and elevated CRP levels showed reduction in post-operative CRP levels even when PSG results showed residual disease. In patients who fail CPAP therapy, surgical treatment may not only improve symptoms but reduce CRP levels as well.

0523

TERMINATION OF OBSTRUCTIVE RESPIRATORY EVENTS WITHOUT CORTICAL AROUSAL FROM SLEEP

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Introduction: Approximately 30% of respiratory events in Obstructive Sleep Apnea (OSA) end without cortical arousal. Cortical arousal (CortAr) may predispose to further respiratory events by promoting hyperventilation and hypocapnia/upper airway dilator muscle hypotonia on return to sleep. The purpose of this study was to: 1) compare the physiological changes at respiratory event termination with CortAr to those events terminated without cortical arousal (noAr); and 2) determine whether subsequent respiratory events are less severe/associated with less dilator muscle hypotonia after noAr compared to CortAr.

Methods: 12 CPAP treated OSA patients were instrumented with an epiglottic catheter (P_{EPI}), intramuscular genioglossus and tensor palatini EMG electrodes (EMG_{GG} and EMG_{TP}) and a nasal mask/pneumotachograph. During stable NREM sleep, CPAP was lowered to induce flow limitation/respiratory events for 3 minute periods or until full awakening occurred. Inspired minute ventilation (V_I) and EMG data were compared between respiratory events which were terminated with CortAr versus noAR. Sudden increases in CPAP (CPAPinc) served as a control.

Results: V_I was greater following CortAr than CPAPinc (p=0.04), but not different to noAR (14.3±1.5 vs. 10.4±0.5 and 13.3±1.2 l/min respectively). P_{EPI} was not different between event types. EMG_{GG} and EMG_{TP} did not change with CPAPinc (change=0.6±0.4 and 0.9±0.6 %max) but increased similarly for both CortAr and noAR events (EMG_{GG} 13.2±3.5 and 7.5±2.6, EMG_{TP} 5.8±1.7 and 4.1±1.3 %max). Subsequent respiratory events were less severe than initial events regardless of whether CortAr or noAR occurred (peak inspiratory airflow increased from 0.22±0.04 to 0.36±0.04 l/sec, p=0.005 and V_I increased from 4.3±0.7 to 6.4±0.6 l/min, p=0.003). In addition, secondary respiratory events tended to have greater EMG_{GG} (7.7±3.2 vs. 4.8±2.1 %max, p=0.06) and EMG_{TP} activity (4.2±0.9 vs. 2.9±1.0, p=0.047) than initial events after both CortAr and noAR events.

Conclusion: The physiological changes occurring upon termination of respiratory events without arousal are not different to when cortical arousal occurs. Contrary to prior understanding, cortical arousal does not lead to genioglossal hypotonia on return to sleep in this setting.

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0524

ASSESSMENT OF UPPER-AIRWAY DILATOR MUSCLE REFLEXES, RESPIRATORY SENSATION, TONGUE FORCE AND FATIGUE CHARACTERISTICS IN UNTREATED OSA PATIENTS VERSUS CONTROLS

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Introduction: The possible role of upper-airway (UA) neuropathy and impaired UA dilator muscle function in OSA pathogenesis/disease progression is debated. To explore this issue, we performed a detailed analysis of the reflex responses of two UA dilator muscles (genioglossus [GG] and tensor palatini [TP]), measured respiratory-related evoked potentials (RREPs), and assessed tongue protrusion force and fatigability in OSA patients and controls.

Methods: To date, GG and TP EMG (wire electrodes), RREPs (Cz and Pz), and UA pressures at the choanae (Pcho) and epiglottis (Pepi) have been recorded in 9 awake, untreated, OSA patients and 12 controls. Reflex and RREP responses were generated via 250 ms pulses of negative UA pressure (-16 cmH_2O at the mask). Maximal voluntary tongue protrusion force was assessed via force transducer and "fatigability" via a repeated isometric contraction protocol (5s on at 70% max force and 5s off until task failure).

Results: The UA collapsibility index ([nadir Pcho-Pepi]/nadir Pcho x100 during pulses) was greater in OSA patients vs. controls (64±7 vs. 44±6 %, p=0.04). GG and TP reflex latencies and amplitudes were not different between OSA and controls (e.g. GG peak onset 20±2 vs. 19±2 ms; peak amplitude 492±127 vs. 318±56 % baseline), nor were RREP component latencies or amplitudes (e.g. P1 latency 25±2 vs. 24±1 ms; P1 peak amplitude 3.2±0.5 vs. 3.6±0.7 μv). Maximal tongue protrusion force was greater in OSA vs. controls (33±2 vs. 26±2 N, p=0.03) but "fatigue" occurred more rapidly (2.4±0.4 vs. 4.3±0.4 min, p=0.01).

Conclusion: These data indicate that UA dilator muscle reflex responses and sensory processing to negative pressure pulses are intact, but there are increased maximal tongue protrusion force and fatigability in awake, untreated, OSA patients compared to controls. While further assessment of functional effectiveness of UA dilator muscles during sleep is required, these data raise the possibility that untreated OSA patients may be more vulnerable to UA dilator muscle fatigue which could contribute to the pathophysiology of the disorder.

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0525

INFLAMMATION AND INSULIN RESISTANCE IN NONOBESE MEN WITH SLEEP APNEA

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Introduction: We have postulated that inflammation, insulin resistance, and visceral adipocity play a major role in the pathogenesis of sleep apnea in obese and the associated cardiovascular morbidities. Although in clinical populations obese patients with sleep apnea are the large majority, in general population samples, apnea is present in nonobese and is associated with cardiometabolic risks, i.e., hypertension, diabetes. The goal of this study was to examine the inflammation and metabolic profile in nonobese, middle-aged men.

Methods: Sixteen nonobese men with OSA and 12 nonobese controls matched for age and BMI were monitored in the sleep laboratory for 4 consecutive nights. Objective measures of sleep, daytime sleepiness and performance, serial 24-hour plasma measures of interleukin-6 (IL-6), TNF receptor 1 (TNFr1), leptin and adiponectin, fasting blood glucose and insulin, and two samples (morning and evening) of C-reactive protein (CRP) were obtained.

Results: Nonobese men with sleep apnea compared to nonobese controls showed higher 24-hour levels of IL-6 and leptin, and single levels of CRP. Furthermore, glucose/insulin ratio was significantly lower in apneics vs. controls, indicating insulin resistance. However, there were no differences between the two groups in terms of 24-hour TNFr1 or adiponectin, a molecule that promotes insulin sensitivity.

Conclusion: Inflammation and insulin resistance are present also in nonobese apneics, although of a lesser degree compared to obese apneics. Inflammation and insulin resistance in nonobese patients with sleep apnea may be the link to cardiometabolic risks associated with this disorder. Whether these abnormalities in nonobese patients with apnea are primary or sequelae to sleep apnea and whether they are ameliorated by current treatments should be the focus of future research.

Support (optional): R01 HL64415

0526

OBSTRUCTIVE SLEEP APNEA (OSA) IN PATIENTS WITH TYPE 2 DIABETES (T2DM): PREVALENCE AND IMPACT ON GLUCOSE CONTROL

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Introduction: There is good evidence for an independent association between OSA and altered glucose metabolism. Our previous cross-sectional analysis showed that perceived sleep debt and poor sleep quality are significant predictors of glycemic control in patients with T2DM but the study did not control for OSA. The present study assesses habitual sleep time and OSA in T2DM and tests the hypothesis that the presence and severity of OSA are determinants of glycemic control.
Methods: Fifty-five patients with T2DM were consecutively recruited from our outpatient clinics. Each patient underwent 5 days of home wrist actigraphy to assess habitual sleep duration and an overnight polysomnography (PSG) to assess OSA (apnea-hypopnea index [AHI] ≥5) and its severity (mild: 5< AHI < 15; moderate:15≤AHI<30; severe:AHI≥30). The duration of PSG was tailored to the individual sleep duration but ≥ 7 hours. Glucose control was assessed by serum hemoglobin A1c (HbA1c).
Results: Mean (±SD) habitual sleep duration was 6.2±1.2 hours with only 18% of the sample obtaining ≥ 7 hours of sleep. 87% of the patients had OSA (mild: 25%, moderate: 35%, severe: 27%). Increasing severity of OSA was associated with worsening glucose control after controlling for age, sex, race, BMI, insulin use, years of diabetes and total sleep time on PSG. Compared to patients without OSA, the adjusted mean HbA1c was increased by 1.82% (p=0.018) in patients with mild-to moderate OSA and 2.44% (p=0.004) in patients with severe OSA. These effect sizes are comparable to those of widely used oral anti-diabetic medications. Adjusted HbA1c values were correlated with markers of OSA severity, including total and REM-related number of obstructive events (p=0.05 and p=0.01, respectively), lowest oxygen saturation (p=0.01), and REM-related number of desaturations >3% (p=0.01).
Conclusion: Thus, OSA is highly prevalent and an important determinant of glucose control in T2DM. Patients with T2DM should be systematically evaluated and treated for OSA.
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0527

IN OBESE INDIVIDUALS, THE EFFECT OF OSA ON VASCULAR FUNCTION IS MODULATED BY AGE AND GENDER

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Introduction: We hypothesize that OSA independently contributes to abnormal vascular function in obese individuals.
Methods: Obese subjects, free of known co-morbidities with a BMI>29 kg/m2, were enrolled. OSA was defined as RDI>10/hr. Vascular function was measured by 3 different methods: 1.measuring the change in brachial artery diameter before and after flow mediated dilation (FMD) 2.measuring skin microcirculatory flow before and after iontophoresis of acetylcholine (Ach, endothelial-dependent) and sodium nitroprusside (SNp, endothelial-independent) and 3.assessing Augmentation Index (AIx), a measure of arterial stiffness.
Results: 72 obese subjects, 38 with OSA, were studied. FMD was impaired in OSA compared to non-OSA subjects (5.7+/-3.8% vs 8.34+/-4.1%, p=0.005). In multiple stepforward linear regression analysis inclusive of age, gender and BMI, age (p=0.013) was a significant predictor of change in FMD. In a subgroup of subjects <50 years old (59 subjects), however, OSA status was the only significant predictor of % change in FMD (p=0.04), adjusted for age, gender and BMI. No statistically significant differences were found between endothelial-dependent and independent vasodilation in the skin microcirculation. AIx, was similar between the OSA and non-OSA groups (16.2+/-11.4% vs. 20.4+/-10.1 % respectively, p=0.10). However, females had a higher AIx than males (23.7+/-8.6% vs. 10.7+/-9.0 % respectively, p=<0.0001). In a step-forward regression analysis of younger subjects (<50 yrs) that included OSA status, age, and BMI, OSA status (p=0.001) predicted AIx in males. In younger females, age was the only predictor of AIx (p=0.001).
Conclusion: The decrease in FMD in OSA vs non-OSA subjects can be explained by differences in age. However, younger OSA subjects have decreased FMD compared to non-OSA subjects, even after controlling for known covariates. With increased age, all subjects have impaired endothelial function regardless of OSA status. OSA, therefore, may be associated with functional impairment ("a premature aging effect") on the endothelium. AIx, on the other hand, is affected by gender with large differences between males and females. In younger subjects, AIx is predicted by OSA in males and age in females. Younger males, therefore, may be more susceptible to the effects of OSA on AIx. In obese healthy individuals, the effect of OSA on vascular function, measured using several different methods, is modulated by age and gender.
Support (optional): National Sleep Foundation, Pickwick Fellowship NIH (R01-HL73146)

0528

THE IMPACT OF END-EXPIRATORY LUNG VOLUME ON PHARYNGEAL COLLAPSIBILITY IN OSA PATIENTS AND CONTROLS

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Introduction: Pharyngeal cross-sectional area increases as lung volume increases from residual volume to total lung capacity, and prior studies have suggested that this change is greater in patients with obstructive sleep apnea (OSA) than in controls. However, these studies were performed during wakefulness, when other factors besides lung volume could influence pharyngeal cross-sectional area. Therefore, we aimed to determine the impact of changes in end-expiratory lung volume (EELV) on pharyngeal collapsibility during sleep in OSA patients and controls.
Methods: CPAP treated OSA patients and controls were instrumented with an epiglottic catheter and a nasal mask/pneumotachograph (for CPAP delivery, airflow and mask pressure measurement). Magnetometers were used to measure changes in EELV. Subjects slept supine in a head-out plastic chamber in which the extra-thoracic pressure could be lowered (to raise EELV) while on nasal CPAP. CPAP was set at the prescribed level for OSA patients and at 4 cmH2O for controls, and was increased if needed to eliminate flow limitation. The pharyngeal critical closing pressure (P_{CRIT}) was measured by sudden reductions of CPAP for 3-5 breaths each minute at baseline and with EELV increased approximately 500cc.
Results: Full data have been obtained in 7 OSA patients (aged 47±13years, AHI 37±21 events/hr) and 3 controls (aged 26±2 years) to date. The average increase in EELV was 579cc and 553cc, respectively. In OSA subjects, P_{CRIT} was 2.6±0.9 cmH_2O at baseline and -0.8±0.6 cmH_2O at increased EELV, a difference of -3.4 cmH_2O. In controls, P_{CRIT} was -5.6±1.6 cmH_2O at baseline and -10.7±2.4 cmH_2O at increased EELV, a difference of -5.1 cmH_2O.
Conclusion: These preliminary data indicate that increasing EELV by 500cc reduces P_{CRIT} substantially and by a similar amount in both OSA patients and controls.
Support (optional): NIH HL048531 HL60292, RR01032 and American Heart Association 0635318N.

0529

PLATELET REACTIVITY IS RELATED TO HYPOXEMIA, NOT RDI, IN NONCOMORBID OBESE

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Introduction: We hypothesize that platelet activation, reactivity and aggregability in obese subjects correlates with OSA severity.
Methods: Obese subjects, free of known cardiovascular co-morbidities with a BMI>29 kg/m2, were enrolled. Subjects were excluded if they were known to be taking aspirin, NSAIDs, SSRIs, as well as other potentially confounding medications. OSA was defined as RDI>10/h. All patients underwent overnight polysomnography (PSG) with collection of blood for platelet studies in a controlled manner the following morning. The following markers of sleep and OSA were analyzed: RDI, SaO2 nadir, %time spent <90% oxygen saturation, total sleep time (TST), arousal index (AI), and sleep efficiency. Five biomarkers of platelet activation were selected and measured by flow cytometry in three states (no stimulation, stimulation with 5uM and 20uM of ADP): PAC-1, P-selectin, and Gp1b surface receptor expression and platelet-monocyte/platelet-neutrophil aggregation. The receptor expression profile was represented by an index which combined platelets positivity with average receptor density.
Results: 34 of 55 subjects were diagnosed with OSA (median RDI 13/h, interquartile range 3.2-27.5, median BMI 37.5kg/m2, interquartile range 33.4-43.4). Platelet function did not correlate with RDI. There was, however, an inverse relationship between time spent at oxygen saturations <90% and gp1b indices at 0, 5uM, and 20uM of ADP stimulation, suggesting higher levels of platelet activation with greater desaturation (rho= -0.45, p=0.001; rho= -0.42, p=0.001; rho= -0.371, p=0.005, respectively). In addition, those subjects with a lower oxygen saturation nadir had an elevated Pac1 receptor index, suggestive of higher basal platelet activation (rho= -0.25, p=0.05). Arousal index was negatively correlated with platelet neutrophil aggregation (rho= -0.28, p=0.03). Sleep efficiency did not correlate with platelet function as assessed by flow cytometry.
Conclusion: In the healthy obese with and without OSA, but no other cardiovascular co-morbidities, OSA as measured by RDI is not associated with increased platelet activation. However, platelet activation is associated with greater oxygen desaturations and a lower arousal index. Thus, measures other than RDI may need to be considered when determining risk of thrombotic events in OSA patients.

0530

A META-ANALAYSIS OF RANDOMIZED CONTROLLED TRIALS EVALUATING THE EFFECT OF NOCTURNAL CONTINUOUS AIRWAY PRESSURE (CPAP) THERAPY ON EJECTION FRACTION IN PATIENTS WITH SYSTOLIC CONGESTIVE HEART FAILURE AND OBSTRUCTIVE SLEEP APNEA

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Introduction: The prevalence of sleep-disordered breathing may be as high as 50 percent among all patients with congestive heart failure (CHF). The pathogenesis of obstructive sleep-apnea (OSA) in CHF involves abnormalities in pharyngeal anatomy, pharyngeal function, and ventilatory control. In patients with heart failure, edema of the upper airway is an additional factor that may contribute to pharyngeal airway narrowing. OSA can increase ventricular transmural wall stress and afterload and worsen CHF. We aimed to study the effect of nocturnal continuous positive airway pressure (CPAP) therapy on left ventricular ejection fraction (LVEF) in patients with systolic CHF and OSA by conducting meta-analysis of the existing literature.
Methods: We searched MEDLINE and citations of all original articles and reviews for studies published in English reviewed using keywords: CPAP, positive pressure ventilation, OSA, CHF, sleep apnea and heart failure. The inclusion criteria for clinical studies was: (1) randomized controlled trials, (2) published in English language, and (3) measurement of LVEF after CPAP therapy in patients with both systolic CHF and OSA as one of end-points. The Mantel-Haenszel method for calculating the weighted summary odds ratio under the fixed effects model was used for statistical analysis. Next, the heterogeneity statistic was incorporated to calculate the summary odds ratio under the random effects model.
Results: Four randomized, placebo-controlled clinical studies were included in the meta-analysis. The cumulative number of patients treated with CPAP was 74. The cumulative number of patients as controls was 83 (48 treated with sham CPAP+medical therapy for CHF, 35 patients treated with medical therapy for CHF). The pooled mean change in LVEF was 3.8±1.2%in CPAP group and 0.8±1.4% in controls (p=0.003). The pooled odds ratio for improvement in LVEF after CPAP therapy was 7.3 (95% C.I.-3.4-12.5) in fixed effects model.
Conclusion: This metanalysis has some limitations: (1) small number of studies, (2) different durations of CPAP were used in included studies (range= 6 weeks-3 months), and (3) different apnea-hypopnea index criteria to treat with CPAP were used in included studies. In conclusion, nocturnal CPAP therapy significantly improves LVEF in patients with both OSA and systolic CHF.

0531

NATURAL HISTORY OF OBSTRUCTIVE SLEEP APNEA TREATED WITH CONTINUOUS POSITIVE AIRWAY PRESSURE(CPAP)

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Introduction: This study examines the clinical history of adults with moderate to severe obstructive sleep apnea treated with CPAP. Baseline in lab PSG and optimal CPAP validation studies were performed. Repeat CPAP study was performed to assess adequacy of control of OSA on CPAP. Daytime sleepiness by the Epworth Sleepiness Scale (ESS) and body mass index are correlated with changes in CPAP pressure.
Methods: A retrospective review of subjects with obstructive sleep apnea treated with CPAP compared initial CPAP study with repeat in minimum of 4 years. All underwent pre and post treatment assessment using the ESS, age, gender, BMI, RDI, oxygen desaturation, and modafinil usage. Means, standard deviations, and t-tests are assessed.
Results: 50 subjects were studied at an interval of 6.8(2.6) years with 33 males (66%) and 17 females (34%); age 50(9); baseline PSG: RDI 46(35); nadir oxygen saturation 79(9). BMI at 1st CPAP study 35(7) and 2nd CPAP study 37(8). 14(28%) were able to maintain or lose weight while 38(72%) gained weight. For the 1st CPAP titration study: the clinical level on CPAP was 9 (3); RDI on ideal CPAP level was 7(7) with mean number of minutes on ideal CPAP=135. For the 2nd CPAP titration study: the clinical level on CPAP was 11(3); RDI on ideal CPAP was 4(4) with mean number of minutes on ideal CPAP=191. Clinical CPAP pressures at 2nd study increased for 46(92%). ESS scores were significant from baseline to CPAP studies 1&2: baseline ESS/CPAP 1st p=0.007 and baseline ESS/CPAP 2nd p=0.02; however, 16 subjects (32%) were taking modafinil at the 2nd CPAP study.
Conclusion: Our results demonstrate that ideal clinical pressure in OSA treated with CPAP increases over time and with increasing BMI and age. Modafinil was used to treat daytime sleepiness in 32% of subjects at the 2nd CPAP study.

0532

ENDOTHELIAL P-SELECTIN EXPRESSION AND PLATELET CONSUMPTION DURING SLEEP IN OBSTRUCTIVE SLEEP APNEA

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Introduction: Patients with obstructive sleep apnea syndrome (OSA) are subject to increased morbidity and mortality from cerebrovascular and cardiovascular diseases associated with arterial thrombosis. However, the detailed mechanism underlying this relationship has not been clearly established. P-selectin (CD62P) is an adhesion molecule that is expressed on the membrane of activated endothelial cells and initiates thrombus formation via the rolling and attachment of platelets. Circulating microparticles derived from endothelial cells (EMPs) and from platelets (PMPs) are shed from the plasma membrane of these cells after stimulation. We aimed to clarify the relationship between the activated endothelium and platelet consumption during sleep in OSA patients.
Methods: We used flow-cytometry to count the CD41-positive PMPs and the P-selectin- and PECAM-1-expressing EMPs from the peripheral blood of 20 male subjects undergoing testing for suspected OSA. Blood samples were collected before and after polysomnography.
Results: The overnight decrease in platelet count ($P<0.05$), increase in PMPs ($P<0.05$), and increase in P-selectin-positive EMPs ($P<0.01$) correlated positively with the longest duration of apnea. The overnight increase in P-selectin-positive EMPs also correlated positively with the increase in PMPs ($P<0.05$), but not with urinary catecholamine or oxidative stress products.
Conclusion: This is the first report of platelet consumption and of the expression of P-selectin on the vascular endothelial surface of OSA patients during sleep. These findings suggest that activated endothelial cells expressing P-selectin initiate the aggregation and consumption of platelets. Severe hypoventilation-causing arterial hypoxia may augment the endothelial P-selectin expression.

0533

IS YOUR PATIENT STILL SNORING? A PREDICTOR OF CPAP NON-COMPLIANCE

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Introduction: Continuous positive airway pressure (CPAP) is effective therapy for obstructive sleep apnea (OSA), but compliance is often suboptimal. Many current CPAP devices allow download of daily use data to assess compliance, but this information is not readily available in many primary care settings. Our study goals were to develop a surrogate tool to assess CPAP compliance and to identify clinical predictors of non-compliance.
Methods: We performed a prospective cohort study to examine the use of a novel questionnaire developed by a multidisciplinary group of sleep providers. Patients with OSA presenting for CPAP follow-up were asked to answer questions addressing three potential domains that impact CPAP compliance: technical issues with the device, OSA symptom improvement and the psychological impact of CPAP therapy. Completed questionnaires were correlated with data download from the corresponding CPAP device. Compliance was defined as CPAP usage greater than 4 hours per night for at least 5 nights per week. Data was evaluated using univariate and multivariate logistic regression analyses.
Results: We analyzed 134 completed questionnaires. Eighty-six percent were male with a mean age of 45.3 ± 12.9 years. Eighty-five percent of CPAP devices were humidified and 76% were heated. The compliance rate was 62%. Non-compliant patients were more likely to report continued symptoms of daytime sleepiness ($p=0.02$) and continued snoring ($p=0.01$). Continued snoring remained an independent predictor of CPAP non-compliance after adjusting for all study responses using multivariate logistic regression (OR=2.92, 95% CI, 1.39-6.18).
Conclusion: Asking OSA patients on CPAP therapy about continued snoring may serve as a rapid, effective assessment tool for primary care providers to identify individuals who would benefit from referral for CPAP data download and further evaluation to enhance compliance. Increasing availability of CPAP download data for primary care providers to review remains an important tool to improve CPAP compliance and patient outcomes.

0534

TO EXAMINE THE CORRELATION BETWEEN CONTINUOUS POSITIVE AIRWAY PRESSURE (CPAP) AND THE TIMING OF LAST MEAL BEFORE BED TIME

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Introduction: Obstructive Sleep Apnea is a chronic disorder characterized by frequent reduction and/or cessation of inspiratory airflow during sleep, with resulting hypoxemia and hypercapnia that are terminated by arousals. This pattern of repetitive arousals and nocturnal hypoxemia leads to disruption of sleep architecture and daytime hyper-somnolence as well as a multitude of neurobehavioral and cardiopulmonary derangements. Despite widespread agreement that continuous positive airway pressure is effective therapy for obstructive sleep apnea, it is estimated that 50% of patients recommended for therapy are noncompliant 1 year later. Many patients have difficulty tolerating nasal CPAP due to nasal airway problems, mouth leak, and general discomfort from the mask and headgear. Interventions to improve compliance in such patients have not been studied. Mechanical and psychological/educational interventions have been proposed to try to increase the hours of use of CPAP therapy. We evaluated the relationship between CPAP and timing of last meal before bedtime affects the compliance and tolerance of CPAP.
Methods: A retrospective data collection study was performed via review of charts of those undergoing CPAP treatment for obstructive sleep apnea. The questionnaire's used as a standard of care gave more information on the relationship between timing of last meal and CPAP compliance and Tolerance.
Results: 50 charts of patients who came for re-titration (HUMC, Institute for Sleep/Wake Disorder during the year 2008) were reviewed. There were 9 females and 41 males. BMI ranged from 24.0-68.3. 56% of the patients self reported that their timing of last meal was 3-4 hours, 26% reported 1-2 hours and 18% reported 5 hours prior to CPAP usage; 18% reported intolerance and poor compliance to CPAP if the timing of the last meal was less than 1 hour prior to its usage, 28% found it extremely difficult to use CPAP right after their last meal. 42% reported increase in weight by more than 5 pounds after starting to use CPAP.
Conclusion: To enhance the treatment of sleep apnea with CPAP, Physicians could easily incorporate patient education on the timing of last meal and its effects on CPAP compliance. This education can take place at the time of initial application of CPAP and/or at the consecutive evaluations. This practice will further improve the goal of adherence to CPAP and the quality of life.

0535

DIFFERENCES IN SLEEP QUALITY AND DAYTIME SLEEPINESS BEFORE AND AFTER CPAP USE

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Introduction: This study is based on chronobiologic and homeostatic models of sleep regulation which hold that chronic partial sleep deprivation is associated with decrements in functioning. Our purpose was to examine the differences in self-reports of sleepiness and sleep quality in adults with OSAHS before and after CPAP use.
Methods: Participants included adults who were ≥ 21 years of age and able to speak English. They completed the Pittsburgh Sleep Quality Index (PSQI) and the Epworth Sleepiness Scale (ESS) before and after CPAP treatment. We used descriptive and correlational statistics and t-tests.
Results: The sample included 16 participants (M age = 53 years ± 9.7; 56.2% male; M BMI = 37.73; 68.8% full time workers; 43.8% married; 50% African American; M Charlson comorbidity index 1.66 ± 1.83; 69% with T2DM; 81.2% with HTN; M AHI 56.84 ± 26.37. Mean CPAP pressure was 11.77 ± 1.8; M 45% of days with usage ≥ 4 hours ± 29.73; M 238.74 days used ± 107 days. CPAP pressure correlated negatively with the number of hours of sleep (-.588 p =.021) but not with falling asleep within 30 minutes (.429 p =.111). Paired sample t-tests were conducted to evaluate the impact of CPAP on excessive daytime sleepiness (EDS) and sleep quality. There was a statistically significant decrease in EDS scores before CPAP (M 11.93 ± 3.94) and after (M 9.25 ± 4.52), t (15) 2.77, p =.014. Sleep quality improved from M 9.37 ± 2.87 to 7.18 ± 4.68, t (15) 2.39, p =.03.
Conclusion: Results of this small pilot should be taken cautiously, though it was not surprising to find that high CPAP pressure correlates with sleeplessness. While suboptimal CPAP use was demonstrated, subjective reports of improvements in EDS and sleep quality even at this level of treatment hold promise as important benefits to communicate to patients.

0536

CLINICAL PREDICTORS OF OBSTRUCTIVE SLEEP APNEA IN A FAR-EAST ASIAN POPULATION (TAIWANESE)

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Introduction: To identify standard clinical parameters that may predict the presence and the severity of obstructive sleep apnea/hypopnea syndrome (OSAHS) in Taiwanese.
Methods: Three hundred twenty-five patients with habitual snoring who underwent a physical examination and polysomnography were included in this study. We recorded the self-reported severity of nasal obstruction, updated Friedman's tongue position (uFTP), tonsil size, neck circumference and body mass index (BMI) and measured thyroid-mental distance and hyoid-mental distance in the study population.
Results: When the physical parameters were correlated singly with the respiratory disturbance index (RDI), we found that sex (P < .0001), uFTP (P < .0001), tonsil size grading (P < .0001), and BMI (P < .0001) were reliable predictors of OSA. When all important factors were considered in a multiple stepwise regression analysis, a significant correlation with OSAHS emerged when an "OSAHS score" was formulated by factoring the gender, uFTP, tonsil grade, and BMI grade (RDI = 14.29 × gender + 12.71 × uFTP + 4.62 × Tonsil Size + 9.05 × BMI - 42.52).
Conclusion: This study has distinguished the correlation between gender, uFTP, tonsil size, and BMI with levels of severity of OSAHS. An OSAHS score would also be beneficial in identifying Taiwanese patients who should have a full sleep evaluation.

0537

DONEPEZIL TREATMENT FOR SLEEP APNEA: PRELIMINARY RESULTS

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Introduction: Previous studies suggested that anticholinesterase drugs may be an effective treatment for OSA (obstructive sleep apnea) in AD (Alzheimer's disease) patients. The present study was designed to evaluate the effect of donepezil in non-AD OSA patients.
Methods: Randomized, double-blind, placebo-controlled design. Twelve patients with moderate to severe OSA, were allocated to two groups, donepezil-treated (n=6) and placebo-treated (n=6). Patients were administered donepezil or placebo. PSG (polysomnography) was performed at baseline and after 1 month treatment. Adaptation PSG was performed the night before baseline PSG. Sleepiness was assessed by Epworth scale. Sleepiness and sleep data were analyzed using two-way ANOVA.
Results: AHI (apnea-hypopnea index) improved after 1 month donepezil treatment (p<0.01 - interaction effect). There was a non-significant trend (p=0.06) to improve Epworth score and REM AHI. Treatment was well tolerated. Mild gastric-intestinal side effects were present in one treated subject.
Conclusion: This preliminary study suggests that donepezil treatment may benefit OSA patients. Further studies are needed to confirm these findings and determine specific target subpopulations for this treatment.
Support (optional): AFIP FAPESP

0538

THE EFFECT OF OBSTRUCTIVE SLEEP APNEA ON SYMPATHOVAGAL BALANCE IN PREECLAMPSIA

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Introduction: Obstructive Sleep Apnea is an independent risk factor for CV disease and is associated with an alteration in sympathetic tone. Preeclampsia is a common complication of pregnancy and has been associated with increased sympathetic tone. We evaluated the effect of OSA on sympathetic/parasympathetic balance in preeclampsia and in healthy pregnant females.
Methods: We compared Heart Rate Variability (HRV) during 5 minutes of stable stage 2 and REM sleep in healthy pregnant females in third trimester (N=6, 31.3±4.4 yrs, BMI 28.2±5.7 kg/m2), pregnant females with OSA (N=2;34.0±4.2 yrs, BMI 39.0±5.7 kg/m2), preeclamptic women without OSA (N=7; 26.1 ±7.4 yrs., BMI 33.5±6.3 kg/m2) and preeclamptic women with OSA (N=6; 27.8 ± 3.6 yrs, BMI 36.9±4.6 kg/m2). Temporal and spectral analysis of the R to R intervals and nonlinear properties of HRV was done using HRV Analysis Software version 1.1. For time-domain analysis mean RR was used. For frequency domain VLF, LF, VLF, and LF/HF ratio of the nonparametric spectrum were used. For the nonlinear method SD1 and SD2 were used. Age, BMI, mean RR, VLF, LF, HF, LF/HF ratio, SD1, and SD2 were determined for each group and statistical analysis was performed using ANOVA (for time domain variables) and nonparametric ANOVA (for frequency domain variables) with GraphPad InStat program version 3.01. P-values less than 0.05 were considered significant; all values are expressed as mean ± standard error of the mean (SEM).
Results: There were significant differences in LF% power (61.93± 13.35 vs. 35.21±13.35; p = 0.02) and LF/HF ratio (8.681±7.285 vs. 1.203±0.629, p=0.016) between patients with and without OSA in the preeclamptic group. There were no differences in HF,LF, LF/HF be-

tween the control group and patients with preeclampsia. The results suggest that presence of OSA adversely affects the sympathovagal balance in patients with preeclampsia.
Conclusion: Preeclamptic patients with OSA have increased LF power and LF/HF ratio suggesting an abnormal sympathovagal balance during sleep.
Support (optional): The authors wish to thank the Lung Association of Saskatchewan, Saskatoon Reagion Health Authority for their support.

0539

PENILE TUMESCENCE PATTERN DURING SLEEP IN PATIENTS WITH OBSTRUCTIVE SLEEP APNEA. PRELIMINARY RESULTS

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Introduction: A growing body of evidence links sleep-disordered breathing and erectile dysfunction. However, during prolonged hypoxia condition increase in penile tumescence had been attributed to counter-regulatory mechanisms that induces smooth muscle relaxation. In this study we examined the oscillation in penile tumescence during sleep in patients with obstructive sleep apnea (OSA).
Methods: Twelve OSA subjects (age 47± 9, BMI 21.3± 2.7, AHI 22±10) underwent monitoring of nocturnal penile tumescence during all-night sleep using RigiScan PlusTM, concomitantly to polysomnography. Increase in penile tumescence above 20% over baseline was considered. Tumescence activity units (TAUs) expressed % increase in tumescence over baseline per minute. Cross-correlation analysis was used to determine the relationship between penile tumescence and the respiratory variables during sleep
Results: The subjects demonstrated an average sleep latency of 14.2 ± 4.0 min, sleep efficiency of 84.4 ± 7.8%, and mean distribution of sleep stages as follows: stage 1, 13.6 ± 1.8%; stage 2, 60.9 ± 5.1%; SWS, 2.8 ± 0.7%; and REM, 20.7 ± 2.1%. The REM latency was 112.3 ± 8.0 min, and arousal index was 13.7 ± 3.1. Penile base TAU positively correlated with apnea/hypopnea index (r=0.43; P=0.04), desaturation events (r=0.57, P=0.03), and arousal index (r=0.72, P=0.02). Maximum negative cross-correlation between penile tumescence and oximety during sleep was observed when penile tumescence was lagged by 0.25 hr, (r = -0.72, P=0.03). suggesting that decrease in oxymetry precede increase in penile tumescence, independently of the sleep stage.
Conclusion: Penile tumescence activity during sleep was associated to respiratory events and sleep fragmentation in OSA patients.
Support (optional): AFIP and CEPID 98/14303-3

0540

AUTONOMIC NERVOUS FUNCTION DURING PENILE TUMESCENCE EVENTS IN REM SLEEP ON PATIENTS WITH OBSTRUCTIVE SLEEP APNEA. PRELIMINARY RESULTS

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Introduction: Erectile dysfunction is reported in sleep-disordered breathing. Since parasympathetic tone due to the loss of the vagolytic effects of chest wall expansion occurs during obstructive sleep apnea events and hypoxemia, this study was conducted to evaluate the autonomic nervous system changes during events of increased penile tumescence that occur in in patients with obstructive sleep apnea (OSA).
Methods: Twelve OSA subjects (age 47± 9, BMI 21.3± 2.7, AHI 22±10) underwent monitoring of nocturnal penile tumescence during all-night sleep using RigiScan PlusTM, concomitantly to polysomnography. Increase in penile tumescence above 20% over baseline was considered. A digital Holter ECG was used to examine heart rate variability (HRV) during sleep in frequency domain: low-frequency (LF) power, high-frequency (HF) power, the LF/HF ratio, and very low-frequency (VLF) power in 5-minute sequential samples of the longest and more stable stage 2 and REM sleep periods.
Results: Among the 12 patients, 57±4% of the apnoeas/hypopnoeas and 77±6% of increase in tumescence events occurred during REM sleep. Tumescence event periods were compared with non-event periods (baseline tumescence) in REM sleep, independently of the presence of respiratory events. Increase in both HFn (131 ± 46 to 708 ± 78 ms2, $p < 0.001$), and LF/HF RRI power ratio (from 3.91 ± 0.4 to 1.9 ± 0.6) was observed during penile tumescence periods. Concomitant obstructive respiratory events were present in 73.7% of the samples with increase in penile tumescence.
Conclusion: Penile tumescence events during sleep was associated to respiratory events and increase in both sympathetic and vagal autonomic activity in REM sleep
Support (optional): AFIP and CEPID 98/14303-3

0541

A DOUBLE BLIND, CROSS-OVER STUDY ON THE EFFECTS OF SILDENAFIL IN BLOOD PRESSURE AND HEART RATE VARIABILITY IN SEVERE OBSTRUCTIVE SLEEP APNEA

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Introduction: The increased availability of nitric oxide by Sildenafil may induce prolongation of sleep apnea events and also peripheral vasodilatation, instead of vasoconstriction, as expected during apnea. Given that both effects may impair compensatory mechanisms in OSA, we conducted this study to clarify the effect of sildenafil on the autonomous nervous functions change with respiratory sleep events.
Methods: Thirteen men with OSA (IAH>30/h aged 43±10, BMI 26,7± 1.9 kg/m2 without cardiovascular and/or chronic respiratory disease) took of sildenafil 50mg or placebo at bedtime. All-night polysomnography, blood pressure (BeatScope 1.0TM) and Holter monitoring to assess heart rate variability (HRV) were simultaneously recorded. Frequency domain techniques were performed during and after apnea events in non REM and REM sleep.
Results: In comparison to placebo, sildenafil significantly decreased the variation of (BP) at the end of apnea events (0.43 ± 0.10 vs 0.20 ± 0.04, t=-8.7, p<.001). Increase in the HF component of HRV was observed during apnea and in post-apnea in non-REM sleep, with the use of sildenafil, in comparison to placebo (P=0.002, and 0.0003, respectively). In the post-apnea condition, reduction in LF/HF index (0.0007) was observed in non-REM sleep.
Conclusion: In severe OSA, a 50-mg dose of sildenafil at bedtime blunts the variation of BP related to apnea, increased vagal and decreased sympathetic tonus in non-REM sleep during apnea event and after it.
Support (optional): AFIP and CEPID 98/14303-3

0542

SLEEP-DISORDERED BREATHING AND SELF-REPORTED GENERAL HEALTH STATUS IN THAI PATIENTS

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Introduction: Objective: To determine the relationship between sleep-disordered breathing and self-reported general health status in Thai patients.
Methods: Design: Descriptive, cross-sectional study. Setting: Data was collected from January 2006 to December 2007 at King Chulalongkorn Memorial Hospital. Subjects: 268 patients (195 men and 73 women), ages 16 - 82 years. Outcome Measurement: A health profile was obtained by self-administered questionnaire. Sleep-disordered breathing severity was assessed by an attended single-night comprehensive polysomnography.

Results: Sleep-disordered breathing was not directly associated with the general health status. Presence of excessive daytime sleepiness, which was the major symptom of obstructive sleep apnea, was associated with decrements in all domains of Short Form 36, and this relationship was of clinical significance. Age, sex and body mass index were also related to a lower physical function. Hypertension and excessive daytime sleepiness were associated with the severity of sleep-disordered breathing.
Conclusion: Sleep-disordered breathing is indirectly related to a lower general health status and this relationship is of clinical significance. Given the growing emphasis of the importance of patients' perceptions of health, these findings are relevant to estimating the overall impact of sleep-disordered breathing.

0543

PRIOR KNOWLEDGE OF AND/OR OPINION ON CONTINUOUS POSITIVE AIRWAY PRESSURE (CPAP) HAS NO IMPACT ON CPAP COMPLIANCE IN PATIENTS WITH OBSTRUCTIVE SLEEP APNEA

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Introduction: Poor compliance with continuous positive airway pressure (CPAP) therapy limits long-term successful control of obstructive sleep apnea (OSA). Poor compliance may result from beliefs and preconceived attitudes towards this therapy. We aimed to examine, using a simple two question survey format, whether the prior knowledge and/or opinion on CPAP affect its acceptance and long-term compliance with it.
Methods: 121 consecutive CPAP-naïve patients with sleep apnea were asked two questions via survey format on initial evaluation: Have you heard about CPAP, a method of treatment of sleep apnea (yes/no)? If the patient answered "yes" to this question, an additional question was asked: Have you heard good things / bad things / both good and bad things about CPAP? Following the diagnosis of OSA, objective compliance with CPAP was assessed at the first visit at 4-6 weeks of CPAP use.
Results: Following CPAP prescription, 14 patients refused CPAP and 107 patients accepted it. Among the whole group, overall compliance with CPAP was 3.5 ± 2.9 hours on 55% of days. Patients used CPAP for more than 4 hours on 42.3 ± 40.1% of days. There was a statistically insignificant trend towards higher usage in patients who have heard of CPAP as a treatment modality, as compared to those who have not; type of prior opinion (good things / bad things / both good and bad things about CPAP) did not affect the compliance. In the multiple regression analysis, only age and AHI were positive predictors of patient's compliance with CPAP.
Conclusion: Patient's knowledge of CPAP or opinion on it prior to sleep evaluation has no impact on the CPAP compliance following the diagnosis of obstructive sleep apnea.

0544

CHRONIC INTERMITTENT HYPOXIA INDUCES COGNITIVE IMPAIRMENTS IN HUMAN APOLIPOPROTEIN E4 TRANSGENIC MICE

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Introduction: Apolipoprotein E4 (ApoE4) is recognized as genetic risk factor for Alzheimer's disease (AD). Our previous studies on ApoE-null mice showed increased cognitive impairments following chronic intermittent hypoxia (IH). While epidemiological associations have emerged between ApoE4, AD, and sleep apnea, no studies have specifically assessed both spatial and reference memory under IH conditions in transgenic mice expressing human ApoE4.
Methods: Two groups of human ApoE4 targeted replacement mice, (age 11 months) and (age 18 months) and its age matched controls, C57BL/6NTac mice were subjected to spatial learning in the Morris water maze. After acquisition of the Morris water maze task, all the mice were exposed to 15 days of IH during rest period (cycling of 5.7% or 21% oxygen every 3 min) starting from 7.00 am to 7.00 pm (light period) followed by room air (RA) until 7.00 am next day, or RA (21% oxygen throughout) in 2 identical commercially designed chambers operated under a 12-hour light-dark cycle, to assess reference memory.
Results: Deficits in spatial reference memory in ApoE4 mice subjected to chronic IH emerged when compared to both the RA- and IH-exposed control groups. In addition, ApoE4 mice showed impairments in the acquisition of spatial learning, which were more pronounced in older mice. Ki-67 immunohistochemistry following water maze, showed decreased proliferation of new cells in the dentate gyrus.
Conclusion: Chronic IH induces deficits in memory retention processes that may be due to compromise of the hippocampal circuitry. Aging further compounds the progression of memory losses, especially in ApoE4 transgenic mice. More studies are underway to understand potential mechanisms underlying the deleterious effects of IH during sleep on learning and memory and plasticity in a murine model of AD. Such studies may potentially lead to development of improved therapeutic strategies targeting AD-associated cognitive impairments.
Support (optional): HL-065270, HL-086662, and HL-083075, and the Children's Foundation Endowment for Sleep Research.

0545

OBSTRUCTIVE SLEEP APNEA SYNDROME VERSUS UPPER AIRWAY RESISTANCE SYNDROME: PREVALENCE IN THE SAO PAULO EPIDEMIOLOGIC SLEEP STUDY

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Introduction: Obstructive Sleep Apnea Syndrome (OSAS) prevalence varies, based on available population-based studies, from 1.2 to 7.5% but the Upper Airway Resistance Syndrome (UARS) prevalence was not established so far. The aim of the present study was to compare OSAS and UARS prevalence by age, gender, and nutritional status in a population based sample of the adult inhabitants of Sao Paulo city.
Methods: A population-based survey adopting a probabilistic three-stage cluster sample of the Sao Paulo city was used to represent the population according to gender, age (20-80 years), and socioeconomic classes. Questionnaires and in-lab full-night polysomnography, using nasal pressure cannula and thermistor were done. OSAS criteria used was the AASM-ICSD-2. UARS diagnosis was established according to Bao & Guilleminault (2004) criteria.
Results: From 1101 questionnaires, 1042 volunteers underwent to polysomnograpy (refusal rate=5.4%). Mean age was 42±14 yrs, 55% were women, and 60% presented BMI>25 kg/m2. Applying the generated sample weight variable, OSAS was observed in 32.9% (95%CI:29.6-36.3) and UARS in 18.75% (95%CI:16.6-21.1). OSAS prevalence was higher in male than female (40.6 vs. 26.0 %). UARS was higher in female (21.8 vs. 15.2%), mostly in normal weight women (29.2%; 95%CI:22.1-37.4). There was an increase in OSA prevalence with age, while UARS group demonstrated a decrease in prevalence in overweight/obese women but not in normal weight men.
Conclusion: OSAS was more prevalent than UARS in a sample of the adult population of Sao Paulo, mostly in men. UARS prevalence differs between genders and nutritional status.
Support (optional): AFIP, FAPESP, CNPq

0546

MODELING FROM MAGNETIC RESONANCE IMAGING: AUTOMATIC CONSTRUCTION OF A THREE-DIMENSIONAL TONGUE COMPLEX

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Introduction: Tracing the upper airway is normally a manual and complex process which restricts fast comparisons and an understanding of upper airways characteristics. Three-dimensional (3D) computer simulation of human anatomy is an increasingly useful tool in medical research. A 3D computer model of the upper airway could elucidate the interactions between the airway and soft tissues in patients with obstructive sleep apnea.
Methods: We have created a 3D tongue model from a magnetic resonance imaging (MRI) data set prior to surface smoothing and error computation. The extracted tongue complex consists of intrinsic, extrinsic (posterior part of styloglossus and palatoglossus excluded), and geniohyoid muscles as well as the submucosal glands. Multiple MRI slices in the sagittal, coronal and axial directions of the head and neck region of a young non-overweight Caucasian male were taken in the supine position with and without a mandibular advancement appliance in place. Data from each of the three slice directions were registered and merged to reconstruct a high-resolution volumetric data set. We have created a patient-specific tongue model by morphing the atlas model (manually traced) to fit the anatomy obtained from a patient's MRI scan. By selecting approximately 25 landmark points on the atlas and their corresponding points on a patient's MRI scan, a morphing algorithm could be applied to deform the atlas model into a model which describes the patient's tongue in considerable detail.
Results: Our 3D tongue extraction results from 75 planar contours; 11, 35 and 29 contours from sagittal, coronal and axial views, respectively. We confirmed a small model error by comparing some 380 manually selected landmarks from the tongue boundary to an automatic morphing algorithm. Accurate models with low to negligible error are generated when deforming the atlas model into a patient tongue with a similar shape.
Conclusion: This automatic morphing algorithm of the tongue may be added to our 3D upper airway model (www.artisynth.org) currently being developed to examine the pathogenesis and effects of treatment in patients with obstructive sleep apnea.
Support (optional): Study supported by the Vancouver Coastal Research Institute.

0547

COMPARATIVE ANALYSIS OF OXIMETRY AND SLEEPSTRIP FOR THE DIAGNOSIS OF SLEEP APNEA-HYPOPNEA SYNDROME IN THE HOME

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Introduction: Previously, we reported that SleepStrip a very useful, easy to manipulate, and low-cost tool for screening a large number of patients with OSAHS. However, the study was carried out in our sleep laboratory, and so the method may be impractical for home use. We therefore examined the practical usefulness of SleepStrip and pulse oximetry when used unsupervised in patients' homes.
Methods: This study analyzed 37 male and 13 female patients, who had undergone their first polysomnography (PSG) study in our sleep center. Patients underwent a standard PSG recording about one month after the use of the home recording devices. SleepStrip (SLP, Israel) and pulse oximetry (Pulsox-Me 300, Konica-Minolta. Co., Osaka, Japan) devices were used for recording for at least 5 hrs in the patients' homes and were then sent to our sleep center by mail. Patients were scored with the device using four levels of apnea-hypopnea severity: level 0 (AHI < 15), level 1 (15 < AHI < 25), level 2 (25 < AHI < 40), and level 3 (AHI > 30), respectively.
Results: Twenty patients (40%) were classified as apneic (AHI > 15) in the PSG study and 38 patients (76%) were classified as having AHI > 15 with SleepStrip. On the other hand, twenty-nine (58%) were classified as apneic (AHI >15) with PSG and 20 patients (40%) were classified with ODI (oxygen desaturation index) 3% > 15 using pulse oximetry. In the comparison of pulse oximetry and PSG, the sensitivity and specificity values were 69 and 100%, respectively.
Conclusion: The sensitivity of SleepStrip monitoring in comparison with the standard PSG was superior to that of the pulse oximeter. In addition, the sensitivity of data obtained in the patients' homes were comparable to those generated in our sleep center, 89.7 and 100%, respectively. These results show that SleepStrip is a useful tool for screening a large number of patients with OSAHS.

0548

FACTORS PREDICTING CARDIAC ARRHYTHMIAS IN PATIENTS STUDIED BY OVERNIGHT POLYSOMNOGRAPHY

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Introduction: Cardiac arrhythmias (CA) have been shown to occur in up to 50% of patients with obstructive sleep apnea (OSA). Few studies investigated Age, BMI, AHI, and oxygen desaturation as predictors of CA with small sample sizes. Our objective was to investigate the impact of these factors in a large number of patients studied by Polysomnography (PSG).
Methods: We retrospectively studied 777 most recent PSGs done at the University of Mississippi Medical Center. Logistic regression analysis was performed to predict factors affecting CA using the parameters of BMI (< 25 vs ≥ 25 kg/m2), minimum oxygen saturation (<70%, 70-89.9%, ≥90%), age (0-35, 36-65, >65) and %REM Sleep(<20% vs ≥20%). OSA was defined as AHI ≥5. Odds ratio (OR) and 95% Confidence Intervals (CI) were calculated.
Results: 54.31% of patients had OSA. Prevalence of arrhythmias were 52% among persons with OSA versus 40% who had no OSA. Those with OSA were 1.6 times (OR=1.9, 95% CI 1.205-2.133) more likely to have CA compared to patients without OSA, but AHI became statistically insignificant in predicting CA after adjusting for other variables. Minimum oxygen saturation during sleep (MinSPO2) and age were better predictors. CA were more likley in patients with MinSPO2<90% (OR=1.64, 95%, CI 1.14-2.36) compared to MinSPO2>90%. Increasing age also increased the odds of having CA independent of AHI comparing the age >65 group (OR=4.47, 95% CI 2.24-8.91) and age 35-65 group(OR=1.62,95% CI 1.18-2.24) to the age <35 group. BMI and %REM sleep were not statistically significant in predicting CA.
Conclusion: The odds of having cardiac arrhythmia is higher in patients with OSA. But rather than AHI, increasing age and degree of oxygen desaturation increase the odds of arrhythmia, possibly reflecting the underlying pathophysiologic process.

0549

POSITIONAL THERAPY FOR THE REDUCTION OF OBSTRUCTIVE SLEEP APNEA

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Introduction: The aim of this study was to assess the efficacy of positional therapy using a recently developed vest type device in positional obstructive sleep apnea (OSA).
Methods: 14 participants with mild to moderate positional OSA were included. To evaluate the efficacy of the vest type device, changes of OSA between baseline and experimental polysomnography were assessed. The authors also estimated adverse event rate and subject's satisfaction.
Results: The AHI was lower in the experimental examination 9.3 ± 8.3 versus 22.8 ± 9.3 ($p<0.001$). The improvement of AHI was about 55% when using the vest type device. Participants' satisfaction after using the vest type device was acceptable level and no adverse effects were reported.
Conclusion: Positional therapy using the vest type device appears to be a valuable treatment for mild to moderate positional OSA patients.

0550

GENDER DIFFERENCES IN MOOD DISTURBANCES IN PATIENTS WITH OBSTRUCTIVE SLEEP APNEA

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Introduction: Mood disturbances have been commonly reported in patients with obstructive sleep apnea (OSA). Previous studies examining gender differences in OSA clinical presentation reported that women had greater mood disturbances, especially depressive symptoms, than men. It remains unclear, however, whether these results arise from gender differences in underlying psychiatric comorbidities or are an effect of OSA. This study examined the effect of gender on mood disturbances in patients with OSA controlling for psychiatric comorbidities.
Methods: Pre-treatment data from 134 men and 97 women in a clinical trial of CPAP treatment efficacy in milder OSA (apnea hypopnea index, AHI 5-30) were analyzed. Mood disturbances were evaluated by the Profile of Mood States. Analysis of covariance (ANCOVA) was used to examine the effect of gender on mood states, adjusting for other pertinent demographic and clinical factors as covariates.
Results: After adjusting for age, body mass index, AHI, and psychiatric comorbidity (any current diagnosed psychiatric conditions), higher levels of Depression-Dejection ($p=.003$), Vigor-Activity ($p=.023$), and Anger-Hostility ($p=.013$) were observed in men compared to women. Depression was the primary known psychiatric condition, occurring in 15.7% of men and 42.3% of women ($p<.001$). Male patients with diagnosed depression had Depression-Dejection mood scores 7.2-points higher than women with depression ($p=.026$) and 7.8-points higher than men without diagnosed depression ($p=.013$). In contrast, no significant difference in the Depression-Dejection mood score was observed between women with and without diagnosed depression ($p=.396$).
Conclusion: The findings emphasize the influence of comorbid psychiatric conditions in mood disturbances in male patients with OSA. Underlying psychiatric comorbidities should be considered when evaluating mood in this population. The mechanism producing a differential impact of psychiatric comorbidities on mood disturbances in men and women with OSA remains unclear. Thus, the relationships between depression and OSA need further exploration.
Support (optional): National Heart, Lung, and Blood Institute American Nurses Foundation ENRS/Council for Advancement of Nursing Science

0551

THE ROLE OF ANATOMICAL ALTERATIONS OF THE UPPER AIRWAYS OF PATIENTS WITH OBSTRUCTIVE SLEEP APNEA SYNDROME WHO ADHERED TO ORAL APPLIANCE TREATMENT

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Introduction: The aim of this study was to correlate the efficacy and the compliance of OSAS treatment with mandible advancement appliances (MAA) with upper airway (UA) findings and to compare the UA findings prior and subsequent to MAA use.
Methods: 28 patients with mild and moderate OSAS were enrolled. All patients were submitted to anamnese, UA and facial skeletal examination and polysomnography, before and after 120 days of MAA use. The success criteria was 50% decrease of the apnea-hypopnea index (AHI) and the compliance criteria was MAA use over 70% of the nights
Results: The average age was 48,8 ± 11,3 years. The clinical and polysomnographic findings that showed statistical differences before and after 120 days of MAA use were: decrease of Epworth somnolence scale score (ESS) ($p=0.02$), decrease of AHI ($p<0.01$), decrease of arousals index ($p<0.01$) and decrease of oxihemoglobin desaturation time above 90% ($p=0.01$). As for compliance, the ESS was higher prior to treatment and within the good compliance group ($p=0.04$). Sleep efficiency was higher in the same group after the treatment ($p=0.02$). The UA alterations were correlated with the success or failure of the treatment, and the only positive correlation was the absence of anatomic nasal alterations and the success group ($p=0.04$), which was not observed for compliance. The UA findings, before and after MAA use, showed improvement of pharyngeal alterations in only 4 patients
Conclusion: The UA alterations did not interfere in MAA compliance in the group that was observed. The MAA efficacy was statistically poor in patients with anatomical nasal alterations, but not in other UA alterations. The UA exam did not present significant alterations after MAA use
Support (optional): AFIP,FAPESP,CNPQ

0552

IMPACT OF SPLIT-NIGHT VERSUS TRADITIONAL SLEEP STUDIES ON CPAP COMPLIANCE

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Introduction: Split-night polysomnography can establish a diagnosis of obstructive sleep apnea (OSA) and titrate continuous positive airway pressure (CPAP) during a single study in patients with sleep-disordered breathing. However less time is devoted to CPAP titration, which may result in incomplete ablation of events. It is unclear what impact split-night studies have on short-term CPAP compliance. We sought to determine if split-night polysomnography could be used in OSA without diminishing short-term compliance.
Methods: Consecutive patients diagnosed with OSA were assessed for short-term CPAP compliance after the initial 4-6 weeks of treatment. The average hours/night and percentage of nights of CPAP use were

compared between patients who underwent traditional and split-night studies. Good compliance was defined as >4 hours/night on more than 70% of nights.
Results: We included 400 consecutive patients (78% male, mean age 47±8 years). 267 patients underwent split-night and 133 patients had traditional studies. Type of study did not impact compliance. Good compliance was observed in 56.9% v 55.6% (split v traditional, p=0.81). Absolute use by quartiles was also similiar (70% had split-night studies in top quartile of use, 66% in bottom quartile of use; p=0.55). Mean number of days between diagnosis and titration in the traditional group was 80.5 days.
Conclusion: Split-night polysomnography does not adversely impact short-term compliance in patients with obstructive sleep apnea, and offers the benefit of reduced number of studies needed and the inherent delay in initiating CPAP therapy with traditional studies.

0553

POLYSOMNOGRAPHIC VALIDATION OF THE MOUTH LEAK SYNDROME

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Introduction: We have observed that some patients with a poor response to nasal continuous positive airway pressure (nCPAP) for obstructive sleep apnea syndrome (OSAS) have developed a mouth leak syndrome (MLS) with a sensation of air rushing out the mouth, nasal congestion and premature removal of the nCPAP during the night. We propose that this is a reaction to nCPAP mouth leak. We sought to test this hypothesis with polysomnography including continuous monitoring of mouth leak (PSGML) in patients treated with nCPAP.
Methods: Consecutive new patients with OSAS (n = 40; age 52.5, SD 12.0) were studied with validated prospective questionnaires and a download every week of fixed pressure nCPAP therapy (mean pressure 9.1 SD 2.0; REMStar, Respironics, USA) which was adjusted to extinguish any residual sleep apnea. After 4 weeks, patients were monitored with PSGML to quantify the time spent in mouth leaks and any sleep interruptions associated with mouth leaks.
Results: Of 40 patients, 16 met published clinical criteria for the MLS. These patients demonstrated less satisfaction and less compliance with nCPAP. PSGML demonstrated more mouth leak with a mean (SD) 46.0 (19.0) events per hour compared to those without MLS 31.9 (11.1; $p < 0.01$) and with more mouth leak as a fraction of sleep time with 55 (17)% compared with 32 (18)% ($p < 0.01$). Mouth leaks were also more often terminated with micro-arousals with 30 (22)% vs. 14 (11)%, hence increasing sleep disruption.
Conclusion: Patients with OSAS treated with nCPAP who develop MLS demonstrate more objective mouth leaks as well as more sleep disruption due to these leaks.
Support (optional): OSR Medical & the Mount Sinai Hospital Research Foundation

0554

THE EFFECTS OF CPAP TREATMENT ON DAYTIME FUNCTION AND QUALITY OF LIFE: A DOUBLE-BLIND, RANDOMIZATION, PLACEBO-CONTROLLED TRIAL

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Introduction: Obstructive sleep apnea (OSA) is reported to be associated with impaired daytime function, depression and quality of life (QoL). The CPAP treatment has been reported to improve daytime function and QoL in OSA patients with excessive daytime sleepiness (EDS). However, the effect of CPAP treatment in patients with high apnea-hypopnea index (AHI) but minimal symptom was unclear. Therefore, this study aimed to test if the CPAP could improve the daytime function and QoL in patients with OSA irrespective of sleepiness.
Methods: Participants: From 2008, Jan. 1st to 2008, Nov. 31st, we recruited consecutive patients of 109 severe OSA (AHI≥30/hr) as eligible patients. 58 patients were excluded and totally 51 patients were enrolled. Enrolled patients were randomized to 12-week therapeutic or subtherapeutic CPAP. Patients remained blinded whether they were receiving therapeutic or subtherapeutic CPAP, as did the investigator. Protocol: Recruited subjects were evaluated on the day of baseline measurement and in the end of 12-week CPAP treatment. Data collected included body composition, exercise amount (IPAQ), daytime sleepiness (ESS, MSLT), hospital anxiety depression score (HADS), and SF-36. Changes of daytime functions were assessed with changes of ESS and sleep latency before and after CPAP treatment. The change of QoL was assessed with changes of HADS and SF-36. The CPAP effect was measured by comparing the changes in therapeutic group with those in the subtherapeutic group. EDS was defined as a global clinical impression by the sleep clinician of excessive tendency to fall asleep. Neither ESS nor MSLT was used to define the presence of EDS.
Results: Among 51 enrolled patients, 11 withdrew from the study and 40 patients finished the study. Twenty-two in 40 received therapeutic CPAP and 18 received subtherapeutic CPAP. Patients receiving the therapeutic and subtherapeutic CPAP were matched in age, sex, body composition, and CPAP compliance. In patients with EDS (ESS 15.5 ±3.6), 12-week therapeutic CPAP had greater impact on anxiety score (p=0.02), body pain (p=0.005), and sleep latency (p=0.04) than subtherapeutic CPAP. In patients without EDS (ESS 6.4 ±3.4), therapeutic CPAP worked the same as the subtherapeutic CPAP.
Conclusion: CPAP affects OSA patients with and without EDS differently. A 12-week CPAP does not appear to improve daytime function and QoL in patients without EDS.
Support (optional): NCT00491088

0555

ACUTE INTERMITTENT HYPOXIA INDUCES HYPOTHERMIA AND SLEEP PROPENSITY IN HUMAN APOLIPOPROTEIN E4 TRANSGENIC MICE

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Introduction: Alzheimer's disease (AD) is accompanied by significant disruption in sleep/wake patterns. The presence of sleep-disordered breathing, i.e., cyclic intermittent hypoxia (IH) in AD patients may ac-

celerate neurodegenerative processes. A significant linkage between apolipoprotein E4 (ApoE4), AD, and sleep apnea has emerged; however, no studies have specifically assessed sleep phenotype, core body temperature (Tb), and gross motor activity (Ag) regulation under acute IH conditions in transgenic mice expressing human ApoE4.
Methods: ApoE4-targeted replacement mice and age matched C57BL/6NTac mice were chronically implanted with a telemetric transponder to measure EEG, EMG, Tb and Ag at 6 months. Following baseline recordings of 24 hours (7am -7am), the recordings were continued for another 24 h during which the animals were exposed to acute IH (cycling 5.7% or 21% oxygen every 3 min) for 6 hours (1pm-7pm) in 2 identical commercially available chambers operated under a 12-hour light-dark cycle.
Results: ApoE4 mice showed an increase in wake and decrease in SWS and REM sleep during IH exposure. However, during dark hours when mice were in room air, there was a marked SWS and REM rebound in ApoE4 mice when compared to controls. IH also elicited marked hypothermia and drastic decreases in gross motor activity. Body temperature returned to baseline immediately after IH exposures during the recovery period; however, gross motor activity remained reduced compared to C57BL/NTac mice.
Conclusion: Using a combination of sleep-wake, Tb, and Ag recordings, the preliminary results support the hypothesis that acute IH imposes global temporal effects on multiple physiological functions, and suggest unique vulnerability among transgenic mice aiming to replicate human neurodegenerative disorders.
Support (optional): NIH grants HL-065270 and HL-086662, the Children's Foundation Endowment for Sleep Research and University of Louisville grant E0606 (RV).

0556

PREVALENCE OF UPPER AIRWAY RESISTANCE SYNDROME (UARS): A POPULATION-BASED SURVEY

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Introduction: Upper Airway Resistance Syndrome (UARS) is characterized by increased respiratory effort during sleep associated with excessive diurnal somnolence (EDS) or fatigue in patients who do not present polysomnografic (PSG) finding suggestive of Obstructive Sleep Apnea (OSA). Until now there are no studies evaluating UARS prevalence in general population. The aim of the present study was to estimate the prevalence of UARS by age, gender, and nutritional status in a population based sample of the adult inhabitants of the Sao Paulo city.
Methods: A population-based survey adopting a three-stage randomized cluster sampling of Sao Paulo city was used to represent the population according to gender, age (20-80 years), and social class. Questionnaires were applied and all volunteers were invited to perform in lab full night PSG using nasal cannula and thermistor. UARS diagnosis was established according to the Bao & Guilleminault (2004) criteria: AHI≤5; nadir of SpO2≥92%, presence of nasal cannula flow limitation episodes and one of the following symptoms: fatigue, EDS, sleep fragmentation, insomnia, pseudo-fibromialgia, parasomnias, headache, parasympathetic manifestations.
Results: A total of 1101 questionnaires were applied and 1042 volunteers underwent to PSG (refusal rate=5.4%). Mean age was 42±14 yrs, 55% were women, and 60% presented BMI>25 kg/m2. The prevalence of UARS for total population was 18.75% Prevalence was higher in female than male (21.87 vs 15.19%) and trends to decrease with aging (20-29 yrs: 31.04%; 30-39 yrs: 24.62%; 40-49 yrs: 14.98%; 50-59 yrs: 8.094%; 60-69 yrs: 5.48%; 70-80 yrs: 0%) independently of BMI (adjusted to 27.6 Kg/m2).
Conclusion: UARS prevalence estimated in a sample of the adult of the Sao Paulo city was high (19%) and predominantly in female and younger subjects.
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0557

MANAGEMENT OF OBSTRUCTIVE SLEEP APNEA: PORTABLE MONITORING FOR DIAGNOSIS FOLLOWED BY TREATMENT WITH AUTO-ADJUSTING POSITIVE AIRWAY PRESSURE

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Introduction: In populations with a high prevalence of obstructive sleep apnea (OSA), the use of portable monitoring (PM) for diagnosis will frequently require a subsequent positive airway pressure titration by polysomnography (PSG) or unattended auto-titration to select an effective level of CPAP for treatment. An alternative to titration is treatment with an auto-adjusting positive airway pressure (APAP) device. We hypothesized that PM followed by treatment with APAP would be an effective alternative to diagnosis and titration with PSG followed by CPAP treatment.
Methods: We retrospectively analyzed all positive airway pressure (PAP) naive patients who had a diagnostic study followed by PAP treatment from January 2006 to December 2007 at the Malcom Randall VAMC. We included patients with an AHI of 5/hour or greater and excluded patients treated with BPAP or PAP + oxygen. Patients who never returned for follow-up or in whom objective adherence information was never collected were also excluded. A clinical pathway consisting of PSG for diagnosis and titration followed by CPAP treatment was compared to one using PM followed by APAP treatment. The number of patients in the PSG pathway was 135 and in the PM APAP pathway was 317.
Results: Demographics: The mean ± SEM of the age (PSG 59.2 ± 0.9 vs APAP 59.1 ± 0.7 years), BMI (PSG 34.7 ± 0.6 vs APAP 34.7 ± 0.5 kg/m2), and Epworth Sleepiness Scale (ESS) pretreatment (PSG 14.5 ± 0.5 vs APAP 13.9 ± 0.3) did not differ. Diagnostic information: The AHI by PSG 55.3 ± 2.6 events/hr TST (total sleep time) and 36.1 ± 2.1 events/hr TRT (total recording time) was higher than the AHI by PM 24.3 ± 1.0 events/hr TRT ($P < 0.01$). The lowest SaO2 (PSG 80.7 ± 1.0 vs PM 77.2 ± 0.9%) did not differ significantly. Treatment: The CPAP pressure in the PSG group (12.7 ± 0.3) cm H2O was higher than the 90% pressure in the APAP group (11.0 ± 0.2 cm H2O)($P <0.05$). Adherence: The average use (all days) was PSG 4.1 ± 0.2 vs APAP 4.5 ± 0.2 hours/night (P=NS). The percentage nights with use > 4 hours was PSG 51.2 ± 3.1 vs APAP 50.9 ± 2.0 % (P=NS). Outcomes: The change in the ESS (PSG - 3.7 ± 0.5 vs APAP - 3.6 ± 0.4) and residual AHI by PAP device (PSG 7.0 ± 0.7 vs APAP 6.2 ± 0.3 events/hour) did not differ.
Conclusion: A clinical pathway using PM and APAP treatment resulted in equivalent adherence and improvement in subjective sleepiness compared to one using PSG.

0558

EFFICACY OF NOCTURNAL CONTINUOUS POSITIVE AIRWAY PRESSURE (CPAP) IN IMPROVING QUALITY OF LIFE MEASURES IN PATIENTS WITH OBSTRUCTIVE SLEEP APNEA

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Introduction: In Obstructive Sleep Apnea (OSA) one standard of treatment involves nocturnal application of CPAP (Continuous Positive Airway Pressure). OSA patients have CPAP applied during a sleep study where the optimum setting is identified by titration. Significant reduction or elimination of apneic episodes is usually seen. To assess functional outcomes of this intervention, a questionnaire specific to lifestyle and daily functioning relative to sleepiness is used to assess quality of life (QOL). We hypothesize that use of CPAP at a properly determined level allows reduction in OSA symptoms, allowing increased sleep qual-

ity, improving patients' lifestyle and quality of life. Via this study, we seek to validate efficacy of CPAP intervention in OSA.
Methods: Subjects complete the Functional Outcomes of Sleep Questionnaire (FOSQ) twice, a pre-treatment baseline, and again after six months of CPAP. Subjects are adults referred with demonstrated OSA. Functionality is assessed in five discrete behavioral subscales, which in combination provide an overall score. A series of metrics are calculated longitudinally as pre-to-post differences in subscale and overall scores, analyzed by paired t-test to estimate strength of the change in score. Mean, standard deviation, t-score, and P-value are calculated. The original study demonstrated a mean score of 13.61±4.25 for OSA-positive patients, and 17.92±1.73 for normals.
Results: A large pool of 2751 baseline scores, and 455 who completed the follow-up, were analyzed separately. The data are stated as mean ± 1 Standard Deviation (SD). Overall score in the 2751 baselines (untreated OSA patients) was 14.93±3.35. In the group of 455 treated patients, baselines were 14.63±3.23. This close match in pre-treatment score between the untreated and treated groups suggests that the smaller sample fairly represents the larger OSA population. In the study group, mean difference was 2.49±3.12, t-score (T453)=17.00 (P<<0.0000001), indicating a very high degree of statistical significance. The mean score pre-treatment was 14.63±3.24 and post-treatment 17.12±3.01, similar to the author's original findings, where our post-treatment values approximate those of the normal group.
Conclusion: The highly significant increase in overall score and subscales affirms increased QOL and daily functioning. From this we infer the efficacy of properly determined CPAP therapy in mitigating symptoms of OSA and increasing sleep quality.

0559

CHRONIC INTERMITTENT HYPOXIA ACCELERATES PROGRESSION OF ALZHEIMER'S LIKE DISEASE IN HUMAN APOLIPOPROTEIN E4 TRANSGENIC MICE

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Introduction: Significant disruption in sleep/wake patterns is observed in patients with Alzheimer disease (AD). In AD patients, the presence of sleep apnea, i.e., cyclic intermittent hypoxia (IH), may accelerate the neurodegenerative processes. While epidemiological associations have emerged between apolipoprotein E4, AD, and sleep apnea, we aimed to assess potential interrelationships between sleep phenotype, body temperature (Tb), gross motor activity (Ag), beta-amyloid and tau deposition, and spatial and reference memory under chronic IH conditions in transgenic mice expressing human apolipoprotein E4 (hApoE4).
Methods: hApoE4 and C57BL/6NTac mice were chronically implanted at age 7 months with a telemetric transponder to measure EEG, EMG, Tb and Ag. After 24h baseline recordings, they were subjected to either IH (cycling of 5.7% or 21% oxygen every 3 min) starting from 7.00 am to 7.00 pm (light period) followed by room air (RA) until 7.00 am next day, or RA (21% oxygen throughout) in identical chambers operated under a 12-hour light-dark cycle. Sleep-wakefulness, Tb, and Ag were recorded every 15 days from ages 7 to 9.5 months. The mice were also evaluated for spatial and reference memory in the Morris water maze. Hippocampal, basal forebrain and cortical sections were labeled for beta- amyloid and tau proteins.
Results: There were marked increases in SWS, number of sleep episodes, and decreases in EEG delta power during SWS during the light period following IH exposures in hApoE4 mice, indicating that IH modulates sleep homeostatic drive. There was a decrease in Tb and Ag in hApoE4 mice during IH exposures. While Tb returned to normal values, Ag was markedly higher during dark period following IH. Modified sleep latency tests showed that hApoE4 mice exposed to IH had shorter sleep latencies compared to RA. hApoE4 mice showed impairments in the acquisition of spatial learning and deficits in memory retention processes. IH was also associated with marked increases in beta-amyloid and tau protein deposits in hApoE4 mice.
Conclusion: This study supports the hypothesis that chronic IH exposures during sleep impose global temporal effects on multiple physiological functions, and reveal unique vulnerability to sleep apnea in a transgenic mouse model of AD. Such studies may potentially lead to development of improved therapeutic strategies targeting AD-associated pathologies.
Support (optional): NIH grant HL-086662, the Children's Foundation for Sleep and Neurobiology Research and University of Louisville grant E0581 (RV)

0560

SNORING AND OBSTRUCTIVE SLEEP APNEA- HYPOPNEA SYNDROME IN GUANGXI,CHINA PREVALENCE, PROFILES AND POTENTIAL RISK FACTORS

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Introduction: China has many Nationalities. In Guangxi Zhuang Autonomous Region, most of the residents are Zhuang people and Han people. The purpose of this study was to investigate the prevalence, profiles and potential risk factors for snoring and OSAHS in Guangxi, China, Therefore to measure the association between OSAHS and National status.
Methods: An urban and a rural population-based cluster samples were randomly selected in each of eight counties/cities. All residents aged 14 years or older in the selected clusters were interviewed with a standardized questionnaire.
Results: Among 12742 sampling subjects, 10819 participants completed the questionnaire (response rate = 84.9%). The overall prevalence of OSAHS was 4.1% (men 5.7% ; women 2.4%), and the overall habitual snoring was 11.5% (men 17.1% ; women 5.6 %). Zhuang subjects 6313, the overall prevalence of OSAHS was 3.2%; Han 3513, the overall prevalence of OSAHS was 6.0% (P=0.000), Others 993, the overall prevalence of OSAHS was 3.3%. Using univariate analysis, the prevalence of OSAHS were significantly higher in following persons: a) urban residents, b) the elders, c) smokers, d) drinkers, e) those with higher body mass index (BMI), f) those who have received more school education, g) those with nasal problems, h) those whose parent is Han, i) those who usually sleep with prone prosition. However, when analysed using Multiple Logistic Regression Analysis, only urban residents, age, smoking status, drinking status and BMI were risk factor for OSAHS.
Conclusion: OSAHS is prevalent in individuals aged 14 years or older in Guangxi, China. There were significantly difference between Zhang and Han.
Support (optional): Supported by Natural Science Foundation of Guangxi, China.

0561

ESZOPICLONE IMPROVES SHORT AND INTERMEDIATE TERM CONTINUOUS POSITIVE AIRWAY PRESSURE COMPLIANCE

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Introduction: Continuous positive airway pressure (CPAP) is recommended as the first-line therapy for most patients with obstructive sleep

apnea (OSA). Unfortunately the effectiveness of CPAP is limited by intolerance and poor compliance. Numerous interventions have had modest to no improvement on subsequent compliance. Long-term compliance is often predicted within the first few weeks of therapy. We hypothesized that a short course of non-benzodiazepine sedative hypnotics would facilitate the initial tolerance of CPAP and subsequently improve long-term use.

Methods: Prospective, double-blind, randomized, placebo-controlled trial. Consecutive adult patients newly diagnosed with OSA were randomized to 14 days of Eszopiclone 3mg or placebo starting the first day of CPAP therapy. Compliance was objectively measured each week for 24 weeks. The primary endpoint was the effect of Eszopiclone on CPAP compliance.

Results: 136 patients were enrolled (70 Eszopiclone, 66 placebo). Mean age was 45.6 ± 9.0 years, mean BMI 30.4 ± 5.3 kg/m. Baseline ESS was 12.5 ± 5.2. The majority of subjects had severe OSA, with a mean AHI of 36.1 ± 27.7. There were no differences between groups at baseline. Eszopiclone resulted in greater use of CPAP throughout the study period. Specifically, CPAP was used on more nights (79.8 ± 3.1 vs 63.6 ± 5.7%, $p<0.001$) and for more hours per night (5.0 ± 0.2 vs 4.1 ± 0.2 hours, $p<0.01$). There was a sustained improvement in compliance among those receiving Eszopiclone. During the 24th week, CPAP was used on more nights (75.3% vs. 46.5%, p=0.003) and for longer durations (5.0 vs 3.7 hours/night,p=0.08) in those receiving Eszopiclone. Significantly fewer subjects receiving Eszopiclone discontinued CPAP during the study period (25.8% vs 11.4%, p=0.03).

Conclusion: A short course of Eszopiclone facilitated initial tolerance of CPAP therapy and resulted in significant improvements in short and intermediate-term compliance.

0562

A PROSPECTIVE POLYSOMNOGRAPHIC STUDY ON THE NATURAL COURSE OF COMPLEX SLEEP APNEA IN 675 PATIENTS TREATED FOR OBSTRUCTIVE SLEEP APNEA

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Introduction: Patients (pts) with obstructive sleep apnea who have ≥ 5 central apneas per hour of sleep (AI) under otherwise sufficient treatment of obstructive sleep apnea by nCPAP (obstructive and mixed AI < 5) are designated to suffer from complex sleep apnea (compSA). It is uncertain which pts develop compSA and how stable over time compSA is. We therefore initiated a prospective study to identify pts with compSA and to observe the natural course of compSA over a period of 3 months.

Methods: Pts with full night polysomnographic diagnosis of obstructive sleep apnea were reevaluated by full night polysomnography (PSG) in the first night with stable nCPAP treatment (after one night nCPAP titration) and after three months nCPAP treatment.

Results: 82 out of 675 pts (12.2 %) developed compSA in the first night with stable nCPAP treatment. These pts were older (59.8 vs. 55.5 years, p = .001) and had a higher Apnea-Hypopnea Index (AHI; 37.5 vs. 31.4. p = .003) in the diagnostic PSG than those who did not develop compSA. The higher AHI was solely due to more central and mixed apneas (both p < .05). Sleep variables in the diagnostic PSG did not differ for pts with and without compSA. In the first night with stable nCPAP treatment, pts with compSA exhibited lower sleep efficiency, more wake after sleep onset and more sleep stage nREM1 (p < .05 respectively). 76 % of pts with compSA and 74 % of pts without compSA showed up for the 3 months follow-up. 13 % of each group did not continue nCPAP treatment. Out of the 54 pts with initial compSA available for follow-up, 40 (74 %) did not have compSA in the follow-up PSG. 16 of the 382 pts (4.2 %) without initial compSA available for follow-up had compSA in the follow-up PSG. Despite the fact that the 30 pts with compSA at follow up are largely different from those with initial compSA, similar differences in age and sleep structure were present at follow up and initial evaluation.

Conclusion: The finding that most pts with initial compSA do not have compSA after 3 months means that compSA is not a stable disorder. While compSA is widely believed to impair sleep quality, we offer an alternate interpretation: compSA is a phenomenon appearing in older pts with a large proportion of central apneas before treatment in nights with spontaneous low sleep quality with many sleep wake transitions which promote central apneas and hypopneas. If pts with compSA had constantly impaired sleep, they should be more sleepy - but they are not (ESS 7.3 vs 6.5 at follow up, p = .3).

0563

EXAMINATION OF QUALITY OF SLEEP BETWEEN SMOKERS AND NON-SMOKERS WITH OBSTRUCTIVE SLEEP APNEA

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Introduction: A study of the effect of smoking on sleep of healthy people reported a lowered quality of sleep due to nicotine withdrawal symptom. The present study examined the effect of smoking on Obstructive Sleep Apnea (OSA).

Methods: The subjects were 489 males who had underwent PSG for OSA diagnosis from January 1st, 2007 to October 31st, 2008. The total subjects had an average age 50.2±15.6 years, and average AHI 30.4±22.8. The subjects were classified into 3 groups (smoker: n=134, age 45.4±13.0 years, AHI 34.3±24.8, non-smoker: n=226, age 49.9±17.2 years, AHI 27.8±22.2, and ex-smoker: n=129, age 55.4±13.2 years, AHI 31.0±21.2, groups) and their PSG was analyzed. Moreover, AHI was classified into 4 groups (AHI <5, 5≤ AHI<20, 20≤AHI<40, and 40 ≤ AHI groups) and analyzed.

Results: There were no differences of average AHI, Slow Wave Sleep, and Sleep latency among the smoker, ex-smoker, and non-smoker groups. In the AHI<5 group, the Slow Wave Sleep (%) tended to be lower in the smoker group (9.5 ± 4.5) than in the non-smoker group (14.9 ± 18.7). The Sleep latency tended to be longer in the smoker group (17.7 ± 22.6) than in the non-smoker group (56.2 ± 84.6).

Conclusion: Lowered Slow Wave Sleep (%) and prolonged Sleep latency in the smoker groups with AHI <5 may be an effect of smoking. Irrespective of smoking history, there was no difference among the groups with 5 ≤ AHI in the evaluation of Sleep architecture. This suggests that Sleep disturbance by OSA covers up the effect of smoking. In the case that Slow Wave Sleep is not obtained or excessive daytime sleepiness is not improved after the beginning of CPAP treatment, a the effect of smoking is suggested and a smoking cessation program will be important along with CPAP treatment.

0564

CPAP TREATMENT VS. CONSERVATIVE TREATMENT IN MILD OBSTRUCTIVE SLEEP APNEA: IMPLICATIONS ON CARDIOVASCULAR MORBIDITY

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Introduction: Obstructive sleep apnea OSA) is associated with significant cardiovascular morbidity and increase in overall mortality. The apnea-hypopnea index (AHI), defines the disease severity (5-4.9 mild, 15-29.9 moderate, > 30 severe). Continuous positive airway pressure (CPAP) is the treatment of choice for moderate to severe OSA resulting in improved daytime functioning and decreased cardiovascular morbidity. No studies have compared the cardiovascular outcomes (here, mean

blood pressure "mbp") between CPAP and conservative therapy in mild OSA.
Methods: Retrospective cohort study of subjects with mild OSA diagnosed between 2004-2006. Subjects > 18 year and < 65 years with a diagnosis of mild OSA by PSG were included; those with a h/o hypertension (>130/90mmHg), angina, stroke, cigarette smoking, alcohol or illicit drugs abuse were excluded. Intervention: CPAP; outcome: mbp two years after the diagnosis.
Results: A total of 255 subjects (CPAP 93, no-CPAP 162) were followed up for a mean duration of 2.8 years. Unmatched for covariates (age, sex, BMI, neck circumference, AHI, arousal index and family h/o cardiovascular problems), subjects with mild sleep apnea on CPAP treatment had a 1.97 points drop while no-CPAP treatment resulted in a 9.61 points increase in mbp ($p<0.0001$). After propensity score matching for covariates, CPAP showed a mean difference of -11.97 (95% CI: -14.03,-9.92, $p<0.0001$). Stratification of propensity scores and quintile analysis revealed a similar result although the net treatment effect was smaller - 3.83(95% CI: -1.92,-5.74). Sensitivity analysis: 2.646.
Conclusion: This study shows worsening of mbp in subjects with mild sleep apnea not getting CPAP treatment. CPAP treatment effectively stabilized or decreased the mbp over a two year period. Further research with large sample and longer follow-up is recommended to determine if mild OSA is also associated with other cardiovascular and cerebrovascular complications and to determine the effectiveness of CPAP in alleviating these complications.

0565

OBSTRUCTIVE SLEEP APNEA IN NON-OBESE PATIENTS: AGE, GENDER AND SEVERITY

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Introduction: Obesity is considered as the most important risk factor for Obstructive Sleep Apnea (OSA). However OSA is frequent syndrome in non-obese patients also: OSA was reported in 28% non-obese patients (based on PSG conducted to evaluate OSA). Our study goal is to determine probability of OSA in non-obese patients based on standard PSG which was conducted primarily due to excessive daytime sleepiness.
Methods: We reviewed 28583 standard PSGs (18 years and older) acquired from November 2004 through November 2008 in 18 sleep centers (SleepTech network). Patients with BMI between 18.5 and 27 were considered as non-obese and patients with apnea-hypopnea index (AHI)>5 were defined as OSA positive.
Results: PSG was conducted in 5426 (57% male, 43% female) non-obese patients and 23157 (61% male, 39% female) overweight patients. OSA was revealed in 2906 non-obese patients (54%), most patients were middle age - 57%. Equal number of patients had mild or moderate/severe OSA: 1465 (50.4%) and 1084 (49.6%) respectively. Male prevalence as well as neck size (NS) were significantly higher in group with moderate/severe OSA ($p<0.005$). AHI<5 was revealed in 2520 (46%) non-obese patients (42% male and 58% female). No significant differences were observed by age, Epworth Sleepiness Scale and NS in comparison with OSA positive group.
Conclusion: Our results demonstrate that more then half (54%) non-obese patients are OSA positive out of 19% non-obese patients with conducted PSG. These results are higher in comparisons with previously reported data based on smaller group of patients. Our results also confirmed prevalence of male, middle age patients and higher NS in OSA positive non-obese group. High prevalence of mild OSA in non-obese patients lowers possibilities using portable monitoring in this group of patients.

0566

THE IMPACT OF SLOW WAVE SLEEP (SWS) AND SLEEP FRAGMENTATION ON FATIGUE VERSUS DAYTIME SLEEPINESS IN PATIENTS WITH OBSTRUCTIVE SLEEP APNEA (OSA)

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Introduction: Fatigue and daytime sleepiness are common complaints in OSA patients. Although fatigue can be a result of many pathophysiological conditions, it has been documented that more patients report fatigue, as compared to sleepiness, in this population. The aim of this study was to determine if fatigue changes after CPAP treatment and whether or not changes in fatigue (as opposed to daytime sleepiness) can be correlated with amount of SWS and degree of sleep fragmentation. This finding could suggest management strategies of fatigue in sleep clinic patients.
Methods: This was a retrospective chart review of 60 (out of 130 charts) sleep clinic patients who were diagnosed with OSA and underwent CPAP treatment. Patients' Fatigue Scale scores, Stanford Sleepiness Scale scores, percentages of SWS, Arousal Indices (AI) and Apnea Hypapnea Indices (AHI) were extracted from the charts before and after CPAP treatment.
Results: Of the 60 patients, 40 were males (age=56 ± 14) and 20 were females (age=57 ± 12). Statistical analysis was performed for males and females separately as well as males and females together. After CPAP treatment, there was a significant ($P<0.05$) decrease in fatigue, daytime sleepiness and arousal index (sleep fragmentation). SWS percentage, however, did not increase significantly after CPAP treatment. The decrease in fatigue was moderately correlated with the decrease in arousal index only in males ($P<0.05$, $r=0.4$). No significant correlations were observed in females and when the males and females were mixed. Daytime sleepiness did not have any significant correlation with neither SWS nor sleep fragmentation before and after treatment in any of the populations.
Conclusion: Fatigue seems to be moderately associated with sleep fragmentation rather than SWS in OSA patients and this association seems to be specific to male patients.

0567

CRANIOFACIAL CHANGES AFTER TWO YEARS OF NCPAP WEAR

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Introduction: Many obstructive sleep apnea (OSA) patients use nasal continuous positive airway pressure (nCPAP) as a first line therapy where a face mask rests on the anterior maxilla during sleep. The purpose of this study was to assess in OSA patients, using standard cephalometric analyses, craniofacial changes in adult subjects after nCPAP wear.
Methods: Some 46 Japanese subjects had a baseline cephalometric radiograph taken before the commencement of nCPAP therapy and a follow-up radiograph was taken after a minimum of 2 years to evaluate possible craniofacial changes. Baseline and follow-up radiographs were analyzed and changes in craniofacial structures were assessed. The evaluated cephalometric measurements were related to face height (UFH, LFH, TFH, MP-H, PNS-P, MPSN, PgNB), interarch relationships (SNA, SNB, ANB, SNPg, GoGn, Convexity, PNS-V) and tooth position (U1L1, U1SN, U1NA, IMPA, L1NB, Overjet, Overbite).
Results: Most of the OSA patients were male (91.3 %) and the mean baseline values for age, BMI and AHI were 53.1±13.3 years, 27.1±5.7 kg/m2 and 42.3±19.5/hour. The average duration of nCPAP use was 35.1±6.4 months. After nCPAP wear, the angular cephalometric vari-

ables of SNA (1.30±1.36), ANB (0.76±1.07), SNB (0.51±0.88) and SNPg (0.65±0.87) decreased significantly (p<0.001) whereas the linear value of NAU1 (0.62±1.04 mm) increased significantly (p=0.005). However, no significant correlations between the craniofacial changes, demographic variables or the duration of nCPAP use were identified.
Conclusion: The use of a nCPAP machine more for than 2 years may change craniofacial form by reducing maxillary and mandibular prominence and the relationship of the dental arches. Since nCPAP is often used for long time periods, the long term side effects of nCPAP wear warrant further detailed analysis to quantify craniofacial changes over time.

0568

EFFICACY OF AN ORAL APPLIANCE (OA) COMPARED TO NCPAP OVER QUALITY OF LIFE AND NEUROCOGNITIVE FUNCTIONING IN OSAS PATIENTS

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Introduction: OSAS patients may present impairment of both neurocognitive functioning (NCF) and quality of life (QL). The purpose of this study was to evaluate the effect of an OA compared with that of nCPAP regarding NCF and QL parameters in OSAS patients with a randomized, double blind and placebo controlled trial.
Methods: 29 patients with moderate to severe OSAS of both genders, BMI<35Kg/m2, 20-65 y-old were included. All patients were submitted to 3 treatments: OA, OA placebo and nCPAP. The evaluation was performed throughout four periods, with one week washout between them: A (baseline), B/C (one month after OA or placebo) and D (one month after nCPAP). The following procedures were undertaken: full night polysomnography, SF-36 QL Inventory, PVT (reaction time test) and NCF tests.
Results: 24 men and 5 women were evaluated (age=47.0±8.9y, BMI=28.4±3.6Kg/m2). nCPAP was more effective than OA in improving respiratory sleep parameters as well as sleep fragmentation. SF36: compared to baseline OA improved Vitality, Mental Health, General Health State and Social Aspects (p<0.05). Compared to baseline CPAP improved Vitality and Social Aspects when compared to placebo (p<0.05). Additionally, OA improved General Health State compared to CPAP (p<0.05). PVT: Both OA (119.5±4.6) and CPAP (112.8±4.8) improved PVT scores compared to baseline (107.6±4.4) and placebo (111.6±4.4) (p<0.05). NCF: Compared to baseline OA improved Trail A (46.4±3.8 X 36.7±2.2), Trail B (106.1±9.9 X 88.6±9.2), Codes (59.2±2.9 X 64.1±2.9) and Number & Letter (4.5±0.2 X 5.0±0.2) (p<0.05). Compared to baseline CPAP improved Search Symbols (29.7±1.4 X 33.7±1.4), Trail A (46.4±3.8 X 36.6±2.1), Codes (59.2±2.9 X 66.7±3.6) and Number & Letter (4.5±0.2 X 5.2±0.2) (p<0.05). Also, compared to baseline placebo improved Search Symbols (29.7±1.4 X 32.5±1.4) and Trail A (46.4± 3.8 X 36.8±2.2) (p<0.05).
Conclusion: OA as well as nCPAP can improve quality of life and neurocognitive functioning in OSAS patients.
Support (optional): AFIP, CNPq, FAPESP/CEPID

0569

DOES ALLERGY SEASON AFFECTS POLYSOMNOGRAPHY STUDY RESULTS?

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Introduction: It has been shown that allergic rhinitis increases sleep disordered breathing (SDB). Anectodally we have observed an increase in severity of SDB events on clinical sleep studies during days with high pollen levels. We sought to study if there was a statistical increase in AHI in relation to days with high allergen counts vs low counts.
Methods: We obtained pollen count information from the American Academy of Allergy, Asthma and Immunology (AAAI). These counts were provided with permission from the National Allergy Bureau and its participating station (Baltimore pollen 2004 to 2008). We chose dates with high and low pollen counts and examined all diagnostic sleep studies done during those dates in our sleep center (2005, 2006, 2007). We extracted polysomnography data including age, gender, BMI, AHI (REM, NREM), SaO2 (baseline, average low, minimum). Continuous variables are presented as mean (standard deviation). We compared demographic and sleep characteristics of patients studied on high vs low allergen count days using Mann Whitney U tests. Our primary outcome of interest was AHI. We created bivariate linear regression models for each independent variable of interest, clustered by date of study. To determine whether the association between pollen count and AHI was due to other patient characteristics, we created a multivariable linear regression model of age, sex, BMI and pollen count (high vs low) on the AHI, clustered by date of study.
Results: Studies performed on high allergen count days (108) were compared to those on low allergen count days (90). Age, gender, BMI, SaO2 indices were were not different between groups. Overall AHI [high pollen, 39.5(35.9) vs low pollen, 28.1(26.2)] and NREM AHI [high pollen 37.9(37.0) vs low pollen 26.0(27.3)] were different (p = 0.019; 0.016) but not REM AHI. In the multivariable analysis, BMI was inversely correlated with AHI alone (increasing AHI associated with decreased BMI), but after accounting for the other factors, this relationship reversed.
Conclusion: This retrospective analysis suggests that AHI may be higher when there are high pollen levels. Additionally, multivariable analysis suggests that in this population, patients with lower BMI's may have been more significantly affected by the high pollen counts. These findings should be considered when evaluating patients in allergy season and may also have an effect on CPAP tolerance and levels required for treatment. A prospective study is needed to confirm these findings.
Support (optional): The AAAAI and the National Allergy Bureau

0570

SUCCESS RATES OF NASAL EXPIRATORY POSITIVE AIRWAY PRESSURE (NEPAP) VIA EXPIRATORY RESISTIVE LOAD FOR THE TREATMENT OF OBSTRUCTIVE SLEEP APNEA

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Introduction: Prior investigations have shown that nEPAP is efficacious at reducing AHI. Presentations of those works were limited by the sample sizes of those studies. To increase power of the calculations and to additionally present those data in the form of therapeutic success rates, data from two prior studies were pooled.
Methods: In both studies, subjects underwent monitored polysomnography with and without nEPAP (Provent™ Professional Sleep Apnea Therapy, Ventus Medical, Inc., Belmont, CA) on separate nights in random order. All sleep data were scored by a blinded reader. In the literature several different success thresholds have been reported for OSA therapies. The majority focused on changes in AHI, in either absolute or percent reduction terms, e.g. AHI<5, AHI<10, or AHI improved by at least 50% and combinations thereof.
Results: nEPAP reduced AHI in the 58 subjects from 26.6±24.8 (mean±SD) to 13.7±20.1, a 49% reduction (p<0.001). During the treatment night, 36% of subjects (21/58) met the success criteria of AHI<5, 59% (26/44) met AHI<10, and 66% (38/58) had an AHI<50% of their baseline value. Further, 72% of subjects (42/58) met either the AHI<10 OR AHI improved by at least 50% criteria, and 50% of subjects (22/44) met both the AHI<10 AND AHI improved by at least 50% criteria. There

was one reported adverse event (a headache) in these studies which was deemed "possibly related" to the device.
Conclusion: Success rates and a significant change in AHI across this group of subjects demonstrate the viability of nEPAP via expiratory resistive loading in the treatment of OSA. Success rates are comparable to those of alternative therapies such as mandibular advancement devices and surgical approaches while incurring fewer adverse events. Since the ease of trial for nEPAP is high in comparison to those alternative therapies, nEPAP could be an early consideration for the treatment of OSA.

0571

SLEEP AND BREATHING: THE PREVALENCE OF OBSTRUCTIVE SLEEP APNEA SYNDROME IN HOSPITALIZED ELDERLY PATIENTS

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Introduction: To explore the prevalence of obstructive sleep apnea syndrome (OSAS) and its characteristics and correlates in hospitalized elderly patients with cardiovascular diseases.
Methods: All of the patients who were hospitalized in department of cardiovascular from January to June in 2005 were invited to participate in the current study. A total of 317 hospitalized elderly patients were recruited into this study. All participants were assessed by portable bedside nocturnal polysomnograph and Epworth sleeping scales.
Results: Among 317 patients, 281(88.6%) met the criterion of obstructive sleep apnea(AHI≥5) and 47(14.8%) met the criteria of obstructive sleep apnea syndrome(AHI ≥5 and ESS≥9). Multiple regression analysis indicated that when the severity of OSAS (as indicated by AHI) was considered as dependent variables, it was significantly associated with minimal SaO2 and the oxygen desaturation index, while age, habitual snoring, ESS, BMI, meanSaO2 and the duration of SaO2≤ 90% did not show significant effects on the severity of OSAS.
Conclusion: High prevalence of obstructive sleep apnea syndrome (with sleepiness) was found in elderly hospitalized patients and the rate of obstructive sleep apnea would be much higher without criterion of sleepiness. Minimal SaO2 and the oxygen desaturation index were the important predicting factors of the severity of OSAS; while age, BMI, habitual snoring, sleepiness were not correlated with OSA after adjusting for Minimal SaO2 and oxygen desaturation index.

0572

EFFECTS OF CPAP ON SLEEP STRUCTURE IN 394 PATIENTS WITH OSA

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Introduction: Obstructive sleep apnea (OSA) is characterized by airflow limitations or breathing cessations during the night, thereby compromising the macro- and microstructure of sleep. Obstructive events are abolished by means of nasal continuous positive airway pressure (nCPAP) therapy. Although compromising effects of OSA on sleep structure are well known, there are only few studies with small sample sizes investigating the restoration of sleep structure in effectively treated patients using nCPAP.
Methods: We investigated in a large sample size of OSA patients the changes in sleep structure prior and with nCPAP. A diagnostic PSG and a follow-up PSG with nCPAP 3 months after initiation of therapy was performed. Sleep parameters were extracted from both PSGs.
Results: 394 patients with good compliance to therapy (> 4.5 h per night) and effective nCPAP therapy (AHI after 3 months of therapy < 10/h) were investigated (348m, 46f, age 55 ± 11.2 years, BMI 32.1 ± 5.9 kg/m^2). While Total Sleep Time showed no significant difference, sleep efficiency significantly improved (72.3 ± 14.8 % vs. 75.3 ± 13.1 %, $p < 0.001$) along with a significant decrease in nREM1 and nREM2 (15.1 ± 13.9 % vs. 9.1 ± 6.9 % for nREM1, 52.5 ± 13.3 % vs. 48.4 ± 10.9 % for nREM2, both $p < 0.001$). Slow wave sleep significantly increased (15.2 ± 9.7 % vs. 22.1 ± 9.7 %, $p < 0.001$) as did REM sleep (17.3 ± 6.8 % vs. 20.5 ± 6.1 %, $p < 0.001$).
Conclusion: We could show a significant improvement in sleep efficiency accompanied by an increase in deep sleep and REM sleep as well as a decrease in light sleep. It can be concluded that nCPAP significantly improves sleep structure. A conclusion regarding the normalization of sleep structure, however, is complicated by lacking meaningful reference values.

0573

RESPIRATORY INDUCTIVE PLETHYSMOGRAPHY DERIVED FLOW CAN BE A USEFUL CLINICAL TOOL TO DETECT PATIENTS WITH OBSTRUCTIVE SLEEP APNEA SYNDROME

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Introduction: Obstructive sleep apnea (OSA) is a common disorder characterized by recurrent episodes of a complete or partial collapse of the upper airway during sleep. The disease is traditionally diagnosed by overnight polysomnography with detection flow limitation by nasal pressure cannula. The aim of this study was to evaluate the accuracy of flow (X flow) from calibrated respiratory inductive plethysmography (RIP).
Methods: We studied 60 males and 26 females, who came to our sleep center in 2007. All the participants received an overnight polysomnography and data were graded blindly and randomly by two experienced technicians.
Results: In our study, patients with OSA were predominantly male, with higher BMI, higher percentage of snorers, and more events of oxygen desaturation and arousal. There is a good correlation of X flow and flow from nasal pressure cannula, regardless of total apnea-hypopnea events, apnea events or hypopnea events. The correlation is strong especially in severe OSA patients. The sensitivity and specificity to find OSA (AHI ≥ 5) from X flow versus standard polysomnography was 98% and 100%, respectively. Positive predictive value is 100% and negative predictive value is 97%.
Conclusion: X flow could be a good clinical tool to be used instead of flow from nasal pressure cannula in OSA patients.

0574

HYPOPLASIA OF WHITE MATTER IN NEWBORN MICE ELICITED BY MATERNAL EXPOSURE TO INTERMITTENT HYPOXIA DURING SLEEP

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Introduction: The prevalence of OSA is increased during pregnancy, with potential adverse consequences. OSA in pregnancy leads to decelerations in the rhythm of fetal heart and may lead to growth retardation. However, little is known about how oligodendrocytes in fetal central nervous system (CNS) respond to maternal occurrence of intermittent hypoxia (IH) during sleep, and what the long-term consequences may be in the offspring.
Methods: Timed pregnant mice (9.5 day-post-coitus) were exposed to either 3 days of IH (8% O2/21% O2/3 min cycle/12hrs during the light phase), or normoxia. After maternal exposures, animals were transferred to room air until sacrifice. Oligodendrocyte-specific proteins, myelin-related proteins and neurocytoskeletal components were assessed at different post-exposure days by means of immunostaining, quantitative real-time PCR, and Western blots.

Results: Olig2 expression analysis revealed a significant decline in the number of Olig2+ OPCs in e12.5 IH-exposed neural tubes. At later e14.5 in IH-exposed spinal cords, Olig2+ progenitors were distributed less evenly in both gray and white matter regions, with more Olig2+ cells in the ventricular zone, suggesting an increased proliferation of neural progenitor cells. Transcriptional levels of mbp and MAG in P6 neonatal brains and spinal cords were significantly inhibited, and were accompanied by remarkable decreases of myelinated fibers labeled with anti-MAG in the regions of corpus callosum and external capsule at P10. However, myelinated axons were restored at P30 despite thinner white matter that was associated with decreased expression of neuromicrotubule and neurofilaments.
Conclusion: These findings suggest that oligodendroglial-axonal development is vulnerable to IH insults, as occurs in OSA, and that acute maternal IH during the critical window of fetal CNS development can induce impairments in neonatal white matter including myelin and axons.
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0575

CARDIO-PULMONARY COUPLING (CPC) MEASURES CORRELATE TO STANDARD SLEEP VARIABLES IN A RANDOM CLINICAL SAMPLE OF PATIENTS SUSPECTED WITH SLEEP DISORDERED BREATHING (SDB)

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Introduction: Scoring rules of sleep variables measured in sleep medicine were recently revised. Some of these variables were reported in subjects selected from the Sleep Heart Health study in addition to cardio-pulmonary coupling (CPC) measures. This study's objective is to determine the correlation of CPC variables to standard sleep variables in a random clinical sample.
Methods: The SleepTech database was searched for polysomnography (PSG) studies of patients (age: 35.7 ± 24.9 years; range: 3 to 78 yrs) suspected with SDB (RDI=14.77±27.80) and a minimum 6 hours of recording. Sixty eight PSGs met criteria for manually sleep staged and respiratory scored and ECG signal with less than 5% artifact of total study time. RemLogic (Embla, Inc; Broomfield, CO) was used to calculate the CPC variables- a measure of autonomic and respiratory interactions. All of the PSGs were scored according to 2007 AASM criteria. Comparison was based upon CPC measures of sleep quality generated in mean percent of the windows analyzed for high frequency coupling (HFC), low frequency coupling (LFC), very low frequency coupling (vLFC), and other frequencies.
Results: Pearson R correlation of CPC values: HFC, LFC, vLFC and Other classifications were compared to the manually scored PSG sleep variables using SPSS. REM duration and REM percent of total sleep time significantly correlated (r=.438, p=.000; r=.327, p=.007, respectively) with HFC. LFC was significantly negatively correlated to REM duration and REM percent of total sleep time (r=-.404; p=.001; r=-.285, p=.019). NREM duration correlated significantly with HFC (r=.360, p=.003) and had a significant negative correlation to LFC and vLFC (r=-.293, p=.015; r=-.245, p=.044; respectively). Total sleep time and NREM duration negatively correlated with vLFC (r=-.462, p=.017; r=-.446, p=.023).
Conclusion: The RemLogic CPC analysis variables correlate with standard sleep metrics in a clinical population suspected with OSA, but seems to detect complementary aspects of sleep physiology.

0576

PARTNER INVOLVEMENT IN CPAP: DOES PRESSURE HELP?

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Introduction: Obstructive sleep apnea (OSA) impacts patient and partner sleep and quality of life. This study assessed partner involvement in continuous positive airway pressure (CPAP) and the impact of specific tactic types on adherence.
Methods: Demographics and relationship quality, measured by the Quality of Relationships Inventory support and conflict subscales, were measured in 23 married/cohabiting male OSA patients before CPAP initiation. Partner involvement in CPAP was assessed at day 10 and 3 months post CPAP initiation using a 25-item measure of tactics to encourage healthful behavior. Subscales included positive (i.e., encouraged), negative (i.e., blamed), bilateral (i.e., worked together), and unilateral (i.e., reminded) tactics. A 32-item interpersonal circumplex-based measure of behaviors to encourage CPAP was also administered at follow-up (Supportive Actions Scale-C) as a conceptual framework to evaluate and compare interpersonal behaviors. This measure includes 2 dimension scores: affiliation (i.e., just tried to be there) and control (i.e., told me what to do) derived from 8 octant scores. Objective adherence was measured at follow-up.
Results: Patients reported an average of 5.5+4.5 tactics used per week at day 10 and 4.0+4.9 tactics used per week at follow-up. Average tactic frequency was < 1-2 times/week and tactic frequency was similar for all subscores with the exception of negative tactics which were lower at follow-up (p=.003). Adherence data was available for 14 patients. Bilateral tactics were positively correlated with adherence (r= .75, p= .002) and showed a trend with relationship support (r= .39, p= .067). On the interpersonal measure, bilateral tactics were positively correlated with both affiliation (r= .55, p=.034) and dominance (r= .57, p=.026).
Conclusion: Results indicate partners are involved throughout the first 3 months of CPAP treatment and use a variety of tactics. Bilateral tactics (i.e., working together), were associated with higher adherence and represent a moderately warm and controlling interpersonal style, such as instrumental support and collaboration. Future research is needed to test interventions to increase partner support for CPAP.
Support (optional): T32 HS00078

0577

IS THERE VALUE TO A SLEEP CLINIC EVALUATION PRIOR TO POLYSOMNOGRAPHY?

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Introduction: The majority of referrals for Polysomnography (PSG) are to evaluate for obstructive sleep apnea (OSA). Direct referrals for PSG are often made by primary care providers (PCPs), who may take limited sleep histories. It is currently not required that direct referrals for PSG by PCPs be seen in Sleep Clinic prior to PSG. We investigated the value of a pre-PSG Sleep Clinic assessment.
Methods: Consecutive patients directly referred to an urban academic sleep laboratory for PSG were enrolled. All referrals documented symptoms suggesting OSA and usually would not have required pre-PSG evaluation. All patients were seen in the Sleep Clinic prior to their PSG and changes made to the PSG order were documented and extracted.
Results: 156 patients were enrolled. Demographics: gender 58% female, age 43 +/- 11 years old, ethnicity: 47% African American, 42%

Caucasian, 8% Hispanic and 3% others. Additional measures include: Body Mass Index 41+/- 10 kg/m2, neck circumference 43 +/- 5 cm, Epworth Sleepiness Scale 12 +/- 6. Thirty seven (24%) of patients had orders placed that could impact their PSG. Twenty eight of the 37 (18% of all patients) had changes made to their PSG order. Changes included 1) cancellation in 4 (3%) due to low clinical suspicion, patient refused or known OSA, 2) change to a day study in 6 (4%), 3) addition of full EEG/video recording in 4 (3%), 4) addition of a sleep aid in 14 (9%). Nineteen of the 37 (12% of all patients), including 5 patients who had PSG order changes, had other orders placed that could impact the quality of their PSGs; these included the addition of nasal steroids in 13 (8%) and workup/treatment for restless legs syndrome in 6 (4%).
Conclusion: Significant changes to PSG orders were made in 18% of patients suspected of having OSA following a pre-PSG Sleep Clinic evaluation. Further investigation is needed to evaluate how this approach might impact outcomes and cost.

0578

GENOME WIDE GENE EXPRESSION PROFILING IN BASAL FOREBRAIN OF MICE FOLLOWING ACUTE INTERMITTENT HYPOXIA

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Introduction: Chronic intermittent hypoxia (IH) is a major component of sleep apnea, and leads to cognitive impairments and sleep disturbances. The cholinergic basal forebrain, including the horizontal limbs of the diagonal band of Broca, magnocellular preoptic area and substantia innominata have a strong influence on the regulation of sleep-wakefulness and cognition. However, there are no studies on how acute single exposure to IH during sleep alters gene expression in the basal forebrain.
Methods: Adult CB57BL mice (n=7/group) were exposed to either acute IH (cycling of 5.7% or 21% oxygen every 3 min) or to room air (RA) for a period of 6 hours from 1pm-7pm (last six hours of light period), in 2 identical commercially designed chambers, operated under a 12-hour light-dark cycle. Basal forebrains were harvested and snap frozen in liquid nitrogen, total RNA was extracted, and hybridized onto whole mouse genome long-oligonucleotide microarrays. Gene ontology (GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway analyses were used to identify significant functionally-related groups of genes, and hierarchical cluster analyses were used to visualize expression changes between RA and IH conditions.
Results: Of the 41,361 viable transcripts, 330 were differentially expressed in IH mice using initial scrutiny based on p-values <0.01. Of the 330 transcripts, 297 transcripts were used to built GO and biological pathways. For GO, 177 transcripts (59%) involved biological functions, 185 (62%) cellular components, and 206 (69%) reflected molecular functions. The major molecular functions consisted of catalytic activity (32.7%), binding (50.2%) and motor activity (2.4%). The KEGG pathway database was also used to characterize the enrichment of specific pathway components into functionally regulated genes groups. The 2 most significantly modulated pathways during preliminary analyses were focal adhesion, and B-cell receptor signaling.
Conclusion: Following exposure to acute IH, significant changes of gene expression patterns are identified in mouse basal forebrain. System biology approaches allows for identification of biologically-relevant gene clusters and pathways and gene-gene interactions that may be functionally relevant in sleep disorders associated with IH.
Support (optional): Supported by NIH grant HL-086662 and University of Louisville grant E0581 (RV).

0579

A FUNCTIONAL NEUROIMAGING STUDY OF THE EFFECTS OF ARMODAFINIL ON CORTICAL ACTIVITY AND WORKING MEMORY IN PATIENTS WITH RESIDUAL EXCESSIVE SLEEPINESS ASSOCIATED WITH OBSTRUCTIVE SLEEP APNEA

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Withdrawn

0580

ARMODAFINIL IMPROVES PATIENT-REPORTED OUTCOMES IN PATIENTS WITH EXCESSIVE SLEEPINESS ASSOCIATED WITH OBSTRUCTIVE SLEEP APNEA OR NARCOLEPSY

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Introduction: Armodafinil, the *R*- and longer-lasting isomer of modafinil, has been shown to improve wakefulness in patients with excessive sleepiness associated with obstructive sleep apnea (OSA) and narcolepsy. This is the first study to evaluate patient-reported outcomes of armodafinil, a non-amphetamine, wakefulness promoting medication.
Methods: This was an open-label, 8-week study with an extension phase. Patients with excessive sleepiness associated with OSA or narcolepsy were administered armodafinil (NUVIGIL®) 150 to 250 mg once daily. Efficacy was assessed using Patient Global Impression of Improvement (PGI-I), Clinical Global Impression of Severity of Illness (CGI-S), BFI, and questionnaires to evaluate patients' ability to engage in life activities and patient satisfaction. Safety and tolerability were assessed.
Results: 246 patients received armodafinil (OSA, n=151; narcolepsy, n=95) for ≤9 months. Median duration for the OSA group was 169 days and for the narcolepsy group was 170 days. Armodafinil improved overall clinical condition in the majority of patients, with 66% of patients reporting their condition as "very much improved" or "much improved" as assessed by the PGI-I, and 81% of patients who were deemed responders on the CGI-S. Armodafinil reduced global fatigue. Improved ability to engage in daily activities was reported in up to 71% of patients with OSA or narcolepsy. At final visit, 68% of patients with OSA or narcolepsy were satisfied with armodafinil treatment. Adverse events were mostly mild to moderate in nature with the most common adverse event being headache.
Conclusion: Armodafinil improved patient reported outcomes, including overall clinical condition and some aspects of functioning and fatigue (as measured by the BFI) in patients with excessive sleepiness associated with OSA or narcolepsy. Patients were satisfied with treatment. Clinicians also rated patients as improved following armodafinil administration. Armodafinil was generally well tolerated.
Support (optional): Study sponsored by Cephalon, Inc.

0581

DIAGNOSTIC ACCURACY OF SPLIT NIGHT POLYSOMNOGRAPHY

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Introduction: AASM practice parameters indicate that split-night polysomnograms (PSG) may be performed when the apnea hypopnea index (AHI) ≥ 20-40 depending on clinical factors. The aim of this study was to determine the diagnostic accuracy of split night PSG, including a lower range of AHI thresholds.

Methods: We reviewed 134 consecutive full night PSGs (FN-PSG) performed at our center prior to November 2008. Subjects had been enrolled in studies investigating the relationship between cardiovascular disease and/or weight gain and obstructive sleep apnea (OSA). We compared the AHI from the first 2-hours (2hr-AHI) or 3-hours (3hr-AHI) of sleep with the "gold standard" AHI from FN-PSG (FN-AHI), considering OSA present if FN-AHI≥5.

Results: The 2hr-AHI and 3hr-AHI correlate very well with the FN-AHI (r=0.9283 and 0.9678, respectively). Using the Bland-Altman technique, the difference between 2hr-AHI and FN-AHI was only -1.58 [95%CI (-2.65)-(-0.54); p=0.0040], but the 3 hr- AHI was not statistically different from FN-AHI (p=0.0522). A 2hr-AHI and 3hr-AHI ≥5 are quite specific (0.92 for both), producing a likelihood ratio of disease of 10.13 [95%CI 4.64-22.10] and 10.44 [95%CI 4.80-22.72], respectively. The area under the receiver operating curves (AUC) for 2hr-AHI and 3hr-AHI using FN-AHI≥5 was 0.92 and 0.95, respectively.

Conclusion: The AHI derived from the first 2 or 3 hours of sleep is of sufficient diagnostic accuracy to rule-in OSA at a threshold of only 5 or 10 in patients suspected of having OSA. This study suggests that the current threshold (AHI≥20-40) for split-night studies may be revised to a lower number, allowing more efficient use of resources.

0582

DIFFERENTIAL PRETREATMENT PREDICTORS OF INITIAL AND LONG-TERM CPAP ADHERENCE

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Introduction: CPAP adherence is complex and multi-factorial. Attitudes towards treatment after seven days on CPAP predict later adherence. However, pretreatment attitude measures have failed to correlate with adherence. This study examined pretreatment attitudes and adherence over time and across multiple adherence parameters.

Methods: Data were collected as routine pre and post-treatment CPAP follow up in the clinic of a licensed psychologist certified in behavioral sleep medicine. Standard care involved pretreatment standardized questionnaires evaluating CPAP-Specific Self-Efficacy Scale (CS-SES), problem solving and coping styles and collection of objective CPAP data at 7-days (N=39) and 30-days (N=19). Multiple linear regressions were completed to analyze the relationships between pretreatment questionnaire scores and adherence.

Results: CPAP average duration of use, per night: The multiple linear regression revealed pretreatment scores on the Personal Control scale were correlated with this adherence variable at 7-days (R = .32; p < .04) and 30-days (R = .46; p < .05). A model adding the Approach-Avoidance scale improved this correlation at 7-days (R = .46; p = .01) and 30-days (R = .71; p = .03). Scores on Strategic Planning and Instrumental Support scales were correlated with this variable at 7-days (R = .43; p < .02) but not 30-days. CPAP average duration of use, per night of use: Correlations existed between Personal Control and Strategic Planning scales and this adherence variable at 7-days (R = .60; p < .001). While CS-SES scores were correlated with this variable at 30-days (R = .504; p < .03), Personal Control and Strategic Planning were unrelated to this adherence variable at 30-days.

Conclusion: Pretreatment CS-SES scores, problem solving, and coping styles are related to 7-day and 30-day adherence. Variation in these predictive factors across time and adherence parameter emphasizes the complexity CPAP adherence. Understanding these relationships may improve identification and treatment of CPAP non-adherence.

0583

ABNORMALITIES IN BAROREFLEX SENSITIVITY AND CARDIAC AUTONOMIC FUNCTION: INDEPENDENT EFFECTS OF SLEEP-DISORDERED BREATHING AND IMPAIRED GLUCOSE METABOLISM

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Introduction: Baroreflex sensitivity (BRS) has been reported to be reduced in normotensive subjects with sleep-disordered breathing (SDB), and also in subjects with impaired glucose metabolism (IGM), even after adjusting for obesity. In this study, we sought to determine the association between BRS with IGM and SDB, each occurring in isolation or together.

Methods: Polysomnograms selected from the Cleveland Family Study database were divided into 4 categories: Normal, SDB only (respiratory disturbance index, RDI > 5/h), IGM only, and SDB+IGM. IGM was defined as an oral glucose tolerance test (OGTT) level > 140 but < 200 mg/dl. Low-frequency (0.04-0.15 Hz) power (LFP-HRV) and high-frequency (0.15-0.4 Hz) power were computed from the ECG using spectral analysis of heart rate variability (HRV). Pulse transit time variability (PTTV), determined from the ECG and the pulse-oximeter photoplethysmograph channel, was used as a surrogate measure of blood pressure variability. From the PTTV and HRV power spectra, we estimated BRS_{PTT}, an indirect measure of BRS based on spontaneous pulse transit time fluctuations.

Results: Based on 19 polysomnograms analyzed to date (age=20.8-65-.2yrs, men/women=9/10, BMI=24.8-55.4kg/m^2), BRS_{PTT} was found to be ~25% lower in IGM and SDB+IGM vs normals (p<0.01), but no different in individuals with IGM contrasted to SDB+IGM. LFP-HRV was lower in SDB, IGM and SDB+IGM vs normals (p<0.05), but not different between IGM and SDB+IGM. BRS_{PTT} and OGTT level were negatively correlated (p=0.001) in NREM stage 1 and 2 sleep, after adjusting for gender, age, and RDI.

Conclusion: Our preliminary analyses demonstrate impaired BRS_{PTT} and cardiac autonomic function in IGM and in SDB compared to controls. Further work is underway to increase sample size in the study and to investigate the potential additive effects of SDB to IGM-related impaired BRS.

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0584

CHANGES IN THE SCORING OF OBSTRUCTIVE SLEEP BREATHING EVENTS: ACCORDING TO THE AASM RECOMMENDATIONS IN 1999 VERSUS 2007

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Introduction: The definition of accurate recording and measuring of sleep related obstructive breathing events are clinically critical as a base

for quantifying disease severity and assessment related to diverse morbidities in obstructive sleep apnea hypopnea syndrome (OSAHS). The aim of the study is to explore the effect of using different scoring recommendations for apnea and hypopnea in polysomnographic studies: 1) The 1999 AASM Task Force (AASM 1999); 2) The 2007 AASM Task Force (AASM 2007).

Methods: 60 total patients who were diagnosed with OSAHS using the 2007 AASM recommendations (20 patients in each severity grade; mild, moderate and severe; 55 males, mean age; 47.9±11.7yrs, mean BMI; 25.9±3.4kg/m2) at the Asan Medical Center were randomly selected and studied retrospectively. All sleep related scoring was derived from two different criteria; AASM 1999 and AASM 2007. We compared the change of apnea index (obstructrive; OI, central; CI, mixed; MI), hypopnea index (HI) and AHI using paired-t test ($p<0.05$).

Results: Of total patients, higher OI with AASM 1999 and higher HI with AASM 2007 was prominent (AASM 1997 vs. 2007; OI; 21.61±20.78/hr vs. 15.10±18.47/hr, $p<0.001$, HI; 7.45±5.94/hr vs. 12.53±9.3/hr, $p<0.001$). There were no significant changes in MI and CI between the two criteria. Total AHI was slightly lower with AASM 2007 compared to AASM 1999 (30.75±23.98/hr vs. 29.26±23.80/hr, $p<0.001$) but only one patient shifted from severe to moderate grade. Also, results were similar for all subgroup analysis according to severity grade and score difference between two criteria were proportional to its severity increment (mean difference AASM 1997 vs. 2007; mild; OI; 3.11±1.48/hr, HI; -2.04±1.14/hr, OHI; 1.08±1.05/hr; moderate; OI; 5.27±2.61/hr, HI; -4.21±2.35/hr, OHI; 1.05±1.34, severe; OI; 11.16±5.29/hr, HI; -8.97±5.08/hr, OHI; 2.33±3.54/hr).

Conclusion: We investigated the variation of OSAHS according to two different scoring criteria for apnea and hypopnea. AASM 2007 criteria is more strict to apnea and sensitive to hypopnea detection than AASM 1999. AHI grade are not influenced by the change of criteria, although there is a lower scoring tendency of AHI with AASM 2007.

0585

THE EFFECTS OF NASAL CONTINUOUS POSITIVE AIRWAY PRESSURE ON THE EARLY SIGNS OF ATHEROSCLEROSIS IN OBSTRUCTIVE SLEEP APNEA SYNDROME

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Introduction: Obstructive sleep apnea syndrome (OSAS) is associated with cardiovascular complication which is considered to be mediated by atherosclerosis. Recent studies showed that repetitive nocturnal hypoxia may be associated with the early signs of atherosclerosis such as arterial stiffness or endothelial dysfunction in OSAS patients. The aim of this study was to investigate whether the nasal continuous positive airway pressure (nCPAP), most effective therapy for eliminating the upper airway obstruction, is effective for improving arterial stiffness or endothelial dysfunction.

Methods: We enrolled 21 OSAS patients (mean age, 50.4 ± 11.5) with moderate to severe degree. After finishing the baseline nocturnal polysomnography (NPSG), carotid-femoral pulse wave velocity (cfPWV) and flow-mediated dilation (FMD) were measured for assessing arterial stiffness and endothelial dysfunction. Also, serum levels of C-reactive protein (CRP), total cholesterol, triglyceride, HDL cholesterol, glucose, or insulin were measured. After applying nCPAP (mean duration, 139.2 ± 46.5 days) to the patients, cfPWV, FMD, and serum laboratory test were performed again.

Results: The mean apnea hypopnea index (AHI) of patients was 64.0 ± 20.0 (26.1 - 99.5)/h prior to nCPAP treatment. Compared to baseline measurements, the value of cfPWV significantly decreased from 11.2 ± 4.8 to 9.2 ± 2.0 ($p=0.038$), and FMD was significantly improved from 5.53 ± 2.58 to 6.50 ± 2.50 ($p=0.027$) after nCPAP treatment. Body mass index (BMI), serum levels of CRP, total cholesterol, triglyceride, HDL cholesterol, or glucose did not significantly changed after nCPAP treatment. Also, degree of insulin resistance was not significantly improved.

Conclusion: The values of cfPWV or FMD were significantly improved after nCPAP treatment, even though there was no significant change in anthropometric measurement, inflammatory reaction, or insulin resistance. We could confirm that the nCPAP treatment significantly improved risk of cardiovascular complication in OSAS patients.

0586

ENDOTHELIAL DYSFUNCTION AND ARTERIAL STIFFNESS IN OBSTRUCTIVE SLEEP APNEA SYNDROME

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Introduction: Obstructive sleep apnea syndrome (OSAS) is associated with an increased risk for developing cardiovascular complications. The purposes of this study were to investigate the influence of nocturnal sleep apnea on the arterial stiffness, and the relationship between arterial stiffness and endothelial dysfunction in OSAS patients.

Methods: This study enrolled 107 male subjects who were referred to sleep laboratory to undergo nocturnal polysomnography (NPSG). After they finished NPSG, FMD was measured on the brachial artery and cfPWV was measured using a noninvasive automatic device. All the subjects fasted at least 8 hours. Subjects aged older than 60 years, taking antihypertensives, antihyperlipidemic drug, diabetes medication or suffering from inflammatory diseases were excluded.

Results: Based on the apnea hypopnea index (AHI), we classified the subjects into three groups; severe OSAS group with AHI ≥ 30 (N=41), mild to moderate OSAS group with AHI ≥ 5 and < 30 (N=40), and normal control group (AHI < 5; N=26). There were significant differences in FMD ($p<0.01$) and cfPWV ($p<0.05$) among three groups, although there were no significant differences in age, body mass index (BMI), neck circumference, and waist-to-hip ratio. Stepwise multiple regression showed that lowest O2 saturation was significant determinant of FMD (beta = 0.23, adjusted R2=4.5%, $p<0.05$), and age (beta=0.27, $p<0.01$) and percentage of time below 90% O2 saturation (beta=0.31, $p<0.01$) were significant determinants of cfPWV (adjusted R2=15%, $p<0.01$). FMD was significantly correlated with cfPWV ($r=-0.24$, $p=0.012$).

Conclusion: FMD and cfPWV were impaired in OSAS, which could be implicated in the pathogenesis of cardiovascular complications of OSAS. Nocturnal hypoxemia rather than AHI might better explain the association of OSAS with FMD or cfPWV. In addition, it should be considered that age may also affect the cfPWV in OSAS patients.

0587

CONTINUOUS POSITIVE AIRWAY PRESSURE THERAPY COMPLIANCE VARIES WITH AGE

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Introduction: Several studies have investigated compliance with Continuous positive airway pressure (CPAP) therapy, but few address CPAP use and compliance in elderly compared with young patients. This study examined predictors of CPAP compliance in these groups.

Methods: Data collection was done through chart review of VA Medical Center patients with diagnosed obstructive sleep apnea (OSA) using CPAP. Patients with diagnosed sleep disorders other than OSA were excluded. Sleep variables from baseline sleep and CPAP titration studies in compliant versus non-compliant elderly (N = 36; age 70 - 80) and

young (N = 36; age 40 - 50) patients were compared. Compliance was determined by self-reported use of CPAP > 5 hours per night for > 6 months. The statistical analysis of data was performed the using T-test, ANOVA and Z score.
Results: Of 72 patients, 44 (22 each group) had follow-up data, 72% young and 40% elderly were compliant (P=0.03). Compared to the young, the elderly group had significantly longer sleep latency; more arousals, limb movements (LM) and LM-related arousals; and less total sleep time (TST) and sleep efficiency (SE) at baseline and with CPAP. Baseline respiratory disturbance indices and post-CPAP improvement were comparable between the young and elderly. In ANOVAs comparing compliance data, arousal indices (prior to CPAP initiation) were higher (44 SD 32) in those failing therapy compared to those who succeeded (25 SD 16) - F = 4.371, p = 0.043. No other variable significantly predicted compliance, and analyses also showed no interactions between age and success. Patients failing CPAP also tended to have less TST (254 versus 293 minutes) and SE (65 versus 73%) than those who succeeded.
Conclusion: These preliminary findings show significant differences in sleep variables between the young versus elderly. However, only the arousal index was predictive of subsequent CPAP compliance regardless of age.
Support (optional): Dayton Department of Veterans Affairs Medical Center, Wright State University, and the Sleep-Wake Disorders Research Institute

0588

EFFICACY OF ORAL APPLIANCE IN SEVERE OSA PATIENTS NOT COMPLIANT WITH CPAP THERAPY

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Introduction: The mandibular advancement devices have been used with good results for patients with primary snoring and mild or moderate sleep apnea, Apnea Hypopnea Index (AHI) ≤ 30 and these results have been proved by many studies. In cases of severe apnea (AHI > 30) in patients not compliant with CPAP therapy, the treatment with oral appliances is indicated, but in these cases, the efficacy of oral appliances is sometimes questioned. In this study we show the results obtained in 18 consecutive patients with severe sleep apnea, not compliant with CPAP therapy, with polissonographyc diagnosis and mean AHI=37.9 ± 9.0 (32/68), treated with oral appliances, and followed with polissonographic records in use of appliance.
Methods: A group of 18 consecutive patients (4 Female, 14 Male) mean age 50.2 years old (SD=7.86, range 37/64), BMI 28.2 (SD=4.3, range 21/35) with severe OSA with polissonographic diagnosis, not compliant with CPAP, were referred to therapy with oral appliance (PLG appliance). After the better adjustments and titration are achieved, the patients were submitted to follow-up polissonography, using the oral appliances in order to observe the improvement in AHI.
Results: The follow up polissonography shows a reduction in AHI, achieving an outcome of 79%, initial mean AHI 37.9 ± 9.0 was reduced to mean AHI 8.0 ± 8.4 with appliance. The results shows an important reduction in AHI in patients with severe OSA, in 10/18 (56%) patients the AHI was reduced to less than AHI 5 and 13/18 (67%) reduced to less than AHI 10.
Conclusion: Patients with severe OSA, not compliant with CPAP therapy could be treated with oral appliances with good outcomes.

0589

THE ROLE OF MAXILLOMANDIBULAR ADVANCEMENT SURGERY IN OBSTRUCTIVE SLEEP APNEA: THE MAYO CLINIC EXPERIENCE

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Introduction: Similar to other surgical treatments for obstructive sleep apnea (OSA), reported outcomes of maxillomandibular advancement (MMA) have varied widely according to differences in definitions of success. We explored the outcomes of MMA at our institution including how often it produced a cure for OSA, defined as an apnea-hypopnea index (AHI)of 5 by polysomnography (PSG) within 6 months of surgery. Additionally, we evaluated pre- and post-MMA lateral cephalometric radiographs with a customized computer analysis to quantify changes in the maxillomandibular complex.
Methods: A retrospective review of records was done for OSA patients who underwent MMA surgery at Mayo Clinic between November 2004-June 2008 and had PSGs done pre-procedure and within 6 months post-procedure. Surgical cure was defined by AHI < 5 post-MMA. Change in anatomic positions of the maxilla and mandible post-MMA was quantified by use of lateral cephalometric point posterior nasal spine (PNS) and cranial base to anterior mandibular position angle (SNB) respectively.
Results: Twenty three of 37 patients (8 females, 29 males with mean age of 47.69 years) had PSGs (28.74 ± 31.15 months) pre-MMA and (6.92 ± 3.95 months) post-MMA. Fifty seven percent achieved AHI < 5; 70% achieved AHI < 10; 91% achieved AHI < 20. No significant differences were found in mean BMI (pre-MMA 30.1 ±5.4 and post-MMA 29.3 ± 5.9, p=0.5349). Mean total AHI decreased significantly from 46.1± 26.4 pre-MMA to 8.1± 10.7 post-MMA (p<0.0001). There was a significant increase in lowest mean oxygen saturation from 81± 7.4 to 86 ± 5.4 (p=0.0073). Daytime sleepiness as measured by Epworth Sleepiness Scale score (ESS) also decreased significantly from 12.9 ± 4.5 to 8.3 ± 3.2 (mean +/-SD) p=0.0009. Mean increase in PNS position post-MMA was found to be 8.29mm ± 2.37. SNB showed a mean increase from 78.86° ± 3.63 pre-operatively to 83.27° ± 3.75 post-MMA.
Conclusion: In the majority of our OSA patients, MMA surgery effectively eliminated sleep disordered breathing. Previous studies have shown high success rates utilizing a definition of success of post-op AHI <20, with at least a 50% reduction from the pre-surgical AHI. Our study suggests that the rate of success is still quite high with an even more robust definition of surgical success of post-op AHI<5. The change in maxillary and mandibular position, quantified by change in PNS and SNB angles respectively, correlated with significant AHI reduction in the majority of our patients.

0590

REDUCTION OF MORNING HEADACHES IN SUBJECTS WITHOUT SLEEP DISORDERED BREATHING: AN OPEN STUDY WITH A JAW RETAINER

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Introduction: Approximately 7.6% of the general population report morning headaches (MHA). Moreover, about 3 of 4 patients with sleep apnea have MHA. Most patients with sleep apnea do report relief of MHA when treated with continuous positive airway pressure or oral appliance (OA). The objective of this open study was whether an OA could benefit subjects with MHA but without sleep disordered breathing (SDB).
Methods: In over 20 subjects with MHA, 12 subjects (7W/5M; 27.6 y.o. ± 2.1, mean±SEM) with frequent MHA and without clinical or sleep recording (habituation night and diagnostic night) evidence of SDB were

selected. An oral appliance (O.R.M., Narval, FR and CAN) was individually fitted. Intensity of MHA was estimated on a 100mm VAS over 5 different periods: P1) 5 mornings without OA, P2) 7 mornings with OA in non-advanced position followed by one overnight polygraphic recording, P3) 5 nights of washout without OA, P4) 7 nights with OA in advanced position followed by one overnight polygraphic recording, and P5) 5 nights of washout without OA.

Results: From an initial MHA intensity of 55±2 (P1), the use of OA was associated with a drop to 16±1 (repeated measures ANOVA, $p<0.0001$) for both P2 and P4. At washout periods (P3 and P5), MHA intensity returned to values similar to those observed at P1. No significant difference was seen for sleep efficiency, sleep stage distribution, oxygen desaturation or arousal index. Although apnea-hypopnea index and upper airway resistance were within normal range, the hypopnea index decreased with OA in advanced position from 0.4 (median; min 0 - max 4.5) to 0 (0-1.9; $p=0.05$).

Conclusion: OA may be a beneficial alternative to manage MHA in absence of SDB. Similar findings need to be reproduced in a randomized controlled trial to assess contribution to results of prevention of jaw retrusion during sleep.

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0591

NASAL EPAP - PHYSIOLOGIC MECHANISM OF ACTION

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Introduction: Provent (Ventus Medical, Inc.) is a nasally applied resistive valve which has been shown to reduce AHI by 80% in half of patients with sleep disordered breathing (SDB), with response independent of SDB severity (JCSM 4:426). It produces nasal expiratory positive airway pressure (nEPAP), but how this improves SDB is unclear since airway collapse is predominantly inspiratory. We evaluated efficacy and physiologic mechanisms by which nEPAP improved SDB.

Methods: 6 SDB patients (BMI 26-39kg/m2) underwent 3 full-PSGs: diagnostic (RDI calculated in supine/lateral positions by nasal cannula); therapeutic (Provent in place—pressure and CO2 were monitored intranasally, while flow was measured by an external pneumotachograph); CPAP study (passive/active Pcrit were determined in supine/lateral positions during NREM/REM). To indirectly assess tracheal traction effects, awake functional residual capacity by N2 washout (FRC) was measured in the sitting/supine/right-lateral positions. 5 normal control subjects (RDI<11; BMI 20-30kg/m2) also underwent positional FRC measurements.

Results: In SDB, diagnostic RDI was 8-97 overall and 37-97 supine; RDI in control subjects was 5-11 overall and 6-25 supine. With nEPAP, 2 patients did not sleep, and 1 had no change in RDI. RDI in the remaining 3 patients fell by 44 to 87% and below 20 in all cases (REM-RDI remained 43 in one patient). In these 3 patients, NREM end-expiratory intranasal pressure increased to a range between 18 and 26cmH20 suggesting development of auto-PEEP. SDB recurred whenever pressure fell transiently, as after an arousal. In the patient without benefit from nEPAP, nasal pressure remained near 0 due to oral expiration. Passive Pcrit (available in only 2 responders so far) decreased from the supine to lateral position, and was unchanged from NREM to REM. FRC in control subjects fell by 23% from sitting to supine, but only 10% from sitting to lateral.

Conclusion: nEPAP produced marked improvement in SDB in 3/6 patients, despite some residual REM SDB. This was associated with elevated end-expiratory pressures suggesting auto-PEEP and tracheal traction as a potential mechanism.

Support (optional): Ventus Medical, Inc.

0592

EFFECT OF EXPIRATORY PRESSURE RELEASE ON UPPER AIRWAY PRESSURE: RELATIONSHIP TO FREQUENCY OF RESPIRATION

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Introduction: During CPAP treatment of Obstuctive Sleep Apnea Hypopnea Syndrome (OSAHS) reduction in mask pressure during expiration (C-flex ™) may improve comfort. Mitigation of expiratory rise in upper airway (UA) pressure would provide a possible mechanism. However, we previously showed that despite fall in mask pressure during C-Flex ™, pressure in the upper airway did not fall in 8/9 subjects. The purpose of this study was to assess the effect of respiratory frequency on this behavior of UA pressure during C-flex ™.

Methods: 12 subjects with OSAHS (AHI 71 +/- 34/hr) had a full NPSG at optimal CPAP using a Respironics BiPAP Auto Series with Bi-Flex ™ (Murrysville, PA). Mask pressure (MP), supraglottic UA pressure (SGP), and airflow were recorded at constant CPAP and the highest C-Flex ™ level (3). Expiratory ΔMP and ΔSGP were averaged over 3 consecutive breaths during N2 sleep. Measurements were repeated at least twice in 9/12 patients. In three patients, additional measurements were made during wakefulness.

Results: A total of 24 respiratory periods were analyzed in the 12 patients (21 asleep / 3 awake). At the mask, application of C-flex ™ produced a decrease of 1.16 +/- 0.54 cm H20 (0.31 - 2.97 cm H20) during expiration. In 4/24 periods there was a proportional decrease in SGP, whereas in 20/24 there was no change. The respiratory frequency in the group with proportional decrease in SGP was 15.1 +/- 4.1 bpm, whereas it was 18.1 +/- 4.7 bpm in the group without decrease in SGP. Furthermore, in the three cases where subjects were measured during sleep and wake, it was a lower frequency which was associated with the expected response of SPG to C-flex ™.

Conclusion: Reduction of expiratory mask pressure during CPAP (C-flex ™) produced the expected reduction in supraglottic pressures only rarely. In these cases this effect appears to be related to lower respiratory frequency, which occurrs mostly during wake. Thus during sleep there was little impact of C-Flex ™ on the UA and the reported benefit may be related to pressure effects seen only during awake.

Support (optional): NCRR00096,ALANY,ISC III,SOCAP,FRSD

0593

ADJUNCTIVE ARMODAFINIL IMPROVES WAKEFULNESS THROUGHOUT THE DAY IN CPAP-TREATED PATIENTS WITH EXCESSIVE SLEEPINESS ASSOCIATED WITH OBSTRUCTIVE SLEEP APNEA

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Introduction: Armodafinil (NUVIGIL®), the *R*- and longer-lasting isomer of modafinil, is a non-amphetamine wakefulness-promoting medication. Compared to modafinil, on a mg-to-mg basis, armodafinil produces higher plasma concentrations later in the day.

Methods: This post-hoc analysis of data from a 12-week, multicenter, double-blind, randomized, placebo-controlled study compared efficacy of once daily armodafinil 150 or 250 mg to placebo for maintaining wakefulness throughout and later in the day in 395 patients with OSA who experienced residual excessive sleepiness even with CPAP use. Maintenance of Wakefulness Test (MWT) evaluated wakefulness over six 30-min test sessions scheduled at two hour intervals beginning at 0900. MWT latency was assessed throughout (0900-1900). Efficacy (0900-1900) was also evaluated for a subgroup of the more sleepy

patients (baseline MWT latency <30 min, n=256). Tolerability was assessed.
Results: At final visit, mean changes from baseline on MWT latency across all 6 daily tests (0900-1900) were 1.3 min for armodafinil 150 mg, 1.6 min for armodafinil 250 mg, and -1.3 min for placebo (armodafinil vs placebo; all $P<0.05$). Numeric separation in the MWT latency was seen between each armodafinil group and the placebo group at the first 5 tests but not at the 1900 hour test. In patients with baseline MWT <30 min, respective findings were 3.1 min, 2.3 min, and -0.2 min (armodafinil vs placebo, all $P<0.05$). The most common adverse event associated with armodafinil was headache.
Conclusion: As adjunctive therapy, armodafinil 150 mg and 250 mg improved wakefulness throughout the day compared with placebo in patients who have OSA and associated residual sleepiness, even with regular CPAP use. Armodafinil was generally well tolerated.
Support (optional): Supported by Cephalon, Inc.

0594

OXYGEN SATURATION IN OBSTRUCTIVE SLEEP APNEA (OSA) AND NORMAL CONTROLS: COMPARISON BETWEEN REM VERSUS NREM AND PHASIC REM (PREM) VERSUS TONIC REM (TREM)

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Introduction: Sleep is divided into REM and NREM. REM sleep is subdivided into phasic (PREM) and tonic (TREM) periods. PREM is characterized by bursts of rapid eye movement, irregularities in heart and respiratory rates and muscle twitches. Limited literature indicates decreases in oxygen saturation (SaO_2) in normal subjects from TREM to PREM periods. A retrospective, single- blind study was done to determine whether subjects with and without OSA have significant changes in, SaO_2 in REM versus NREM sleep and SaO_2, time and number of events in PREM versus TREM periods.
Methods: Subjects were divided: normal, Group 1 (AHI <5, n=14); mild OSA, Group 2 (AHI 5.1-15, n=13); moderate OSA, Group 3 (AHI 15.1-30, n=11) and severe OSA, Group 4 (AHI>30.1, n=8). Eye movements separated by <2 respiratory cycles equal one PREM event and >2 respiratory cycles a different PREM event. PREM/TREM event was defined as ≥10 seconds. SaO_2 was averaged for 30 second following PREM/TREM event. Eye movements <2 respiratory cycles were not considered as PREM/TREM events. Inclusion criteria: diagnostic PSG; TST≥4.5 hours and normal REM time(age and gender). Some exclusion criteria: no lung, neuromuscular or upper airway diseases; no ENT/chest surgeries; non-smokers and no REM sleep modifiers. Over 100,000 data points were processed.
Results: Sixty-three percent of the sample (n=46) was men. The mean data for all subjects: age 48.8±15.2; BMI 27.4±5.9; TST 366.6±38.8 and REM time 79.8±16.5. All groups were equivalent in age, TST, REM time and PREM or TREM (SaO_2, time and number of events). There were statistically significant differences between average and lowest REM SaO_2 when compared with average and lowest NREM $SaO_2$for groups 1 and 2; the lower SaO_2 were in NREM sleep. Twelve patients (six pairs) with AHI within 0.0-0.5 and BMI within 3-15 were compared; there were no statistical significant differences with respect to REM or NREM SaO_2, TST, REM time, PREM or TREM (SaO_2, time and number of events).
Conclusion: Statistically significant differences in oxygen saturation between groups occurred in normal and mild OSA subjects in NREM when compared with REM sleep; the lower oxygen saturations occurred in NREM not in REM. In subjects with or without OSA, there were no significant differences between PREM or TREM(SaO_2, time and number of events), TST and REM time. Subjects with similar AHI but different BMI had no differences in REM versus NREM SaO_2, TST, REM time and PREM versus TREM (SaO_2, time and number of events).

0595

SEDATED ENDOSCOPY DIAGRAM FOR OBSTRUCTIVE SLEEP APNEA

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Introduction: Airway evaluation for Obstructive Sleep Apnea(OSA) have focused on methods to predict OSA or identify levels of obstruction to guide surgery. Describing levels of obstruction have not generally improved surgical outcomes. We have described a novel method that models the airway as a series of muscle buttresses and may more accurately depict airway structure. This study assess the reproducibility of this method.
Methods: Video endoscopic recordings of 21 sedated endoscopies (propofol and a standardized algorithm) were reviewed. Structural buttresses were scored on 3 and 4 point the scales and included the salpingo/palatopharyngeus, levator, and uvular muscle groups for the epi-pharynx and the epiglottis, lateral hypopharynx, vallecular and proximal tongue base for the hypopharynx. Exact matching of results from two blinded observers was assessed.
Results: Structural agreement for all measures was 74.83%. The highest level of agreement was on the structure of the levator paltine (85.7%) with the lowest the epiglottis (57.14%).
Conclusion: The current method demonstrates a high level of agreement between observers. The method holds the potential of allowing more widespread structural description of the upper airway using clinical endoscopy.

0596

HYPERVENTILATION AS A PREDICTOR OF CPAP-EMERGENT CENTRAL SLEEP APNEA

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Introduction: Central sleep apnea (CSA) may develop during CPAP titration while treating obstructive sleep apnea (OSA). Risk factors for the development of this type of complex sleep apnea include male sex, history of cardiac disease and CSA on the diagnostic polysomnogram (PSG). The aim of this study was to determine whether we could predict CPAP-emergent central sleep apnea (CECSA) on the basis of the end-tidal CO_2 ($PetCO_2$) without CPAP.
Methods: We performed a retrospective review of the polysomnograms (PSGs) performed between 2006 and 2008. Diagnostic PSGs were performed with end-tidal capnometry (Smiths Medical BCI Capnocheck Sleep). We included those patients with OSA and no central apneas during the diagnostic night, who subsequently developed central apneas with CPAP therapy (CECSA). The control group was comprised of OSA patients without CSA during both the diagnostic and CPAP studies, matched for sex, age and BMI. Demographic, baseline, pre and post titration parameters were compared between these groups. We defined alveolar hyperventilation as a $PetCO_2 < 35$ torr and compared the percentage of total sleep time (TST) spent below this value.
Results: We reviewed 10 CPAP emergent CSA patients and 13 controls that were matched for sex, age (mean 53 ± 14 years (SD)) and BMI (mean of 33.6 ± 7.3 kg/m^2). There was a predominance of males in both groups (M: F ratio 12:1) The AHI was not statistically different between the groups (mean 43.5, $p = 0.20$). Those with CECSA had a statistically higher percentage of TST below 35 torr (mean 55% of TST vs. 14% for the control group, $p = 0.002$).
Conclusion: Patients with CECSA tend to be hypocapneic compared to those with simple OSA. CECSA may be predicted by estimating alveolar hyperventilation as determined by the percent of TST below 35 torr on PSG without CPAP. $PetCO_2$ may therefore be an invaluable tool in predicting those at risk for CECSA.

0597

WEIGHT AND POSITION - PROFILE OF OBSTRUCTIVE SLEEP APNEA (OSA) IN A SUBURBAN SLEEP CENTER

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Introduction: OSA is related to weight and can change with sleeping positions. An observational review was performed of initial diagnostic polysomnograms ordered for AASM indications. The purpose was to establish the patterns of weight and positional changes with OSA seen in a suburban AASM accredited center.
Methods: All initial full-night diagnostic or initial split-night (diagnostic portion) studies performed for any indication on patients >18y/o were reviewed. All studies were performed following AASM guidelines. Weight data was reviewed for the presence and severity of apnea (none AHI < 5, mild AHI 5-15, moderate AHI 15-30, severe AHI >30, and very severe AHI > 60). The effect of position on apnea severity was measured by the change of AHI in the supine position compared to the entire diagnostic study in the no apnea, mild and moderate apnea studies.
Results: Data was reviewed from 628 studies performed between 6/07 and 10/08 (37% females and 63% males). Studies were classified by apnea (179 no apnea, 195 mild, 103 moderate and 151 severe apnea [60 with AHIs >60]) and weight (BMI). BMIs<30 were seen in severe apnea 30% and very severe apneas 22% of the time. Of individuals with BMIs <20, three (33%) had apnea. Of individuals with BMIs <25, 44 (44%) had apnea. Of individuals with BMIs >40, one did not have apnea (1.6%). Positional increase in apnea occurred in AHI<5 - 12%, AHI 5-15 - 31%, and AHI 15-30 - 50%.
Conclusion: Individuals with a normal BMI can have apnea, including severe apnea. Very severe obesity (BMI>40) is almost always associated with apnea. Excessive weight should be an indication for testing, but normal weight should not exclude individuals with appropriate symptoms. Positional apnea is common in the mild and moderate apnea individuals. Some individuals have apnea only in the supine position.

0598

ADHERENCE TO POSITIVE AIRWAY PRESSURE THERAPY — EFFECTS OF REM-RELATED APNEA, GENDER AND INSURANCE

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Introduction: REM-related apnea occurs in patients with mild to moderate obstructive sleep apnea and may be more prevalent in women. Adherence to positive airway pressure (PAP) therapy has not been described in this population. Our objective was to determine whether REM-related apnea, and other factors, affect adherence to PAP therapy.
Methods: Adherence data was reviewed from 75 consecutive adult patients presenting to the Vanderbilt Sleep Disorders Center. All patients had modem-equipped PAP devices, allowing adherence data to be monitored using commercial software (Respironics' EncoreAnywhere). Demographic and polysomnographic data were obtained, along with adherence at 7, 14, 28 and 56 days following start of therapy.
Results: Overall adherence rates exceeded minimum standards of adherence for all time points (approximately 90%, > 4.4 hours per night). 25.3% of the 75 patients had REM-related apnea (AHI ≥ 5; NREM AHI < 15; REM AHI/NREM AHI > 2). These patients were predominantly women with mild to moderate sleep apnea (average AHI = 12). Patients with REM-related apnea had increasing difficulty adhering to PAP therapy over time, resulting in one hour less of nightly use at 56 days compared to patients without REM-related SDB (4.4 versus 5.7 hours; p=0.007). This finding was unrelated to SDB severity. Men wore PAP devices less than women through the first 28 days (p=0.04), but usage was equivalent at 56 days (p=0.10). While Medicare patients wore PAP therapy less at 7 days (p=0.01) compared to patients with private insurance, adherence was comparable at 56 days (p=0.54).
Conclusion: Men and those with Medicare, while initially less adherent, were comparable in PAP use to women and those with private insurance at 56 days. In contrast, patients with REM-related apnea showed decreasing PAP use over time, despite similar adherence rates through the first two weeks of therapy. Patients with REM-related apnea represent an important group to target in programs aimed at increasing CPAP adherence.
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0599

MODELING THE EFFECTIVENESS OF TREATMENTS FOR OBSTRUCTIVE SLEEP APNEA/HYPOPNEA

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Introduction: The standard treatment for Obstructive Sleep Apnea (OSA) is continuous positive airway pressure (CPAP). CPAP can be very effective in the laboratory, but is limited by poor patient acceptance and adherence. Alternative mechanical treatments which, while less efficacious in reducing the apnea/hypopnea index (AHI) in the laboratory, may be more likely used by the patient. One of these is a new treatment device (Provent, Ventus Medical, Inc.) that causes expiratory positive airway pressue (nEPAP). The purpose of this model analysis is to compare the effectiveness of CPAP versus nEPAP taking into consideration both apneas and hypopneas prevented during hours of use and those not prevented due to lack of use (dAH%). Our hypothesis is that a therapy which is slightly less effective in the lab than CPAP will provide more benefit if higher adherence results in fewer abnormal breathing events over a patient's lifetime.
Methods: Efficacy and compliance data on CPAP from the literature were contrasted with current nEPAP data. dAH% took into account the hours of use of a device, its efficacy during use, and the hours of non-use (with its associated apneas/hypopneas). A higher dAH% indicates a more effective treatment.
Results: The dAH% for minimally adherent CPAP users ranged from 32% - 40%, while the higher usage patients experienced a 52-66% apnea/hypopnea prevention. For nEPAP the range was 53%-58% in minimally adherent users, whereas in highly adherent users the efficacy of nEPAP in preventing abnormal breathing events was 67%-72%.
Conclusion: Models created using AHI reduction and adherence rates from clinical literature and studies of CPAP and nEPAP suggest that nEPAP prevents a similar or greater number of AH events than CPAP. While nEPAP studies report smaller AHI reduction than CPAP in the lab, the higher reported adherence rates for nEPAP therapy more than offset the in-lab differences.

0600

THE FREQUENCY OF PARASOMNIA SYMPTOMS IN PATIENTS WITH OBSTRUCTIVE SLEEP APNEA

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Introduction: Parasomnias are disruptive events occurring in either rapid eye movement (REM) or non-REM (NREM) sleep. These disorders may occur alone or result from another sleep disorder such as obstructive sleep apnea (OSA). The overall occurrence of parasomnias in the general population has not been reported. Among the more common parasomnias (confusional arousals, sleep terrors and sleepwalking), the reported prevalence is 2-5%. We sought to identify the frequency of

parasomnia symptoms in patients with OSA and the response of these disorders to OSA treatment.
Methods: A retrospective chart review was performed on all new patient referrals for evaluation of OSA from July 2006 through December 2007. Patients who met inclusion criteria (n=537) were at least 18 years of age, had a polysomnogram diagnostic of OSA (apnea-hypopnea index (AHI) > 5) and documentation of the presence or absence of parasomnia symptoms.
Results: 51 patients (59% women, 84% of non-Hispanic origin and average age of 47 years) had one or more types of parasomnia complaints. Twenty-one (38%) reported sleep paralysis, sixteen (29%) reported sleep-related hallucinations, eleven (20%) reported acting-out dreams (or symptoms suggestive of REM sleep behavior disorder), five (9%) reported sleepwalking, one reported sleep-related eating and one had an unusual complaint of a "pulling sensation" down her spine at sleep onset. The frequency of parasomnia symptoms in those with OSA was 9.5%. Ten patients (20%) reported an improvement in their parasomnia symptoms with continuous positive airway pressure (CPAP) treatment. However, many patients' records lacked follow-up documentation, they did not return for subsequent visits or they were non-compliant with treatment.
Conclusion: There is a higher occurrence of parasomnia symptoms in patients with OSA compared to the prevalence rates of individual parasomnias. Fragmentation of sleep caused by recurrent episodes of upper airway obstruction and episodic desaturations likely contributes to state transition instability predisposing to parasomnia expression. Additional investigation is needed to assess the response of parasomnia symptoms to OSA treatment.

0601

INTERACTION OF ALLERGIC RHINITIS AND CPAP ON NASAL CONGESTION

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Introduction: Clinicians have noticed that following the initiation of continuous positive airway pressure (CPAP), some patients experience worsening of nasal congestion while others have no change or improvement of nasal congestion. The primary aim of this study is to determine if baseline allergic rhinitis interacts with CPAP to impact the effect of CPAP on nasal congestion.
Methods: This prospective observational cohort study included patients with newly diagnosed obstructive sleep apnea, follow up at 3 months, and any CPAP use (self report) within 4 weeks of their follow up. Baseline allergic rhinitis was assessed prior to CPAP exposure and was defined as a history of reaction to a skin allergen test. Nasal congestion outcome was measured at baseline before CPAP and at follow up while on CPAP, using both a visual analog scale (VAS) of subjective nasal congestion and the Nasal Obstruction Symptom Evaluation Instrument score (both range 0-100, higher is worse nasal congestion). Nasal congestion scores were compared in each group before and after initiation of CPAP (paired t-tests), and nasal congestion change scores were compared between groups (t-test).
Results: The patients with allergic rhinitis (N=9) and without allergic rhinitis (N=45) were of similar age, gender, nasal surgery history and baseline nasal steroid use ($p>0.05$). Allergic rhinitis patients had insignificant worsening of nasal congestion on CPAP, with the mean (standard deviation) subjective nasal congestion on VAS not changing from baseline to 3 months: 44 (24) to 47 (23), paired t-test $p=0.60$. Those without allergic rhinitis had significant improvement of nasal congestion with CPAP, with a decrease in VAS from 44 (26) to 28 (28), $p<0.001$. The change in nasal congestion was significantly different between the groups with allergic rhinitis (VAS change 4 [22]) and without allergic rhinitis (-16 [28]), $p = 0.04$. Negative VAS change represent improvement in nasal congestion. Similar results were found with nasal congestion measured by the Nasal Obstruction Symptom Evaluation score.
Conclusion: Patients with allergic rhinitis had insignificant worsening in subjective nasal congestion after CPAP initiation, while those without allergic rhinitis experienced significant improvement in nasal congestion. The relative change in subjective nasal congestion after CPAP initiation was significantly worse in those with baseline allergic rhinitis relative to those without baseline allergic rhinitis.
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0602

CPAP USE AND CHANGE IN BMI IN PATIENTS WITH OBSTRUCTIVE SLEEP APNEA

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Introduction: Obstructive sleep apnea (OSA) is closely associated with obesity and a bidirectional relationship between these two conditions has been suggested. Studies assessing effects of continuous positive airway pressure (CPAP) therapy on body mass index (BMI) have produced conflicting results.
Methods: We reviewed the charts of 108 patients with newly-diagnosed OSA who were started on CPAP therapy. BMI at the time of CPAP initiation was compared to that obtained 1-36 months later. CPAP adherence was assessed 2-6 weeks after the CPAP therapy was initiated. Average daily CPAP use and usage index (percentage of nights CPAP was used for >4 hours) were used as indicators of adherence.
Results: The mean age of the 108 patients (105 men and 3 women) was 61.8±10.2 years. The mean BMI was 36.57±7.66 kg/m^2 (23.01-57.33 kg/m^2) at CPAP initiation and 36.11±7.57 kg/m^2 (22.01-61.02 kg/m^2) after an average of 10 months of follow up. Paired t-tests revealed a small but significant decrease in BMI (-0.41±1.79 kg/m^2, range -6.30 kg/m^2 to 3.08 kg/m^2, P=0.019) with CPAP use. Sixty one patients (56.5%) had a decrease (-1.56±1.46 kg/m^2) and 47 had an increase (1.07±0.86 kg/m^2) in BMI at follow up. There was no significant difference in age, initial BMI or apnea-hypopnea index on the diagnostic polysomnogram between these two groups of patients. The average daily CPAP use was 4.9±2.4 hours and the usage index was 63.2%±33.2%. There was no difference in the adherence variables between those whose BMI increased or decreased at follow up. Conversely, there was no significant difference in change in BMI between those who used CPAP 4 hours or more a night versus those with average nightly CPAP use less than 4 hours. Use of other indicators of adherence including average CPAP use cutoffs of 5 or 6 hours a night or usage index cutoffs of 60%, 70% or 80% revealed similar results. The proportion of patients whose BMI decreased was higher, but not statistically significant, in obese (BMI ≥ 30, n=92) patients compared to that in non-obese (BMI < 30, n=16) patients (59.8% vs. 37.5%, P=0.083).
Conclusion: We found a small but significant decrease in BMI with long-term CPAP use in this predominantly male population with OSA. No clinical or demographic variables evaluated in this study predicted whether BMI would increase or decrease with therapy.

0603

OXIMETRY, POLYSOMNOGRAPHY AND CPAP ADHERENCE IN OBSTRUCTIVE SLEEP APNEA

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Introduction: Polysomnography is considered the reference standard for diagnosis of obstructive sleep apnea (OSA). Oximetry can provide a convenient and inexpensive tool for identifying OSA.
Methods: We reviewed charts of 125 patients who underwent oximetry and/ or polysomnography (PSG) for diagnosis of OSA. The oximetry was followed by either an in-laboratory PSG or an in-home titration using auto-titrating positive airway pressure (APAP) device, followed by fixed pressure PAP administration. We compared the oxygen desaturation index (ODI) on oximetry with apnea-hypopnea index (AHI) in the PSG in the patients who underwent both these procedures. Patients were classified as no, mild, moderate or severe sleep apnea on the basis of oximetry if they had ODI<5, ODI 5-15, ODI 16-30 or ODI>30, respectively. Similar values were used to classify sleep apnea based on AHI obtained from PSG. We also studied the correlation of CPAP adherence variables with ODI and AHI.
Results: Of all patients, 90 underwent oximetry, 85 underwent PSG and 50 underwent both these procedures. The mean age of the patients was 61.1±10.0 years, the mean ODI was 30.0±24.5 and the mean AHI was 34.1±26.2. While we did not find a significant correlation between the AHI and the indicators of CPAP adherence, ODI significantly correlated with both nightly CPAP use (R=0.26, P=0.019) and usage index (percentage of nights CPAP was used for >4 hours, R=0.25, P=0.024). Patients with high nightly CPAP use (>=4hours/night) had a higher ODI than those who used CPAP <4hours/night (34.1 vs. 21.9, P=0.04). Similarly, the mean ODI was higher in patient with usage index above 60% than those with a lower usage index (35.7 vs. 22.6, P=0.02). The AHI, however, was not different in patients with good or poor CPAP adherence. The interval between the oximetry and the PSG recordings in the patients undergoing both procedures was 2.8±2.1 months. There was a high correlation between DI and AHI (R=0.71, P<0.001). Using PSG as gold standard, oximetry misclassified the severity of sleep apnea in 56% of the mild, 77% of the moderate and 15% of the severe sleep apnea patients. The sensitivity of oximetry for diagnosing severe sleep apnea was 69%, specificity was 89%, positive predictive value was 85% and negative predictive value was 76%.
Conclusion: While there were significant differences between oximetry and PSG in diagnosis of OSA, the association of ODI, but not AHI, with CPAP adherence suggests the importance of oximetry in evaluation of patients with OSA.

0604

INSOMNIA SYMPTOMS AND CPAP USE IN OSAS PATIENTS: A DATA MINING ANALYSIS

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Introduction: Insomnia complaint and OSAS are two frequent comorbid situations. But there is no data about the impact of insomnia symptoms on CPAP use. The aim of the study was to assess the occurrence of insomnia symptoms in OSAS patients and its consequences on short and medium-term CPAP use.
Methods: Retrospective study, data collected prospectively. Baseline data were: -Insomnia symptoms, assessed by the Insomnia Severity Index (ISI) -Subjective sleep quality, assessed by the Pittsburgh Sleep Quality Index (PSQI) -Sleeping medication intake (sedatives, antidepressants, hypnotics). CPAP use (hrs/night) was measured at the end of the 1st and 6th month. Data were analyzed using the Segmentation method (Decision Tree learning) which helps to identify very homogeneous groups of subjects with regard to the median value of the ISI score and of the 6th month-CPAP use in the study sample, and to model compliance.
Results: In 156 OSAS patients (AHI=39±21/hr), 128 men, 28 women (age=55±12 yrs, BMI=29.1±6.3 kg/m2, baseline Epworth Score=12±6), with CPAP treatment, median ISI score was 15 and median 6th month-CPAP use was 4.38. ISI score was 14±5, PSQI index was 8±3, and CPAP use at month 1 and month 6 were 3.96±2.44 and 3.83±2.41 respectively. In the homogeneous groups defined by segmentation, CPAP use was not different at the 1st (3.8±2.4 vs 4.1±2.7) and at the 6th month (3.7±2.3 vs 4.2±2.3) in subjects with an ISI score≥15 vs those with an ISI score<15. The ISI scores were not different (12.3±5 vs 14.5±5.7) in subjects whose CPAP use was≥4.38 vs those whose CPAP use was<4.38. Sleeping medication intake was not an explanatory factor for CPAP use.
Conclusion: Insomnia symptoms were highly prevalent in OSAS patients, but had no impact on compliance.

0605

STROKE OR TRANSIENT ISCHEMIC ATTACK AMONG OUR CASES FOLLOWED-UP FOR OSAS

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Introduction: The results of many studies underline the association between sleep-disordered breathing (SDB) and cerebrovascular disorders. SDB, mostly obstructive sleep apnea syndrome (OSAS), is believed to be an independent risk factor of stroke and is related to poor outcome and increased long-term stroke mortality. The present study evaluated the frequency of stroke or transient ischemic attack in OSAS patients.
Methods: Since 1995, 12,548 questionnaires have been completed by the clients of our disorders centers. In 6,356 cases, this was followed by cardiorespiratory polygraphy, intended for assessing the severity of OSAS objectively. Subjects were categorized according to the following criteria: preclinical OSAS (AHI=5-10); mild OSAS (AHI=11-20); moderate OSAS (AHI=21-40); severe OSAS (AHI>40). The prevalence of stroke or transient ischemic attack was ascertained in the patient population studied.
Results: Verifying the independence of stroke or transient ischemic attack from severe OSAS using Pearson's khi square test revealed that in this population, the occurrence of stroke or transient ischemic attack is influenced by OSAS severity (df: 3; p<0.0001). According to evidence from a prospective study, the risk of concomitant stroke or transient ischemic attack is 1.5 times higher in severe, than in mild or preclinical OSAS (RR: 1.58). The odds ratio for OSAS accompanied by stroke or transient ischemic attack was higher for all RDI classes in younger (aged <50 years), than in elderly (more, than 50 years old) patients. Furthermore, the relative influence of BMI was smaller in the subset of younger patients.
Conclusion: RDI is independently associated with the presence of stroke or transient ischemic attack - as well as with BMI and age - as seen in our patient population. The odds ratio (OR) for OSAS and stroke or transient ischemic attack is higher in the younger (50 years old) age group, than among the elderly. Therefore, young patients suffering from severe OSAS stand a higher chance of undergoing stroke or transient ischemic attack.

0606

EFFECT OF POSITIVE AIRWAY PRESSURE USE ON URINARY ALBUMIN EXCRETION IN OBSTRUCTIVE SLEEP APNEA PATIENTS

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Introduction: Albuminuria which reflects the state of microvascular endothelial dysfunction predicts cardiovascular events in subjects with and without established cardiovascular risk factors. Recent study found that Obstructive sleep Apnea was significantly associated with increased urine albumin excretion and this increase may result from the influence of sleep related pathophysiologic changes like intermittent hypoxemia that results in endothelial dysfunction. The relationship between albuminuria in Obstructive Sleep Apnea patients and Positive Airway Pressure treatment has not been previously described.
Methods: Subjects with polysomnography established obstructive sleep apnea were prescribed positive airway pressure treatment according to titration study. Patients with Diabetes, Hypertension, Previous positive airway therapy or medications such as Angiotensin Converting Enzymes were excluded. Urine albumin to creatinine ratio was measured before starting therapy and four weeks after that. Digital compliance cards were analyzed and patients who used their machines less than 4 hours every night were excluded from final analysis.
Results: A total of 16 patients were recruited for the study, All patients were male, And mean age was 43.4, Mean Apnea hypopnea index was 25.9, Mean urine albumin to creatinine ratio was 6.488. One month after positive airway pressure treatment their mean Urine albumin to creatinine ratio was 5.765. P value 0.26
Conclusion: Preliminary results of this study did not reach statistical significance for improvement of microalbuminurea by Positive Airway Pressure treatment. More patients will be recruited to power the study.

0607

OPTIMAL CUT-OFF POINTS FOR THE ADJUSTED NECK CIRCUMFERENCE IN PREDICTING OBSTRUCTIVE SLEEP APNEA

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Introduction: Obstructive Sleep Apnea (OSA) is the most common reason for referrals to sleep laboratories in the United States. Since polysomnography (PSG) is a limited resource, there is considerable interest in clinical prediction rules that could help physicians in prioritizing patients for PSG. The Adjusted Neck Circumference (ANC) [Flemons, AJRCCM 1994] represents such a rule that adjusts measured neck circumference for the presence of snoring, choking or gasping, and hypertension to clinically predict which patients are likely to have OSA as documented on PSG. Our aim was to validate the ANC in our study population.
Methods: We reviewed a database of 799 adult patients who underwent PSG at our hospital-based sleep center between 2/05 and 11/07. We calculated the ANC by extracting the neck circumference (in cm), h/o hypertension (add 4cm), h/o snoring (add 3cm), and h/o choking or gasping (add 3cm). We defined significant OSA as a respiratory disturbance index (RDI) of ≥5 events/hr and calculated the sensitivity, specificity, and area under the receiver-operating characteristic (ROC) curve for various ANC cut-off points in males and females. We then validated the optimum cut-off point obtained by the ROC method using the Youden index (YI), an optimization criteria that identifies the point on the ROC curve with the largest vertical distance from the line of chance.
Results: In males, an ANC of 43.8 cm was the best predictor of OSA with an Area under the ROC Curve (AUC) 0.83, sensitivity-0.84, specificity-0.7 and a YI of +0.54. In females, an ANC of 40.32 cm was the best predictor of OSA with an AUC 0.73, sensitivity-0.74, specificity-0.63 and a YI of +0.38.
Conclusion: ANC is a useful and easily obtainable clinical prediction rule that helps guide selection of patients for PSG, especially in males.

0608

PRESERVED SLEEP QUALITY UNDER SIMULATED ALTITUDE AS ASSESSED BY EEG POWER AND THE ECG-DERIVED SLEEP SPECTROGRAM

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Introduction: Chronic nocturnal hypoxia for 14 successive nights has been demonstrated not to alter attention and working memory in young healthy adults. We hypothesized that preserved sleep stability across hypoxic exposures would explain stable cognitive function. Delta spectral power on EEG during stable sleep as well as high frequency coupling (HFC) on ECG-based spectrogram was adopted as measures of sleep quality.
Methods: Eleven healthy, non-smoking subjects (7 men, 27±1.5 years) were exposed to 9 hours of continuous hypoxia (FiO2 0.13) for 13 consecutive nights. Polysomnography was done at baseline and during 3 time points, at night 3, 7, and 14. In each study, delta spectral power was obtained during stable N2 and N3 sleep. Stable sleep was defined when there was no significant fragmentation in EEG and fluctuation in EMG and cardiorespiratory signals. The time threshold was 2 or 5 continuous minutes for N2 and 2 minutes for N3. The amount of HFC for the sleep period on the ECG-based spectrogram was computed. Randomized block ANOVA was used with EEG delta power and HFC as dependent variables with post hoc Tukey test.
Results: Delta spectral power during stable sleep was not significantly different across the entire hypoxic exposures (p=0.98 for N2; p=0.32 for N3). HFC was different between pre-exposure and mid-exposure (night 7; 52.5±23.6% vs. 39.0±16.7%, p=0.02) but returned to the baseline level at the post-exposure (night 14; 45.4±18.2%, p=0.39).
Conclusion: Preserved EEG delta power during stable sleep and HFC might explain the preserved cognition across the chronic nocturnal hypoxic exposures.

0609

INFLUENCE OF OBSTRUCTIVE SLEEP APNEA ON NOCTURNAL VENTRICULAR ARRHYTHMIAS IN PATIENTS WITH AUTOMATIC IMPLANTABLE CARDIOVERTER DEFIBRILLATORS

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Introduction: Patients with automatic implantable cardioverter defibrillators (AICD) continue to suffer from ventricular arrhythmias that are associated with significant morbidity. Obstructive sleep apnea (OSA) results in recurrent intermittent hypoxia and sympathetic nervous system activity surges which provide the milieu for cardiac arrhythmia development. We postulate that the prevalence of nocturnal clinically significant ventricular arrhythmias is higher among patients with AICD and OSA.
Methods: We prospectively studied 21 men with AICD without concomitant anti-arrhythmic agents. The presence of OSA was determined by overnight polysomnography. Obstructive apneas and hypopneas were classified according to standard criteria. An apnea-hypopnea index

(AHI) >10 events/hour established the diagnosis of OSA. AICD interrogation was used to determine the type and time of onset of clinically significant ventricular arrhythmia (non-sustained VT, sustained VT and VF) in each patient. All patients were monitored for a 6 month period.
Results: Using the threshold of AHI >10 events/hour, OSA was present in 13 patients (61.9%, mean AHI: 24.5 ± 17.5; Age: 66.5 ± 10.8 yrs; BMI: 28.3 ± 3.6), while 8 had AHI<10 (38.1%; AHI: 5.8 ± 2.2; Age: 62.6 ±9.9; BMI: 28.0 ± 3.8). There was a trend toward higher episodes of ventricular arrhythmias in patients with OSA (mean 1.6 ± 1.7 vs. 0.6 ± 1.2 per patient, P = 0.09). However, the higher number of ventricular arrhythmias in patients with OSA was solely due to a significant increase in ventricular arrhythmias occuring between midnight and 6 AM (0.8 ± 1.0 vs. 0.3 ± 0.7, P=0.04).
Conclusion: The results of this study suggest that patients with AICDs and OSA have a higher frequency of clinically relevant ventricular arrhythmias during the night.

0610

MIXED SLEEP APNEA: COMPLEX CONCEPT RATHER THAN OBSTRUCTIVE SLEEP APNEA/HYPOPNEA SYNDROME (OSAHS)

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Introduction: Both mixed apnea and obstructive apnea often coexist in the same individual of OSAHS. Mixed breathing pattern has been included into the concept of obstructive apnea emphasis on ventilatory overshoot. But recently growing evidence of complex sleep apnea was introduced to it. We investigated the variation of apnea patterns focused on mixed apnea in OSAHS patients and compared to the patients without mixed apnea.
Methods: Total 135 patients who diagnosed to OSAHS at the Asan Medical Center since 2006 were studied. Diagnosis of OSAHS was based on the combined assessment of 1) relevant clinical features; 2) overnight polysomnography(AHI>5, scoring was performed by AASM 2007). We compared the change of apnea index(obstructrive;OI, central;CI, mixed;MI)/hypopnea index(HI) in two group('Mixed group; MI=0', n=30 vs. 'Non-mixed group; MI>0 ', n=105) according to sleep stage(REM vs. NREM), body position(supine vs. non-supine) and time of night(early half vs. late half).
Results: In total 135 OSAHS patients (OI=23.4±18.9, MI=4.5±10.0, CI=1.68±4.3, AHI=48.0±21.1), higher MI was positively proportional to CI. In group comparison, 'Mixed group' had significantly higher OI and AHI and marginally higher CI than 'Non-mixed group'. In 'Non-mixed group', there was a significant increment of OI in REM period, dominant OI and HI in supine position and obstructive apnea had the incremental tendency in late half of night. 'Mixed group' showed that MI, CI and HI except OI were higher in NREM period but body position dependent breathing pattern was similar to 'Non-mixed group'. In 'Mixed group', hypopnea was dominant in early half of night, same result as 'Non-mixed group' but mixed apnea was prominent in late half of night.
Conclusion: We investigated the variation of OSAHS according to with or without mixed apnea. Mixed apnea occurred predominantly in NREM period and late half of night with position dependency and had proportional increment to central apnea. Although both type of obstructive apnea and mixed apnea have similar feature such as position dependency and vulnerability to late phase of night, NREM dominance and positive correlation with central apnea of mixed apnea may imply dysregulation of respiratory control rather than classical airflow obstruction in obstructive sleep apnea. Mixed apnea may not subset of OSAHS but another complex pattern.

0611

THYROMENTAL DISTANCE AS A PREDICTOR OF OBSTRUCTIVE SLEEP APNEA-HYPOPNEA IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE PATIENTS

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Introduction: Low thyromental distance has been found to be an independent predictor of obstructive sleep apnea-hypopnea (OSAH) in obese patients. We have analyzed thyromental distance in chronic obstructive pulmonary disease (COPD) patients in order to predict obstructive sleep apnea-hypopnea.
Methods: A cross-sectional study was conducted at the referral sleep laboratory of a tertiary care teaching hospital. 75 eligible patients with a diagnosis of COPD were included. Thyromental distance was measured along straight line from thyroid notch to the lower border of the mandibular mentum with the head fully extended. Whole night polysomnography (Medcare polygraph, Medcare Flaga, Reykjavik, Iceland) was done in all the patients. Cut-off values for thyromental distance was taken as 7.5 cm. OSAH was diagnosed if AHI exceeded 5 per hour.
Results: 36 out of 75 (48%) patients had OSAH. Out of these 36 OSAH patients only five (13.89%) had thyromental distance ≤ 7.5 cm (p value 0.66).
Conclusion: Thyromental distance can not be used as an independant predictor of OSAH in COPD patients.

0612

CEREBRAL HEMODYNAMIC IN SNORERS, MILD AND SEVERE OBSTRUCTIVE SLEEP APNOEA: A NEAR INFRA-RED SPECTROSCOPY (NIRS) STUDY

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Introduction: Sleep disordered breathing (SDB) of obstructive type causes hemodynamic consequences leading to an increased cerebrovascular risk. The severity of SDB at which detrimental circulatory consequences appear is matter of controversy. Aim of the present study is the investigation of cerebral hemodynamics in SDB patients of variable severity using near infra-red spectroscopy (NIRS).
Methods: Nineteen patients with SDB were investigated by nocturnal video-polysomnography (VPSG) coupled with cerebral NIRS. NIRS data were averaged for each patient and a new method (integral) was applied to quantify cerebral hemodynamic alterations.
Results: Nocturnal VPSG disclosed various severities of SDB: snoring (7 patients, apnoea-hypopnoea index (AHI)=2±2/h, range: 0.5-4.5); mild SDB (7 patients, AHI=14±8/h, range: 6.3-28.6); and severe obstructive sleep apnoea syndrome (5 patients, AHI=79±20/h, range: 39.6-92.9). Relative changes of NIRS parameters were significantly larger during obstructive apnoeas (compared to hypopnoeas; mean deoxygenated haemoglobin (HHb) change of 0.72±0.23 and 0.13±0.08 micromol/l per sec, p-value=0.048) and in patients with severe SDB (as compared to mild SDB patients and simple snorers; mean HHb change of 0.84±0.24, 0.02±0.09 and 0.2±0.08 micromol/l per sec respectively, p-value=0.020). In this group NIRS and concomitant peripheral oxygen saturation changes correlated.
Conclusion: This study suggests that acute cerebral hemodynamic consequences of SDB lead to a failure of autoregulatory mechanisms with brain hypoxia only in the presence of frequent (AHI>30) and obstructive respiratory events.

0613

GRADUATION FROM CPAP: IS IT REALLY POSSIBLE?

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Introduction: We occasionally encounter questions from patients with obstructive sleep apnea (OSA) whether CPAP can be discontinued if they reduce weight. Only limited data is available weather it is possible to discontinue CPAP with weight reduction, though weight reduction has been encouraged for almost every over-weighted patients routinely.
Methods: We performed retrospective review of medical charts of all patients diagnosed as OSA who underwent polysomnogram (PSG) and CPAP titration in Toyohashi Mates clinic, Toyohashi, Japan from September 2001 to November 2008. After initial CPAP titration, follow up PSG was performed when the patients requested to be reexamined whether CPAP was able to be discontinued. The demographic and PSG data was analyzed.
Results: We identified total 1459 patients who were followed in our clinic after introduction of CPAP treatment. 1246 were men and 213 were women. Average age, average AHI, mean BMI and mean follow up period were 51.4 years, 52.0, 26.8 kg/m2 and 571.8 days. In 28 patients, CPAP treatment was discontinued due to improvement of AHI to less than 20 in the follow up studies, cause CPAP treatment is not approved by Japanese national insurance system if AHI is less than 20. CPAP was discontinued in 6 patients without intervention (group 1). 16 patients required oral appliances (OA) (group 2) and 6 patients required surgical interventions (tonsillectomy or uvulopalatopharyngoplasty) (group 3). Average BMI change in group 1, 2, and 3 was -1.71, -0.49 and -1.16. Average ESS was 5, 10.4 and 10.33. Average AHI was 11.5, 8.44 and 9.66. Compared with average BMI change, ESS and AHI in patients currently on CPAP (-0.12, 5.25 and 3.89), BMI is more reduced in group 1 (p=0.018), ESS is higher in group 2 and 3 but not in group 1, and AHI is higher in all groups with statistical significance.
Conclusion: Discontinuation of CPAP treatment without intervention seems possible in small group of patients with significant weight reduction. In our patients, ESS was not deteriorated, though AHI score was higher.

0614

POSITIONAL THERAPY FOR OBSTRUCTIVE SLEEP APNEA: AN OBJECTIVE ASSESSMENT OF ITS EFFICACY AND USAGE AT HOME

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Introduction: Positional therapy preventing patients from sleeping supine has been used for many years to treat positional obstructive sleep apnea (OSA). A few studies have demonstrated its efficacy but the actual usage of this therapy at home has never been objectively assessed.
Methods: Ten patients with positional OSA, who refused or could not tolerate CPAP were identified. Nine of these patients, in whom the efficacy of a positional therapy device was confirmed during an overnight study, were instructed to use it every night for 3 months. Objective usage of the device was assessed by an actigraph placed inside the positional device (open study, patients were informed). A third night study was performed at the end of the 3 months period.
Results: During the diagnostic night study, mean apnea-hypopnea index (AHI) was 24.2±10 events/h (49.7±21.8 supine and 6.5±6.6 non-supine), with an average of 48.6±30% of the night spent supine. During the night study with the positional therapy, mean AHI was reduced to 5.7±3.2 events/h (p=0.0018) and the % of time spent supine dropped to 8.1±8.4% (p=0.011). Two of the nine patients stopped using the positional device, one because of a back pain and another because of a clavicle fracture in an accident. Overall the positional device was worn 63±34% of the night (range 9.1 - 96.6%) for an average of 8.2±2.3 hours per night. Six of the seven patients who were still using the device at the end of the study had a third night study with the device: Mean AHI was 5.8±4.1 events per hour with 4.5±5.9% of the night spent supine.
Conclusion: Usage of a positional therapy for OSA over a 3 months period is comparable to the reported CPAP usage and its efficacy persists at the end of this period.
Support (optional): Lausanne University young researcher grant. Swiss Pulmonary Society grant for research.

0615

EFFECT OF MAXILLOFACIAL SURGERY ON THE MORPHOLOGY OF NASOPHARYNGEAL SPACE IN JAPANESE PATIENT

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Introduction: The role of Maxillofacial surgery as a treatment for adult obstructive sleep apnea syndrome (OSAS) remains controversial. Especially in Asian country, skeletal abnormalities are thought to be the great factors of OSAS. So we need more study about application of Maxillofacial surgery to OSAS patients. The aim of this study was to evaluate the effect of Maxillofacial surgery on the morphology of nasopharyngeal space.
Methods: The subjects were 18 adult patients who were operated Maxillofacial surgery at the Ichikawa general hospital with chief complaints of malocclusion. After maxillary or mandibular bone was departed, we pulled maxillary and mandibular bones maximally as a simulation of Maxillary mandibular advancement (MMA) procedure. The fiberoptic pharyngoscope was positioned transnasally before and after maxillary and mandibular simulation to measure the nasopharyngeal space actually.
Results: After maxillary movement, the mean occipitofrontal and lateral diameter of the nasopharyngeal space were significantly enlarged from 7.2mm and 24.0mm to 13.3mm and 26.0mm, respectively. After mandibular movement, the mean occipitofrontal and lateral diameter of the nasopharyngeal space were significantly enlarged from 10.5mm and 28.2mm to 14.3mm and 36.0mm, respectively. The mean area of the nasopharyngeal space were also enlarged significantly after maxillary and mandibular movement (from 128.5mm2 and 300mm2 to 320mm2 and 542mm2 respectively). Compared maxillary movement with mandibular movement, the occipitofrontal diameter was enlarged more widely when maxillary bone was pulled, though the lateral diameter was enlarged more widely when mandibular bone was pulled.
Conclusion: The results indicated that Maxillofacial surgery affect the soft tissue of the upper airway. This study also suggested the difference of the enlargement pattern of the nasopharyngeal space, compared maxillary advancement with mandibular advancement. This difference was considered according to the anatomy of the Upper airway dilator muscles(UAE).

0616

POTENTIAL ROLE OF FATTY ACID BINDING PROTEIN 4 IN INTERMITTENT HYPOXIA-INDUCED FOAM CELL FORMATION

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Introduction: Obstructive sleep apnea (OSA) which is characterized by intermittent hypoxia (IH) during sleep, has emerged as an independent risk factor for cardiovascular disease, and more specifically coronary heart disease. IH is associated with disruption of lipid metabolism, activation of inflammatory pathways, and endothelial dysfunction. More recently, IH was shown to induce atherosclerotic lesion formation in a mouse model of atherogenesis. However, the molecular mechanisms underlying IH-associated atherogenesis remain largely unknown. Adipocyte fatty acid binding protein (FABP4) plays a critical role in the process of atherosclerosis and inhibition of FABP4 effectively reduces atherosclerotic lesion formation, supporting the notion FABP4 may also play a potential role in IH-induced atherogenesis.
Methods: We used an in vitro monocyte cell line model to test cellular cholesterol accumulation, cellular cholesterol efflux, and foam cell formation under carefully controlled IH exposures with or without treatment with FABP4 siRNA. The THP-1 cell line was exposed to IH for 3, 6, 12 and 24 hours. The mRNA expression of receptors for cholesterol uptake (CD36, SRA) and cholesterol transporter for cholesterol efflux (ABCA1) were also examined by real-time RT-PCR.
Results: IH induced increased mRNA and protein expression of FABP4 in a time-dependent manner. IH was associated with increased level of intracellular cholesterol and decreased cholesterol efflux, and increased foam cell formation. IH increased expression of CD36 and SRA and decreased the expression of ABCA1. Furthermore, down regulation of FABP through a specific siRNA markedly decreased IH-induced cellular cholesterol accumulation and foam cell formation and partially reversed the alterations in gene expression (CD36, SRA and ABCA1) and cholesterol efflux induced by IH.
Conclusion: FABP4 plays an important role in IH-induced foam cell formation and may become a viable therapeutic target aiming to prevent and potentially reverse OSA-associated atherosclerosis.
Support (optional): University of Louisville SOM Research Award, AHA SDG 0930129N, NIH grants HL-086662 and HL65270, and the Children's Foundation for Sleep and Neurobiology Research

0617

PREDICTORS OF CONTINUOUS POSITIVE AIRWAY PRESSURE ADHERENCE IN A RANDOMIZED CONTROLLED TRIAL

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Introduction: Optimal continuous positive airway pressure (CPAP) adherence is often difficult to attain in clinical research involving obstructive sleep apnea consequently affecting interpretability of data. We therefore sought to identify characteristics that may predict CPAP adherence in an interventional trial.
Methods: CPAP adherence was assessed in consecutive participants randomized to receive active CPAP or sham (sub-therapeutic) CPAP over an eight-week period as part of the Oxidative Stress in Sleep Apnea and Cardiac Disease study. Objective adherence data was obtained as recorded with electronic compliance meters. Acceptable adherence was defined as CPAP usage of ≥4 hours for 70% of the days. Logistic regression analyses were performed to examine the association of acceptable adherence and subject characteristics.
Results: The analytic sample comprised 38 participants: 49.7 ± 11.3 years of age, 55.3% men, 55.3% Caucasian, Body Mass Index (BMI): 35.7 ± 8.0 kg/m2, treatment CPAP 9.5 ± 2.1cm H2O, RDI= 38.9 ± 23.1 (median=34.7) and CPAP adherence= 60.1 ± 31.3% (median=68.1%). No significant association was observed with CPAP adherence and sex, race, BMI, RDI or optimal CPAP pressure. CPAP adherence was associated with age and randomization assignment. Mean age of subjects with acceptable and unacceptable adherence was 56.0 ± 10.2 vs. 43.4 ± 8.8 years respectively (p=0.0002). For every year increase in age, subjects had a 17% increased odds of having acceptable adherence (OR=1.17, 95% CI: 1.05-1.31). Of subjects randomized to treatment, 70.0% had acceptable adherence; while only 22.7% of those assigned to sham CPAP had acceptable adherence (p=0.02). Subjects randomized to treatment were 7.8 times more likely to have acceptable adherence than those randomized to sham CPAP (OR=7.84, 95% CI: 1.85-33.23).
Conclusion: Increasing age and randomization to treatment are predictors of CPAP adherence in this interventional trial.
Support (optional): This work was supported by NIH HL079114-02, RR00080, and RR024989.

0618

TC-99M HMPAO BRAIN SPECT FINDINGS IN PATIENTS WITH OBSTRUCTIVE SLEEP APNEA SYNDROME

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Introduction: The incidence of stroke is high in patients with obstructive sleep apnea syndrome (OSAS) especially in the early morning hours. As an underlying mechanism several studies demonstrated reduced cerebral blood flow velocities in patients with OSAS during sleep, but the corresponding findings of regional brain perfusion are not well established. The aim of this study was to evaluate the regional brain perfusion findings in OSAS patients.
Methods: Brain perfusion SPECT studies were done in 23 OSAS patients (8 F, 15 M; aged 51 ±9 years). Patients were divided into two groups according to their apnea hypopnea indexes (AHI) as mild OSAS (8 patients with AHI= 5-15) and severe OSAS (15 patients with AHI >30). Tc-99m HMPAO (740 MBq) was injected in the morning of polysomnography during patients' awakening. Brain images were acquired 60 minutes later with a dual-headed gamma camera.
Results: In patients with severe OSAS cerebral blood flow ratios were significantly lower in the entire cerebrum, right and left cerebral hemispheres ($p<0.05$). Region based comparison revealed bilateral decreased perfusion in frontal and parietal lobes of patients with severe OSAS ($p<0.01$). No difference was observed between the two groups in respect to cerebellum, temporal and occipital lobes.
Conclusion: We conclude that severe obstructive sleep apne syndrome is associated with the risk of ischemic stroke because of significantly decreased cerebral perfusion.

0619

ROLE OF LEUKOTRIENE B4 IN INTERMITTENT HYPOXIA-INDUCED ATHEROGENESIS

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Introduction: Obstructive sleep apnea (OSA), which is characterized by intermittent hypoxia (IH) during sleep, has emerged as an independent risk factor for cardiovascular disease. Indeed, IH may induce atherosclerotic lesion formation in a mouse model of atherogenesis. The LTB4-BLT1 axis appears to play a critical role in the formation of atherosclerotic lesions in an animal model of apoE-/-/Blt1-/- transgenic mice. Furthermore, LTB4 production was increased in OSA patients and negatively correlated to hypoxic levels during sleep, with CPAP therapy decreasing LTB4 production.

Methods: We used an in vitro monocyte cellular model to test macrophage transformation, activation of inflammatory pathways, cellular cholesterol accumulation and foam cell formation following IH exposures. The THP-1 cell line was exposed to IH for 3, 6, 12 and 24 hours. LTB 4 production was assessed by ELISA. Macrophage transformation was assessed by flow cytometry using specific cell lineage markers. Induction of inflammation was examined by measuring TNF-α, IL-1, and IL-6 production, and standard assays were used for cholesterol trafficking and foam cell formation before and after exposure to oxidized LDL.
Results: IH induced increased production of LTB4 as well as the expression of 5-LO and LTA4H, the key enzymes for producing LTB4. IH was associated with transformation of monocytes to activated macrophages, as evidenced by increased expression of CD11b, CD14 and CD68. In addition, IH also induced the expression pro-inflammatory cytokines, TNF-α, IL-1, and IL-6. IH exposures promoted increased cellular cholesterol accumulation and foam cell formation. Furthermore, U-75302, a specific antagonist for LTB4 receptor 1 (BLT1) markedly attenuated IH-induced changes.
Conclusion: LTB4 plays an important role in IH-induced atherogenesis and may become a potential therapeutic target aiming to prevent and potentially reverse OSA-associated atherosclerosis.
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0620

IMPACT OF TIME ON THE TREATMENT EFFICACY OF MANDIBULAR REPOSITIONING DEVICES

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Introduction: A limited number of studies have measured changes in sleep-disordered-breathing subsequent to treatment with mandibular repositioning devices (MRD). This pilot study assesses changes in efficacy and/or need for routine adjustment to optimize outcomes.
Methods: Seven females and eight males underwent in-home sleep studies (ARES Medical, Carlsbad, CA) at baseline, and one-, two-, three- and six-months subsequent to MRD insertion. Eighty-seven percent (13/15) maintained the same MRD-advancement prior to the month-two study. In all cases no adjustments were made between month-three and -six. Ten of 15 cases were treated by a dentist with no prior experience with MRD therapy but followed validated treatment protocols. Repeated-measures ANOVA and t-tests were used to assess changes across the five time-points.
Results: Pre-treatment, the group mean AHI was 22 events/hr, range 7-54, mild=5, moderate=6 and severe=4. Males and females differed in weight, height, age, BMI, and %-time snoring >30dB ($p<0.05$) and snoring >40dB ($p<0.01$). There was no effect of treating dentist on outcome. There were no significant changes in weight, neck size, BMI, %-time-Supine, level of MRD adjustment, or valid recording time that could have contributed to outcomes. The overall ($F=9.31$, $p<0.0001$), supine ($F=8.25$, $p<0.0001$) or non-supine AHI-4% ($F=3.65$, $p<0.01$) as well as Epworth scores ($F=3.62$, $p=002$) were significantly higher pre-treatment vs. all other time points, but once treatment was initiated, no significant changes were observed between months one, three and six. No significant differences in %-time snoring >30dB or >40dB before and during the treatment was likely a result of between-subject variability.
Conclusion: These pilot data are part of a longitudinal study assessing the benefits of MRD therapy. These results suggest that once an MRD is properly adjusted, it provided consistent efficacy across the first six-months of therapy. Additional studies are underway to assess how routinely patients must be retested to confirm efficacy.
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0621

BENEFIT OF MANDIBULAR REPOSITIONING DEVICE THERAPY IN PATIENTS WITH MODERATE AND SEVERE OSA

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Introduction: Practice parameters recommend mandibular repositioning devices (MRD) in patients with mild- to moderate-obstructive sleep apnea (OSA). This study investigates the benefit of therapy in patients with moderate to severe OSA.
Methods: Sixteen females and forty-one males were diagnosed with moderate- (n=33) or severe-OSA (n=24) based on an ARES in-home sleep study. Automated algorithms were used to compute an Apnea Index and an Apnea/Hypopnea Index based on >4% reduction in SpO2 (AHI-4%). Sleep studies were repeated at one- (37%) or two-months (63%) post-insertion, depending on when the MRD was determined to be optimally adjusted based on validated protocols. Outcomes includes changes in AHI, %-time snoring, and changes in Epworth-Sleepiness-Scale (ESS) and Beck-Depression-Index (BDI).
Results: An AHI-reduction >50% was observed 82% of moderate and 96% of the severe patients. For those classified with moderate-OSA (AHI =16-30), 61% had a post-treatment AHI in the normal range (AHI<5), 30% shifted to the mild range (AHI=6-15), 9% were unchanged. For patients with severe-OSA (AHI>30), 13% shift into normal range, 62% into mild and 21% into moderate, and 4% unchanged. Significant reductions in %time SpO2<90% occurred from both moderate-OSA (5+1.2 vs. 2+0.9 SE, $p=0.02$) and severe-OSA (9+1.8 vs. 3+0.9 SE, $p=0.001$) patients. The %-time snoring>40dB in the moderate-OSA group (24+3.1 vs. 13+2.7 SE, $p<0.0001$) showed a greater decrease compared to the severe-OSA group (31+3.3 vs. 22+3.6 SE, $p<0.01$). Only six of 19 case with moderate-OSA and a pre-treatment ESS>10 remained ESS>10 post-treatment. Fifty-seven percent of the moderate-OSA and 83% of the severe-OSA patients with BDI>10 pre-treatment were in the normal range after MRD therapy.
Conclusion: Significant improvement in sleep-disordered-breathing, hypoxemia, snoring, daytime somnolence and depression were achieved in patients with moderate- and severe-OSA with MRD therapy. All patients who fail CPAP should be considered for MRD therapy.
Support (optional): NIH SBIR grant 2R44-DE016772-0

0622

CLINICAL UTILITY OF NECK CIRCUMFERENCE AS A SURROGATE MEASURE OF SLEEP DISORDERED BREATHING IN PREGNANCY

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Introduction: Measurement of neck circumference is considered a standard part of physical examinations in patients with suspected sleep-disordered breathing (SDB) and may be a better correlate of apnea severity than BMI. Recent studies suggest that SDB during pregnancy is associated with hypertension. Pregnant women may be particularly vulnerable to SDB due to relatively rapid weight gain and edema. Therefore simple, non-invasive markers of SDB in pregnancy may be clinically useful.
Methods: A retrospective record review was undertaken of women admitted to the labor and delivery unit. Data extracted included airway assessments obtained on admission as well as demographics. Measurement of neck circumference by anesthesiologists has been a routine procedure in our institution for over 12 months. Diagnoses of chronic hyperten-

sion, gestational hypertension, and pre-eclampsia were obtained from discharge codes.
Results: Data from 1601 records are included. Mean age was 28.8±6.0 years and mean parity was 1.5±1.2. The racial composition was as follows: 70% Caucasian, 14% African American, 11% Asian, 4% Hispanic, and 1% mixed race. Three percent of subjects had a neck circumference ≥40cms which is considered to identify, high risk for SDB in women. African Americans had larger neck circumferences than other races (36.1±3.1cm vs. 35.1±3.0cm in Caucasians vs. 34.2±2.0cm in Asians). A diagnosis of gestational hypertension was present in 8.5% of women and 4.5% received a diagnosis of pre-eclampsia. In a logistic regression neck circumference ≥40cm was an independent predictor of gestational hypertension (odds ratio 2.2 95%CI 1.2-3.9; p=0.01), as well as pre-eclampsia (odds ratio 3.4 95%CI 1.7-6.5; p<0.001) after controlling for covariates such as chronic hypertension, age, BMI, and race.
Conclusion: Neck circumference may have clinical utility in helping to identify pregnant women at risk for pre-eclampsia. The known association between neck circumference and SDB raises the possibility that SDB may potentially explain in part this observed association.

0623

DOES BELIEF IN ONE'S ABILITY AND CONFIDENCE TO USE CPAP PREDICT COMPLIANCE?

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Introduction: A big challenge with CPAP therapy is compliance and predictors of its use. Several studies suggest that behavioral aspects and self-efficacy could be indicative of treatment compliance. This study provides preliminary data using the CPAP Self-Efficacy Scale (CSES) to predict CPAP compliance based upon Bandura's self-efficacy theory: belief in one's perceived capability of a situation.
Methods: Eighty-three patients who underwent diagnostic and CPAP titration PSG in a Midwestern metropolitan sleep center completed the CSES the morning following titration. The CSES consisted of 20 questions asking about one's "level of confidence" with each statement between 0-100%. The scale had four categories: OSA Consequences, Use of CPAP, Barriers to Use, and Outcomes. Scores on the CSES were compared to the initial CPAP download to assess relationship with compliance. Demographics, subjective sleep and daytime functioning measures, and PSG data were also evaluated for relational context to self-efficacy and compliance.
Results: Overall score of CSES significantly correlated with age (r= -.352, p< .01) CPAP titration sleep time (r= .301, p< .01), and optimal pressure sleep time (r= .262, p< .05). Comparing to average CPAP compliance/day (range: 14-230 days) CSES total (r= .308, p< .05) and component CSES Outcomes (r= .354, p< .01) were significantly correlated. To determine variables predictable of CPAP compliance, a forward stepwise regression was performed. Of all the variables assessed, only the Outcomes component of the CSES entered the model (p<. 05), and accounted for 12% of the variance. Excluded variables included age, BMI, gender, daytime functioning, diagnostic AHI and arousal index, CPAP sleep time, and the optimal pressure.
Conclusion: Although preliminary, using a CPAP self-efficacy scale based on Bandura's model predicted CPAP compliance. Further work is needed to assess the benefit of this measurement in a larger population and to determine other factors that could mediate the relationship between treatment self-efficacy and compliance.

0624

CHRONIC INTERMITTENT HYPOXEMIA IN PATIENTS WITH OSAS REDUCES THE MOTOR NERVE FIBERS (UNIT NUMBER) OF MEDIAN NERVE

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Introduction: Intermittent hypoxemia is one of the burden of obstructive sleep apnoea syndrome (OSAS. Our aim is to investigate electrophysiologically the effect of chronic intermittent hypoxemia on motor unit number of the patients with OSAS.
Methods: Sixty two patients with OSAS and fifty seven normal controls were included. Neurological examination in all patients revealed normal findings. Ninety five of patients with a mean age of 45.3 ± 10.6 (14-77) years were male and twenty four with a mean age of 46.7 ± 11.5 (25-70) years were female. According to apnea-hypopnea index (AHI), they were divided in two group (group 1: AHI< 15 and group 2: AHI >15.1). Motor and sensory conductions on median and ulnar nerves were measured and, those with normal conduction values were included; thus, carpal tunnel syndrome or polyneuropathy were excluded. According to automatically incremental method MUNE studies were completed by using Keypoint system (Dantec, Denmark).
Results: There were no statistical differences between two groups in terms of peak amplitudes, distal latency of motor and sensory nerves (p>0.5) and max values of M amplitudes. The mean max. M area was 50.8 ± 20.4 (16.1-121.7) in group 1 and 48.6 ± 20.05 (10.5-111.4)in group 2 (p: 0.55). The mean motor conduction velocity of median nerve in NC and in patients with OSAS were 60.6 ± 5.2(50-71.2) m/s and 58.4 ± 4.3 (51.2-70.8) m/s, respectively (p: 0.010). The mean MUNE values in group 1 and in group 2 were 155.3 ± 41.17 (ranged 46.6 and 251.7) and 127.7 ± 40.2 (ranged 22.8 and 235), respectively (p<0,000).
Conclusion: The significant reduction of the motor nerve fibers estimated by MUNE method led the conclusion that chronic recurrent hypoxemia during sleep may be an independent risk factor for the decrease of motor units and subclinical neuropathy in patients with OSAS.

0625

A COMPARISON OF THE EFFICACY OF CPAP TREATMENT IN SMOKERS VERSUS NON SMOKERS

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Introduction: The current study aims to investigate whether the smoking of cigarettes has any effect on the difference in the Apnea Hypopnea index once Continuous Positive Airway Pressure (CPAP) therapy is introduced to patients diagnosed with sleep apnea.
Methods: A stratified random sample of 50 initial patients diagnosed with sleep apnea was taken from the clinic's database. Twenty five of the subjects were smokers and twenty five were non smokers. Smokers were defined as those who reported smoking half of a package of cigarettes a day, and non smokers were defined as those as who do not smoke at all. First, the difference was found between AHIs of all of the subjects pre and post treatment. Then the mean difference in AHI between smokers and non smokers were compared using an unpaired t-test.
Results: The results of the unpaired t-test comparing average change in AHI once CPAP treatment was introduced showed that there was a significant difference between the mean AHIs for each group (n=48, p=0.005).
Conclusion: The results showed that the smoking of cigarettes had an effect on the difference in the Apnea Hypopnea index once CPAP therapy was introduced to patients diagnosed with sleep apnea.

0626

COMPLIANCE CARD (CC) LIMITATIONS IN PATIENTS WITH A HIGH APNEA-HYPOPNEA INDEX (AHI) ON POSITIVE PRESSURE THERAPY (PPT)

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Introduction: CC use with patients on PPT has been an objective tool in sleep medicine and will be even more relevant with CMS requirements for data in patients on PPT. A common dilemma however is how to manage patients with a high AHI despite good compliance. CC data does not distinguish if the residual events are central or obstructive. Our goal for this study was to establish the spectrum of respiratory events from CC's of patients with a high AHI on PPT.
Methods: We are retrospectively reviewing a series of patients from the Overton Brooks VA Hospital sleep clinic with a high AHI while on PPT. The AHI was determined by the PPT machine CC data. The first 10 patients are reported. All subjects had an AHI>15 based on the CC. These subjects then underwent a sleep study while on PPT to characterize the cause of the high AHI.
Results: Subjects were male, age 55±8.5 with a BMI 36±5.3. CC data showed a mean AHI of 31±12. The sleep study on their PPT machine corroborated the CC data, revealing an AHI 20±10(central apnea index 7.9±9.8). For 40% of our subjects, central apnea (>50% central apnea) was predominant (central index 17±9.0). All four patients take narcotics for pain, but three were not taking narcotics at the time of the original diagnosis of obstructive sleep apnea. As a result, three patients developed central sleep apnea in addition to their obstructive sleep apnea causing the high AHI on the CC.
Conclusion: CC's are a useful tool in sleep medicine but their limitations may hinder the proper management for patients on PPT. From our data set, central sleep apnea must be in the differential for patients with a high AHI on CC's, especially if empirically increasing pressure does not improve the AHI or risk factors are present.

0627

MULTINIGHT RECORDING AND ANALYSIS OF CPAP AIRFLOW IN THE HOME FOR TITRATION AND MANAGEMENT OF SLEEP DISORDERED BREATHING (SDB)

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Introduction: Auto-titrating CPAP machines are increasingly being used for treatment of SDB. Data do not show consistently better outcomes, perhaps because pressure "runaways' and insufficient pressure may offset any benefit of continuous titration. An alternate approach to initial and ongoing titration of CPAP is to repeatedly maintain a fixed pressure (e.g. for an entire night), analyze airflow and change the pressure in the next period as indicated. This has the added advantage of not responding to transient behavior of the airflow signal. The present study is proof of concept for this approach to adjusting CPAP in home.
Methods: 15 male subjects with SDB (RDI 15-100/hr) were given a custom home CPAP device (Fisher & Paykel Healthcare) with a removable USB memory stick to use for several weeks. 11/15 were chronic CPAP users and 4 had had only one conventional in-laboratory CPAP titration night. Using a file on the memory stick, nightly CPAP was varied ± 3 cmH2O around prescription pressure. Machine flow was continuously recorded for at least 2 nights at each pressure. Scoring was manual and offline. From the flow signal alone apnea, hypopnea (airflow < 30% lasting 10s-120s with inspiratory flow limitation) and runs of sustained flow limitation >2min were identified. RDI = (apnea + hypopnea)/ valid signal time was calculated for each night. Obstruction Index (OI), which includes sustained runs of flow limitation, was also calculated (Proc Am Thoracic Soc, Vol 2: A764, 2005). Automation of this scoring is being implemented.
Results: Subjects collected 17±5 nights of data at 4-6 different pressures. As pressure was increased RDI fell and tended to be consistent at each pressure. In each subject, a pressure existed where the RDI and OI were consistently below 10. A clear inflection in the pressure/RDI curve was seen in 6/15 subjects and 11/15 subjects for pressure/OI curve. The inflection point on OI (OI<10 if no inflection point seen), was within 3 cmH20 (average absolute difference,1.5 cmH2O) of the previously prescribed CPAP pressure.
Conclusion: Recording multiple nights of CPAP airflow in the home and analyzing the data for residual SDB provided valuable and consistent information. It shows promise as an alternative to initial in-lab titration and provides the opportunity for re-evaluation of effectiveness of existing titration pressures. Automation of this process, including nightly adjustment of CPAP based on the scoring, may represent an new direction in auto- titration.
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0628

LARYNGEAL DESCENT AND THE SEVERITY OF OBSTRUCTIVE SLEEP APNEA IN JAPANESE

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Introduction: We examined the hypothesis that the evolutionary changes of supralaryngeal vocal cord tract (SVT) to create speech also increased the risk for OSA.
Methods: 139 Japanese patients (113 males, 26 females, mean age 46.3 ± 14.2, mean BMI 27.3 ± 27.2 kg/m2) who visited our sleep clinic suspected having obstructive sleep apnea were included in this study. They has performed polysomnography, and 3-dimentional CT for the evaluation of upper airway. We defined the horizontal segment (SVTH) are the distance between upper incisor and upper anterior edge of the third cervical vertebrae(C3), and the vertical segment (SVTV) are the distance between C3 and vocal cord. SVTH and SVTV are measured using 3-D CT. Ratio of SVTH and SVTV were calculated, and relationship between SVTH/SVTV and AHI were evaluated by Pearson's correlation test.
Results: Mean AHI was 38.6 ± 27.4, SVTH/SVTV was 1.2 ± 0.2. SVTH/SVTV had a significant relationship with AHI, and was found even divided into obese and non-obese group.
Conclusion: Laryngeal descent may be an important factor in development of obstructive sleep apnea in Japanese population.

0629

ASSESS PREVALENCE OF EXCESSIVE DAYTIME SLEEPINESS (EDS) AMONGST POLICE OFFICER: PILOT STUDY

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Introduction: Sleep is an important part of health of police workers and vital to their remaining alert and vigilant at work. We studied sleep/wake habits, as well as prevalence of excessive daytime sleepiness (EDS) amongst a group of police officers and assessed the role of unrecognized sleep apnea if any.
Methods: After IRB approval, we enrolled healthy, police workers who volunteered to participate in the study. Exclusionary criteria included

known sleep disorder or significant cardiopulmonary disease. Officers were administered Epworth Sleepiness Scale (ESS) and Berlin Sleep questionnaires (BQ). They were given an actigraph to wear for a minimum of 4 days and a maximum of 7 days. All of them underwent an overnight portable sleep test using a two-channel recorder - Apnealink® to screen for sleep disordered breathing. Descriptive statistical tests were used along with tests for sensitivity and specificity.

Results: We studied 12 male police officers with mean (SD) age 34 (+/- 7) years and mean (SD) BMI 29 (+/- 2.6). Though mean(sd) total bedtime was 414 min (+/- 106) per night, sleep efficiency for the group was reduced, with a mean(sd) value of 76 (+/- 17) %. Five out of the 12 officers (41%) of the group had an abnormally high ESS of >/== 10. Of those with abnormal ESS, only 1 had OSA defined as an AHI >10. Another officer had abnormal AHI, but had normal ESS. BQ was positive in both officers with abnormal AHI, but was also positive in 3 more subjects with negative Apnealink studies. Sensitivity and specificity of BQ in this small cohort was 100% and 70% respectively. Predictive value of a negative BQ was 100% while the predictive value of a positive BQ was 40%. There was no correlation between ESS, and either total sleep time or sleep efficiency.

Conclusion: Sleep quality in this cohort of police officers is compromised by significantly reduced sleep efficiency. Excessive daytime sleepiness as defined by an abnormal Epworth is seen in as many as 41% of police workers. OSA is seen in only a small proportion of these and other factors including insufficient sleep, inadequate sleep hygiene among others, may be responsible for this. BQ as a screening tool for OSA seems to have good specificity in this population.

0630

LIFESTYLE INTERVENTION AS A FIRST LINE TREATMENT FOR PATIENTS WITH MILD OBSTRUCTIVE SLEEP APNEA - A RANDOMIZED CONTROLLED STUDY

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Introduction: Obesity is the most important risk factor for obstructive sleep apnea (OSA). Although included in clinical guidelines, no randomized controlled studies have been carried out on the effects of weight reduction upon mild OSA. The aim of this prospective randomized 1-year follow-up study was to determine whether supervised lifestyle counseling including an early very low calorie diet (VLCD) could be an effective treatment for adults with mild OSA.

Methods: Seventy-two consecutive overweight patients (BMI 28-40) with mild OSA were recruited. The intervention group (N=35) completed the VLCD program with supervised lifestyle modification, and the control group (N=37) received routine lifestyle counseling. The treatment effect was evaluated with cardio-respiratory monitoring at baseline and after the 12-month intervention. The apnea-hypopnea index (AHI) was the main outcome variable, and the other measurements used were the change in symptoms and the 15D-Quality of Life (QoL) tool.

Results: The lifestyle intervention was found to effectively reduce 1) body weight (-10.7±6.5 kg, mean±SD), 2) AHI (-4.0±5.6) compared to control group (0.3±8.0), (P=0.017). Moreover, according to AHI, the mild OSA was objectively cured in 22/35 (63%) patients in the intervention group, and in 13/37 (35%) patients in the control group (P=0.033 Fisher's exact test). The adjusted odds ratio for having mild OSA was also markedly lowered [OR 0.24 (95% CI 0.08-0.72, P=0.011)] in the intervention group. All common symptoms related to OSA, and some features of QoL improved after the lifestyle intervention. Changes in AHI were strongly associated with changes in weight and waist circumference.

Conclusion: Lifestyle counseling, including an early VLCD is a feasible and effective treatment for the majority of patients with mild OSA. The achieved benefits from the intervention were maintained at 1-year follow-up. The study is an on-going trial with 1 year post-intervention results available shortly.

Support (optional): The study was funded by the Hospital District of Northern Savo. Kuopio University Hospital, the Juho Vainio Foundation, the Yrjö Jahnsson Foundation, the Jalmari and Rauha Ahokkaan Foundation and the Finnish Anti-Tuberculosis Foundation have supported the study with grants.

0631

NONLINEAR COMPLEXITY OF BREATHING IN A MOUSE MODEL OF STROKE AND CHEYNE-STOKES RESPIRATION

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Introduction: Cheyne-Stokes respiration (CSR) often results from ischemic stroke. We hypothesized that cerebral ischemia would produce irregular breathing reminiscent of CSR in the AJ mouse, a strain known for its regular breathing.

Methods: The middle cerebral artery occlusion (MCAo) model was used to induce stroke in four male AJ mice. Four additional male AJ mice underwent a similar sham procedure without artery occlusion. Mice were left to recover for 24 hours after which respiration was sampled at 200 Hz by whole body plethysmography. Measurements included inspiratory time (Ti), expiratory time (Te) and respiratory rate (RR). Linear analysis included comparison of means for Ti, Te and RR and the coefficient of variation of respiratory rate (CVrr). Sample entropy was computed for separate 10s windows within 60s respiratory epochs and compared to 19 dataset surrogates with preserved linear but eliminated nonlinear information. The statistic of nonlinear complexity in breathing pattern was calculated by summing values of significant differences in sample entropy between surrogates and original nonperturbed data.

Results: Each of the four stroke mice and none of the sham mice exhibited a waxing and waning pattern of respiration. No differences between groups were seen in linear analyses. There was a trend toward difference between stroke compared to sham animals in RR (157.4±57.0 vs. 226.9±25.8; p=0.09), Ti (0.12±0.03 vs. 0.09±0.01; p=0.12), Te (0.32±0.13 vs. 0.18±0.04; p=0.12) and CVrr (21.4±8.1 vs. 15.4±6.2; p=0.29). In distinction, there was a statistically significant increase of nonlinear complexity in breathing pattern when comparing stroke to sham animals as measured by the statistic of nonlinear complexity (0.15±0.04 vs. 0.09±0.01; p=0.02).

Conclusion: Ischemic stroke in the AJ mouse results in Cheyne-Stokes respiration. This complex waxing and waning respiratory pattern is not reflected by conventional linear statistics including measurements of variability, but is demonstrated by determinants in nonlinear complexity.

0632

POSITIVE AIRWAY PRESSURE DEVICES AND DELIVERY INTERFACES: WHAT'S A DOCTOR TO DO?

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Introduction: Various new devices and mask interfaces have been introduced into the market over past few years for management of sleep disordered breathing. Despite the increase in available options, patient

compliance continues to be a problem. Two major factors that can impact compliance are (1) lack of clear understanding among the prescribing clinicians of the ever changing devices and delivery interfaces available and (2) manufacturers using different terminologies to describe similar features leading to confusing language. These factors may negatively influence optimal equipment being issued and impair patient tolerance and adherence. Proper education for clinicians is an important strategy for ensuring compliance.

Methods: We compared companies that manufacture Positive Airway Pressure (PAP) devices and mask interfaces for the US market. A review of product profiles was carried out using manufacturer internet websites, brochures, user manuals, handouts and patient usage information. A Medline literature search was then conducted to review clinical outcomes using these devices and develop an educational tool for providers.

Results: We identified 54 different machines for PAP therapy. Key concepts in determining the type of PAP device are level of pressure needed, central vs. obstructive processes, co-morbidities, nasal vs. mouth breathing, and facial structure. We have created a progressive strategy for lab titration based on these characteristics. Innovative features like heated humidification, ramp, respiratory pressure relief, data cards and an array of mask interfaces are available to help achieve better overall outcomes.

Conclusion: In the rapidly changing market of durable medical equipment for PAP therapy, a well developed conceptual algorithm can improve clinician's knowledge and provide structured support for delivering optimal patient care.

0633

PATIENTS WITH ACCENTUATED REM-RELATED OBSTRUCTIVE SLEEP APNEA (OSA) MAY HAVE INCREASED HEART RATE VARIABILITY

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Introduction: REM sleep involves relative autonomic instability. Some people have a disproportionate worsening of their OSA during REM sleep, as compared to NREM sleep. While structural abnormalities account for some of this worsening, poor regulation of cardiorespiratory interactions may also be involved. Deranged cardiac parameters may be present in those with accentuated REM-related OSA.

Methods: 89 consecutive patients were identified with respective REM and NREM apnea-hypopnea indices (AHI) from polysomnography. The baseline heart rate (HR) and heart rate variability (HRV) were attained from NREM sleep via sleep study reports in those with a NREM AHI <10 to minimize the tumultuous pairing between sleep apnea and cardiac parameters. Those with a NREM AHI > 10 were excluded. The experimental group included subjects with a REM AHI ≥ 5 that was at least four times greater than the NREM AHI (High REM AHI group). Leftover subjects that did not meet these criteria were placed in the control group (Low REM AHI). The relationship between cardiac parameters and the High REM AHI & Low REM AHI groups was examined.

Results: High REM AHI patients (n=32) had a mean HR of 70.4 bpm, mean HRV of 26.5 bpm, and a mean REM AHI of 36.0. Low REM AHI patients (n=34) had a mean HR of 72.2 bpm, mean HRV of 24.0 bpm, and a mean REM AHI of 4.3. The NREM AHI was similar between groups. Increased heart rate variability was associated with the High REM AHI group (Pearson, p = .063), but there was no correlation between the baseline heart rate and the High REM AHI group (Pearson, p = .492).

Conclusion: Patients with REM related OSA may have increased heart rate variability during sleep. Future research can utilize more specific methodology to validate this finding and assess the significance.

0634

SLEEP AND BREATHING: CARE OF CPAP EQUIPMENT A FACTOR IN COMPLIANCE AND HYGIENE

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Introduction: Compliance with CPAP therapy for obstructive sleep apnea is sub optimal at 30-80% with difficulties of CPAP maintenance and hygiene largely unexplored. This study was designed to test whether patients have difficulty adequately cleaning CPAP interfaces and if contaminated equipment increases problems and eventual abandonment. Regular washing of equipment should be an effective means of controlling bacterial and fungal growth with older interfaces more likely to be contaminated.

Methods: 30 patients on CPAP for more than one month were studied. Clinical global improvement on CPAP was measured as was frequency of cleaning, and type and age of interface. Bacterial and fungal cultures were taken from the interfaces and humidifiers. Cultures were classified, photographed, and colonies counted. Culture growth was so significant on the first 20 patients, that a secondary trial of mask washing and repeat culture was added.

Results: CGI scores noted 63% of the patients much improved or improved. Although the cultures grew mostly normal flora, the colony counts were high; 21% of the patients had 100-500 colonies and 48% grew >2000 colonies per plate. There was no significant correlation of severity or cleaning frequency with colony counts. Mask age was important; with fungal growth from 100% > 1 year old, and only 25% aged 1-3 months. Gram negative bacteria increased almost linearly with mask age. In the secondary trial, interfaces were rewashed, resulting in 90% lower colony counts, unless they were > 1 year old when washing was ineffective.

Conclusion: This pilot study suggests there are high counts of bacterial and fungal flora on CPAP interfaces, despite routine washing, with the older interfaces, more contaminated and resistant to cleaning. Further research will be required to determine whether increasing the frequency of mask replacement is effective at reducing bacterial contamination, and ultimately improve patient outcome by influencing CPAP adherence or infection risk.

0635

SELF-REPORTED SLEEP APNEA IS A POOR PROGNOSTIC FACTOR FOR MOARTLITY IN PATIENTS FROM THE SWEDISH OBESE SUBJECTS STUDY

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Introduction: It is not clear whether severely obese patients reporting sleep apnea have a worse prognosis than could already be explained by other established mortality risk factors.

Methods: The Swedish Obese Subjects (SOS) Study is a non-randomized controlled trial of bariatric surgery versus conventional treatment for the treatment of severe obesity and associatied complications (mean BMI ca. 41kg/m2, see Sjostrom et al NEJM 2007 357 741-52). Self-re-

ported sleep apnea was measured in 3953 patients at baseline who were observed for 54,236 person-years (Mean=13.5 max=21.0 years).
Results: Sleep apnea was reported by 934 patients and was a significant univariate predictor of mortality (HR=1.74 95%CI= 1.40, 2.18). In a range of multivariate models of mortality risk controlling for up to 16 other potential confounders and well-established mortality risk factors sleep apnea remained a significant prognostic factor (Fully adjusted HR=1.29 95%CI=1.01, 1.65).
Conclusion: Self-reported sleep apnea appears to be a significant, but modest, independent prognostic marker of all-cause mortality in obese patients. The apparent relative weakness of this association compared with hazards associated with untreated sleep apnea in the 2 general community cohorts (Hazard ratios above 3.0 Young et al SLEEP 2008 31 1071-8 and Marshall et al SLEEP 2008 31 1079-85) may be caused by the misclassification of patients according to their apnea status using only a self-report measure in the SOS study. It is also possible that this is an indication that the relative risk of mortality attributable to sleep apnea decreases as obesity and other risk factors worsen.
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0636

ORAL APPLIANCE THERAPY FOR TREATMENT OF RESIDUAL OBSTRUCTIVE SLEEP APNEA AFTER UVULOPALATOPHARYNGOPLASTY

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Introduction: Uvulopalatopharyngoplasty (UPPP) is the most common surgical procedure performed to treat obstructive sleep apnea (OSA) with an overall success rate of approximately 40%. To our knowledge, there is currently only one publication regarding the use of oral appliance (OA) as a salvage intervention after UPPP (1). The University of Michigan has established a multi-disciplinary Alternatives to CPAP clinic in which patients with OSA who are unable to use CPAP are evaluated for alternative treatments. Data from this clinic was used to evaluate the efficacy of OA for persistent OSA after UPPP.
Methods: We performed a retrospective chart review to identify patients with residual OSA after UPPP who were subsequently treated with an OA between December 1997 and August 2007. Demographics included age, sex, and BMI. Three polysomnograms were analyzed for each patient; diagnostic baseline, post-UPPP, and while using the OA. Successful treatment of OSA was defined as AHI<10 or AHI<20 with ≥50% reduction while using OA compared both to baseline and to the post-UPPP results.
Results: Sixty-three patients underwent UPPP, with 12 (all male) who subsequently received an OA. Mean age was 41.3±13.7 years and 8 of these (66.7%) met the criteria for successful treatment of OSA. There were no significant differences in demographics between the group who was considered successfully treated versus the group who was not. Mean baseline AHI was 31.8±21.0 and did not change after UPPP (31.2±14.9). There was no significant change in any sleep parameters between baseline and post-UPPP polysomnograms. There was a reduction in total AHI between post-UPPP and OA from 31.2±14.9 to 13.5±15.6 ($p<0.05$). This change was mostly due to a reduction in NREM AHI (30.6±19.0 to 10.3±13.9; $p<0.05$).
Conclusion: The use of an OA for the treatment of residual OSA after UPPP should be considered as a salvage treatment after unsuccessful UPPP.
Support (optional): Reference: (1). Millman R, Rosenberg C, Carlisle C, et al. The efficacy of oral appliances in the treatment of persistent sleep apnea after uvulopalatopharyngoplasty. Chest 1998; 113:992-996

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PARA-MEDIAN TONGUE BASE REDUCTION IN OBSTRUCTIVE SLEEP APNEA

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Introduction: The tongue base may contribute to airway obstruction in patients with obstructive sleep apnea. Recent technologic advances now permit use of radiofrequency energy to ablate soft-tissue. Current methods favor creating a single, wide central zone of tongue muscle reduction. We present a technique whereby two narrower parallel para-median tongue base troughs are fashioned to selectively reduce hypertrophic musculature.
Methods: A polysomnogram establishes a diagnosis of obstructive sleep apnea. Flexible laryngoscopy, preferably performed with the patient supine, determines if the tongue base "statically" and/or "dynamically" obstructs the airway. Intra-operative exposure is achieved with use of a tonsil gag. 10 cc of a suitably diluted anesthetic-vasoconstrictor:saline mixture is injected intra-muscularly to provide tumescence. The radiofrequency-generating hand piece is set at 6. The wand is repeatedly swept posterior-to-anterior from the valleculla to the circumvallate papillae, centered approximately 1.5 centimeters off the midline. The width of each para-median trough is approximately 1.5 cm. A 1.5 cm central zone of tongue tissue is preserved. Exposure is easy when compared to midline tongue reduction procedures because the midline-situated endotracheal tube does not require re-positioning. Each para-median trough is half as wide as the central trough and thus heals more rapidly. Furthermore, healing is facilitated from adjacent untreated medial and lateral tissue as opposed to only lateral healing in the central zone method. If ancillary oral or nasal airway procedures are being performed, the posterior tongue should be treated first.
Results: Early healing reveals moderate edema, a thin-layer eschar, and regional hyperemia. Most patients are symptom-free within fourteen days. Late healing finds tapering of the lateral and medial tongue toward both para-median troughs due to the deposition of collagen. The untreated median zone is of reduced height as a result of scar contracture.
Conclusion: Creating para-median troughs in the tongue base musculature with radiofrequency energy causes primary lateral and secondary central depressions, promotes more rapid healing, and reduces airway obstruction in patients with macroglossia.

0638

BERLIN QUESTIONNAIRE DIAGNOSTIC PERFORMANCE IN PUBLISHED VALIDATION STUDIES

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Introduction: The Berlin Questionnaire (BQ) is an instrument identifying subjects at high risk for Obstructive Sleep Apnea (OSA). Since its initial publication in 1999 the BQ has been validated by polysomnography (PSG) in many studies. Yet the overall diagnostic performance of the BQ across these published studies and the OSA severity threshold that is best detected by the BQ are unknown.
Methods: A search of the indexed literature, and archived SLEEP meeting abstracts identified 26 papers and 32 abstracts making reference to the BQ. Of these, studies that validated the BQ by PSG were included in this analysis. Published data were analyzed and pooled at each OSA polysomonographically defined AHI/RDI severity level to calculate sensitivity, specificity, positive and negative predictive values (PPV &

NPV), positive and negative likelihood ratios (LR+ & LR-), diagnostic odds ratios (DOR) and Youden's J statistics for the BQ.
Results: A total of 10 studies involving 1162 total patients satisfied the inclusion criteria. Using a criteria of AHI/RDI>5 with a daytime sleepiness criteria for OSA the BQ had a sensitivity, specificity, PPV, NPV, LR+, LR-, DOR, and Youden's J static of 0.84, 0.75, 0.93, 0.55, 3.31, 0.21, 15.7 and 0.59, respectively. At this same AHI/RDI without regard to daytime sleepiness, these values were 0.78, 0.63, 0.79, 0.61, 2.09, 0.36, 5.88, and 0.40, respectively. At higher AHI/RDI criteria for OSA sensitivity, NPV, and LR- remained high while specificity, PPV, LR+, DOR, and Youden's J statistic were lower.
Conclusion: In PSG-based validation studies the BQ demonstrated good diagnostic utility for OSA defined by an AHI/RDI>5 with daytime symptoms. The BQ remained a sensitive, but less specific tool for the detection of more severe OSA. These findings support the application of the BQ as a screening tool for OSA with this disease threshold.

0639

PSYCHOLOGICAL AND BEHAVIOR FACTORS IN PATIENTS WITH COMORBID OBSTRUCTIVE SLEEP APNEA AND INSOMNIA

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Introduction: A great proportion of patients with obstructive sleep apnea syndrome (OSAS) also complain of insomnia. It is usaually assumed that these patients' insomnia is secondary to the respiratory disturbances and should resolved after the treatment of their OSAS. However, many of them still complain of insomnia symptoms after the treatment with continuous postive airway pressure (CPAP). The present study was to explore the psychological and behavioral factors that are associated with primary insomnia in patients with comorbid OSAS and insomnia.
Methods: 17 patients with comorbid OSA and insomnia, 22 with OSA only, and 15 with primary insomnia (all males) participated in the study. Insomnia was diagnosed according to DSM-IV criteria. PSG was conducted to all subjects for the diagnosis of OSA (5≤RDI≤30, mild to moderate level). A package of questionaires, including Dysfunctional Beliefs about Sleep Scale (DBAS), Sleep Hygiene Practice Scale (SHPS), Beck Anxiety Inventory (BAI), Beck Depression Inventory (BDI), and Presleep Arousal Scale (PSAS), were administered to evaluate the psychological and behavioral factors that are associated with insomnia.
Results: Patients with comorbid insomnia and OSAS show significant higher level dysfunctional beliefs about Sleep ($F = 5.01$, $p<.05$), maladaptive sleep practices ($F = 5.38$, $p =.005$), anxiety ($F = 7.76$, $p<.005$), depression ($F= 15.59$, $p<.001$), and presleep arousal ($F =13.81$, $p<.001$) comparing to OSAS group. In addition, there is no significant difference between comorbid group and insomnia group.
Conclusion: The results suggest that patients with comorbid OSAS and insomnia demonstrated a psychological and behavioral profile similar to primary insomnia. In addition, previous research showed no correlation between OSA and insomnia symptoms in comorbid patients. The cognitive and behavioral aspects of sleep should be addressed in the evaluation and treatment for the sleep disturbance in patients with comorbid OSA and insomnia.

0640

MODAFINIL EFFECTS DURING ACUTE CPAP WITHDRAWAL: A RANDOMISED CROSSOVER DOUBLE-BLIND PLACEBO-CONTROLLED TRIAL

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Introduction: Obstructive sleep apnea (OSA) patients may temporarily stop continuous positive airway pressure (CPAP) therapy for reasons such as travel, or upper respiratory tract infection. Such treatment "holidays" may be associated with neurobehavioural decline. Pharmacotherapy with a wakefulness promoter may prevent or ameliorate this decine. We hypothesised that treatment with 200mg modafinil during acute CPAP withdrawal would improve neurobehavioral performance.
Methods: CPAP compliance was monitored at-home for 7 nights. Patients were then admitted to the laboratory for 3 consecutive nights: CPAP was used for the first night, followed by a baseline day and then withdrawn for the two subsequent nights (nasal airflow monitored). On each of the mornings, following the two CPAP withdrawal nights, patients received treatment A (200mg modafinil or placebo) in a randomised, double-blind, cross-over fashion. Participants repeated the protocol but received the alternate treatment (treatment B) after 5 weeks washout. From 30min post administration patients completed a Karolinska Sleepiness Scale, a 10min psychomotor vigilance task (PVT) and a 20min driving simulation (AusEd) bi-hourly from 08:00 to 20:00. The effects of treatment were analysed using mixed models of changes from baseline.
Results: 21 male OSA (mean±SE; Age 55±2 years, CPAP used 7.1±0.2 h per night at-home) completed the protocol. During CPAP withdrawal, modafinil treatment resulted in faster mean reaction time (-11.0±6.7 vs. 20.8±6.8 ms) and fewer lapses of attention (-0.5±0.4 vs. 0.7±0.4) on the PVT, compared to placebo (all $p\leq 0.0002$). In addition, modafinil reduced the StD of the median lane position (-6±1 vs. 0±1 cm; $p<0.0001$), improved mean reaction time (-0.01±0.02 vs. 0.06±0.02 s; $p\leq 0.0002$) and resulted in fewer lapses to a concurrent task (-0.02±0.04 vs. 0.09±0.04; $p\leq 0.01$) during a driving simulation, compared to placebo. Modafinil also improved subjective sleepiness, compared to placebo ($p\leq 0.01$). Sleep disordered breathing was evident during CPAP withdrawal with a combined mean AHI for the two nights of 39.5±20.
Conclusion: Modafinil may prevent the decline of daytime function and sleepiness in OSA patients who require short-term cessation of CPAP.

0641

THE USE OF NONINVASIVE AUTOMATA SERVOVENTILATION IN ACUT ISCHEMIC STROKE

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Introduction: The BiPAP AutoSV (ASV) devices are specifically designed to be the best choice for managing complicated sleep-disordered breathing (SDB) patients. We have observed the usefulness of BiPAP AutoSV among patients suffered SDB and diagnosed with acut ischemic stroke. We hypothesized that ASV would be improving the apnea/hypopnea index (AHI) and oxygen saturation index (ODI).
Methods: Overnight polysomnography (PSG) was performed in 13 subject /mean age: 67 SD13 y, NIH scores: 10 SD 4) with acut ischaemic stroke, after it had been diagnosed on second days in the ICU. We have not seen hypnoid disfunction of consiousness in any patient. BIPAP AutoSV had been used for 7 days during sleep time on all patients, following PSG was performed on the seventh day.

Results: Cheynes-Stokes (CSR) breathing disorder 4 patients /apnea-hypopnoe index (AHI): 44,3 SD 7,5, oxygen saturation index (ODI): 43,2 SD 5,9, and mixed, central (CAS) and obstructive apnea (OSA) at 7 patients (AHI: 40,1 SD 174, ODI: 44,4 SD 13,2) were observed. Treatment AHI and RAI were both significantly lower using ASV. At patients with CSR the AHI were 3,8 SD 1,7, the ODI 3,8 SD 3,4, at patients with mixed apnea the AHI turned to 4,8 SD 2,4, ODI 4,83 SD 1,8. The BIPAP AutoSV was unsuccesfull in two cases cause of complex aphasia.
Conclusion: The AutoSV device appears to be an effective treatment of both CSR and mixed central and obstructive apnea syndromes in acut ischemic stroke. The AutoSV is hardly useful in patients with aphasia because of their low compliance.

0642

AFTER TRANSITION FROM LABORATORY BASED TO PORTABLE SLEEP STUDIES, ARE PATIENTS WHO NEED BILEVEL AIRWAY PRESSURE RECEIVING IT?

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Introduction: Bilevel airway pressure (BPAP) is used for patients unable to tolerate CPAP. In November, 2004 the JAH-VA implemented extensive changes in OSA diagnosis and treatment. Prior to changeover, patients were diagnosed in the sleep laboratory, and the technician determined per protocol whether to use BPAP. After changeover, staff triaged patients to receive a portable home sleep monitor (PHSM) or in-lab polysomnogram, depending on patient willingness to do PHSM and concomitant diagnoses. Patients with inconclusive/negative PHSM were followed-up in the laboratory. For PHSM patients, auto-titrating CPAP was prescribed when warranted, so BPAP prescriptions were curtailed. We questioned if sicker patients were better able to comply with BPAP than CPAP, and whether patients who needed BPAP were receiving it after the changeover.
Methods: We included all patients receiving a sleep study at JAH-VA from January 2001-September 2006 and divided them into Group A: After-changeover and Group B: Before-changeover. We compared proportions of patients receiving BPAP between Groups A and B using chi-square, and compliance between BPAP and CPAP overall and among sicker patients as indicated by the Charlson morbidity index (CMI).
Results: Of N=1286 and N=1515 in Groups A and B respectively, 186 patients received BPAP. 100% and 56% of Groups B and A were seen in the sleep lab. Overall, 7.85% vs 5.61% of Groups A and B received BPAP (p=0.018). 13.3% of Group A patients seen in the sleep lab received BPAP. Among those with a CMI $\geq$ 2, 10.1% versus 6.6% received BPAP in Groups A and B (p=0.037). Compliance was better for BPAP than CPAP for patients with a CMI $\geq$ 2 (OR =2.3, p=0.003) but not for those with a CMI =0 (OR =0.88, ns).
Conclusion: BPAP enables sicker patients to better comply with treatment. Competent triage of sicker patients to the sleep lab helps assure that BPAP prescriptions reach the appropriate patients.

0643

EFFECTS OF LOW-DOSE ACETAZOLAMIDE ON SLEEP IN MOUNTAINEERS AT HIGH ALTITUDE

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Introduction: Altitude sickness is a problem for mountaineers; to combat altitude sickness, they take acetazolamide, a carbonic anhydrase inhibitor that speeds up acclimatization. The present study evaluates the effects of acetazolamide on sleep parameters at high altitude.
Methods: Twenty healthy mountaineers (19 men, 1 woman) completed this study during their climb from Lukla to base camp at Mount Everest (Kathmandu, 17,800 ft), an approximate 9-day climb. Subjects were randomized into 2 groups (acetazolamide [125 mg] vs. placebo) in a double-blind manner. Subjects were assessed for OSA with portable monitors for 3 nights while at base camp, and sleep diary and actigraphy data were collected for 10 nights. Sleep quality (SQ) and sleep refreshment (SR) % were obtained from the sleep diaries. Total sleep time (TST, hrs), number of awakenings (#W, #/night), sleep efficiency (SE, %), % sleep, wake after sleep onset (WASO, min), and sleep latency (SL, min) were obtained from actigraphy.
Results: For the majority of the objective sleep parameters (TST, # W, SE, WASO) and one of the subjective sleep parameters (SR), the placebo group's sleep parameters consistently dropped at day 3 and then rose steadily until day 7. For TST, # W, SE, and WASO, the lowest sleep parameters of the entire week occurred on day 3. From day 3 on, most of the sleep parameters dramatically improved, with increasing improvement of the sleep parameters for the drug vs. placebo groups observed starting at day 3. Five (drug group) and 6 (placebo group) subjects were diagnosed with OSA. Higher TST, SE, % sleep, SQ, and SR, and lower # W and WASO were found for subjects in the drug group who had OSA than those who took the placebo. The subjects who didn't have OSA in the drug group showed positive results in some of their sleep parameters (TST, #W, SE, WASO, %sleep, SQ, SR). Paradoxically, in the placebo group, the subjects who had OSA had better sleep parameters in TST, SL, and SQ, than those without OSA.
Conclusion: There was an advantage for the group taking acetazolamide. The subjects in the placebo group had more decreases in sleep quality and quantity, since they may have had more difficulty adjusting to the high altitude compared to those in the drug group. During the first 3 days of the study, all of the objective sleep parameters demonstrated that subjects in the drug group acclimated faster than those in the placebo group. Lastly, subjects with OSA in the drug group acclimated faster than those with OSA in the placebo group.
Support (optional): Respironics, Inc. loaned portable monitoring equipment for the study.

0644

CHRONIC VERSUS PREGNANCY-ASSOCIATED HABITUAL SNORING AND MATERNAL BLOOD PRESSURE

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Introduction: Several reports suggest that habitual snoring (HS) during pregnancy (as a marker for sleep-disordered breathing) is associated with gestational hypertension. One potential confounding factor may be the duration of symptoms. New onset HS during pregnancy conceivably could have health ramifications that differ from those of chronic HS, to which cardiovascular and other systems might adapt over a more extended timeframe. However, whether new onset HS during pregnancy is a risk for hypertension is unknown.

Methods: Pregnant women were recruited from obstetric clinics during their last trimester of pregnancy and invited to complete several sleep questionnaires. Habitual snoring was defined as snoring ≥3 nights/week and was considered pregnancy-associated if it began during pregnancy.
Results: Of 429 women studied (mean age 30.1±5.8 years), 66% reported HS (28% with chronic HS and 38% with pregnancy-associated HS). There was a significant difference in pre-pregnancy BMI between chronic HS, pregnancy-associated HS, and non-HS (29.2±8.5kg/m^2 vs. 26.8±7.5kg/m^2 vs. 24.0±5.5kg/m^2 respectively; p<0.001). In total 22% of women with HS had gestational hypertension compared to 9% of women without HS (p<0.001). The proportion of women with gestational hypertension was similar between those with chronic HS and those with pregnancy-associated HS (21% vs. 23% respectively). In a logistic regression model with age, race, gestational age at delivery, smoking status, and pre-pregnancy BMI, HS was independently associated with gestational hypertension (odds ratios 2.0 [95%CI 1.1-3.7] p=0.02). The risk of gestational hypertension was not different between those with chronic HS or pregnancy-associated HS.
Conclusion: Our findings suggest that any adverse impact of habitual snoring during pregnancy on maternal blood pressure is similar regardless of whether habitual snoring preceded pregnancy or developed in association with pregnancy. Obstetricians should be aware of the importance of asking about habitual snoring not only initially but also during routine prenatal visits later in pregnancy.
Support (optional): University of Michigan Institute for Research on Women and Gender; University of Michigan Institute for Clinical and Health Research Seed Pilot Grant F021024; Gilmore Fund donation

0645

QUALITY OF PORTABLE MONITORING STUDIES WITH AUTOMATIC CPAP TITRATION FOR SLEEP APNEA IN HOSPITALIZED PATIENTS

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Introduction: Portable monitoring (PM) studies with auto-CPAP titration have been used in selected patients with obstructive sleep apnea syndrome (OSAS) in the outpatient setting. Inpatient data using this approach is lacking. We aim to assess the quality of PM tracing in highly suspected OSAS (CPAP-naive) subjects placed on auto-CPAP treatment in hospitalized patients.
Methods: We enrolled CPAP-naive patients hospitalized in a tertiary medical center with a high probability of OSAS, previously determined by validated clinical prediction models. Each subject underwent a full-night unattended auto-CPAP titration studied with a type III PM. Quality of PM tracing was assessed by an investigator blinded to the study results. Patients were followed up with a full-night attended split study in a sleep laboratory.
Results: 138 patients were screened and 5 patients withdrew during auto-CPAP titration session. 33 patients completed PM with auto-CPAP titration. Mean BMI was 46.3 (SD±12.9). Data loss occurred in one patient. Quality of PM recordings was diagnostic in 20 patients (62.5%), suboptimal but readable in 7 (21.9%), and unreadable in 5 (15.6%). Intermittent mask air leaks occurred in 78.1% of patients; however, 84.9% were willing to use CPAP at home. 18 patients had follow-up attended overnight split-study polysomnograms, 14 (90.9%) of which were diagnostic of OSAS. There was no statistically significant difference in CPAP level obtained by auto-CPAP vs. split-study attended polysomnogram (P>0.05); mean difference in CPAP pressure was -1.9 (range -4.2 to 0.4).
Conclusion: Frequent mask air leaks occurs in unattended inpatient auto-CPAP titrations. No statistically significant differences in optimal CPAP pressures were obtained between auto-CPAP and attended sleep laboratory CPAP titration. Quality of PM with auto-CPAP recordings in this population varied. We recommend a careful patient selection for auto-CPAP titration, and PM recording assessment by a sleep specialist and follow-up attended sleep lab studies in all patients.

0646

THE ALTERED CORTICAL EXCITABILITY IN PATIENTS WITH UNTREATED OBSTRUCTIVE SLEEP APNEA SYNDROME

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Introduction: To investigate cortical excitability in patients with obstructive sleep apnea syndrome (OSA) during wakefulness,
Methods: we consecutively recruited 33 untreated OSA (30 male, mean age 47.2 yrs, mean apnea-hypopnea index 35.3/hour) and 38 age-and sex- matched normal subjects mean apnea-hypopnea index 3.1/hour. Obtained TMS parameters were resting motor threshold (rMT), motor evoked potential (MEP) amplitudes, cortical silent period (CSP), and intracortical inhibition (ICI) and facilitation (ICF). The parameters were measured in the morning (9-10am) more than 2 hours after arising and compared them between patients and controls. The Epworth Sleepiness Scale (ESS), and Stanford Sleepiness Scale (SSS) were also measured before TMS study.
Results: ESS was significantly higher in OSA patients (10.3±5.2) than in normal controls (2.5 ±1.8, p < 0.001). OSA patients showed significantly a higher rMT and a longer duration of CSP at 120, 140, 150% rMT intensities (t-test, p< 0.001). ICI (2, 3 ms) and ICF (10, 15 ms) were also increased in patients compared to normal subjects (p < 0.05). MEP amplitudes were not different between patients and normal subjects in all stimulus intensities (120, 140, 150% rMT). ESS showed the positive correlation with rMT and ICI and the negative correlation with CSP and ICF values.
Conclusion: The present TMS study suggests that OSA patients have alterations of cortical excitability in untreated OSAS patients during wakefulness. Our findings may show the result of an imbalance of cortical excitability toward a state of enhanced inhibition in OSA brains.

0647

TREATMENT EFFECT OF CONTINUOUS POSITIVE AIRWAY PRESSURE ON EVENT-RELATED POTENTIALS AND CONTINUOUS PERFORMANCE TEST IN UNTREATED PATIENTS WITH OBSTRUCTIVE SLEEP APNEA SYNDROME

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Introduction: To evaluate the changes of attention before and after therapeutic continuous positive airway pressure (CPAP), we measured the P300 and Continuous Performance Tests (CPT) in obstructive sleep apnea syndrome (OSA) patients before and after CPAP treatment.
Methods: Auditory & visual P300 studies and CPT were performed in 47 patients (M:F=45:2, mean age 42.3 ± 5.3 years) with OSA (mean apnea-hypopea index=53.7/hr, range 10.4~99.6/hr) and 35 healthy control (M:F=22:13, mean age 40.6 ± 10.1 years). The diagnosis of OSA was based on standard criteria using nocturnal polysomnography. OSA

patients had repeated auditory & visual P300 studies after 6 months of therapeutic CPAP.
Results: The auditory P300 was significantly prolonged mean latency and decreased mean amplitude at fronto-centro-parietal areas in OSA patients compared to those of normal controls ($p < 0.05$). The visual P300 was significantly prolonged mean latency and non-significantly decreased mean amplitude at fronto-centro-parietal areas in OSA patients. In all three steps of CPT, mean correction rate was non-significantly lower in OSA patients than that in control group ($p>0.05$). After CPAP treatment, the auditory P300 latency was shortened at all electrodes although it did not reach statistical significance ($p>0.05$). The visual P300 latency, amplitudes of auditory and visual P300 was not changed by therapeutic CPAP for 6 months ($p>0.05$).
Conclusion: Our findings in ERP and CPT may support that untreated OSA patients had significantly impaired attention deficits. Successful CPAP treatment induced a shorter latency of auditory P300 but not in visual P300 latency, amplitudes of auditory and visual P300.

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INVESTIGATING THE PREVALENCE OF OBSTRUCTIVE SLEEP APNEA IN PATIENTS REQUIRING MEDICAL INTENSIVE CARE

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Introduction: Obstructive sleep apnrea (OSA) may be caused or exacerbated by severe systemic illness due to a general adverse effect upon a variety of central respiratory centers. However, OSA is common and its occurrence in any given patient might be the result of chance. Nevertheless, previous studies including documentation of the autonomic effects of OSA suggests that extremely ill patients are at great health risk when OSA is a concomitant issue. As such, more information concerning the prevalence of OSA in the MICU is needed.
Methods: Prospective Observational Study. Data was compiled over a 47 day period. Forty-four of 131 consecutively encountered MICU patients (33.6%) were entered into this study. Eighty-seven individuals were excluded; 44 required ventilatory support, 3 were less than 18 years of age, 2 died during screening, 20 were discharged or unavailable for intended polysomnography (PSG) and permission could not be obtained in 18 cases. Attended, overnight, portable PSG studies, utilizing standard methodologies were performed on every patient. All studies were scored by an individual board certified in sleep medicine.
Results: The 44 subjects in the study consisted of 21 males (48%) and 23 females (52%). The mean (+/-SD) age of the subjects was 57.2 +/- 21.1, with a range of 19 to 91. The mean body mass index was 28.5 +/- 7.3. Using an apnea/hypopnea index (AHI) of 5, 10, 15 and 20 respectively as criteria for the diagnosis of OSA, 91%(95% CI: 78%~97%), 82% (67%~92%), 68% (52%~82%),and 52%(37%~68%) were diagnosed with OSA. The median AHI was 22.5 (interquartile range, IQR, of 13 to 41.5), with a median baseline waking oxygen saturation of 98% (IQR of 97% to 100%), and median oxygen saturation low value of 88% (IQR 84% to 92.5%). Two severity of illness scores (APACHE II and SOFA respectively) did not correlate with the severity of OSA as defined by AHI. The mean score of APACHE II and SOFA were 17.7 +/- 7.0 and 4.7 +/- 2.9 respectively. The only sleep variable that correlated with either of the severity of illness scores was the percentage of stage 1 NREM sleep (Pearson coefficient 0.42, $p=0.003$).
Conclusion: Sleep apnea is a relatively common multifactorial health problem which is a known risk factor for hypertension, and vascular disease including stroke. Recognizing the high prevalence of OSA in the MICU population, as such presents an opportunity for therapeutic intervention which might reduce overall morbidity and mortality in this patient population.

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UPPER AIRWAY MEASUREMENT IN KOREAN MALE PATIENTS WITH OBSTRUCTIVE SLEEP APNEA SYNDROME

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Introduction: To investigate the upper airway changes in obstructive sleep apnea-hypopnea syndrome (OSA) patients, we measured cross-sectional areas of the upper airway [retropalatine (RP) and restoglossal (RG) regions] and volumes of upper airway structures on upper airway MRI in OSA patients and healthy subjects.
Methods: The Apnea/Hypopnea index (AHI) of OSAHS patients was calculated by overnight polysomnography whereas apnea-hypopnea screening for healthy subjects was performed by a portable screening device. Upper airway MR images were obtained in healthy subjects and OSAS patients using a 1.5-T MRI scanner. The following parameters were measured on MRI using Analyze 6.0 software: (1) mean area, minimal area, vertical and horizontal lengths of the minimal area in RP and RG region; (2) volumes of RP and RG airway, soft palate, lateral pharyngeal wall, lateral pharyngeal fat pad and tongue.
Results: Twenty-three OSA patients and 17 healthy subjects were included. Body mass index (BMI) and AHI were significantly higher in patients (BMI 27.7±2.5, AHI 56.8±22.3) than healthy subjects (BMI 24.6±1.8, AHI 3.7±2.4). OSA group had significantly smaller mean RP and RG area, smallest area in RP and RG regions and horizontal length of smallest area in RP and RG regions. The volumes of soft palate and lateral pharyngeal wall were larger in the OSA group.
Conclusion: Korean male OSA patients had smaller mean RP and RG area, minimal RP and RG area and horizontal length in minimal RP and RG region and larger volume of soft palate and lateral pharyngeal wall than healthy subjects.

0650

A NOVEL EPIDEMIC OF CPAP INTOLERANCE

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Introduction: CPAP intolerance complicates effective sleep apnea therapy and has several known causes. We describe a novel iatrogenic epidemic of awakenings resulting in easily corrected CPAP intolerance.
Methods: Two private CPAP vendors (VW, JL) independently recognized a series of thus far ten (10) patients repeatedly waking on CPAP with unique clinical and monitoring features. A PUBMED review using the search terms “CPAP” and “complication” was conducted to identify any similar prior reports.
Results: Awakenings on CPAP were characterized by: a.) sudden emergence from sleep, b.) transient inability to sense previously discernible applied pressure, and c.) transient inability to sense an oral egress of pressurized air with mouth opening. Physiological recordings from these CPAP units showed steep and brief supplied pressure drops to zero or near zero pressure without a corresponding sharp increase in mask leak. Patients were sometimes able to correlate their awakening time with the time of the observed pressure drop. No further awakenings were reported when these malfunctioning CPAP units were replaced. No similar reports of awakenings on CPAP resulting from sudden temporary loss of applied pressure were found.
Conclusion: Brief and intermittent mechanical failure of CPAP devices to deliver prescribed pressure may cause awakening with characteristic symptoms and monitoring signs. These specific symptoms and signs should be sought in patients with CPAP intolerance. Internal CPAP monitors could be modified to automatically recognize and report such mechanical failures.

0651

THE EFFECT OF UPPER AIRWAY SURGERY ON POSITIONAL CHANGE DURING SLEEP IN OBSTRUCTIVE SLEEP APNEA SYNDROME

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Introduction: There is rare information available on the changes of sleep position in adult with obstructive sleep apnea syndrome (OSAS) after upper airway surgery. The aim of this study was to evaluate the difference of the positional change during sleep as determined by polysomnography in improved subjects with OSAS before and after upper airway surgery.
Methods: The subjects with OSAS who were treated by upper airway surgery and then performed follow-up polysomnography enrolled in this study. Total 51 subjects divided into surgical success (n=26) and non-success (n=25) group as change of apnea-hypopnea index (AHI) after surgery. We compared the pre- and post-operative difference of the frequency of positional change during sleep and the distribution of sleep position between both groups.
Results: In surgical success group, the positional change index ($P < .05$) was significantly decreased but the proportion of sleep time spent in each position was not significantly changed. In surgical non-success group, the positional change index and the proportion of sleep time spent in each position were not significantly changed.
Conclusion: We found out that the frequency of positional change during sleep significantly decreased with the improvement of AHI in adult with OSAS after upper airway surgery.

0652

WHY POSITION CHANGE OCCURS IN PATIENTS WITH POSITIONAL OBSTRUCTIVE SLEEP APNEA-HYPOPNEA SYNDROME ?

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Introduction: It is well known that respiratory disturbance index (AHI) in sleep with lateral position is on average about 40-50% lower than during sleep supine in patient with obstructive sleep apnea-hypopnea syndrome(OSAHS). We investigated that the pattern of nocturnal body position change in patient with OSAS differs among patient with OSAHS and control.
Methods: We reviewed the polysomnographic finding of 283 patients with OSAHS. We assessed the frequency of positional change, sleep stage that positional changes were occurred, sleep events that could cause the positional change, according to the severity apnea-hypopnea index (AHI) and positonal apnea-hypopnea index difference. We defined positional OSAHS that supine-lateral index [(supine AHI- lateral AHI)/ supine AHI] is more than 0.5.
Results: There were no difference in position change frequency and time of lateral position during sleep and body mass index among positional(supine-lateral index <0.5)and non-positional OSAHS (supine-lateral index >0.5) patients. And also position change frequency and time of lateral position during sleep were not different beween mild (AHI=5-15), moderate (AHI=15-30), severe (AHI= 30>) OSAHS patients. Positional change commonly occurred in NREM stage II sleep in normal control group, but usually noted in NREM stage I sleep in OSAS group.
Conclusion: Nocturnal positional change is common phenomenon in control and patients with OSAS. In patient with OSAS, respiratory events could provoke the positional change during sleep.

0653

BLOOD PRESSURE MEDICATION COSTS IN PATIENTS WITH OSA - A PROSPECTIVE TRIAL

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Introduction: Obstructive sleep apnea (OSA) has been identified as an independent risk factor for development of arterial hypertension by several studies in the literature. Data from randomized controlled trials in OSA suggest a role in blood pressure reduction for continuous positive airway pressure (CPAP) treatment. Blood pressure reduction due to CPAP therapy could have an effect on blood pressure medication costs. This, however, has not been investigated so far.
Methods: We measured office blood pressure and calculated daily blood pressure medication costs of OSA patients prior and after 3 months of CPAP therapy. A diagnostic polysomnography (PSG) and a follow-up PSG with 3 month nCPAP therapy was performed. Sleep and respiratory parameters were extracted from both PSGs.
Results: 162 patients (132 male, 30 female, mean age 60.2 ± 9.1 years) were investigated. Respiratory disturbance index (RDI) was significantly improved with CPAP therapy (47.2 ± 27.7/h vs. 6.1 ± 9.2/h, $p<0.001$) as well as systolic blood pressure (142.6 ± 17.1mmHg vs. 137.8 ± 16.2 mmHg, $p<0.05$) and the Epworth Sleepiness Score (10.4 ± 5.0 vs. 6.5 ± 4.0, $p<0.05$). Decrease in diastolic blood pressure was not significant (85.1 ± 11.0 mmHg vs. 82.0 ± 11.5 mmHg, $p=0.05$). Daily blood pressure medication costs were 0.70 ± 0.66€ [~0.94 USD] vs. 0.71 ± 0.63€ [~0.95 USD], this difference was not statistically significant.
Conclusion: Systolic blood pressure was reduced with CPAP therapy by 4.8 mmHg on average, but the blood pressure medication and therby blood pressure medication costs remained relatively unchanged - possibly indicating that general practitioners are not aware of the beneficial effect of the CPAP therapy on the blood pressure. This may be a specific effect in the german healthcare system, but we can conclude that potential beneficial effects of CPAP therapy should be more emphasized in order to reduce medication costs.

0654

SLEEP DISORDERED BREATHING IN AN ELDERLY COMMUNITY-LIVING POPULATION - RELATIONSHIP TO CARDIAC FUNCTION, INSOMNIA SYMPTOMS AND DAYTIME SLEEPINESS

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Introduction: The relationship between sleep disordered breathing (SDB), systolic function/heart failure in elderly people living in community has not been investigated, nor has insomnia and excessive daytime sleepiness (EDS). The aim of this study was to describe the prevalence of SDB and its relationship to systolic function, the different insomnia symptoms as well as EDS.

Methods: 331 subjects (71-87 years), healthy enough to living in their own homes, underwent echocardiographic examinations and sleep respiratory recordings during one-night in the patients homes with polygraphic equipment(Embletta, ResMed, Trollhättan,Sweden). Questionnaires were used to evaluate insomnia symptoms and EDS.
Results: Mild SDB (AHI 5-15), was found in 32%. Moderate SDB (AHI 15-30) occurred in 16%, and 7% had severe SDB (AHI >30). Median AHI was significantly higher ($p<0.001$) in those with mild impaired systolic function (AHI 11.7) and moderate impaired systolic function (AHI 10.9) compared to those with normal systolic function (AHI 5.0). Impaired systolic function was also independently associated to SDB as indicated by AHI≥10 and AHI≥15. Concerning insomnia symptoms and EDS, only difficulties in initiating sleep correlated significantly ($p<0.05$) with AHI.
Conclusion: SDB is common among the elderly and may be related to impaired systolic function/heart failure. However, detection of SDB in such population may be problematic since insomnia symptoms and EDS correlated poorly with SDB.

0655

THE RELATIONSHIP BETWEEN INSOMNIA AND OSA SEVERITY

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Introduction: Recent studies have suggested a considerable prevalence of co-morbid insomnia in groups referred for suspected obstructive sleep Apnea (OSA) ranging between 20-60%. However, few studies have evaluated the relationship between insomnia severity and OSA severity. It may well be the case that co-morbid insomnia is mainly confined to relatively mild OSA suggesting a possible negative relationship between insomnia severity and OSA severity. This would be the case if severe OSA produced extreme sleepiness and thus provided some protection against insomnia. The present study investigated these relationships.
Methods: Subjects consisted of consecutive patients (N=257) over a two month period in the Adelaide Institute for Sleep Health Clinic undergoing full PSG for suspected OSA. Those with diagnosed narcolepsy, RLS/PLMS, REM behavior disorder, Cheyne-Stokes Breathing, and those with insufficient data to measure a reliable respiratory disturbance index (RDI) were excluded (total of 41). OSA severity was measured as the RDI (total obstructive apnea and hypopnea events per hour according to the AASM criteria). Insomnia severity was measured with the Insomnia Severity Index (ISI) scale in which a score >14 is considered indicative of at least moderately severe insomnia. Other measures included the Epworth Sleepiness Scale (ESS), body mass index (BMI), daytime fatigue (FFS), age, and gender.
Results: In those with some OSA (RDI>15) the prevalence of insomnia (ISI>14) was 39%. However, the prevalence of co-morbid insomnia was not lower for more severe OSA (moderate 30<RDI<45, insomnia was 40%, severe RDI>45, insomnia was 43%). In fact the correlation between RDI and ISI was small but positive ($r=0.13$, $p<0.03$) suggesting a trend for higher RDI to be associated with higher ISI. Sleepiness had small positive correlations ($p<0.01$) with RDI and ISI (0.156, 0.186). Daytime fatigue was strongly correlated with ISI ($r=0.41$, $p<0.001$) but not RDI (n.s.). BMI was strongly correlated with RDI ($r=0.42$) but not ISI. A factor analysis of all these measures aligned ISI with fatigue and sleepiness while RDI was grouped with only BMI.
Conclusion: The prevalence of co-morbid insomnia in those with OSA was considerable (39%) in this study. Contrary to the possibility that this degree of co-morbidity is mainly a function of overlap in the mild regions of both disorders, the prevalence of co-morbid insomnia did not decrease with more severe OSA.

0656

IMPACT OF AGE AND POSITION ON SEVERITY OF GENDER-SPECIFIC SLEEP DISORDERED BREATHING

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Introduction: This study investigates the impact of age on gender-specific positional and non-positional OSA.
Methods: Sleep study results obtained with the ARES Unicorder yielded data from 98 females and 261 males between age 30-45 years, and 106 females and 268 males between 55-70 years. By gender group, there were no statistically significant differences in weight, neck size and BMI, although older males were slightly shorter. Variables for analysis included: supine and non-supine AHI values with 10-sec cessation in airflow for apneas, hypopneas with a 4% desaturation (AHI-4%), hypopneas with a 1% desaturation and accompanying arousal indicator (AHI-1%), %-time SpO2<90%, and %-time snoring<30dB.
Results: As compared to the younger group, older males had significantly greater AHI values in both the supine (AHI-4%=23/18, AHI-1%=33/27) and non-supine (AHI-4%=16/12, AHI-1%=25/19) positions ($p<0.01$). There were no differences in %-time snoring or SpO2<90%. The Epworth scores were lower for older men (9.2/10.4, $p<0.01$). There were no differences between younger and older males in prevalence of self-reported snoring (88/85%), waking up choking (63/54%), witnessed apneas (68/58%), depression (15/18%) and positional OSA (60/64%). Significant distributions by older/younger males included hypertension (55/21%,$p<0.0001$), heart disease (18/2%, $p<0.0001$) and diabetes (17/5%, $p<0.001$). Compared to the younger cohort, older females had significantly greater AHI values only in the supine position (AHI-4%=20/15, AHI-1%=31/26,$p<0.05$), and snored more often during the night (%-time >30dB=34/28,$p=0.02$). The %-time SpO2<90% was close to significant (4.0/2.3,$p=0.076$). There were no differences in prevalence of self-reported snoring (76/75%), waking up choking (59/50%), witnessed apneas (54/50%), heart disease (9/2%), diabetes (16/9%), depression (44/26%) and positional OSA (56%/54%). Significant difference in prevalence of hypertension (55/29%,$p<0.01$) was noted.
Conclusion: Older women are susceptible to increased sleep apnea/hypopnea severity only in the supine position. The increased incidence of daytime somnolence in younger males may impact referrals for a sleep study at a younger age.
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0657

PARABRACHIAL (PB) AND BASAL FOREBRAIN (BF) UNIT ACTIVITY DURING HYPERCARBIA INDUCED AROUSALS FROM SLEEP IN RATS

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Introduction: In obstructive sleep apnea (OSA), frequent arousals from sleep are caused by the collapse of the upper airway, resulting in hypercarbia/hypoxemia, and an increase in respiratory effort. Recent work using anatomical and lesion methods suggests that the pontine parabrachial nucleus (PB) is important for wakefulness and cortical EEG activation. Here we test the hypothesis that the PB is activated by visceral and respiratory signals arising during OSA, and drives wakefulness & cortical activation via ascending excitatory glutamatergic projections. The PB projections to the basal forebrain (BF) are especially important, since extensive evidence indicates the BF has cortically projecting, wakefulness-promoting neurons critical for cortical activation.

Methods: Fine time resolution was provided by tetrode/ multiple single unit recordings in rats to determine the activity of PB and BF neurons in natural sleep-wake cycles, and during arousals from sleep that are: 1) spontaneous; 2) provoked by acoustic stimulation; and 3) provoked by hypercarbia (10s infusions of 10% CO2 at 14L/min, alternated with long periods of air flow at 14L/min), thus mimicking the stimuli from OSA. The onset of CO2 infusion was determined by an experimenter monitoring the rat's vigilance state on-line.
Results: Rats were aroused from sleep in over 90% of the CO2 trials. Arousals from sleep occurred at an average CO2 concentration of ~ 6 % (at ~ 7s into the 10s period of CO2 infusion). These CO2 induced arousals were transient as the rats returned to sleep within ~30s. The pattern of BF unit activity across sleep-wake and arousals from sleep indicated state-related discharge consistent with previous work. During spontaneous arousals from sleep the activity of a slow wave sleep active BF neuron was suppressed, whereas the activity of wake-active BF neurons was elevated. Preliminary findings indicate PB neuronal activity may mediate hypercarbia-induced arousals, but not spontaneous arousals from sleep. The discharge activity of some PB units correlated with heart rate, consistent with previous work.
Conclusion: Understanding the neural control mechanisms that underlie spontaneous & pathological arousals from sleep may provide a rational basis for development of therapies aimed at reducing arousals from sleep.
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0658

WEEKLY PHONE CALLS VS. BRIEF PATIENT EDUCATION TO IMPROVE CPAP COMPLIANCE: A RANDOMIZED CONTROLLED TRIAL

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Introduction: Effectiveness of Continuous Positive Airway Pressure (CPAP) as a treatment for Obstructive Sleep Apnea (OSA) can be limited by poor compliance. Our goal is to explore prospectively the effects of short-term phone sessions (weekly phone calls for 4 weeks) or educational handouts, compared to usual care on CPAP compliance in our clinic population. We aim to specify the most commonly expressed reasons for CPAP non-adherence and suggest modalities for early interventions.
Methods: All adult OSA patients, who have been prescribed CPAP, were asked to participate in this randomized control trail. Patients were randomized to one of three groups: Group A. weekly 15-minute follow-up phone calls for 4 weeks, Group B, CPAP handout and educational material approved by our institute, and Group C. usual care (verbal discussion about their diagnosis). Groups were correlated with three non-compliance measures obtained from the digital electronic compliance card (average minutes/day of use (CPAPmin), percent of days more than 4 hours of use(CPAP4hrs)and percent of days the device was ever used(CPAPday)) using bivariate correlations, independent sample- t tests and one-way ANOVA.
Results: 128 patients were enrolled at the time of submission of this abstract. 19 patients (15 males and 4 females) had compliance card information and were included in the data analysis. Mean (SD) for age =51.58 (12.05), BMI=37.77 (8.64), and AHI= 30.82(26.53). There were no significant differences of baseline characteristics (age, BMI, ESS, AHI, Lowest O2, limb movement and CPAP pressure needed) among the three groups. Although there were trends for higher CPAPmin and CPAPday in groups A and B, when compared to group C, but they were not significant. CPAPmin (SD) =[318.17(110.78)// 348.00(77.90)//279.25(159.71); p=0.640], CPAP4hrs (SD)=[0.65 (0.30)// 0.78(0.19)// 0.66 (0.33); p= 0.733], and CPAPday (SD)=[0.89(0.15)// 0.93(0.07)//0.79(0.24); p=0.391].
Conclusion: We find no significant differences in compliance outcomes among OSA patients who were started on CPAP and followed with weekly phone calls for 4 weeks, received educational materials, or had usual care. Collecting more compliance information from the rest of the study subjects and enrolling more patients will help increase the power of our study.

0659

OBSTRUCTIVE SLEEP APNEA (OSA) AND FLOPPY EYELID SYNDROME

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Introduction: Floppy eyelid syndrome (FES) is an often unrecognized ocular condition characterized by flaccid, easily everted upper lids. Chronic papillary conjunctivitis, ptosis, and eyelid imbrication are common manifestations. Although an association between FES and OSA has been described, this has been under recognized and unrecognized. Rarefraction of elastin fiber density within the tarsus has been proposed as the pathophysiologic mechanism. The objective of this study is to describe the association of Obstructive Sleep Apnea (OSA) and Floppy Eyelid Syndrome.
Methods: We present three cases referred to the Neurology/Sleep clinic at JFK Medical Center, who had overnight polysomnographic studies for suspected/ sleep apnea.
Results: One patient presented with frequent morning headaches, ptosis, and conjunctival erythema with associated blurring of vision. The second patient was referred for evaluation for myasthenia gravis due to presenting complaints of bilateral ptosis, daytime fatigue, and hypersomnolence. The third patient had symptoms suggestive of sleep apnea with droopy eyelids as an incidental finding. All three patients had a BMI greater than 30, and Obstructive Sleep Apnea (OSA) in the moderate-severe range. No other cause for their droopy eyelids was found on appropriate workup and subsequent examination by an Ophthalmologist.
Conclusion: Patients with Floppy Eyelid Syndrome (FES) might be referred to a Neurologist's office for evaluation of ptosis. In obese patients with easily everted eyelids and a history suggestive of OSA, FES needs to be kept in mind and these patients should be referred for a diagnostic sleep study and appropriate management to prevent long term sequelae of untreated OSA.

0660

INCREASED CAROTID-ARTERY INTIMA-MEDIA THICKNESS IN OBSTRUCTIVE SLEEP APNEA/HYPOPNEA SYNDROME

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Introduction: Obstructive sleep apnea/hypopnea syndrome (OSAHS) is strongly linked with increased cardio- and cerebrovascular diseases. The aim of this study was to investigate whether the carotid intima-media thickness (IMT), a useful indictor of early atherosclerosis, was associated with the presence and the severity of OSAHS.
Methods: One hundred and sixty-three OSAHS patients (apnea/hypopnea index ≥ 5/hr.) and 22 simple snorers as the control group were enrolled in this study. Carotid IMT was investigated with B-mode high-

resolution ultrasonography. All IMT measurements were carried out blindly to the status of the patients.
Results: The IMT of the carotid arteries of OSAHS patients was significantly higher than that of control subjects (0.686 ± 0.176 mm versus 0.581 ± 0.112 mm; P = 0.004, Wilcoxon rank sum test).
Conclusion: This study shows that the carotid IMT is significantly increased in patients with OSAHS. Our findings might further strengthen the hypothesis that patients with OSAHS increase the risks of developing cardio- and cerebrovascular morbidities.

0661

MAGEMENT OF TMJ PAIN IN ORAL APPLIANCE THERAPY FOR SNORING AND SLEEP APNEA

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Introduction: A number of studies have showed TMJ pain as one of the most common side effect with oral appliances ranging 15% to 40%, sometimes related to not titratable appliances. The aim of this study is to show the percentage of complains in clinically significant pain in TMJ and the number of patients who have improvement in symptoms with temporally reducing in mandibular advancement, with posterior titration of oral appliance.
Methods: A group of 171 consecutive patients (49 F and 122 M, mean age 50.42y) treated with oral appliance (PLG Appliance), are clinically followed for complains of pain in the TMJ at least 15 days after the appliance was fitted in mouth or during the titration of appliance. The protocol used of titration initially uses an advancement of 50% of maximal protrusion and titrates 1mm each 15 days to reach 80% of total protrusion. In patients that report pain in TMJ, the madibular advancement was reduced in 1mm or 2mm until pain reduction, 15 days after pain relief we resume titration and separate the patients in two groups, responders (patients with improvement in symptoms and successful titration) and non-responders (patients with no improvement of pain or no successful titration).
Results: 10 patients did not finish all procedures, 161 patients finish the protocol of titration completely. 27/161 (17%) patients complain TMJ pain after fitted with appliance and have reduced the initial advancement. We found 3/27 patients (11%) have no relief pain and not reach complete titration and consider non-responders, 24/27 patients (89%) improve pain in TMJ and finish titration successfully (responders). The number of patients with TMJ pain, using this protocol of titration, decrease from 17% (23/161) to 2% (3/161) of patients treated.
Conclusion: TMJ pain during titration of mandibular appliances could be controlled successfully reducing mandibular advancement and posterior titration, with titratable appliances, achieving better outcomes.

0662

MOUTH OPENING DURING SLEEP MAY BE A CRITICAL PREDICTOR OF SURGICAL OUTCOME AFTER UVULOPALATOPHARYNGOPLASTY FOR OBSTRUCTIVE SLEEP APNEA

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Introduction: To identify clinical implication of mouth opening in assessment of surgical outcomes after uvulopalatopharyngoplasty (UPPP) and to give preoperative guidelines for surgical indication of UPPP
Methods: A total of 69 consecutive patients with obstructive sleep apnea who underwent UPPP. All the subjects underwent cephalometry, nocturnal polysomnography and sleep videofluoroscopy (SVF) before and after surgery. Multiple parameters of polysomnography, cephalometry and SVF including angle of mouth opening, retropalatal and retrolingual airway space were evaluated as predictors of UPPP.
Results: Increased angle of mouth opening and decreased retropalatal airway space during SVF were significantly related with surgical failure (P<0.001). The combination of angle of mouth opening and retropalatal ariway space could predict surgical outcome with predictive values of 92.3% and 100% for successful and non-successful outcome, respectively.
Conclusion: Sleep videofluroscopy could provide us with useful clinical information not only on dynamic airway but also on important prognosticators before UPPP. Mouth opening and retropalatal airway space during sleep could be an important prognostic factor determining surgical outcome of UPPP.

0663

RELATIONSHIP BETWEEN DAYTIME SLEEPINESS AND SLEEP ARCHITECTURE IN PRIMARY SNORING PATIENTS

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Introduction: Daytime Sleepiness (DS) is one of the main symptoms in Sleep Breathing Disorders, nevertheless the presence of DS in Primary Snoring (PS) has been a matter of controversy. The relationship between DS and the particular features of the sleep pattern in PS patients has not been determined yet.
Methods: The objective was to determine the relationship between the Epworth Sleepiness Scale (ESS) and the features of the sleep pattern in untreated PS patients. This is a retrospective study which included 236 patients (mean age: 44.8 years old, range: 18-82) with PS. Diagnosis was based both on clinical examination as well as on the Polysomnographic (PSG) recordings. PS patients were grouped in four categories according to ESS scores obtained: No DS = 0 - 6; Mild DS = 7 - 12; Moderate DS = 13 - 18 and severe DS = 19 - 24. Analysis of variance were done to compare the PSG features between the four ESS categories.
Results: No changes were found in Total Sleep Time, Nocturnal Wake Time, Sleep Efficiency, Light Sleep or REM sleep latencies; but unexpectedly, we found a significant decrease in Light Sleep and a significant increase in both Slow Wave Sleep (SWS) and REM sleep particularly in the group of severe DS.
Conclusion: In the present study no correlation was observed between Total Sleep Time and ESS in PS patients, however, in the group with severe DS, significant changes on Light Sleep, SWS and REM sleep duration were detected. It is possible that these modifications could be an expression of chronic partial sleep deprivation usually observed in patients affected with chronic PS.
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0664

RATS EXPOSED TO CHRONIC INTERMITTENT HYPOXIA (CIH) HAVE REDUCED SEROTONIN TYPE 2A RECEPTOR IMMUNOREACTIVITY IN THE HYPOGLOSSAL (XII) MOTOR NUCLEUS

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Introduction: Obstructive sleep apnea (OSA) patients adapt to the anatomical vulnerability of their upper airway by generating a higher level of activity in upper airway-dilating muscles. Serotonin mediates a part of wake-related excitatory drive to XII motoneurons, of which some innervate major upper airway-dilating muscles. However, XII motoneurons of rats exposed to CIH, an important pathogenic factor in OSA, exhibit attenuated excitatory response to microinjection of serotonin into the XII nucleus (Veasey et al., 2004. Am J Respir Crit Care Med 170:665-672). To investigate the basis of this attenuation, we examined the effect

of CIH on expression of serotonin type 2A (5-HT_{2A}) receptor, the main serotonergic excitatory receptor in XII motoneurons.
Methods: Five male rats were subjected to CIH and another 5 rats to matching room air exchanges. The hypoxic/normoxic cycle comprised 10% O_2 for 90 s and 20.9% for 90 s for 10 h/day (7am-5pm) for 35 days. At the end of exposure, one CIH and one sham-treated rat were perfused and coronal medullary sections from each animal pair were subjected to 5-HT_{2A} receptor immunohistochemistry. The density of receptor immunostaining was quantified within the caudal half of the XII nucleus from digital images of four sections per rat and background staining was subtracted.
Results: CIH rats had 10%±3(SE) lower levels of 5-HT_{2A} receptor immunostaining than sham treated animals ($p<0.01$).
Conclusion: The moderately decreased 5-HT_{2A} receptor levels may contribute to the reduced response of XII motoneurons to exogenous serotonin in rats exposed to CIH, but these findings cannot explain the observation that OSA patients have enhanced, rather than reduced, upper airway motor tone during wakefulness. If effects elicited by CIH in rats also occur in humans with OSA, additional adaptations to the disorder must occur to compensate for the reduced XII motoneuron responsiveness to serotonin.
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0665

IS USEFUL RHINOMANOMETRY TO EVALUATE NASAL RESISTANCE ON OSAS PATIENTS USING NCPAP

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Introduction: It is reported that high nasal resistance is a risk factor of nasal CPAP failures. But it is not clear that which patients need nasal therapy when using nasal CPAP? How do we know the indication of nasal therapy? Is useful rhinomanometry to evaluate nasal resistance on Obstructive Sleep Apnea patients using nasal CPAP?
Methods: We enrolled cohort of 664 patients who was diagnosed as OSAS in Ota Sleep Disorder Center (Japan) from January 2005 to November 2005. All patients were diagnosed by overnight polysomnography. And measurements of nasal resistance were performed using anterior rhinomanometry method. We followed up those patients for CPAP treatment up to 6 months after the prescription.
Results: 24.4%, which is 96 out of 407, rejected CPAP titration or dropped out from nCPAP within 2 months. Nasal resistance with such patients which is defined as the early CPAP failure group was significantly higher than with CPAP tolerant group, which is the patients group who could continue CPAP treatment for more than 2 months. Out of 359 patients who started nCPAP, 90 patients udnerwent nasal treatment at sleep onset and 18 patients received nasal surgery such as septoplasty because of nasal obstruction. Consequently, 30.1% required nasal treatment for nasal-CPAP. Statistically, the patients who received nasal treatment had higher nasal resistance than the patients without nasal treatment.
Conclusion: The results suggest that Obstructive Sleep Apnea patients with high nasal resistance should receive nasal treatment to improve the compliance of nasal-CPAP. Rhinomanometry is useful tool to evaluate nasal resistance and can be used as an indication for nasal treatment for Obstructive Sleep Apnea patients using nCPAP.

0666

EFFECT OF HUMIDIFICATION ON TITRATION PRESSURES IN OBSTRUCTIVE SLEEP APNEA

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Introduction: A number of clinical investigations have attempted to define the role humidification plays in Positive Airway Pressure (PAP) therapy, whether this be heated humidification or cool pass-over humidification. Although considerable work has focused on whether or not humidification in PAP therapy has the ability to impact subjective concerns and thereby increase therapy compliance, little effort has been undertaken to investigate the role humidification may play in titrated pressures for PAP therapy. The present authors hypothesize the delivery of higher and more consistent humidification can impact not only patient subjective concerns related to PAP therapy tolerability, but tighter humidity control can impact nasopharyngeal physiology in such a way as to reduce nasal airway resistance. Therefore, the purpose of the present investigation was to determine what effect humidification type has on titrated PAP therapy in a controlled laboratory environment.
Methods: Enrollment included twenty participants prospectively recruited from two outpatient sleep medicine centers in Tulsa, Oklahoma between March and June 2008. The present investigation employed a randomized, crossover design. Upon completion of the diagnostic polysomnogram and once inclusion criteria had been satisfied and informed consent obtained, subjects were randomized to either heated humidification utilizing a heated breathing tube (CPAP A (SleepStyle™ 604, Fisher & Paykel Healthcare)) or conventional heated humidification (CPAP B (Heated breathing tube deactivated)). Patients were required to undergo two consecutive positive pressure titration nights, one night for each treatment arm.
Results: The average effective CPAP pressure was significantly different between the two treatment groups, $t(19) = -6.015$, $p = 8.70$ E-06. Average therapeutic pressure for CPAP A was 9.8 ±1.89 cm H2O and CPAP B 10.9 ±1.98 cm H2O. CPAP pressure in the combined groups ranged from 7 to 15.5 cm H2O. No statistical differences were observed based on patient mask selection. No gender differences or general demographic parameters were significantly different.
Conclusion: Titrated laboratory CPAP pressures are demonstrated to be significantly impacted by the methond of humidification used. Therapeutic CPAP press,ures were observed to be significantly lower when ThermoSmart™, a heated breathing tube humidification system, was utilized as compared to a conventional humidification systems.
Support (optional): Support provided by Fisher & Paykel Healthcare.

0667

EVOLUTION OF SLEEP PATTERN AND SLEEP BREATHING DISORDERS DURING FIRST SEVEN NIGHTS AFTER SURGERY - A PILOT STUDY

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Introduction: Anesthetics, analgesics and surgery may have a tremendous impact on the sleep architecture of postoperative patients. We investigated the effect of surgery and anesthesia on sleep for seven nights postoperatively
Methods: After REB approval, patients consented to undergo polysomnography (PSG) with a 10-channel portable device (Embletta x100) preoperatively at home; postoperative night 1, 3, 5 and 7 in hospital or at home. The device was installed by well trained technicians. The PSG recordings were scored by a certified sleep technologist. Data were entered into a specifically designed Microsoft Access database and analyzed with SAS 9.1 for Windows.
Results: Fourteen patients completed 5 nights of PSG, 9 male and 5 female. Age was 65± 5 and BMI 31 ± 6. Surgeries were 11 orthopedics, 1 urology, 1 spine and 1 gynecological. Anesthesia type included 4 general and 10 regional. Preoperative apnea hypopnea index (AHI) was 13.3 ± 29 and 6 patients (43 %) were AHI>5. The REM sleep on postoperative night1 was significantly decreased. It was gradually recovering, but it was still significantly lower by night7. Preoperative REM sleep was 22±7%, night1: 6±7 ($p<0.05$ vs preop), night3: 13±5%($p<0.05$ vs preop), night5: 17±7%($p<0.05$ vs preop) and night7: 18±10%($p<0.05$ vs preop).

Stage 2 sleep was significantly increased postoperative night1 vs preop (78±16% vs 61±15% p<0.05). AHI was increased following surgery and returned close to preoperative level by night7. AHI for preoperative, postoperative night 1,3,5,7 was 13.6±29., 21.3±30, 25±34, 20.6±29 and 15.5±27, respectively. Possibly because of small sample size, the change of AHI was not statistically significant. Respiratory arousal index also followed a similar pattern as AHI.
Conclusion: After surgery, REM sleep was significantly decreased and not fully recovered by night 7 after surgery. AHI and respiratory arousal index was increased and returned close to preoperative level by night 7.

0668

AIRWAY PROTECTION: THE MISSING LINK BETWEEN NOCTURNAL BRUXISM AND OBSTRUCTIVE SLEEP APNEA

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Introduction: In 2008 we presented that Nocturnal Bruxism (NB), defined as a grinding or clenching of the teeth during sleep, occurs as part of a protective reflex in situation were there is a collapsing airway, such is in patients with OSA. To our knowledge we are the first to make this claim that would explain the link between NB and OSA. We additionally presented that in many patients this protective mechanism successfully minimizes the degree of obstructive respirations making the diagnosis difficult, frequently only possible by way of esophageal pressure monitoring (Pes). We present here additional data to support our claim and to shed light on the importance of enhanced diagnostic measurements with the Pes during polysomnography so that subtle cases do not go undiagnosed.
Methods: We retrospectively reviewed 729 consecutive charts of patients diagnosed with OSA or Upper Airway Resistance Syndrome (UARS) treated with CPAP at least six months prior to initiating our assessment (296 F, 433 M, average age 51 +/- 13.8). NB was determined by either sleep questionnaire or from the clinical history and exam. All patients who's charts were reviewed had NPSG testing to diagnose OSA or UARS. UARS was established by Pes monitoring using a water catheter technique. Follow up interviews were performed to assess outcome in patients with NB placed on CPAP for treatment.
Results: Of the 729 OSA patient, 183 demonstrated Bruxism (25.1%) 95 females and 88 males. Of these 119 underwent a follow-up interview for the study, by which time 17 were using bite guards as part of their treatment. Statistical assessment was performed on the remaining 102 patients who were only using CPAP for treatment. CPAP compliance was assessed by self report. A multivariate analysis was performed and demonstrated a significant relationship between degree of CPAP use and degree of improvement in NB (p=.0054). Of the 102 patients 25 had AHI < 6 but found to have the UARS. Of these 14 used CPAP nightly, 12 of whom demonstrated improvement in NB, representing 85.7% of the 100% CPAP compliant UARS group.
Conclusion: Again, to our knowledge, we are the first to postulate that Nocturnal Bruxism is a compensatory mechanism of the upper airway to overcome upper airway collapse. This process may reduce the obstruction, masking the proposed relation of NB and OSA in some, thus increasing the need for Pes monitoring as part of NPSG testing in UARS patients. This study supports that airway protection is the missing link between Bruxism and OAS.

0669

COMPARISON OF HYPOPNEA SCORING USING TWO SEPARATE CRITERIA SETS

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Introduction: Untreated obstructive sleep apnea (OSA) is a modifiable risk factor associated with diabetes, coronary artery disease, hypertension, congestive heart failure, stroke, and myocardial infarction. Two criteria sets (Criteria 1 and 2) have been proposed for scoring hypopneas. One approach entails meeting more stringent criteria (Criteria 1) for diagnosis of obstructive hypopneas. Should this strategy gain widespread adoption, many patients who only qualify for diagnosis of OSA by the less stringent criteria will not be diagnosed and treated. Given the sequelae of untreated OSA, a comparison of the two criteria is warranted, and results from this study may be useful for future diagnostic strategies of sleep disorders centers.
Methods: Criteria 1: Nasal pressure signal shows a drop by greater than 30% from baseline, duration of the events is at least 10 seconds, with a 4% or greater desaturation from pre-event baseline. Criteria 2: Nasal pressure signal shows a drop by greater than 50% from baseline, duration of the events is at least 10 seconds, with a 3% or greater desaturation from pre-event baseline, or the event is associated with an arousal. 23 patients who fulfilled criteria for OSA by Criteria 2 were identified from overnight polysomnography (PSG) records at the Vanderbilt CRC over 19 months. 20/23 (86.96%) had initially presented with excessive daytime sleepiness. One AASM board-certified physician, blinded to the original scoring, scored the PSGs according to the two criteria sets from the AASM Manual for the Scoring of Sleep and Associated Events (2007).
Results: Mean apnea-hypopnea index (AHI) by Criteria 1 was 9.83 $\pm$ 10.83 (mean $\pm$ SD); mean AHI by Criteria 2 was 20.33 $\pm$ 16.87 (mean $\pm$ SD) with p-value < 0.001 by the paired t-test. 11/23 patients (47.8%) did not qualify for OSA diagnosis by Criteria 1.
Conclusion: Our results indicate that patients diagnosed with OSA by Criteria 2 are significantly less likely to be diagnosed with OSA by Criteria 1. Criteria 1 would thus exclude many patients who would otherwise be diagnosed and treated for OSA. We recommend using Criteria 2 to avoid preventable sequelae of OSA in these patients. Further large scale studies are needed to evaluate the impact of missed opportunities to treat OSA when the more stringent criteria are used.

0670

RATS SUBJECTED TO CHRONIC INTERMITTENT HYPOXIA (CIH) HAVE INCREASED DENSITY OF NORADRENERGIC (NE) TERMINALS IN THE HYPOGLOSSAL (XII) MOTOR NUCLEUS

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Introduction: Obstructive sleep apnea syndrome (OSAS) patients have higher levels of upper airway motor tone in wakefulness than healthy persons. This allows them to maintain the airway open, but the mechanisms underlying this adaptation are unknown. NE activation of XII motoneurons plays an important role in the maintenance of upper airway motor tone. We tested whether exposure to CIH, a major pathogenic factor in OSA, alters the density of NE terminals in the XII nucleus.
Methods: Six male rats were subjected to CIH and another 6 rats to sham room air exchanges. The hypoxic/normoxic cycle comprised O_2 at 10% for 90 s and 20.9% for 90 s for 10 h/day (7am-5pm) for 35 days. Five days prior to perfusion, tetramethylrhodamine-dextran was injected into the base of the tongue (20 µl, 5%) to retrogradely label XII motoneurons. Paired sets of coronal medullary sections (35 µm), one from CIH and one from sham-treated rat, were immunohistochemically

processed for dopamine β-hydroxylase (DBH, a marker for NE cells and fibers) and rhodamine. DBH terminals, including those closely apposed to retrogradely labeled XII motoneurons were counted in 100x100 μm counting box positioned in the ventromedial quadrant of the XII nucleus.
Results: The average numbers of DBH terminals were significantly higher in CIH than sham-treated rats (647±53(SE) vs. 473±50 per counting box; $p<0.01$). The average numbers of DBH terminals closely apposed to cell bodies and proximal dendrites of retrogradely labeled XII motoneurons were similarly increased in CIH rats.
Conclusion: Increased density of NE terminals in the XII nucleus in CIH rats suggests an elevated excitatory NE drive to XII motoneurons. In OSAS patients, this could lead to increased level of upper airway motor tone in wakefulness.
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0671

SNORING DURING PREGNANCY AND ITS RELATION TO PRE-ECLAMPSIA

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Introduction: Pre-eclampsia is a feared complication of pregnancy. Previous retrospective studies have indicated that women who snore are especially at risk. In this prospective study development of snoring and obstructive breathing was correlated to blood pressure and development of preeclampsia.
Methods: 503 consecutive pregnant women answered questionnaires concerning snoring, fatigue, daytime sleepiness and edema. Epworth Sleepiness score (ESS) and symptoms of restless legs syndrome (RLS) were also included. The questionnaire was presented in the 1st, 2nd and 3rd trimester. Blood pressure was also recorded. Data concerning pregnancy and delivery complications were taken from the maternity clinic's records. Women snoring often-always at visit 2 and/or 3 were denoted habitual snorers. They were offered a sleep respiratory recording; 34 volunteered.
Results: 36/503 women (7, 2%) snored habitually already at the first visit, and 19,5% at the end of pregnancy. There was no difference concerning weight increase during pregnancy between habitual snorers and non-snorers. Habitual snorers reported more edema at visit 2 and 3, and significantly higher scores in morning and daytime tiredness and ESS score compared to non-snorers. 22% of the habitually snoring women reported RLS-symptoms already in the 1st trimester, 33% in the 2nd and 32% in the 3rd. For non-snorers the corresponding figures were 14%, 25 % and 29%. Systolic blood pressure increased significantly more in habitual snorers already between 1st and 2nd visit. Weight and Apgar scores of the newborns showed no difference. Pre-eclampsia developed in 18 women, twice as common among habitual snorers (6/93 = 6,5%) as in non-snorers (10/354 = 2,8%). They had higher snoring scores at all visits, with the greatest difference in the third trimester ($p=0,058$), and their diastolic pressure increased significantly more already at the 2nd visit compared to women without pre-eclampsia. They had more edema ($p<0,001$, 3rd visit) and higher increase in BMI ($p<0,001$). There was no relationship to RLS. 9/34 sleep recordings showed supine AHI >5. Two women who later developed pre-eclampsia were recorded; both had AHI >10.
Conclusion: Habitual snorers had more daytime tiredness and higher ESS scores and their systolic blood pressure increased more already during early pregnancy. The incidence of RLS was higher. Pre-eclampsia was twice as common among snorers as non-snorers, but the difference was not significant due to the low number of cases.

0672

COMMUNICATION GAPS EXIST IN THE INITIAL DIAGNOSIS AND MANAGEMENT OF PATIENTS WITH OBSTRUCTIVE SLEEP APNEA

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Introduction: Newly emerging sleep disorders clinics offer important diagnostic and management resources for patients experiencing a variety of sleep disorders. However, the key to achieving therapeutic patient outcomes is the continuity and coordination of care between such clinics and the ordering physician. To ensure long-term patient adherence accurate diagnosis, test and treatment strategies must be thoroughly communicated to all patients with sleep disorders. Reviewing a series of obstructive sleep apnea (OSA) patient visits; this study evaluated one component of that continuity of care model: ordering physician communication of test results with the patient.
Methods: Patients are referred to the sleep disorders center (SDC) for testing based upon the ordering physician's written prescription. The overnight polysomnogram, as well as any related testing, is completed with the results forwarded to the ordering physician within two weeks. As part of the routine follow up of those patients who are prescribed positive airway pressure (PAP) therapy, patients receive a telephone follow-up by a member of the sleep disorders center staff. If the patient is having difficulty with compliance with PAP therapy, he/she is offered an appointment to meet with the sleep disorders center physician and therapy staff. At the time of the patient's visit with the sleep disorders center physician, a questionnaire was completed by the patient. The patient was asked whether their treating physician has reviewed the results of their sleep study with them.
Results: Over a six month period (May 2008-October 2008), 167 new patient visits were conducted by the sleep disorders center physician. Of these, 145 were diagnosed with obstructive sleep apnea and were receiving positive airway pressure therapy for at least a two week period. 126 (87%) of these noted that their treating physician did not review any of the tests results with them while 19 (13%) noted that they had received information regarding their test results from their primary care physician.
Conclusion: Most patients who are newly diagnosed with obstructive sleep apnea have received no information from their primary care provider regarding their diagnosis. In each instance the patient had been prescribed (and was receiving) therapy for his/her obstructive sleep apnea by that primary care physician.

0673

MONOCYTE ADHESION TO ENDOTHELIAL CELLS: EFFECTS OF INTERMITTENT HYPOXIA AND ANTIOXIDANTS

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Introduction: Monocytes of co-morbidities free OSA patients are activated and produce larger amounts of reactive oxygen species (ROS), inflammatory cytokines and adhesion molecules than healthy controls. Consequently, adhesion to endothelial cells (ECs) is increased. The aim of the present study was to investigate the adhesion of monocytes to intermittent hypoxia (IH) treated ECs as compared to normoxia (NOX) and to sustained hypoxia (SH) conditions in vitro, and how tumor necrosis factor-α (TNF-α) and antioxidants affect this interaction.
Methods: Adhesion assay of monocytes (THP-1) to ECs (EA.hy926) was performed by plating $4x10^4$ ECs/well onto Fibronectin-coated 96-well plates and culturing for 48 hrs until confluence. ECs were treated with various conditions as IH (4 alternating cycles, in each cycle hy-

poxic period lasted 10 min. at 2.5% O2, 5% CO2, 92.5% N2 and was alternated with 50 min. NOX), SH (continuous - 2.5% O2, 5% CO2, 92.5% N2) and NOX (19% O2, 5% CO2, 76% N2). Additionally TNF-α and antioxidants were used in the IH condition. After ECs were treated, LeukoTracker™ fluorescence labeled monocytes ($2.5x10^5$ cells) were added to ECs for 30 min. after which adherent monocytes were lysed and quantified by a fluorescence reader. ECs were treated with antioxidants for 1 hr prior to exposure to IH and during the IH treatment period. Antioxidants used included: rotenone (0.05 mM, mitochondrial oxidase inhibitor); apocynin (0.5 mM, NADPH oxidase inhibitor); allopurinol (0.05 mM, xanthine oxidase inhibitor) and N-acetyl cysteine (NAC, 0.1 mM, ROS scavenger).

Results: Monocyte adhesion to ECs was considered as 100% at NOX. It significantly increased with IH (155±26%, p=0.0000002), SH (137±31%, p<0.02) and TNF-α treatment (162±37%, p<0.01) (n=14-17 determinations). A combined IH and TNF-α treatment further increased monocyte adhesion to ECs (205±25%, p<0.0002). Antioxidants used significantly attenuated monocyte adhesion to IH treated ECs (Rotenone decreased from 100% to 56±12% p<0.006; Apocynin to 77±5%, p<0.003; Alloporinul to 67±2%, p<0.002; NAC to 70±7%, p<0.003, n=4-5 determinations).

Conclusion: IH and TNF-α increased monocyte adhesion to ECs and their combined treatment had a syneristic effect. On the other hand, treatment with antioxidants attenuated the adhesion. These findings suggest the involvement of inflammation and oxidative stress in the adhesion process particularly through mitochondrial function.

0674

DAYTIME VIGILANCE AND SIMULATED DRIVING PERFORMANCE AFTER CPAP TREATMENT IN OSAS PATIENTS

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Introduction: Patients with obstructive sleep apnea syndrome [OSAS] have excessive daytime sleepiness [EDS], increased risk of traffic accidents and poor Simulated Driving Performance [SDP]. CPAP treatment improves EDS, therefore we tested its impact on EDS and SDP.

Methods: Sixteen male with severe OSAS (mean age=53±9y, mean AHI=61±19/h) were tested before and after CPAP treatment with maintenance of wakefulness test [MWT] and 4 sessions of a monotonous 30min SDP test. Subjective (Epworth sleepiness scale score [ESS]) and objective sleepiness (sleep latency at MWT [MWTSL]) and SDP (lane position variability [LPV], number of crashes [Crashes], time from the beginning of the driving simulation to the occurrence of the first crash [TTC]) performed at different times of the day were compared by means of Kruskall - Wallis test, and performed before and after CPAP were compared by means of Wilcoxon signed rank test. MWTSL was correlated with SDP parameters using Pearson's correlations in baseline conditions and after CPAP treatment.

Results: OSAS patients did not show significant differences in MWT-SL and SDP performed at different times of the day. Mean EDS and SDP significantly improved after treatment, as shown by the following results obtained before and after CPAP: mean MWTSL =17±12' and 29±10' (p=0.002), mean ESS = 12±5 and 5±4 (p=0.0004), mean LPV= 0.56±0.29m and 0.43±0.17m (p=0.026), mean Crashes = 2±5 and 0.4±0.4 (p=0.1), mean TTC = 23±7' and 28±3' (p=0.034). Mean MWTSL significantly correlated with SDP parameters in both conditions: r=-0.50 (p=0.050) and r=-0.57 (p=0.020) for mean Crashes, r=0.52 (p=0.039) and r=0.58 (p=0.019) for mean TTC, r=-0.59 (p=0.015) and r=-0.64 (p=0.007) for mean LPV, respectively before and after n-CPAP.

Conclusion: CPAP therapy significantly improved SDP in severe OSAS. Objective sleepiness correlated with SDP parameters in baseline conditions as well as after CPAP treatment.

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0675

THE PREVALENCE OF SLEEP RELATED BREATHING DISORDERS IN CHRONIC PAIN MANAGEMENT

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Introduction: Chronic severe pain may require treatment with opioid medication. Opioid medication is known to affect breathing during sleep. Much of the data available has studied the acute effects of opioids. Conventional assumptions are that many of the respiratory side effects of opioid medication disappear over time.

Methods: To assess the prevalence of this problem we conducted full night diagnostic polysomnography (PSG) in patients from two pain clinics. All were under the care of a pain management specialist for at least 6 months with no changes in opioid pain medication for the previous four weeks.

Results: We describe an interim analysis of 56 patients on oral opioids. 38 (67%) were female, with mean age of 45 (±10.4 SD) years, BMI 30.2 (±6.5 SD) kg/m2, Epworth sleepiness score 9.9 (±4.6 SD), Oswestry pain disability score 24.1 (±6.9 SD), Pittsburgh sleep quality index 12.7 (±3.7 SD) underwent full night diagnostic polysomnography (PSG). PSGs were scored by a central scoring center blinded to patient clinical information. Patient's morphine equivalents (MEq) were calculated on the day of the PSG with a mean value of 42.5 (range 4.5-427.5) mg/day. In this group of patients total sleep time averaged 358 (± 64) min and median sleep efficiency was 80 (range 45-98%). Obstructive sleep apnea (AHI > 5/hr) was present in 59% (95%CI 45-72) and central sleep apnea (central apnea index > 5/hr) was present in 12.5% (95%CI 5-24), all of whom had concomitant obstructive sleep apnea. Severe sleep apnea (AHI > 30/hr) was present 14 (95%CI 6-26%); 5 of these 8 patients had central sleep apnea. Sleep related hypoxemia occurred in 46% (95%CI 33-60%).

Conclusion: Patients on chronic stable opioid pain medications experience significant sleep disordered breathing and have substantial sleep related hypoxemia. Sleep disordered breathing can persist over time in some patients on long term opioid medications.

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0676

OBSTRUCTIVE SLEEP APNEA: DOES HEAD POSITION DURING SLEEP MATTER?

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Introduction: Obstructive sleep apnea is a significant medical problem affecting up to 4 percent of middle-aged adults. Thoracic position has been shown to have an impact on obstructive sleep apnea. The clinical importance of head position during sleep is unknown. The purpose of this study is to assess the role of head position on a patient's obstructive sleep apnea.

Methods: The study included 58 patients who underwent a polysomnography at TriHealth Sleep Center in which head and thoracic positions were measured. In addition to the head and thoracic sensors, digital video was also used to view and verify the head and body positions. The apnea-hypopnea index (AHI) was measured during four different

sleep positions: thorax supine, thorax non-supine, head supine, and head non-supine.
Results: Overall, half (29) of the subjects were male and half (29) were female. The average age was 54 and the average body mass index was 34. During REM sleep, there was a significant difference in AHI between thorax supine position (42.9) and thorax non-supine position (21.6) ($p = 0.006$). Additionally, there was a significant difference in AHI between head supine position (45.3) and thorax non-supine position (21.6) ($p = 0.003$). During non-REM sleep, there was a significant difference in AHI in thorax supine position (30.8) and thorax non-supine position (12.8) ($p = 0.001$). There were also significant differences between head supine (34.0) and head non-supine (18.6)($p = 0.008$) and head supine (34.0) and thorax non-supine (12.8) ($p < 0.001$). However, when comparing thorax supine and head supine positions in both REM and non REM sleep, there were no significant differences.
Conclusion: Head position can impact a patient's obstructive sleep apnea. However, there is not a significant difference in AHI when comparing head supine and thorax supine positions.

0677

NOCTURNAL OXIMETER: A SENSITIVE TOOL TO DETECT THE SURGICAL PATIENTS WITH MODERATE AND SEVERE OSA

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Introduction: Undiagnosed OSA is associated with increased occurrence of perioperative adverse events. It is impractical to do polysomnography (PSG) in all patients at high risk of OSA before surgery. The objective of the study is to explore the capacity of nocturnal oximeter in detecting the undiagnosed OSA in the surgical patient
Methods: Following REB approval, the surgical patients at preoperative clinic consented for 8h sleep study at home with a portable PSG device (Embletta X100) and simultaneously SaO2 monitoring with pulse oximeter wristwatch (PULSOX-300i). Embletta X100 has 10 channels: 2EEGs, EOG, EMG, snoring, nasal flow, abdominal and thoracic movement, oximetry and position. The devices were installed by well trained technicians. The PSG recordings were scored by a certified sleep technologist. The oximetry recordings between 00:00h and 6:00h were processed with software Profox. Oxygen saturation index (ODI) was defined as hourly number of desaturation ≥4% and lasting ≥10s. The data were analyzed with SAS 9.1 .
Results: 354 patients completed the study:167 male and 187 female. Age was 61 ± 12 and BMI 31 ± 7. Number of patients with AHI≤5: 142, AHI> 5~15: 98, AHI>15~30: 98, and AHI>30: 48. There was a strong correlation between parameters from oximeter and PSG : AHI and oxygen desaturation index (ODI) ($r=0.808$, $p<0.01$), AHI-REM and ODI ($r=0.456$, $p<0.01$), AHI-NREM and ODI ($r=0.802$, $p<0.01$), respiratory arousal index and ODI ($r=0.785$, $p<0.01$). The sensitivity for ODI >5 to predict AHI>5 was 95% (95% CI: 92-98%), specificity: 67%(CI:57-76%), PPV:85 %(CI:81-90%) and NPV: 87% (CI:77-94%). The sensitivity for ODI >5 to predict AHI>15 and >30 was 99% (CI:97-100%) and 100%.
Conclusion: There was a strong correlation between ODI from nocturnal oximetry and AHI from portable PSG. ODI was a sensitive parameter to identify undiagnosed OSA in the surgical patients preoperatively, especially moderate and severe OSA.

0678

NEIGHBORHOOD-LEVEL DEPRIVATION DOES NOT EXPLAIN THE ASSOCIATION OF AFRICAN-AMERICAN ETHNICITY WITH SLEEP APNEA SEVERITY

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Introduction: The risk of SDB is higher in African Americans than in Caucasians. Both biological and psychosocial explanations for this disparity have been proposed. We examined whether neighborhood-level socioeconomic status (SES) factors explained some of this racial disparity.
Methods: Study subjects were African-American or Caucasian adult patients (≥18 years) undergoing diagnostic PSG at HFH between 2001 and 2008, excluding those with incomplete demographic data and those residing outside of southeastern Michigan. Sleep apnea severity was stratified into four categories using the apnea-hypopnea index (AHI); individuals with no sleep disordered breathing (SDB) (AHI <5 events/hour); mild SDB (AHI between 5-14.9 events/hour); moderate SDB (AHI between 15-29.9 events/hour) and severe SDB (AHI ≥30 events/hour). Four factors were obtained from the 2000 US Census based on patient address: poverty level; single female head-of-household; high-school drop-out rate; and working age males unemployed. Neighborhoods where ≥3 factors indicated deprivation were considered deprived. Age and sex-adjusted ordinal logistic regression models were fit to examine the association of race and neighborhood deprivation on SDB.
Results: A total of 3,916 adults (59.1% male; 44.0% African-American; mean age 51.8±13.8 years) were available for analysis. The prevalence of none, mild, moderate and severe SDB was 42.9%, 22.8%, 13.9% and 20.3%, respectively. 13.8% of patients lived in a deprived neighborhood; more African-Americans (27.9%) than Caucasians (2.8%) lived in deprived neighborhoods ($P<0.001$). After adjusting for age and gender, compared to Caucasians, African-Americans were at a 1.14 (95% CI: 1.01, 1.28) times increased risk of being in a worse relative to a better SDB category ($P=0.034$). Adjusting for neighborhood deprivation did not attenuate the relationship between African-American race and SDB (OR: 1.15; 95% CI: 1.02, 1.32; $P=0.026$). Neighborhood deprivation was not associated with SDB ($P=0.488$).
Conclusion: In this clinic-based sample, the association of African-American ethnicity with sleep apnea severity was not explained by selected neighborhood-level SES indicators. Future studies that assess additional neighborhood-level factors (e.g. housing conditions, crime) and individual-level SES are needed.

0679

THE EFFICACY OF PALATAL IMPLANTS FOR THE TREATMENT OF MILD TO MODERATE OBSTRUCTIVE SLEEP APNEA/HYPOPNEA SYNDROME: A SYSTEMATIC REVIEW

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Introduction: The aim of this study is to perform a systematic review and meta-analysis to determine the success rate of palatal implants for the treatment of mild to moderate obstructive sleep apnea/hypopnea syndrome (OSAHS).

Methods: A systematic review was performed to identify English language studies that evaluate the treatment of mild to moderate OSAHS patients with palatal implants alone. Outcome measures include Apnea-Hypopnea index (AHI), a visual analog scale (VAS) of snoring, and the Epworth Sleepiness Scale (ESS). Eight studies met the inclusion criteria and a meta-analysis was performed to determine the overall success in improvement of each parameter.
Results: The meta-analysis included 214 subjects (mean sample size of 31 patients) with a mean age of 48.35±11.09 years and a mean body mass index (BMI) of 27.83±2.58. Follow-up time differed among studies and was approximately 3 months. Random effects model demonstrated that postoperatively, there was a significant decrease in AHI (17.97±9.32 to 14.49±12.16), VAS of snoring (8.43±1.67 to 4.79±2.69) and ESS (9.64±4.08 to 8.26±7.76). In 32.6% of patients post-treatment PSG showed a 50% reduction in AHI and a level <20 events/hour, classically considered to be a cure. 26.8% of patients had an increased AHI postoperatively.
Conclusion: A systematic review of current literature demonstrates that small but significant improvements occur in AHI, snoring, and sleepiness following the palatal implant procedure. Palatal implants alone were able to successfully treat 32.6% of patients with mild to moderate OSAHS.

0680

DIFFERENT CPAP START PRESSURES DURING CPAP TITRATION BASED ON VARIOUS PATIENT PARAMETERS

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Introduction: Continuous Positive Airway Pressure is the mainstay of therapy for Sleep Apnea. As per the American Academy of Sleep Medicine, the recommended start CPAP pressure should be 4 cm for all patients. We attempted to decipher if the start CPAP pressure should be different based on various patient parameters.
Methods: Retrospective and Prospective analysis was done for patients with Sleep Apnea diagnosed by Polysomnography (>12 leads) at an Accredited Sleep Center from 1/06-4/07.All studies were interpreted by a Board Certified Sleep Specialist. Sleep Apnea was defined by a Respiratory Disturbance Index (RDI) of 5 or more. Mild OSA was defined as an RDI of 5-14.9,Moderate OSA was defined as an RDI of 15-30 & Severe OSA was defined as an RDI of >30. CPAP titration was conducted as per AASM protocol. Patient parameters which were studied include Age, Sex, Height, Weight, Neck Size, BMI, RDI, Apnea Index, Lowest& Average Oxygen Saturation, Sleep Efficiency, Sleep Time, Time Below 90% Saturation, REM/Supine RDI, Maximum & Average time of Apnea, PLMi, Use of medications (Benzodiazepines, Sedatives, Antidepressants), history of Hypertension/Depression, Epworth Sleepiness Scale, Average Oxygen Saturation and Sleep Efficiency on Optimal CPAP, Optimal Pressure, Need for Oxygen, Total Time and Time Below 90% Saturation on Optimal CPAP, Need for BiPAP, & New Central Apneas after Titration. Data was analyzed using the Pearson Correlation Coefficient.
Results: Data for 150 patients was reviewed, which included 300 studies (NPSG and CPAP). There were 95 men and 52 women. Patients' age ranged from 11-84 years old. 92% of patients with Moderate (31) and Severe (73) OSA were titrated to optimal pressure of 8 cm or more. All patients who had a BMI>35, Neck Size >17 & RDI >30 required a pressure of 10 cm or more. 100% of Mild OSA patients (39) were titrated to an optimal pressure of 12 cm or less.
Conclusion: For successful CPAP titration, reaching & having adequate time on optimal pressure in different sleep stages & body positions is very important. Deciphering start CPAP pressure can make this process more efficient. As per our data, patients with Moderate/Severe OSA, should be started at 8 cm. In patients who have a BMI >35, Neck Size >17, and RDI>30, titration should begin at 10 cm. Finally, titration in Mild OSA patients should be done cautiously as most will require a pressure less than 12. Additional prospective randomized trials are needed to further evaluate the benefits of customized start CPAP titration pressures.

0681

TESTING THE NEW CMS GUIDELINES: WHAT DO THEY MEAN IN TERMS OF TREATMENT OUTCOMES?

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Introduction: CMS guidelines (in certain states) require OSA patients to demonstrate 90-day adherence to CPAP of 4+ hours over 70% of nights within any 30-day consecutive period. Non-adherers may lose their CPAP devices. There are currently no studies that have employed this adherence definition, making it difficult to appreciate the effect this might have on patients.
Methods: We examined a retrospective database from a large-scale clinical trial of 208 newly diagnosed patients with OSA who also received neuropsychological testing prior to treatment and 3 and 6 months post-treatment. We categorized patients according to the CMS criteria. Comparisons were made between the two groups on demographic and neuropsychological variables. Tests included measures of memory, executive functioning, and subjective sleepiness.
Results: 119 participants met the criteria for adherence, although the intent of the original study was to improve CPAP adherence, which may have inflated these numbers. The two CMS groups were similar in all demographic and disease severity measures and on all baseline cognitive measures. RM ANOVAs for cognitive tests demonstrated only time effects and no group nor time by group effects. Additional repeated measures ANOVAs were employed to assess change in function between 3 and 6 months for the "non-adherent" group (N=57). Continued improvements were noted on 2 of 3 measures of executive functioning (PASAT D, 3mo=24.4±11.9, 6mo=27.1±12.0; COWA 3mo=42.0±12.7, 6mo=44.5±12.7).
Conclusion: CMS guidelines for CPAP run the risk of taking treatment from "non-adherent users. Our data suggest that these patients demonstrate similar improvements in cognitive outcomes over 3 months and continue to improve on executive functions between 3 and 6 months. These continued improvements are not likely related to practice effects, which would be minimal between the second and third testing sessions, especially when separated by 3 months.
Support (optional): This study was supported by research grant R01 HL67209

0682

OSA PATIENTS DEMONSTRATED A SIGNIFICANT INCREASE IN OCCURRENCE OF SLEEP BREATHING DISORDERS AFTER SURGERY UNDER REGIONAL ANESTHESIA

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Introduction: Obstructive sleep apnea (OSA) is a risk factor for adverse perioperative events. Regional anesthesia may produce less respiratory depression and less interference with sleep. The study is to investigate the effect of surgery under regional anesthesia on the occurrence of sleep breathing disorders.
Methods: Following REB approval, preoperative patients consented for polysomnography (PSG) with a portable device (Embletta x100) be-

fore surgery at home, postoperative night1 ,3. The PSG recordings were scored by a certified sleep technologist. Data were analyzed according to the preoperative apnea-hypopnea index (AHI)>5 vs. AHI≤5 with SAS 9.1 for Windows.
Results: Sixty patients completed the study, 24 male and 36 female, including 58 orthopedics and 2 general surgeries. Age was 63 ± 9 and BMI 33 ± 8. Twenty patients had AHI≤5 (AHI≤5pt) on preoperative PSG and 40 pt AHI>5 (AHI>5pt). There is no significant difference between two groups in gender, age and BMI. The recovery of decreased REM sleep is slower in patients with AHI>5. On night 3, the REM sleep in patients with AHI>5 vs AHI≤5 was 14±11% (P<0.05 vs. preop) vs. 18±12%(p>0.05 vs. preop). AHI, REM AHI, NREM AHI, respiratory arousal index and oxygen desaturation index (ODI) were increased after surgery in both groups. But the significant increase was only observed in AHI>5pt on postoperative night 3 vs preop baseline: AHI: 52±39 vs 27±19 (p<0.05), REM AHI: 47±37 vs 38±22 (p<0.05), NREM AHI: 51±41 vs 24±20 (p<0.05), hypopnea index: 33±26 vs. 15±13 (p<0.05), ODI: 41±37 vs. 24±20 (p<0.05) and respiratory arousal index: 35±31 vs. 19±15 (p<0.05).
Conclusion: After regional anesthesia, OSA patients demonstrated a slower recovery in REM sleep and a significant increase in AHI, respiratory arousal index and ODI on postoperative night 3.

0683

CARDIAC NA/CA EXCHANGER-1 MEDIATES CARDIAC INJURY IN MICE WITH CHRONIC INTERMITTENT HYPOXIA

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Introduction: Chronic intermittent hypoxia (CIH), seen in patients with obstructive sleep apnea, leads to hypertension, ventricular hypertrophy and dysfunction, myocardial oxidative stress and apoptosis in rodents. We hypothesized that Na/Ca exchanger-1 (NCX1), a ubiquitous mechanism for control of intracellular Ca homeostasis, is involved in cardiac injury induced by CIH.
Methods: Cardiac-specific NCX1 knockout mice (KO) and their wild type (WT) littermates were exposed to CIH with nadir FiO2 of 5%, once per minute, 10 hours per day for 8 weeks. CIH was compared with similarly handled normoxic controls (HC). Four groups of 12 to 15 mice each were studied: WT/HC, WT/CIH, KO/HC, and KO/CIH. Outcomes included blood pressure (BP, by cath), left ventricular (LV) geometry (echo) and function (echo and cath), and myocardial gene/protein expression (real-time PCR or Western Blot).
Results: Myocardial mRNA expression of atrial natriuretic peptide, a gene marker for cardiac hypertrophy, was ~2-3 fold higher in both CIH groups than their HC groups (p<0.01). Myocardial NCX1 expression elevated by ~4 fold in WT/CIH compared to WT/HC (p<0.01). It was reduced by ~90% in KO/HC as in WT/HC (p<0.01), but there were no differences between the two KO groups. Mean BP was higher in both CIH groups compared to HC (WT/CIH 95.6+/-10.1 vs. WT/HC 82.0+/-7.3 mmHg, p<0.05; KO/CIH 93.8+/-8.3 vs. KO/HC, 80.8+/-6.9 mmHg, p<0.05). WT/CIH had significantly greater LV posterior wall thickness and LV end diastolic pressure (EDP), and lower fractional shortening and cardiac output than WT/HC. There were no significant differences between WT/HC and KO/HC in these cardiac parameters, or between KO/CIH and KO/HC except a significantly lower LVEDP in KO/CIH.
Conclusion: CIH in mice elevates BP, causes cardiac injury, and upregulates cardiac NCX1 expression. Cardiac-specific NCX1 knockout attenuates cardiac injury but not the elevated BP, suggesting that cardiac injury in CIH is independent to BP changes and mediated by cardiac NCX1.
Support (optional): American Heart Association

0684

A SIGNIFICANT EXACERBATION OF SLEEP BREATHING DISORDERS IN OSA PATIENTS UNDERGOING SURGERY WITH GENERAL ANESTHESIA

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Introduction: It is assumed that the sleep breathing disorder would be worse following surgery and anesthesia. The study is to investigate the change in frequency and severity of sleep disorder in OSA patients after surgery under general anesthesia.
Methods: Following REB approval, preoperative patients over 18 years old were recruited and invited for polysomnography (PSG) with a 10-channel portable device (Embletta x100) preoperatively at home, night 1 and 3 postoperatively in hospital. The PSG recordings were scored by a certified sleep technologist. Data were analyzed according to the preoperative AHI>5 vs. AHI≤5.
Results: Fifty-seven patients completed the study, 17 male and 40 female. Age was 60 ± 13 and BMI 30 ± 6; including 25 orthopedics, 10 general, 12 spine and 10 other type of surgery. There were 17 patients with AHI≤5 (Group I) on preoperative PSG and 40 patients with AHI>5 (Group II).There is no significant difference between two groups in gender, age, BMI and type of surgery. Compared with group I, the recovery of decreased REM and slow wave sleep was significantly delayed in Group II. AHI, REM AHI, NREM AHI, obstructive apnea index hypopnea index, respiratory arousal index and oxygen desaturation index (ODI) were increased after surgery in both groups. However, the significant increase was only observed on the third postoperative night in patients with AHI>5 (Group II), AHI: 49±34 vs. 24±17 preop (p<0.05), REM AHI: 49±38 vs. preop 31±27 (p<0.05), NREM AHI: 49±35 vs. proep 23±17 (p<0.05), obstructive apnea index: 17±18 vs. preop 9±10(p<0.05), hypopnea index : 28±25 vs. preop 14±11 (p<0.05), ODI: 34±29 vs. preop 19±16 (p<0.05) and respiratory arousal index: 29±27 vs. preop 17±13 (p<0.05).
Conclusion: Following surgery under general anesthesia, OSA patients had a slower recovery in sleep architecture and a significantly increased occurrence of sleep breathing disorders.

0685

WEIGHT CHANGE AFTER TREATMENT OF OBSTRUCTIVE SLEEP APNEA WITH POSITIVE AIRWAY PRESSURE

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Introduction: Obesity is causally linked to obstructive sleep apnea (OSA). It has been postulated that treatment of OSA leads to weight loss via increased daytime activity, however results are conflicting. We have examined weight change in OSA patients before and after treatment with positive airway pressure (PAP).
Methods: A retrospective chart review identified 432 subjects who were diagnosed with OSA and prescribed CPAP or BiPAP between 1999 and 2005. Change in BMI over intervals of 1, 2 and 3 years was compared before and after initiation of PAP. Student t-test was used to compare demographic, clinical and polysomnography (PSG) data between those who gained and those who lost weight (≥1kg/m^2) after PAP initiation.

Results: Mean BMI was 35.2±7.17 kg/m^2, mean age was 57.3±9.98 years, and 95% of subjects were male. Mean sleep parameters at diagnosis were as follows: apnea-hypopnea index (AHI) was 37±30.8 per hour, mean SpO2 was 88±4.1%, and nadir SpO2 was 80±12.7%. BMI increased significantly more during the year after PAP initiation compared to the year before PAP initiation (0.63±2.21kg/m^2 vs. 0.12±2.04kg/m^2, $p<0.05$). More patients gained weight the year after compared to the year before PAP initiation (69% vs. 57%, p=0.0005). BMI change over 2- and 3-year intervals did not differ significantly before and after starting PAP. Using regression analysis, none of the baseline variables (age, BMI, AHI, mean SpO2, and patient acceptance of PAP) predicted weight gain.
Conclusion: This retrospective study of clinical data suggests that weight increases during the first year of treatment with positive airway pressure, and may subsequently return to pre-treatment rates. Physicians treating obese patients with OSA should consider an aggressive plan for weight reduction when CPAP or BiPAP is initiated.

0686

FMRI STUDY OF CPAP TREATMENT ON VERBAL MEMORY ENCODING IN OBSTRUCTIVE SLEEP APNEA PATIENTS IN COMPARISON TO HEALTHY CONTROLS

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Introduction: Functional magnetic resonance imaging (fMRI) was used to investigate cerebral correlates of verbal memory (VM) encoding in patients with untreated obstructive sleep apnea (OSA) as compared to healthy controls.
Methods: Forty patients with untreated moderate or severe OSA and ten age and gender-matched healthy controls were scanned. Brain activation during word encoding was measured using a block-design fMRI task. Task blocks alternated between semantic and letter case decision blocks. A delayed recall task was administered after the scan.
Results: As expected, semantic decision condition yielded a higher level of subsequent recollection as compared to the letter case condition. No difference in accuracy was observed between the two groups for either condition. Significantly lower BOLD activation was found in OSA patients as compared to healthy controls (whole brain analysis, $p<0.001$, uncorrected) in right hippocampal and right frontal regions (BA 9, BA 24, BA6). There were no brain regions displaying higher BOLD activation in patients' group as compared to healthy volunteers.
Conclusion: Our results suggest that even in the absence of significant differences in behavioral VME performance, there are significant differences in brain activation between OSA patients and healthy controls.
Support (optional): Respironics, Covidien, Resmed and Swiss National Science Foundation.

0687

TESTING THE CMS GUIDELINES: WHAT DO THE NON-ADHERERS LOOK LIKE?

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Introduction: New guidelines put forward by CMS will, in certain states, require newly diagnosed OSA patients to demonstrate 90-day adherence to PAP of 4+ hours over 70% of nights within any consecutive 30-day period. Patients may ultimately lose their devices if they do not meet these criteria. Adherence has not previously been defined in this way. We attempted to describe the characteristics of the sample that would naturally meet or not meet these new criteria.
Methods: We examined a retrospective database from a large scale clinical trial of 208 newly diagnosed patients with OSA whose adherence to PAP was monitored objectively. Of these, 63 patients received no intervention geared toward increasing adherence. We categorized those patients according to the CMS criteria and compared the two groups on age, AHI, gender, prescribed pressure, BMI, Epworth, self-reported use of PAP, and objective hours of use per night.
Results: 46% of the 63 participants met criteria for adherence. T-tests demonstrated differences between the groups on self-reported and objective adherence only. Non-adherers used CPAP consistently less from week 1 through week 12 (Non-adherers: week 1 = 2.8±1.7, week 4 = 2.2±1.4, week 12 = 1.7±1.3, Adherers: week 1 = 4.8±2.5, week 4 = 5.4±1.9, week 12 = 5.6±1.6). Self-reported use was inflated for each group, but more so for the non-adherers (Non-adherers: week 12 = 4.4±1.9, Adherers: week 12 = 7.0±1.0).
Conclusion: Our findings suggest that non-adherence cannot be reliably predicted by typical demographic variables, including AHI, pressure, or sleepiness. Additionally, in this study, non-adherers seemed to overestimate their actual CPAP use, which would support the requirement of objective adherence monitoring as put forth by CMS.

0688

MAP INDEX SCORES IN MIDLIFE WOMEN WITH VARYING DEGREES OF OSA SEVERITY

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Introduction: The Multivariable Apnea Prediction (MAP) Index has been validated as a predictor of the presence of obstructive sleep apnea in general sleep clinic and other populations. We wanted to determine whether the MAP Index and MAP Apnea subscale are also good predictors among women during the menopausal transition.
Methods: As part of a longitudinal cohort study of sleep-disordered breathing in mid-life women, we are performing yearly overnight full polysomnography on pre, peri and postmenopausal women who are current or former residents of Philadelphia County. Each subject also completes the MAP Index on the evening of her study. PSG data were categorized by Apnea-Hypopnea Index (AHI, 0-<5, 5-<15, 15-<30, >30 events/hr). Data were analyzed using repeated measures ANOVA to test for group differences while taking advantage of all observations, since some subjects contributed repeated measurements.
Results: 74 women have completed at least 1 and up to 2 home sleep studies. The mean age of our subjects was 52.5 (SD 3.5) years. 45.9% of women were Caucasian, 51% African-American, and 3% of other races. For all subjects, the mean MAP score was 0.27 (0.22) and mean BMI was 30.8 (8.3) kg/m2. When categorized by AHI, there were 9 women with a normal AHI, 33 with mild, 43 with moderate, and 15 with severe OSA. Mean MAP Apnea subscale scores (range 0-3.67) were highest in the group with severe OSA (0.989 (1.319), compared to 0.630 (0.655) in normals, 0.626 (0.889) in mild OSA, 0.651 (0.630) in moderate OSA). However, scores were similar among women with normal and mild or moderate OSA, and these differences were not statistically significant (P=0.63). When the total MAP score, which incorporates BMI, AHI, age and sex, was compared between groups, mean total MAP Index was also higher in women with severe OSA (0.44 (0.25), v. 0.12 (0.06) in normal, 0.27 (0.26) in mild, 0.26 (0.16) in moderate OSA) compared to other groups, but differences were not statistically significant (P=0.18).
Conclusion: We found no significant differences in Apnea subscale or total MAP Index scores among mid-life women with varying degrees of OSA severity. Research has shown that women tend to under-report apnea symptoms such as snoring, and often report symptoms differently than do men. This may help to explain why the MAP Index, which is based on symptom self-report, was not significantly higher with increasing OSA severity in this all-female cohort.
Support (optional): NIH R01HL085695

0689

HYPOTHALAMIC SIRT1 IS DOWN REGULATED IN A MURINE MODEL OF SLEEP APNEA OXYGENATION PATTERNS

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Introduction: SIRT1, the mammalian ortholog of Sir2, is a nuclear enzyme that governs essential metabolic and physiological processes. SIRT1 renders cells more resistant to oxidative stress and promotes insulin sensitivity. SIRT1 requires NAD+ for activity. We hypothesized that the oxidative stress incurred by exposure to sleep apnea hypoxia/reoxygenation patterns would reduce SIRT1 protein levels and activity.
Methods: We exposed adult male C57BL/6J mice to intermittent hypoxia (IH) or sham treatment (sham) modeling moderate-severe oxyhemoglobin desaturations at 40 events/hr for 8wks. The percentage of DAB-immunolabeled nuclei was counted in hypothalamic nuclei. As a measure of SIRT1 activity, acetylated p53 (a SIRT1 target) was measured in the same regions.
Results: SIRT1 immunoreactivity was present within the hypothalamus in the lateral hypothalamus(LH) arcuate(ARC), ventromedial(VMH), dorsomedial(DMH), and paraventricular(PV) nuclei. Overall, the percentage of nuclei immunoreactive for SIRT1 was reduced in mice exposed to IH, varying across nuclei. LH sham vs. IH: 82%±5 vs. 54±6,$p<0.001$; ARC, sham vs. IH: 87%±10, 62±8,$p<0.01$; VMH, 57±4, 41±4,$p<0.05$; DMH, 67±7, 40±5, $p<0.01$; PV, 25±2, 15±3, N.S. The percentage of cells labeled with acetyl-p53 increased across the hypothalamus in mice exposed to IH, $p<0.001$. Sham vs. IH: LH, 32%±6 vs. 84%±4,$p<0.001$; ARC, 40%±5, 75±10,$p<0.001$; VMH, 12%±2, 24±4,$p<0.05$; DMH 35%±4, 51%±7,$p<0.05$; PV 7%±3, 10±3,N.S. LH Orexinergic neurons evidenced IH-induced SIRT1reduction and acetyl-p53 augmentation.
Conclusion: Intermittent hypoxia reduces SIRT1 immunoreactivity in select hypothalamic nuclei. Reduced SIRT1 activity is supported by the increased acetylated p53. Reductions in SIRT1 activity are expected to increase appetite, impair mitochondrial function and redox capacity, while promoting both insulin resistance and fat deposition. It is anticipated that hypoxia/reoxygenation patterns observed in moderate-severe obstructive sleep apnea could worsen several of the co-morbidities of obstructive sleep apnea through the down regulation of hypothalamic SIRT1.
Support (optional): This work was supported, in part, by NIH HL079555 and HL080492.

0690

EFFECT OF A SELF-MANAGEMENT INTERVENTION ON CPAP ADHERENCE AND TREATMENT EFFICACY

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Introduction: CPAP is the gold standard treatment for OSA and it is generally accepted that adherence to CPAP can be substantially improved. A key advantage to using CPAP is its ability to objectively measure and store both treatment efficacy and adherence data. Unfortunately, under usual and customary care, there is generally a time lag ranging from days to weeks between adherence data collection and data availability to care providers.
Methods: This was a randomized, controlled trial of usual care compared to a self-management intervention, which consisted of group-based self-management education and is based on a chronic illness care approach. The self-management education consisted of three weekly sessions over the first 2 weeks of CPAP use, and included group review of each patient's nightly CPAP adherence level and efficacy data, along with a focus on troubleshooting any problems. Only new CPAP patients were included in this study.
Results: 240 patients diagnosed with OSA and prescribed CPAP were studied. At baseline, mean age=58.1±12.3, mean AHI=37.5±20, and mean body mass index = 33.4± 6.3 (mean±SD). There were no baseline differences in sleep apnea severity or body mass index between the groups. Nightly CPAP adherence measured over the follow-up period was 3.4±3.0 and 4.5±2.9 hrs/night ($p=.032$) for the usual care and self-management and groups, respectively.
Conclusion: Self-management education has the potential to be an effective and practical way to improve CPAP adherence. Key advantages of the self-management intervention are that it can be easily taught to sleep apnea patients, and helps them focus on troubleshooting problems collaboratively with their sleep providers. This intervention has the potential to help patients better manage their OSA by helping to establish optimal and enduring patterns of CPAP treatment adherence from very early in the treatment initialization process.
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0691

DIFFERENCES IN CEREBRAL ACTIVATION ON A VISUO-SPATIAL WORKING MEMORY TASK IN OBSTRUCTIVE SLEEP APNEA PATIENTS AND HEALTHY CONTROLS

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Introduction: Functional magnetic resonance imaging (fMRI) studies enable investigation of neural correlates underlying behavioral performance. In the present study we used a visuo-spatial n-back task to investigate the working memory (WM) function of patients with untreated obstructive sleep apnea (OSA) as compared to healthy controls.
Methods: A parametric fMRI experiment with four levels of a spatial N-back task was used to investigate the pattern of cortical activations across the various degrees of load in 25 patients with moderate or severe OSA and 11 age and gender-matched healthy controls.
Results: As expected, we found activations in a similar cortical network in patients and healthy subjects, involving bilateral supplementary motor area, dorsolateral prefrontal cortex (DLPFC) as well as precentral and parietal regions. The activity in these regions increased linearly with increasing load. Whole brain group analysis using random effect modeling of the two groups (patients and controls) demonstrated a significantly ($p<0.001$, uncorrected) higher BOLD activation in right frontal regions (BA 32, BA 6) in healthy controls at maximum WM loads. There were no brain regions displaying higher BOLD activation at maximal WM load in patients' group as compared to healthy volunteers.
Conclusion: Our results indicate that at maximal WM loads (3-back) healthy controls display higher brain activation in several right frontal regions as compared to OSA patients.
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0692

SURFING FOR SLEEP APNEA: A REVIEW OF THE QUALITY OF INFORMATION FOR PATIENTS ON THE INTERNET

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Introduction: The internet is a powerful source of information, but the quality of patient-education and its reliability is largely unregulated. The aim of this study was to assess the quality of patient- related sleep apnea

information available on internet sites. Given its chronic nature, accurate and effective patient education is key to long-term treatment success.
Methods: Sleep apnea websites that are publicly available to consumers were reviewed and coded. Websites were analyzed for the quality of patient-education and their accessibility. Coding of each website was classified into two groups: descriptive variables and process variables. The descriptive variables included: the type of website; actively maintained; representation of general disclaimer and web certification. Process variables included: level of interactivity, user friendliness, Elasy patient education criteria, social support availability and type, and incorporation of Chronic Care Model elements.
Results: A total of forty-nine relevant websites were found and assessed. Of these, 20.4% were in blog format and 24.5% included forums. 83.7% of the sites were recently maintained or updated within the last six months. 44.9% provided a general disclaimer statement that addressed the limits of the information provided on the website, while only 16.3% had a valid web certification such as TRUSTe or HON. The level of interactivity was divided into two groups: general interactivity, which included the presence of any online interactive assessments, personal data tracking or the ability to email content experts; and graphical interactivity, which included the graphic illustration of personal health data. 14.3% of the websites included some form of general interactivity while only 2% of websites offered graphical interactivity.
Conclusion: Further studies are needed to further evaluate the quality of patient-education on the web for guiding consumers to a high quality of health information. Sleep apnea websites do not appear to be taking full advantage of state-of-the-art technologies on the internet as it relates to patient education.
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0693

SIDE EFFECTS OF CPAP TREATMENT AT 2 WEEKS AND 6 MONTHS AND THEIR CORRELATION TO ADHERENCE

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Introduction: Side-effects to CPAP treatment are common, and a cause of observed low adherence. There is a lack of research on whether these side-effects vary over time. The SECI is a new, validated instrument to assess side-effects in CPAP treated patients. The aim of this study was to describe the self-rated negative consequences on adherence by different side-effects at 2 weeks and 6 months.
Methods: A prospective, descriptive design was used. 143 consecutive OSA/OSAS patients at three CPAP clinics were enrolled. They filled in the SECI after 2 weeks and 6 months of CPAP use. SECI lists 15 common side-effects and asks the respondent to rate the frequency, magnitude and negative effect on adherence on a 5-point Likert scale for each side effect. Descriptive statistics and correlations were used to describe data.
Results: 75% of the subjects were male. Mean age was 55+-11 yrs, BMI 30,8+-4,7, ESS 10+-5,7 and AHI 43+-21. The dropout rate after 6 months was 24%. The side-effects that were correlated to a decreased objective CPAP use at 2 weeks were dry mouth, being seen with the device by others, nocturnal awakenings, disturbing noise and difficulties to exhale. Correlations between all SECI items and objective CPAP use after 6 months were generally weak.
Conclusion: There are several significant correlations between individual side-effects and decreased CPAP use at two weeks, but not at six moths. This might in part be due to a higher dropout rate among patients experiencing more side-effects. Further research is needed to understand what causes late dropouts from treatment.

0694

REDUCING DIETARY GLYCATION END-PRODUCTS PROTECTS MURINE MODEL OF SLEEP APNEA FROM MOTONEURON INJURY

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Introduction: Hypoxia/reoxygenation events are important physiological disturbances in obstructive sleep apnea and have been shown to induce neural injury. Long-term exposure to intermittent hypoxia (IH) in mice induces endoplasmic reticulum stress (ERS) injury in select upper airway dilator motoneurons, including hypoglossal motoneurons. Motoneurons most susceptible to hypoxia/reoxygenation evidence ERS at baseline. We hypothesized that dietary advanced glycation end products (AGE) contribute to basal ERS in motoneurons and predispose the neurons to IH injury.
Methods: Adult male C57BL/6J mice were randomized to low or normal AGE diets (by altering cooking times/temperatures for food) for 4 weeks prior to IH or sham- IH(8wks, n=5/group), continuing dietary AGE. Motoneurons were analyzed for overall AGE content, oxidative stress dependent AGE, carboxy-(methyl)-lysine (CML) and ERS injury.
Results: On normal AGE diet, there were significant differences across motor nuclei for AGE immunoreactivity in motoneurons: highest in spinal motoneurons, hypoglossal and facial and least in occulomotor. Low-dietary AGE reduced AGE: III($p<0.001$), moV($p<0.01$), VII($p<0.001$), XII($p<0.001$) and cervical spinal motoneurons,$p<0.001$. Lowering dietary AGE improved basal ERS response by increasing p-eIF-2a ($p<0.05$) and lowering basal CHOP immunoreactivity($p<0.01$). IH increased CML in facial($p<0.001$) and hypoglossal($p<0.01$). Mice fed low AGE diet conferred resistance to IH ERS injury with no increased in CHOP or caspase-7(N.S.).
Conclusion: We have discovered a novel source of increased basal ERS in motoneurons: AGE. Motoneuronal AGE content was lowered effectively by modifying dietary AGE intake, and the unfolded protein response improved. Mice fed the low-AGE diet conferred protection from IH ERS injury. Herein, we have identified dietary AGE as an important modifier of motoneuron ERS response in general and an important variable in susceptibility to injury in a murine model of sleep apnea. It is anticipated that this dietary factor influences motoneuronal injury in obstructive sleep apnea and potentially other motoneuronal disorders.
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0695

MEASURES OF MARITAL QUALITY SIGNIFICANTLY IMPACT OBSTRUCTIVE SLEEP APNEA (OSA) SUBJECT'S COMPLIANCE WITH CONTINUOUS POSITIVE AIRWAY PRESSURE TREATMENT

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Introduction: Compliance with CPAP is low despite the efficacy of this treatment in Obstructive Sleep Apnea (OSA). There is little data concerning the effect of marital quality on compliance with CPAP. The aim of this study was to determine whether marital quality affects compliance with CPAP therapy, and whether the association between marital quality and compliance varies with gender.
Methods: 116 subjects (M/F- 87/29, mean age 62.4, age range 31-85) were recruited from subjects participating in the Apnea Positive Pressure

Long-term Efficacy Study (APPLES), a study evaluating the long term effectiveness of CPAP therapy for OSA. Inclusion in the current analysis required that subjects were married during the APPLES study and still be married at the time of questionnaire administration. The Dyadic Adjustment Scale (DAS), a validated quality of marriage questionnaire was utilized in this study. This is a 32-item self-report questionnaire measuring dyadic consensus, satisfaction, cohesion, and affectional expression. A high score in the DAS is indicative of a person's adjustment to the marriage. Additionally, questions related to spouse involvement with general health and CPAP use were asked.
Results: Three years after completing APPLES, 63 patients were still compliant by self-report and 53 were noncompliant with CPAP treatment. There were no significant differences in overall marital quality between the compliant and noncompliant groups. However, the Consensus dimension was significantly higher in the compliant versus the noncompliant group (p=0.045). The level of spouse involvement in subject use of CPAP was significantly higher in the compliant group (p=0.005). Spouse general involvement in subject's health was significantly higher in the compliant group (p=0.005). Males (63.9%) were significantly more compliant than females (41.4%) in compliance with CPAP (p=0.035).
Conclusion: Marital quality measures, such as spouse involvement in general health, CPAP use, and level of consensus in marriage are important factors in CPAP compliance amongst OSA patients.
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0696

SLEEP DISORDERED BREATHING (SDB) RELATED CHANGES IN EEG POWER SPECTRA

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Introduction: Patients with SDB experience sleep fragmentation with arousals, increased stage 1, and decreased slow wave (SWS)and/or REM sleep. The temporal pattern in the EEG power spectra (PS) has not previously been examined. This study sought to investigate SDB-related changes in the sleep EEG using power spectral analysis (PSA).
Methods: Sixty subjects with an AHI > 30 events/hr were matched to 60 normal subjects (AHI = 0 events/hr) on gender, race, age and BMI. Participants with a history of cardiovascular disease, type 2 diabetes mellitus, or smoking were excluded. Conventional sleep staging and techniques of spectral analysis were used to analyze the EEG during sleep. The power spectrum was determined for the entire sleep period and categorized into four frequency bandwidths (δ,θ,α,β). Average and relative power were ascertained for each 30 second epoch. Generalized linear mixed models and regression splines were used to describe the evolution of spectral power during the sleep period.
Results: The median AHI in the subjects with SDB was 38.6 events/hr. Conventional sleep staging showed no differences in the percentages of stage 1, 2, SWS, or total sleep time between the two groups. Spectral analysis showed a decrease in α-power of 1.2% and 1.4%, respectively for subjects with and without SDB ($p< 0.05$). Linear mixed models showed that the trajectories of power spectra for subjects with and without SDB were different during the sleep period. The time-dependent changes of δ-power and α-power during the sleep period were blunted in subjects with SDB ($p < 0.001$).
Conclusion: Spectral analysis of the sleep EEG revealed significant differences in the magnitude and temporal structure of δ-power and α-power in subjects with and without SDB who were noted to have similar amounts of visually scored stages 1,2 and SWS. Furthermore, trajectories of α-power and δ-power suggest that SDB modifies the normal evolution of EEG activity during sleep and imposes profound alterations in sleep structure that are more evident when using PSA or multi-state survival analysis compared to conventional staging.

0697

THE RELATION BETWEEN INSOMNIA COMPLAINTS AND CPAP USE IN A PATIENT SAMPLE

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Introduction: Increasing evidence suggests a frequent co-occurrence between insomnia and sleep-disordered breathing. Further, evidence suggests that patients experiencing both insomnia and SDB suffer greater daytime impairment and are at increased risk for negative health outcomes, relative to patients with only one disorder. One aspect of combined insomnia and SDB that has received surprisingly little research attention is the effect of insomnia complaints on subsequent CPAP adherence.
Methods: The current sample includes 147 consecutive OSA patients (54.2% men, mean age= 51.1±11.8 years, mean BMI=34.4±8.0) in the Johns Hopkins Sleep Disorder Center who returned for CPAP follow-up visits and provided consent for their health information to be included in an IRB-approved research database. Prior to their CPAP titration PSG, patients completed a questionnaire asking about insomnia symptoms including difficulty initiating sleep, difficulty maintaining sleep, and early morning awakenings, with all responses scored on a 5-pt scale. CPAP use was measured via objective monitoring cards provided by patients at follow-up. All patients provided minimum 28 days of data.
Results: Mean CPAP usage was 4:12±2:33 across all nights and 5:18±2:09 on nights when CPAP was used. Among women, insomnia complaints were not significantly related to either measure of CPAP use (all p's > .2). However, among men, complaints of sleep maintenance insomnia displayed a statistically significant negative relation to CPAP use averaged across all nights ($r=-.35$, $p<.01$) and on nights used ($r=-.30$, $p=.01$). Further, among men complaints of early morning awakening displayed a nearly statistically significant negative trend toward decreased use on night used ($r=-.22$, $p=.07$).
Conclusion: In this clinical sample, complaints of sleep maintenance insomnia and early morning awakenings were related to poorer CPAP adherence among men but not among women. Reducing insomnia complaints among selected men prescribed CPAP may be a straightforward and cost-effective way to increase CPAP adherence.

0698

VALIDATION OF THE SIDE-EFFECTS TO CPAP TREATMENT INVENTORY - A NEW TOOL FOR THE MEASUREMENT OF SIDE-EFFECTS TO CPAP TREATMENT

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Introduction: Side-effects are common to continuous positive airway pressure (CPAP) and long-term adherence low. No validated self-rating scale measuring side-effects to CPAP treatment exists today. The aim of this study was to investigate the validity and reliability of the Side-Effects to CPAP-treatment Inventory (SECI) among patients with obstructive sleep apnea syndrome (OSAS).
Methods: A cross-sectional descriptive design was used. A total of 350 OSAS patients (60% men) with a mean use of CPAP treatment for 45 months (2 weeks-182 months) were included. Data collection was achieved with SECI, as well as from medical records. SECI includes 15 different types of side-effects related to CPAP treatment. Each one includes 3 sub-questions (focusing frequency, magnitude, and decrease of CPAP use) answered on a five-point Likert type scale. All items re-

flecting frequency and magnitude of side-effects, as well as decrease of CPAP use are treated as separate scales. The possible range for each scale can be 15-75 with a higher score indicating a higher frequency and magnitude of side effects, as well as a decreased self-rated CPAP use (i.e., adherence).
Results: The median score for the three scales varied between 22-31, with the highest score for the frequency- and the lowest for the adherence scale. The strongest correlation between the three scales was demonstrated between the frequency- and magnitude scale (0.874). A principal component analyses of SECI resulted in a two factor solution describing a device- and a symptom scale. Most of the SECI scales demonstrated satisfactory internal consistency reliability. Highest reliability was demonstrated in the adherence- (0.869) and the magnitude (0.828) scales, while the frequency scale demonstrated lowest internal consistency (0.749).
Conclusion: The high values of reliability and validity of this new instrument are promising and indicates that SECI can be used to measure side-effects to CPAP-treatment in patients with OSAS.

0699

RIGHT VERSUS LEFT LATERAL DECUBITUS POSITION AND THE SEVERITY OF OBSTRUCTIVE SLEEP APNEA

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Introduction: The severity of obstructive sleep apnea (OSA) is worse when the patient is in supine position. However, the difference between the right lateral decubitus (RLD) and left lateral decubitus (LLD) positions on sleep related breathing disorder is still unknown. The aim of this study is to evaluate the severity of Apnea Hypopnea Index (AHI) in the RLD, LLD, and supine position of patients with moderate to severe OSA.
Methods: Fifteen consecutive polysomnograms of adult patients with moderate to severe OSA (AHI >15/hour) referred to JFK Sleep Center between September and November 2008 were reviewed. Only those patients who spent at least 15% of their total sleep time (TST) in the LLD, RLD and supine sleep were included in the study. Data on Total Sleep Time (TST), % TST in NREM/REM sleep, % TST per body position, and AHI per body position were collected. The data was processed using the SPSS software for Windows. Friedman and Wilcoxon ranked sign tests were used for statistical analysis.
Results: The mean age was 54.75 +/- 8.66 with mean BMI of 34.60 +/- 8. Sixty seven percent of the patients were males. TST was 362.960 minutes +/- 49.63, and 85.45% +/- 4.4 was spent in NREM sleep. AHI was 47.91 +/- 30.99, with Arousal Index of 31.91 +/- 17.623. There was a significant difference in the AHI in the supine, right lateral decubitus (RLD), and left lateral decubitus (LLD) position of patients in the study ($p < 0.015$). Patients had higher supine AHI (65.19 +/- 30.66) compared to RLD AHI (43.58 +/- 36.79) and LLD AHI (42.49 +/- 39.65) position. There was a significant difference between the supine AHI compared to non supine AHI ($p < 0.023$). However, there was no significant difference between the AHI of patients in the RLD and LLD positions ($p > 0.776$).
Conclusion: The severity of AHI among adult patients with moderate to severe OSA is worse in the supine compared to the RLD and LLD positions. However, there is no difference between the AHI of patients in the RLD and LLD positions.

0700

TESTING THE CMS GUIDELINES: DO BEHAVIORAL INTERVENTIONS INCREASE LIKELIHOOD OF ADHERENCE?

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Introduction: New guidelines put forward by CMS will require, in some states, new OSA patients to demonstrate 90-day adherence to PAP of 4+ hours over 70% of nights within any consecutive 30-day period. Patients ultimately may lose their devices if they do not meet these criteria. We attempted to determine whether various behavioral interventions would improve the likelihood of being defined as "adherent" using these criteria.
Methods: We examined a retrospective database from a clinical trial of 207 newly diagnosed patients with OSA whose adherence to PAP was monitored objectively. These patients were randomly assigned to either a Motivational intervention (ME: N=71), an Educational intervention (ED: N=73), or to Standard Care (SC: N=63). Interventions were conducted over only 2 sessions within the first two weeks of CPAP. We analyzed the effect of these interventions on whether the patient would or would not have met the new CMS criteria.
Results: The three groups were similar in all demographic and disease severity variables with the exception of age, where the Education group was younger than the other two groups. Overall, 88 (43%) of the 208 participants did not meet the new CMS criteria. ED demonstrated an advantage over SC ($p<.05$), even when age was co-varied in the model. Individuals in the ED group were 2.7 times as likely as those in the SC group to meet criteria for adherence (Percent meeting criteria ED: 67%, ME: 58%, SC: 46%).
Conclusion: Our data support the notion that intervening with patients at or near their CPAP initiation can positively affect the likelihood of good adherence. In particular, the educational intervention was highly associated with patients' having met criteria to keep their devices.

0701

MICROGLIAL RESPONSE TO SLEEP APNEA OXYGENATION PATTERNS IN VITRO AND IN VIVO

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Introduction: In humans with sleep apnea, intermittent hypoxemia is the strongest predictor of an inflammatory response. Animal models of sleep apnea oxygenation patterns evidence proinflammatory responses. The mechanisms by which intermittent hypoxia (IH) promotes inflammation are unknown. We hypothesized that microglia, CNS inflammatory cells, develop a proinflammatory response to IH We then sought to determine whether the microglia can respond directly to hypoxia and whether this injury includes an endoplasmic reticulum stress response.
Methods: For in vivo studies, adult male C57BL/6j mice were exposed to 8 wks of IH. Brains were labeled with F4/80, TNF-a and CHOP. We developed an in vitro system by which immortalized murine microglia are continuously perfused for 18hrs with culture medium (normoxia-55-mmHG) and hypoxia-25mmHG).
Results: Mice exposed to IH showed increased TNF-a and CHOP in microglia in the hypoglossal nucleus ($p<0.01$, $p<0.05$). CHOP immunoreactivity followed TNF-a immunoreactivity. In our in vitro model, hypoxic medium increased TNF-a and CHOP in, $p<0.001$, $p<0.001$. There was a direct correlation between the TNF-a and CHOP immunoreactivity, $r2 = 0.65$, $p<0.001$. Quantitative RT-PCR showed: TNF-a copy numbers/2ug RNA, IH:44, 023±5623 vs. sham:5135±438, $p<0.001$. CHOP copy numbers/2ug RNA were IH:8040±145 vs. sham: 1415±120, $p<0.01$.

Conclusion: IH activates the proinflammatory response in microglia in vivo. Increased CHOP, a pro-apoptotic factor, in microglial cells suggests that microglial cells, are susceptible to IH injury. Findings with the in vitro system support the concept that microglial cells are directly vulnerable to hypoxia, and likely IH. That TNF-a predicts CHOP suggests that ER stress may contribute to the inflammatory response. It is anticipated that individuals with severe obstructive sleep apnea have a microglial proinflammatory response. This response could render neurons more susceptible to other neural injuries.
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0702

REDUCED CORTICAL THICKNESS IN OBSTRUCTIVE SLEEP APNEA PATIENTS

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Introduction: Obstructive sleep apnea patients show reduced gray matter volume in many sub-cortical regions, as well as indications of injury to white matter tracts. However, previous studies have used whole-brain voxel-based analyses to locate regions of structural deficits, and these techniques are not specific to cortical regions. We hypothesized that cortical areas overlapping and adjacent to previously-identified regions of injury would specifically show alterations, as measured by cortical thickness.
Methods: We collected high-resolution T1-weighted anatomical MRI brain scans in a 3 Tesla scanner from 39 recently-diagnosed, untreated moderate-severe OSA (AHI mean ± stdev 35.8 ± 3.0 events/hour; age 46.1 ± 1.4 years; female:male 7:32) and 64 healthy control (age 47.5 ± 1.1; female:male 23:41) subjects. We calculated and analyzed cortical thickness using FreeSurfer software, and performed surface-based analysis using ANCOVA to compare cortical thickness between OSA and control groups (threshold: t-statistic > 2.5), with total intracranial volume as a covariate (to account for skull size).
Results: Decreased cortical thickness in OSA vs. controls appeared in multiple regions. The bilateral mid-parahippocampal gyrus was especially affected, as was the right amygdala region. The right medial prefrontal cortex, adjacent to regions of compromised white matter, showed reduced thickness, as did a region in the left ventral medial prefrontal cortex. Other impacted regions included the left posterior cingulate, and isolated areas in the right temporal cortex and left post-central gyrus.
Conclusion: Cortex overlying areas of previously-demonstrated structural injury showed reduced thickness in OSA patients. Thinning of the cortex represents a loss of neurons or supportive tissue, likely from a combination of hypoxic processes, elevated stress hormones, and inadequate perfusion occurring in the syndrome. The consequences are likely manifested in the neuropsychological characteristics of OSA, especially those that do not fully resolve with treatment, such as mood disturbances and cognitive deficits.
Support (optional): National Institutes of Health HL-60296

0703

MANDIBULAR ADVANCEMENT DEVICES SIGNIFICANTLY IMPROVE NEUROCOGNITIVE FUNCTION FOR PATIENTS WITH OBSTRUCTIVE SLEEP APNEA

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Introduction: Obstructive sleep apnea is routinely treated with Mandibular Advancement Devices (MADs). We previously reported preliminary baseline and one-month post-treatment neurocognitive changes for OSA patients treated with MADs compared to CPAP treatment and healthy controls. This report extends the analysis to three months post-treatment with MAD.
Methods: The Alertness and Memory Profiler (AMP) quantified EEG/performance and neurocognitive factors during: 3-Choice-Vigilance-Test(3C-VT), Standard Image-Recognition (SIR), IR with Interference(I-IR), Number IR(NIR), Verbal Paired-Associate-Learning(VPA), and Sternberg-Verbal-Memory-Scan(VMS). OSA patients treated with MAD (n=51, 33male, mean age=52.88, SD= 9.63, range=28-71; mean RDI= 28.19, SD=15, range=5-77) were evaluated with AMP pre-treatment, one-month and three-months post-treatment and were compared to OSA patients treated with CPAP and healthy controls.
Results: 3(group)X3(time) RMANOVA showed significant effects for both MAD and CPAP groups across several EEG performance metrics from pre-treatment to one-month and three-months post-treatment including: improved Visuospatial Processing Speed($F=5.611$, $p<.001$) and Sustained Attention($F=3.04$, $p<.05$); faster reaction times on SIR1($F=4.749$, $p=.001$), VMS($F=2.703$, $p<.05$), and VPA ($F=3.541$, $p<.01$); improved percent correct scores on 3CVT($F=3.749$, $p<.01$), IIR ($F=3.558$, $p<.01$), NIR($F=2.757$, $p<.05$), and VMS($F=6.826$, $p<.001$); and decreased percent missed on 3CVT($F=2.734$, $p<.05$). Furthermore, our apnea risk measure, ACES, measured by an EEG composite evaluation score (2-class Linear Discriminant Function Analysis using 60 EEG variables) improved for MAD($F=11.638$,$p<.001$), indicating a reduction in apnea probability. This data indicates that MAD patients show continued and/or sustained improvement from one month to three months post-treatment.
Conclusion: At baseline, OSA patients exhibited significant impairment across alertness/memory tasks relative to healthy controls. MAD and CPAP therapies significantly improved neurocognitive function one and three-months post-treatment. After three months of therapy, MAD patients improved to normal levels on a number of EEG and performance metrics. This data highlights MAD therapy as a viable treatment option for patients with OSA.

0704

USE OF RESPIRATORY IMPEDANCE SENSING AS RESPIRATORY EFFORT SENSOR FOR IDENTIFICATION OF OBSTRUCTIVE EVENTS

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Introduction: Airflow and respiratory effort signals are required for the identification and classification of sleep disordered breathing (SDB) episodes. Respiratory effort is used to distinguish central from obstructive events, depending on whether inspiratory effort and airflow signals dissociate during tidal breathing. Current non-invasive sensors (piezo-belts and inductance belts) serve as surrogates for respiratory effort by detecting tidal changes in chest and abdominal circumferences. Recent work in dogs has suggested that tidal changes in diaphragmatic position can be detected with respiratory impedance monitoring, which may prove to be a reliable measure of respiratory effort. The present study was conducted to compare respiratory impedance to standard effort signals in the detection and classification of SDB episodes.
Methods: Seven sleep apnea patients (males, age 56±12, BMI 28.1±2.4, AHI 43±29) were studied during sleep using standard polysomnography (PSG), including EEG, EOG, EMG, ECG, oximetry, nasal pressure/airflow, snoring sounds, and respiratory inductance plethysmography (RIP) belts. Respiratory impedance (Zresp), via adhesive skin-surface electrodes, was measured using 2 sets of electrodes overlying the right hemidiaphragm on each subject. Six to fourteen 3-minute epochs were selected at regular intervals from each subject. A Registered PSG Technician scored each epoch twice, once blinded to RIP and once blinded to Zresp signals, for the presence and type (central, mixed, obstructive)

of SDB events. Counts of SDB events for each method were cross-tabulated and compared. The percent raw agreement and Cohen's kappa statistic were used to compare the two scoring methods.
Results: 87% (167/192) of all SDB episodes were scored identically, yielding a kappa statistic of 0.36 (p=0.001). 92% (159/173) agreement was achieved for detecting obstructive events.
Conclusion: RIP and Zresp were comparable methods in detecting SDB events, and especially in detecting obstructive events. Our finding suggests that impedance-based sensing of respiratory effort may be useful for diagnosing and treating OSA.
Support (optional): This study was sponsored by Apnex Medical Inc., St. Paul, MN, USA.

0705

CPAP IMPROVES EXECUTIVE FUNCTION IN ALZHEIMER'S PATIENTS WITH OSA

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Introduction: Obstructive sleep apnea (OSA) is known to have a negative effect on cognitive functioning. We have previously shown that CPAP treatment of OSA in patients with mild-moderate Alzheimer's disease (AD) results in improvement in a neuropsychological test battery composite score. We now examine which specific cognitive domains show improvement.
Methods: 54 men and women with AD and OSA were randomized to either therapeutic CPAP (tCPAP) for 6-weeks or placebo CPAP (pCPAP) for 3-weeks followed by tCPAP for 3-weeks. At baseline, 3-weeks and 6-weeks, participants were administered a complete neuropsychological test battery which examined changes in cognitive abilities related to AD (learning/memory), to OSA (learning/memory and frontal/executive skills), to sleep-disturbance (attention, vigilance), and to normal aging (mental processing speed). Scores were converted to z-scores. The analysis consisted of a two-sample nonparametric Wilcoxon rank sum test to compare changes in domains from baseline to 3 weeks between treatment groups. In addition, a paired analysis of changes in domains after 3 weeks of tCPAP in both groups was also undertaken (defined as baseline to 3 weeks in the tCPAP group, and 3 to 6 weeks in the pCPAP group) using a Wilcoxon signed rank test. All hypotheses were two sided and were tested at the 5% significance level.
Results: There were no significant differences in any domains found between treatment and placebo at three weeks, similar to the findings of the composite score. However, in the paired analyses comparing three weeks of therapeutic CPAP to baseline, there was significant improvement in executive functioning ($p = 0.038$)
Conclusion: These findings suggest that treating OSA with CPAP in patients with AD may result in improvements in executive functioning. These data lend support to the idea that clinicians should not hesitate to treat sleep disorders in patients with dementia.
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0706

BI-LEVEL POSITIVE AIRWAY PRESSURE DEVICE FOR HYPERTENSION IN OBSTRUCTIVE SLEEP APNEA

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Introduction: Evidence suggests device-guided paced respiration (<10 breaths/minute) may reduce blood pressure in hypertensive patients. Although the mechanism by which breathing manipulations exert their antihypertensive effects remains unknown, we believe slow deep breathing may have sympatholytic properties. We hypothesized that patients with obstructive sleep apnea (OSA) performing daily slow deep breathing may experience reduced sympathoexcitation - evidenced by reductions in blood pressure.
Methods: We enrolled 29 subjects previously diagnosed with hypertension and OSA, currently on CPAP, into a one-armed pilot study. Subjects were instructed to perform bi-level PAP-guided paced respiration (using a novel proprietary device) for 30 minutes a day while awake for 8 weeks. Our primary outcome was change in office systolic and diastolic blood pressure between baseline and 8 weeks.
Results: Twenty-eight (98%) of subjects completed the study. The mean baseline blood pressure was 137.2 ± 12.7 mmHg systolic and 85.5 ± 7.6 mmHg diastolic, 81% used anti-hypertensive medications, mean BMI was 35.6 ± 7.1 kg/m2, and mean AHI was 52.7 ± 32.2events/hour. Complete device data were available for 21 (75%) of subjects. Mean device compliance was 82% ± 22, 52% of subjects achieved a mean breath rate <10 breaths/minute over 8 weeks. Four (4) subjects with complete device data had changes in their blood pressure medication regimen during the study. Among the remaining 17 subjects, the mean difference in office blood pressure from baseline to 8 weeks was -6.5 ± 14.4 mmHg systolic ($p=0.08$) and -2.7 ± 9.9 mmHg diastolic ($p=0.29$).
Conclusion: Bi-level PAP-guided paced respiration may lower systolic blood pressure in patients with hypertension and OSA, although mechanisms remain unclear. Larger, randomized controlled trials that include measures of autonomic indices would help to elucidate the efficacy and mechanisms of paced respiration in patients with OSA.

0707

BEYOND SLEEP DISORDERED BREATHING, GENDER DOES MATTER PLASMA TRIGLYCERIDE, URIC ACID LEVELS AND BLOOD PRESSURE

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Introduction: Sleep-disordered-breathing, more male-prevalent, is associated with a systemic inflammation, hypertension and metabolic syndrome. Through sexual hormones' effects, female have better metabolic/cardiovascular functions, partially caused by better upper-airway conductivity and central-breathing control during sleep. The aim of this study is to assess whether these female superiorities actually exist if taking into account an apnea-hypopnea index.
Methods: Retrospective data review analysis.84 randomly selected female just with sleep disturbance enrolled to be matched with a male individually for apnea-hypopnea index (AHImt) or not (nAHImt), besides for age (< and 50 years; Junior and Senior) and body mass index.
Results: In nAHImt/Junior, female (35.7+/-8.3 vs. 35.5+/-8.1 years for male) had shorter neck circumference, better sleep quality and lower AHI (16.2+/-17.5 vs. 30.3+/-24.3 events/hr), blood pressure (BP), and lower serial levels of total cholesterol (TC), triglyceride (TG) (97+/-51

vs. 147+/-142 mg/dL) and uric acid (UA) (5.1+/-1.4 vs.6.3+/-1.5 mg/dL). In AHImt/Junior, female (38.6+/-7.9 vs. 38.9+/-8.5 years) appeared shorter neck circumference, lower waist/hip ratio (0.85+/-0.07 vs. 0.91+/-0.06), BP, TG (96+/-43 vs.142+/-115 mg/dL) and UA (4.7+/-1.4 vs. 6.4+/-1.62 mg/dL). While in nAHImet/Senior, female (56.3+/-5.1 vs. 56.5+/-5.7 years) had lower AHI, neck circumference, and waist/hip ratio, with lower diastolic BP and UA (5.4+/-2.0 vs. 6.4+/-1.7 mg/dL). In AHImt/Senior, female (56.9+/-5.1 vs. 57.5+/-5.8 years) had similar waist/hip ratio, sleep architecture, BP, the lipid profile values, C-reaction protein, and UA. UA positively correlated with TG in Junior male and Senior female. UA positively correlated with systolic BP in Junior/AHImt male and Senior/AHImt female. UA or TG positively correlated with waist/hip ratio in Junior/Senior female or Junior female, respectively, but not in male.

Conclusion: Beyond sleep-disordered-breathing, gender effects on TG, UA and BP persist till menopause age, potentially through central fat evolution.

0708

PREDICTIVE ACCURACY OF APNEA-HYPOPNEA INDEX ESTIMATED FROM A CPAP DEVICE

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Introduction: In order to assess the adequacy of continuous positive airway pressure (CPAP) titration from studies performed at home, we determined the predictive accuracy of the estimated apnea-hypopnea index (AHI) from an autoadjusting continuous positive airway pressure (ACPAP) device compared with the AHI measured in the sleep lab using standard overnight polysomnography (PSG). In this study, we calculated the appropriate estimated AHI from the ACPAP device that corresponds to threshold AHI of 5 and 10 events/hr chosen from the AASM guidelines of the manual titration of PAP in patients with obstructive sleep apnea.

Methods: We studied 99 patients with obstructive sleep apnea at the Veteran Affairs Medical Center at Buffalo, NY. After the diagnostic polysomnography, patients were given an ACPAP device (Respironics, Pittsburgh, PA) and underwent a further PSG while using ACPAP. The scorer of the PSG was blinded from the estimated AHI from the data stored in the ACPAP. We analyzed the estimated AHI from the ACPAP device (AHI-CPAP) and the AHI measured from data recorded during a standard PSG (AHI-PSG). Apneas were scored as cessation of airflow of 10 sec, and hypopneas as at least 30% reduced airflow for 10 sec or more with a 4% desaturation or an arousal.

Results: The mean age of patients was 56.7 years (range: 25-83 years) and the mean body mass index (BMI) was 35.0 (range, 22.4-52), 22% (19 male, 1 female) patients had mild (AHI >=5 to <15/hr), 33% (29 male, 1 female) had moderate (AHI >=15 to <30/hr) and 45% (41 male and 1 female) had severe obstructive sleep apnea (AHI >=30/hr) as assessed from the diagnostic PSG performed in the sleep lab. With a AHI-CPAP of 6 events/hr, the predictive accuracy for a AHI-PSG threshold level of 5 events/hr had a sensitivity of 0.92 (95%CI: 0.75 to 0.99), a specificity of 0.90 (95%CI: 0.81 to 0.96), a positive likelihood ratio of 9.6 (95%CI: 5.1 to 21.5) and a negative likelihood ratio of 0.085 (95%CI: 0.02 to 0.25). With a AHI-CPAP of 8 events/hr, the predictive accuracy for an AHI-PSG threshold level of 10 events/hr had a sensitivity of 0.94 (95%CI: 0.71 to 1.0), a specificity of 0.90 (95%CI: 0.82 to 0.96), a positive likelihood ratio of 9.6 (95%CI: 5.2 to 20) and a negative likelihood ratio of 0.065 (95%CI: 0.004 to 0.28).

Conclusion: The estimated AHI from an autoadjusting CPAP device can be used to assess the adequacy of therapy with reasonable level of accuracy. A limitation of these data is that only one manufacturer's CPAP device was used.

0709

ANALYSIS OF VENTILATORY RESPONSE POST-CENTRAL APNEA BIJAN SADRNOORI M.D. CARITAS HFH. METHUEN, MA 01844

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Introduction: Post-apnea ventilation is a complex interaction between central and peripheral chemoreceptors, as well as chemical hemostatis during each respiratory event. The objective of this study was to determine if recovery breaths following central apnea are able to differentiate various types of CA.

Methods: A total 50 patients with central apnea (CA) of various pathologies were retrospectively studied. Ages of participants ranged from 25-63 years; males and females were equally distributed. All patients met the adult criteria for central apnea. The recovery breath was calculated from the end of the flow and the NP, and the RIP signal. The VT and RR were calculated from the RIP signal. TC02 results from patients who were monitored were plotted and observed. CA was studied under the following conditions: idiopathic, post-arousal, sleep-onset, CSB, narcotic, NMD, COPD, CPAP-induced and complex sleep apnea.

Results: The amplitude of the first breath and respiratory rate were highest under the idiopathic and lowest in the narcotic-induced conditions, respectively. In post-arousal and sleep-onset states, the recovery breaths had intermediate amplitudes with short durations and occurred once or twice. The recovery breaths occurred two to three times under the CPAP condition and were short in duration. In complex sleep apnea, the amplitude and frequency of the recovery breaths were similar to that of the recovery breaths in the idiopathic conditions. In NMD and in COPD, the recovery VT was low; however, the RR was higher in COPD than in NMD. In CSB, the recovery breath was gradual.

Conclusion: This study concludes that the VT and RR of recovery breaths are dependent upon the etiology of central apnea with the highest and longest durations in idiopathic and complex sleep apnea and the lowest in narcotic-induced central apnea. This finding is attributed to the CO2 load and the elimination, the ventilatory response to CO2 and O2, and the perhaps endogenous endorphins. The amplitude of the first breath was related to the duration of central apnea.

0710

ASSOCIATIONS OF LINEAR AND NON-LINEAR INDICES OF HEART RATE VARIABILITY DURING SLEEP WITH SLEEP DISORDERED BREATHING AND DIABETES

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Introduction: Extracting Heart Rate Variability (HRV) data from nocturnal polysomnography (PSG) may provide information on between subject or within subject (across sleep stages and the sleep period) differences in autonomic activity. Although current common used methods for quantifying low and high Heart Rate (HR) frequency spectra are simple, it is not clear that this approach is the most informative one for predicting abnormalities in autonomic tone. Alternative approaches, such as entropy measures which quantifies the temporal characteristics of HR may provide better discrimination in identifying individuals with differences in autonomic tone, such as those with sleep disordered breathing (SDB) or diabetes.

Methods: The sample is 380 adult participants in the Cleveland Family Study who underwent overnight PSG. HRV was quantified using spectral analysis, Poincaré analysis, Detrended Fluctuation Analysis (DFA) and entropy analysis, using data from the entire sleep period as well as sleep stage specific periods. Correlation analysis and logistic regression models, unadjusted and adjusted for age and BMI were used to examine the association between indices of HRV to SDB (quantified by the Apnea Hypopnea Index; AHI) and diabetes (defined as use of diabetes

medication or abnormal fasting or 2 hour post-glucose loading glucose levels.)
Results: Relatively weak associations were observed between all measures of HRV and the AHI, with the strongest association observed between HRV quantified using conditional entropy in Stage 2 sleep (spearman correlation= -0.16, P-value <.01). The negative correlation is an indication that the complexity of heart rate decreases as the severity of SDB increases. In unadjusted analyses, diabetes also was most strongly associated with the measure of regularity defined as the reverse of conditional entropy index (OR=1.18, 95% CI: 1.03, 1.36, p=0.02). Associations were attenuated in adjusted analyses.
Conclusion: Sleep-stage specific analyses of HRV indicate that the complexity of the R-R interval time series as quantified by conditional entropy decreases as the number of apneic events per hour increases. Complexity of the R-R interval time series also is lower in diabetics compared to non-diabetics. These data suggest that quantifying HRV using nonlinear complexity measures may provide useful information regarding abnormalities in autonomic nervous system activity.

0711

EFFECTS OF OROPHARINGEAL EXERCISES ON PATIENTS WITH MODERATE OBSTRUCTIVE SLEEP APNEA:A RANDOMIZED,CONTROLLED STUDY

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Introduction: Obstructive sleep apnea is a public health problem due to the high prevalence and high morbidity. Continuous positive airway pressure (CPAP) is the treatment of choice for severe cases. However, adherence to CPAP is variable among moderate OSA patients and alternative treatments are necessary. Upper airway muscle weakness plays an important role in the genesis of OSA. Oropharyngeal exercises
Methods: Patients with moderate OSA (IAH 15 to 30ap/h) were randomized to 3 months in general. We included 37 moderate OSA patients, that were randomized to 3 months of general measures, including nasal lavage, orientation of alternated bilateral chewing and exercises of inspiration and expiration in the seated position (control group).The treatment with myofunctional therapy consisted of, in addition to the orientations given to the control group, oropharingeal exercises performed without supervision daily and under supervision once a week (20 minutes).Anthropometric measurements, questionnaires evaluating snoring frequency and intensity (Berlin), daytime subjective sleepiness (Epworth),sleep quality (Pittsburg) and full polysomnography were performed at and in the end of the study.
Results: 45 patients were included in the study,8 were excluded because they failed to return regularly. The final group consisted of 37 patients age (mean±SD)=51±9,body mass index =30±kg/m2 and AHI 23±5ap/h,17 were randomized to the control group and 20 to the treatment group. The control group did not change in all parameters along the study. In contrast, the patients treated with myofunctional therapy presented a significant decrease (p<0.05) in neck circumference (39.5±3.4 vs. 38.3±3.7 cm),daytime somnolence (13.2±8.2±6.0),sleep quality (10.3±3.5 vs. 7.1±2.3),snoring frequency (3.9±5.4 vs. 1.8±0.9),snoring intensity (3.4±0.5 vs. 1.8±0.9) and AHI (23.2±4.8 vs. 14.6±8.1 events/h; p,0.01.Considering the entire group, changes in neck circumference correlated with the changes in SHI (r=0.55;p,o.oo1).
Conclusion: Myofunctional therapy, over 3 months, reduced symptoms and severity of moderate OSA. The improvement correlates with the decrease of cervical diameter, suggesting that the musculature tonus of upper airway while awake correlates with the severity of OSA and can be modified with myofunctional therapy.

0712

A PROSPECTIVE EVALUATION OF TREATMENT OUTCOMES IN MILD OSAS

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Introduction: Approximately 24% of men and 9% of women in the adult population have a respiratory disturbance index (RDI) greater than 5. Patients with an RDI >5 but < 15 who have symptoms of daytime sleepiness meet diagnostic criteria for mild obstructive sleep apnea syndrome (OSAS). Treatment outcomes for mild OSAS have been inconsistent, and guidelines state therapy with positive airway pressure (PAP) is optional. We sought to evaluate the symptomatic benefits of PAP in a cohort of patients with mild OSAS.
Methods: A cohort of patients diagnosed with mild OSAS was prescribed PAP therapy and followed prospectively for 3 months. We evaluated changes in quality of life (QOL), fatigue, sleepiness, urinary frequency, and sexual function.
Results: 41 patients (age 44.6±9.9, BMI 29.4±5.4, 56% male) with mild OSAS (RDI 10.7±3.1) were enrolled in this study. Across the cohort, hours of PAP use per night at 1 and 3 months were 5.3±2.2 and 5.1±2.5 respectively. Using the modified sleep apnea quality of life index (SAQLI), patients had significant improvements in QOL in comparison to baseline at both one (+15.8±15.7; p < 0.005) and three months (+17.8±19.7; p<0.005). The functional outcomes of sleep questionnaire (FOSQ) also showed significant improvement at one (+6.6±14.5; p = 0.03) and three months (+6.8±4.5; p = 0.03). Changes in the Epworth Sleepiness Scale (ESS) reached significance at one (-3.1±4.8; p=0.005) and three months (-3.5±3.5; p<0.005), while improvements in fatigue were significant only at one month (-1.5±2.7; p=0.03). There was no improvement in urinary symptoms. Of the multiple measures of sexual function assessed, only libido and the ability to achieve climax were significantly improved.
Conclusion: In a small cohort of patients with mild OSAS who use their machine > 5 hours per night, we found significant improvement in QOL, sleepiness, and fatigue.

0713

DIAGNOSTIC ACCURACY OF HOME SLEEP STUDIES FOR SLEEP APNEA

Grant B
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Introduction: Since the Centers for Medicare and Medicaid Services have approved the use of home studies for diagnosis of sleep apnea, we compared the accuracy of apnea hypopnea index (AHI) and central apnea index (CAI) obtained with the limited channels used for home studies with AHI and CAI from standard overnight polysomnography (PSG) in the sleep laboratory
Methods: We used Rembrandt (Embla, Broomfield, CO) in 95 consecutive full night diagnostic PSG performed in a single sleep laboratory (MedOneMedical, Sandy UT). The PSG (full study) was scored by a technician who then deleted the scoring and analysis and eliminated all channels except the body position, pulse oximeter, thoracic and abdominal inductance recordings used by Embletta (Embla, Broomfield, CO) home sleep study equipment (Embla, Broomfield, CO). These recordings (limited study) were reanalyzed by another scorer naïve to the full study and blinded to the results obtained by the other technician
Results: As judged by the full PSG, 51 patients has no sleep apnea: (AHI < 5/hr), 30 has mild sleep apnea (AHI >=5 to <15/hr), 10 had moderate sleep apnea (AHI >=15 to <30/hr) and 4 had severe sleep apnea (AHI >=30/hr). Bland-Altman analysis revealed an overestimate of the AHI in the limited study compared with the full study: 35% (95%CI: 22 to

49%) but no significant bias for the estimate of CAI: -5.7% (95%CI: -21 to +12%). When the limited study AHI is used to predict an full study AHI of 5/hr or more, the positive likelihood ratio was 3.6 (95%CI 2.3 to 5.5) and negative likelihood ratio of 0.015 (95%CI 0.001 to 0.24). When the limited study AHI is used to predict an full study AHI of 15/hr or more, the positive likelihood ratio was 5.1 (95%CI 3.2 to 8.1) and negative likelihood ratio of 0.041 (95%CI 0.003 to 0.63). When the limited study CAI is used to predict a full study CAI of 5/hr or more, the positive likelihood ratio was 15 (95%CI 6.5 to 35) and negative likelihood ratio of 0.089 (95%CI 0.006 to 1.2).
Conclusion: The severity of sleep apnea can be assessed with reasonable accuracy but this study is limited to one manufacturer's equipment. The presence of central sleep apnea can be assessed with good accuracy which is important for the detection of central sleep apnea and complex sleep apnea. The tendency to overestimate AHI in mild sleep apnea may be of particular importance in some circumstances for example, mild sleep apnea in holders of commercial driver's license.

0714

PATIENTS WITH THE MOUTH LEAK SYNDROME IMPROVE LESS IN SLEEP APNEA HEALTH STATUS

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Introduction: One third of patients with obstructive sleep apnea syndrome (OSAS) treated with nasal continuous positive airway pressure (nCPAP) develop a mouth leak syndrome (MLS) with air leaking out the mouth, nasal congestion and premature removal of the nCPAP. With less compliance we expect that the measures of health status (sometimes called quality of life measures) would not improve as expected. We tested this hypothesis with 2 parallel sleep apnea specific questionnaires in patients initiating treatment with nCPAP.
Methods: Forty consecutive new patients with OSAS (Epworth mean 13.3 SD 5.0) were studied prospectively with the Sleep Apnea Quality of Life Index (SAQLI) as well as the Quebec Sleep Questionnaire (QSQ). They were treated with nCPAP therapy (mean pressure 9.1 SD 2.0). At baseline and after at 4 weeks, patients were queried with the SAQLI and the QSQ. Scores were standardized to a maximum of 100% for comparison.
Results: Of 40 patients, 16 met published clinical criteria for the MLS. These patients demonstrated less satisfaction and less compliance with nCPAP. At baseline, patients who later developed MLS had similar total scores on the SAQLI (MLS mean 57 SD 14% vs. 65 SD 17%; p = 0.19) and the QSQ (MLS mean 57 SD 21% vs. 62 SD 19%; p = 0.41). With nCPAP, their scores improved to levels inferior to those who did not develop MLS on SAQLI (MLS mean 66 SD 15% vs. 83 SD 9%; p = 0.0040) and the QSQ (MLS mean 71 SD 20% vs. 82 SD 13%; p = 0.045).
Conclusion: Patients with nCPAP who develop MLS demonstrate less improvement in measures of sleep apnea specific health status. This may be due to less compliance and more leak-related sleep disruption seen in patients who develop the MLS.
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0715

RISK OF OBSTRUCTIVE SLEEP APNEA IN WIND MUSICIANS

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Introduction: Obstructive sleep apnea (OSA) is caused by collapse of the upper airway. Respiratory muscle training with a wind instrument (didgeridoo) in patients with moderate OSA has been shown to improve OSA symptomology in a laboratory setting. Respiratory muscle training is most effective when resistance is added to the airway. However, it is unclear whether practice with other instruments with various degrees of airway resistance may also reduce risk for OSA. Therefore, we surveyed a national sample of professional musicians. It was hypothesized that playing wind instruments, especially, high resistance instruments, would reduce the risk for OSA.
Methods: 847 professional musicians (age M = 42.5; 62.2% male; 37.8% female), including 760 instrumentalists (M = 30.2 years experience, M = 15.0 hours practice weekly) and 87 conductors/vocalists, completed the Berlin Questionnaire (BQ) for sleep apnea, the Epworth Sleepiness Scale (ESS), and a demographic questionnaire assessing general health and musical experience.
Results: 29.2% of musicians were high risk for OSA as defined by the BQ. ESS scores were significantly different in high OSA risk (M = 7.3, SD = 3.5) as compared to low OSA risk (M = 8.2, SD = 4.0; p = .002) participants. 4.3% of participants carried an OSA diagnosis. Results revealed no significant difference in risk for OSA in instrumentalists (29.1%) vs. non-instrumentalists (33.3%; p = .14). However, when type of instrument (non-wind instruments, low and high wind resistance brass, and low and high wind resistance woodwinds) was considered, results revealed a significant difference in OSA risk (p = .049). Such that, high resistance woodwinds (i.e. double reed instruments) had a lower risk of OSA than other instrumentals. However, high resistance brass instruments (i.e. trumpet, horn) showed no difference in OSA risk.
Conclusion: Results of this study suggest that naturalistic respiratory muscle training with high resistance wind instruments may potentially reduce risk for OSA. Specifically, double reed woodwind instrumentalists (e.g. oboe, bassoon) have lowest risk for OSA.

0716

POSITIONAL THERAPY FOR THE REDUCTION OF OBSTRUCTIVE SLEEP APNEA

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Introduction: Obstructive sleep apnea (OSA) is a common clinical problem. The prevalence of OSA in middle-aged people (40-69 years) is 27% in men and 16% in women. CPAP has become the standard treatment, especially for moderate to severe OSA patients. However, despite its efficacy in sleep apnea, up to 50% of patients are not willing to start or to comply with CPAP therapy. Positional therapy, designed to maintain a non-supine posture during sleep, have been effective in treating mild to moderate positional OSA patients. However, there is little effort in developing effective and comfortable devices that prevent patients to sleep in the supine position. The aim of this study was to assess the efficacy of positional therapy using a recently developed vest type device in 14 patients with mild to moderate positional OSA.

Methods: 14 participants with mild to moderate positional OSA were included. To evaluate the efficacy of the newly developed vest type device, changes of OSA between baseline and experimental polysomnography were assessed. The authors also estimated adverse event rate and subject's satisfaction.
Results: The AHI was lower in the experimental examination 9.3 ± 8.3 versus 22.8 ± 9.3 ($p<0.001$). The improvement of AHI was about 55% when using the vest type device. The arousal index decreased significantly during positional therapy from a 33.1 ± 8.0 to 24.6 ± 9.0 ($p=0.0057$). The ODI also decreased significantly during treatment from a 19.0 ± 9.9 to 8.6 ± 8.2 ($p=0.0006$). Participants' satisfaction after using the vest type device was acceptable level and no adverse effects were reported.
Conclusion: Positional therapy using the vest type device appears to be a valuable treatment for mild to moderate positional OSA patients.

0717

A RANDOMIZED, IN-LAB COMPARISON OF TWO TYPES OF AUTO TITRATING POSITIVE AIRWAY PRESSURE MACHINES TO CONVENTIONALLY TITRATED CONTINUOUS POSITIVE AIRWAY PRESSURE FOR TREATING OBSTRUCTIVE SLEEP APNEA

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Introduction: Increasingly, auto titrating positive airway pressure (APAP) is being used in lieu of conventional CPAP to treat obstructive sleep apnea. A recent trend towards home testing has brought about the question of APAP efficacy and whether or not it can ultimately replace an in-lab titration study. This study is a comparison of the initial efficacy of two types of APAP machines to each other and to CPAP.
Methods: Forty eight CPAP naïve subjects with confirmed moderate to severe OSA on diagnostic polysomnography were randomized one of two types of APAP or to a conventional CPAP titration. Primary efficacy was measured by control of OSAHS, with adequate treatment considered a residual AHI <5 during optimal treatment.
Results: Baseline characteristics were similar when comparing conventional CPAP, Resmed Autoset Vantage™, and Respironics REMstar® Auto in regards to age (50.1±9.2, 48.7±9.8, 44.2±10.1), BMI (34.3±7.5, 35.9±11.0, 35.6±10.5), neck circumference (16.2±1.5, 15.9±2.0, 19.6±10.5), baseline AHI (28.3±23.7, 25.9±27.3, 19.6±10.5). Of the 24 subjects randomized to CPAP, 67% were fixed during the initial titration while 58% of subjects randomized to APAP were treated adequately. Of the 10 subjects with inadequate OSAHS control on APAP, 80% were subsequently adequately treated with conventional CPAP. Residual AHI at optimal PAP pressure was also similar among groups (1.6±1.9, 2.2±2.1, 2.4±1.2.
Conclusion: Efficacy results of the in-lab titration of conventional CPAP titration compared to APAP are similar, with a trend toward more patients having complete normalization of their AHI on conventional CPAP than APAP. It is striking the frequency with which both PAP modalities are incapable of normalizing the AHI in this quaternary referral population. A comparison of the two types of APAP machines to one another is currently being conducted.

0718

COMPLIANCE WITH TWO SERVO VENTILATION DEVICES - VPAP-ADAPTSV® AND BIPAP-AUTOSV® OF PATIENTS WITH CENTRAL AND COMPLEX SLEEP APNEA

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Introduction: Servo ventilation (SV) devices generate positive airway pressure with a variable pressure support that changes in response to patient's own respiratory output. They have been successfully used in treatment of central and complex sleep apnea. There are currently two SV devices on the market - VPAP-AdaptSV® and BIPAP-AutoSV®; their proprietary algorithms used to determine pressure support differ, which may result in a different compliance in patients who use them. We aimed to compare compliance with both devices of patients with central and complex sleep apnea.
Methods: Data of 48 consecutive patients who were prescribed an SV device for central or complex sleep apnea were retrospectively analyzed. Patients underwent a diagnostic polysomnogram, followed by a continuous positive airway pressure (CPAP) titration, and a SV titration study. Choice of the SV device was at the discretion of the managing physician. Objective compliance with the device was assessed at the first visit at 4-6 weeks of its use.
Results: 23 patients received a VPAP-AdaptSV® device, while 25 patients were treated with BIPAP-AutoSV® device. The two groups did not differ in age, sex, Epworth Sleepiness score, apnea-hypopnea index, arousal index at the diagnostic and CPAP titration. Final expiratory pressure during SV titration study was lower in VPAP-AdaptSV® group compared to BIPAP-AutoSV® group (8 (7-9) cmH2O vs. 11 (8-12) cmH2O, $p=0.001$). Compliance data were available on 16 patients treated with VPAP-AdaptSV® and 21 patients treated with BIPAP-AutoSV®. There was no difference between the groups in the percentage of days with the device use (80 (21-100%) vs. 99 (65-100%)), nightly use (4.1 (0 - 6.8 h) vs. 6.1 (3.4 - 7.3 h)), or percentage of nights with more than 4 h use (54 (0-90%) vs. 79 (34-95%)).
Conclusion: Among patients with central and complex sleep apnea, the compliance with VPAP-AdaptSV® and BIPAP-AutoSV® devices is comparable and high.

0719

GENDER AND AGE DIFFERENCES OF REM SLEEP-DEPENDENT OBSTRUCTIVE SLEEP APNEA (REM-OSA) PREVALENCE AMONG KOREAN PATIENTS

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Introduction: Obstructive Sleep apnea (OSA) intensity and frequency are generally severer and increased during rapid eye movement (REM) sleep due to muscle atonia and increased upper airway resistance. 'REM sleep-dependent OSA (REM-OSA)' is defined as the one in which apneas and/or hypopneas occur predominantly during REM sleep. We aimed to evaluate differences of REM-OSA prevalence according to gender and age.
Methods: We reviewed on the nocturnal polysomnographic records of 1,791 consecutive OSA patients with an apnea-hypopnea index (AHI)≥5/h). AHIs during total sleep time (TST), non-REM (NREM) sleep, and REM sleep (AHI_{TST}, AHI_{NREM}, AHI_{REM}, respectively) were calculated. REM-OSA was defined as the one with AHI_{REM} / AHI_{NREM} >2. Statistical comparisons were made between males and females according to the severities of OSA (mild as AHI<15, moderate as 15~30, severe as >30) and the ages (younger as age≤55, older as >55). The independent t-test and χ^2-test with linear by linear association (each with significance level of $p<0.05$) were used for analyses.
Results: Out of 1,791 OSA patients (1,489 males, 302 females), total of 604 patients (429 males, 175 females) fulfilled the criteria for REM-OSA, yielding the overall prevalence of 33.7%. Females had significantly higher prevalence of REM-OSA than did males (58.3% vs. 28.8%, $\chi^2=95.4$, $p<0.01$). Prevalence of REM-OSA differed according to the severities of OSA. In females, prevalence of REM-OSA decreased as the severity of OSA increased (mild 74.9% vs. moderate 51.5% vs. severe OSA 6.1%) ($\chi^2=299.2$, $p<0.01$). In males, result was the same as that of females (mild 51.7% vs. moderate 31.6% vs. severe OSA 4.6%)

(χ^2=299.2, p<0.01). Younger females had a higher prevalence of REM-OSA than did older females (65.5% vs. 51.9%, χ^2=5.7, p<0.05). But, no difference of prevalence was found between younger and older males.
Conclusion: Our results show that REM-OSA is more prevalent in females with OSA vs. males with OSA and in those with mild or moderate OSA vs. those with severe OSA. In females with OSA, REM-OSA seems to be more prevalent in the younger ones vs. the older ones.

0720

THE IMPACT OF WEIGHT LOSS ON OBSTRUCTIVE SLEEP APNEA (OSA) SEVERITY: RESULTS OF A META-ANALYSIS

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Introduction: The extent to which weight loss decreases disease severity in patients with OSA is not well understood. To address this issue, we conducted a meta-analysis of literature comparing reductions in body mass index (BMI) and apnea-hypopnea index (AHI). We hypothesized that mean AHI would decrease proportionally with the mean reduction in BMI.
Methods: Our eligibility criteria included clinical trials of weight loss (regardless of intervention: lifestyle, pharmacological, surgical) in patients with OSA. To be included, studies had to report changes in BMI and changes in AHI. Our search was limited to studies in English and those that reported quantitative results. We used an iterative strategy to identify appropriate search keywords, such as sleep apnea syndromes, weight loss, diet, bariatric surgery and obstructive sleep apnea. We searched Medline from 1966 - April 2008. Data was abstracted in duplicate from articles with the relevant data (JW, VRC) and analyzed by our statisticians (EM, MS).
Results: This search yielded 398 articles, of which 18 were considered relevant for our study question. All 18 studies were single-arm studies with no control group. There was no significant relationship between the mean reduction in BMI (either absolute magnitude of BMI or % change) and reductions in disease severity (absolute or % change in AHI). The lack of association was surprising, with all studies showing a reduction in AHI with weight loss. However, potential explanations could include the following: type of intervention may have differential effects on OSA severity (e.g., surgery vs. medical), heterogeneity in study characteristics (variations in baseline AHI, duration of follow-up, etc.), and multiple contributing factors for OSA in a given patient apart from weight gain (genetics, upper airway structure/function, etc.).
Conclusion: Based on a comprehensive review of the currently available literature, the improvement in OSA from weight loss is highly variable.
Support (optional): MSFHR (Infrastructure, Scholar Award)

0721

MORNING HEADACHE AND REM DEPENDENT OBSTRUCTIVE SLEEP APNEA

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Introduction: The association between morning headaches (AMHA) and Obstructive Sleep Apnea (OSA) has been recognized. Nevertheless, the character of this association remains unclear. Also, the significance of OSA that is exclusively present during REM sleep and its relationship with the complaint of AMHA remain uncertain.
Methods: This was a retrospective review of questionnaires and Polysomnograms (PSG) of adult subjects who on PSG (performed 3/2008-11/2008) had an overall RDI<5, and during REM sleep RDI was ≥5(N=50) or <5(N=50). The questionnaires included baseline characteristics, as well as sleep history. Statistical comparisons of the groups were performed using the Chi-square test for sex, REM-RDI, AMHA, cataplexy, sleep paralysis, hypnagogic/hypnopompic hallucinations, total sleep time(TST), total REM sleep and lowest oxygen saturation.
Results: The baseline characteristics were similar between the two groups. 22/50 subjects reported AMHA in each group (p=1). Although more subjects in the REM-RDI≥5 group reported sleep paralysis than in the REM-RDI<5 group (19/49 vs 11/50 p=0.069), this, as well as reports of cataplexy and hallucinations were not significantly different. Overall 25% of men and 52.94% of women reported AMHA. Among subjects with REM-RDI≥ 5 12.5% of men and 58.82% of women reported AMHA (p=0.0021) vs 37.5% of men and 47.06% of women in the REM-RDI<5 group (p=0.52). Among subjects who reported AMHA compared to no AMHA, there was a trend towards a higher REM-RDI (N=100 7.75 vs 5.97 p=0.34). There was no significant difference in the lowest oxygen saturation (N=100 90.97% vs 90.58% p=0.61), TST or total REM sleep.
Conclusion: In adult subjects with RDI<5, those with REM-RDI≥5 were as likely to report morning headaches as subjects with REM-RDI<5. Women seem to be at higher risk than men for morning headaches if their REM-RDI is ≥5 but not if their REM-RDI is <5. Prospective studies are needed to further explore these findings.

0722

OBSTRUCTIVE SLEEP APNEA IN HEALTHY HYPOGONADAL OLDER MEN

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Introduction: Obstructive sleep apnea (OSA) is characterized by recurrent episodes of upper airway obstruction during sleep. We report preliminary baseline data describing OSA in older hypogonadal men enrolled in a longitudinal RCT assessing testosterone and exercise in aging men.
Methods: Ninety-six hypogonadal men (avg age 67 yr, range 60-84 yr, total testosterone 204-358 ng/dL) were evaluated for OSA using home sleep studies (Stardust, Respironics Inc.). All studies were scored by RPSGT's and evaluated by a boarded sleep specialist. Apneas were defined as 10-second cessations of airflow, and hypopneas were defined as at least a 30% reduction in airflow lasting at least 10 seconds and generating ≥ 4% oxygen desaturation. Apneas and hypopneas were combined and reported as an AHI (apneas and hypopneas per hr of study time).
Results: Of 96 baseline tests, 79% of subjects had OSA [35 mild OSA (AHI 5-14.9), 25 moderate OSA (AHI 15-29.9), 16 severe OSA (AHI ≥30)]. No subject exhibited daytime hypoxemia (O2 sat ≤ 88%) or Epworth Sleepiness score of > 16. Using standard multiple regression analysis with age and total testosterone to predict AHI, R for regression was significantly different from zero, (F2,93)=8.49, p<0.0001. The regression coefficients for age 0.97 ± 0.26 (95%CI: 0.445 to 1.49) and total testosterone -0.06 ± 0.03 (95%CI: -0.13 to 0.001) contributed 12.3% and 3.4% of the variability in AHI, respectively. There were no differences in subjective reporting of apnea symptoms, fatigue, or measures of central adiposity (neck and waist circumference, % trunk fat, visceral fat) between subjects with no OSA (AHI<5) and severe OSA (AHI ≥ 30).
Conclusion: We found a high prevalence of OSA in older men in the Denver area. This may be related to the low/low normal testosterone levels in our selected population. Our subjects with OSA frequently lacked typical OSA signs and symptoms.

0723

EXTENDED VOLUMETRIC TONGUE REDUCTION IN OBSTRUCTIVE SLEEP APNEA

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Introduction: Macroglossia may be a contributing factor in obstructive sleep apnea. In patients with severe macroglossia the tongue base obstructs the oro- and hypo-pharyngeal airway. Volumetric tongue reduction is a surgical method utilizing radiofrequency energy to selectively reduce hypertrophic tongue base musculature. In extreme cases we modify the usual "eight probe" insertion technique to distribute slightly more thermal energy over a larger area to more effectively reduce tongue bulk.
Methods: The two-prong tongue probe device (Gyrus/Olympus Corp., Memphis, TN) settings are lowered from the standard 600J to 500J, allowing the practitioner to safely increase the number of bilateral probe insertions from four (total: 4800J) to five (total: 5000J). The 4.17% increase in energy is distributed into a larger quantity of tongue mass, therefore, representing a decrease in the risk of insertion site thermal injury. After placement of the tonsil gag the ten sites of intended probe insertion are marked using methylene blue following a staggered, parallel zigzag configuration (i.e., left-lateral posterior, right-medial posterior, etc.). Injection of the tumescent agent prior to probe insertion allows for small modifications of probe site placement. Subsequent insertions are staggered apposed to the first (i.e., left-medial posterior, right-lateral poster) to avoid same site entry.
Results: The extended volumetric tongue reduction from the vallecula to the circumvallate papillae, incorporating the extreme medial and lateral aspects of the tongue base, results in a greater distribution of increased radiofrequency energy at safer levels, more effectively ablating tongue musculature.
Conclusion: Utilization of lower regional doses of radiofrequency energy over a greater mass of tongue musculature offers a safe and effective means to perform volumetric tongue reduction in patients with obstructive sleep apnea attributable to severe macroglossia.

0724

CEPHALOMETRIC ASSESSMENT OF CRANIOFACIAL MORPHOLOGY IN JAPANESE MALE PATIENTS WITH OBSTRUCTIVE SLEEP APNEA HYPOPNEA SYNDROME

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Introduction: Craniofacial morphological anomalies fall into two principal categories, skeletal anomalies such as small jaw or mandibular retrusion, and soft tissue anomalies such as elongation of soft palate, macroglossia, or narrow pharynx. This abnormalities as a cause of obstructive sleep apnea hypopnea syndrome (OSAHS) may be greater in Asian populations. Craniofacial morphology as a risk assessment of OSAHS should be determined based on a balance between the jaw as a container and soft tissue as its content. We assessed indices representing skeletal and soft tissue features by cephalometric analysis.
Methods: Cephalometric analysis was performed on 112 male Japanese patients diagnosed with OSAHS by polysomnography to evaluate craniofacial morphological anomalies. The measurement sites were as follows: skeletal morphology; soft tissue morphology; mixed morphology including mandibular plane - hypoid bone (MP-H), the jaw soft tissue (JS) ratio, and soft plate excess (SPE).
Results: MP-H ($r = 0.394$, $p < 0.001$), SPE ($r = 0.412$, $p < 0.001$), and JS ratio ($r = 0.396$, $p < 0.001$) had significant correlations with apnea hypopnea index (AHI). Multivariate analysis results indicated that all MP-H ($p < 0.01$), SPE ($p < 0.001$), and the JS ratio ($p < 0.001$) were significant variables for predicting severe OSAHS (AHI > 30). Receiver-operating characteristics (ROC) curve to analyze the diagnostic accuracy of mixed morphology factors for predicting severe OSAHS. The SPE showed the highest AUC (0.749, $p < 0.001$), followed by JS ratio (AUC 0.718, $p < 0.001$), and MP-H (AUC, 0.711, $p < 0.001$).
Conclusion: The results showed that mixed craniofacial skeletal and soft tissue morphology correlated with AHI. The JS ratio, SPE, and MP-H are useful parameters for diagnosing and predicting the severity of OSAHS in male patients. The results suggest that craniofacial morphology evaluation is a clinically valid method for predicting severe OSAHS.

0725

WHICH IS MORE IMPORTANT FOR OBSTRUCTIVE SLEEP APNEA SYNDROME, APNEA OR HYPOPNEA? AND IS THE IMPORTANT VARIABLE ONLY THE NUMBER OF EVENTS OR ALSO THEIR DURATION?

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Introduction: Apnea and hypopea are generally considered equivalent in calculating the apnea-hypopnea index (AHI) regardless of their kind and duration. However we envisaged that apnea and hypopnea could differ in their effects on arousal and oxygen desaturation, and that the duration of the occurrences of apnea and hypopnea could also be important. The objective of this study was to investigate separately the effects of apnea versus hypopnea on arousal and oxygen desaturation, as well as the influence of the duration of disordered breathing episodes on arousal and oxygen desaturation.
Methods: One hundred and eighty two patients with obstructive sleep apnea underwent full polysomnography. 1) The correlations between variables such as AHI, arousal index, oxygen desaturation index (ODI), apnea index (AI), hypopnea index (HI), mean apnea duration (MAD), mean hypopnea duration (MHD), and mean apnea hypopnea duration (MAHD) were calculated. 2) AHI, arousal index and ODI were compared in patients divided into short and long MAD groups.
Results: 1) AHI, arousal index, ODI, MAD, MAHM, and AI were highly correlated with each other, but MHD and HI were not correlated with the other variables. 2) Arousal index and ODI were higher in the long MAD group than in the short MHD group.
Conclusion: Apnea is more important for arousal and oxygen desaturation during sleep than hypopnea. Longer apnea duration is associated with more severe obstructive sleep apnea syndrome as well as with greater arousal and oxygen desaturation.

0726

OPTIMIZATION OF HUMIDIFICATION WITH THE ADDITION OF A HEATED HOSE IN PATIENTS RECEIVING POSITIVE AIRWAY PRESSURE THERAPY

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Introduction: Non-compliance to positive airway pressure therapy (PAP) effects half of sleep apnea patients. Frequently non-compliant patients complain of symptoms of inadequate humidification. Conversely, condensation in the mask or hose from over-humidification can also result in patients rejecting therapy. We present a retrospective case series of 100 patients who added an actively heated hose to their PAP therapy.
Methods: Retrospective chart review of 100 patients being treated with PAP therapy for sleep apnea at an independent sleep center in San Diego, California, from April 2006 to December 2008. Patients with sleep apnea who were using PAP therapy with a heated humidifier, were loaned an actively heated hose to replace their current hose. After a trial period of 1 to 4 weeks, data were collected and patients were given the option to

purchase the heated hose. Data analysis included downloads from PAP equipment, chart notes and the percentage of patients who chose to purchase the heated hose.
Results: Over 90% of patients elected to purchase the heated hose at an average cost of $115 US. Close to 75% of patients reported an increase in the number of hours of PAP per night. (This was confirmed by machine downloads). Improvement in daytime nasal congestion, sneezing, and rhinorrhea, (symptoms which usually proceeded the use of any PAP) was reported in 20% of patients.
Conclusion: Optimization of humidification in patients receiving PAP for sleep apnea resulted in improvement in both compliance to therapy as well as subjective symptom relief. Patients valued this addition to their PAP therapy enough to pay a significant amount of their own disposable income to continue it.

0727

MEDIAL AND LATERAL TONGUE BASE REDUCTION IN OBSTRUCTIVE SLEEP APNEA

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Introduction: The tongue base can cause upper airway obstruction, contributing to obstructive sleep apnea. Current surgical treatments to reduce hypertrophic tongue base musculature include partial glossectomy and volumetric tongue reduction. In extreme cases of macroglossia we combine both methods to achieve reduction of the lateral aspects of the tongue and elimination of the obstructing central tissue component.
Methods: The hand piece (PROcise XP Coblation Wand, ArthroCareENT) emits radio-frequency energy from the triple-electrode tip to vaporize soft-tissue. The two-prong probe (Gyrus/Olympus Corporation) radially ablates soft-tissue from each probe tip using PlasmaKinetic technology. Both methods have been proven clinically effective, though each has certain advantages and disadvantages with respect to ease and time of use, morbidity, risks, and costs. The volumetric procedure is performed first. With the tongue advanced anteriorly, the tonsil gag is placed, providing suitable exposure. Following injection of a suitably-diluted anesthetic-vasoconstrictor solution to achieve tumescence, three-staggered probe-insertions are performed on the lateral aspects of the tongue. The medial base of tongue is then ablated using repeated poster-to-anterior sweeps of the radio-frequency device.
Results: The bilaterally-perfused medial tongue base tissue is intended to be the site of greater thermal trauma because of its superior capacity to recover from tissue injury. Thus, this area undergoes the glossectomy procedure, in which the mucosa is breached and hypertrophic muscle is vaporized. The lateral tongue tissue is less traumatized, with the mucosa being preserved and the muscle ablation being less extensive.
Conclusion: Medial partial glossectomy and lateral volumetric reduction of the base of tongue are complimentary procedures that effectively diminish areas of the tongue that contribute to upper airway obstruction.

0728

SLEEP DISORDERED BREATHING IN PATIENTS WITH PRIMARY AND SECONDARY POLYCYTHEMIA

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Introduction: Hypoxia is a strong stimulator for erythropoietin production and erythropoiesis. Obstructive sleep apnea (OSA) is characterized by intermittent hypoxia during sleep. The aim of this study is to describe the association of sleep disordered breathing in patients with primary and secondary polycythemia.
Methods: We reviewed the histories of patients with diagnosis of primary and secondary polycythemia who also were diagnosed with OSA at the Mayo Clinic. Demographic information, sleep history, physical examination, laboratory and polysomnographic (PSG) data was collected and analyzed. Diagnosis of primary polycythemia (polycythemia vera) was confirmed by erythropoietin level, JAK2 V617F mutation and bone marrow biopsy.
Results: We identified 8 patients with primary polycythemia and 41 patients with secondary polycythemia who also were diagnosed with obstructive sleep apnea. 75% were male in the primary group as were 73% in the secondary. Epworth sleepiness scale score mean (SD) was 7.7 (2.4) vs. 11.2 (5.8), BMI 31.6 (5.5) vs. 32.4 (8.0) Kg/m2 and age at the time of PSG 67.1 (9.8) vs. 63.6 (13.9) years respectively in primary vs. secondary polycythemia group. Apnea hypopnea index was 14.3 (12.0) vs. 20 (20.5) in primary and secondary groups. Lowest O2 saturation (O2Sat), mean O2Sat during sleep and % of total sleep time with O2Sats <90% were 83.9 (7.5) vs. 80.5 (9.1), 92.9 (1.3) vs. 91.2 (3.7) and 5.2 (7.6) vs. 17.5 (25.5) respectively in primary and secondary polycythemia. Mean hemoglobin was 15.4 (3.2) vs. 17 (1.4) (p=0.0497), mean hematocrit 46.8 (9.5) vs. 49.8 (4.2), erythropoietin level 3.9 (3.1) vs. 16.9 (20.7) (p=0.0006). JAK2 V617F mutation status was positive on all patients with primary polycythemia and 1 of 22 patients checked for this mutation in secondary polycythemia group was positive.
Conclusion: Although the two groups have similar baseline and polysomnographic characteristics the secondary polycythemia patients have relatively higher hemoglobin levels. Further research including control groups should be carried out to better describe the relationship.

0729

POSTOPERATIVE COMPLICATIONS IN SURGICAL PATIENTS AT RISK FOR OBSTRUCTIVE SLEEP APNEA

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Introduction: Obstructive sleep apnea (OSA) is common and undiagnosed among adult surgical patients. Patients with OSA are thought to be more likely to experience peri-operative complications. We designed a prospective, observational study of adult surgical patients to determine an association between screening high risk for OSA and peri-operative complications.
Methods: Consecutive adult surgical patients were screened for OSA risk with the Berlin Questionnaire and Flemons' Index. Patients with known OSA were included. Records were audited for perioperative complications and in-hospital mortality. Odds ratios were calculated using logistic regression.
Results: Of the 4427 surgical patients screened 1716 (39%) had a positive Berlin questionnaire, 1270 (29%) had a positive Flemons' Index, 959 (22%) were positive with both screens, and 549 (12%) had a history of OSA. Odds ratios (OR) for intensive care unit (ICU) admission, postoperative intubation and mortality were calculated. Patients who screened high risk for OSA on any of the questionnaires were more likely to have diabetes mellitus, arrhythmias, coronary artery disease, stroke, congestive heart failure, or chronic obstructive pulmonary disease than those who did not screen high risk for OSA (ps < 0.05). A positive score on either screening tool was associated with increased risk of ICU admission or postoperative intubation but not mortality; the greatest risks were with a positive screen on both questionnaires.
Conclusion: Data from this large prospective study suggest that 22-39% of patients undergoing surgery are at high risk for OSA. Screening is preferable to OSA history alone to help identify patients who are at increased risk for certain peri-operative complications. Further research is required to determine whether OSA risk is directly associated with certain peri-operative complications or whether it represents an epiphenomenon.

0730

TRANSCUTANEOUS CARBON DIOXIDE ANALYSIS DURING POLYSOMNOGRAPHY: VALIDATION OF PRE AND POST STUDY MEASURES

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Introduction: The measurement oxygen and carbon dioxide is integral to monitoring the presence and severity of respiratory failure as well as the response to ventilatory and oxygen strategies in many patients undergoing polysomnography. Though oximetry is the accepted standard for assessing oxygenation in this setting, there is unclear consensus regarding the choice of non-invasive strategies for measuring carbon dioxide. In the present study we sought to assess the validity of transcutaneous monitoring (TCM) device in measurement of carbon dioxide in patients undergoing overnight polysomnography in the sleep laboratory.
Methods: We performed a retrospective review of 121 consecutive patients studied over the past years at two AASM sleep centers who had TCM and blood gas sampling who had a mean age of 53 +/-14 and mean BMI of 37 +/12. Comorbid conditions potentially affecting breathing in the population included CHF (14%), pulmonary hypertension (12%), COPD (18%), interstitial lung disease (7%) and neuromuscular disease (15%). Arterial carbon dioxide (PaCO2) obtained pre and post polysomnography [range 29-81mmHg] were compared with the CO2 levels from the TCM device (Radiometer or Novametrix). The error between PaCO2 and TCM [PaCO2-TCM] in 150 instances in which both TCM and PaCO2 were obtained was 1.1 +/- 6.4 mmHg before PSG and 3.2 +/- 13 mmHg in the morning after the PSG.
Results: The error between PaCO2 and TCM [PaCO2-TCM] in 150 instances in which both TCM and PaCO2 were obtained was 1.1 +/- 6.4 mmHg before PSG and 3.2 +/- 13 mmHg in the morning after the PSG.
Conclusion: The TCM provides reliable estimation of arterial carbon dioxide during wakeful periods before and after polysomnography. In order to extend the validation of the device to the application for assessing sleep-associated hypoventilation in patients with sleep-related breathing disorders, simultaneous arterial and transcutaneous obtained during sleep will need to be compared.

0731

ADDITION OF NECK CIRCUMFERENCE MEASUREMENT TO BERLIN QUESTIONNAIRE AS A SCREENING STRATEGY FOR OBSTRUCTIVE SLEEP APNEA

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Introduction: Obstructive sleep apnea (OSA) is a common clinical condition and recent literature suggests that it widely prevalent. Due to the high costs of attended polysomnography(PSG), efforts to develop screening strategies aimed at improving detection in primary care settings have met with mixed results. The Berlin questionnaire (BQ) is one such strategy that has in particular had modest success, as a well-validated screening tool. What the BQ lacks is data on basic anthropometry besides the body-mass index. We hypothesized that a strategy that combines the BQ with a simple anthropometric measure - neck circumference (NC) would greatly improve its specificity as well as the predictive values.
Methods: Patients >18 yr without previously diagnosed OSA and who were referred for a sleep evaluation were included. BQ was administered in addition to routine sleep questionnaire, and in addition all patients had measurements of NC. NC was dichotomized with a cutoff of 17 in males and 15 in females. All patients underwent overnight full PSG, and a RDI of > 15 was used as the gold standard to define OSA.
Results: We included a total of 1052 subjects - 617 males and 435 females. Mean age and BMI was 55 +/- 14 and 35 +/- 8 respectively. In our study population, BQ had a sensitivity of 90% and specificity of 22%. Positive and Negative Predictive values were 92% and 18% respectively. Addition of NC to BQ had a composite sensitivity and specificity of 83% and 47% respectively. Positive and Negative Predictive values were 94% and 21.3% respectively. Area under curve (AUC) for BQ was .6574, while for composite BQ+NC was 0.7443.
Conclusion: Adding NC measurement is a simple and cost-effective measure to improve the utility of the BQ as an effective screening strategy for OSA.

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RESTFUL SLEEP AFTER CPAP TITRATION FOR OBSTRUCTIVE SLEEP APNEA (OSA)

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Introduction: Subjective improvement in sleep quality after CPAP titration for OSA enhances short term compliance. We sought to evaluate predictors of restful sleep (RS) in patients with OSA after CPAP titration.
Methods: This retrospective study was performed at a tertiary university sleep center. Patients were included if they had a CPAP titration for OSA. Standard admission forms were reviewed for age, gender, and body mass index (BMI) in addition to polysomnography parameters that included apnea-hypopnea index (AHI), periodic leg movements index and with arousal (PLMI and PLMAI). We also compared values for sleep efficiency (SE), REM and N3 sleep before and after CPAP titration. Post-titration questionnaires were reviewed specifically for quality of sleep after CPAP. Patients were categorized into two groups based on the presence of absence of RS. Univariate analysis was performed first followed by logistic regression to discern independent predictors for RS. Only non parametric tests were used due to small sample size. Significance was defined as $p<0.05$ and all tests were two sided.
Results: 93 patients were included in this analysis. Median age, BMI and AHI were 55.26, 36.6 and 15.2 respectively. 60% were males. RS group comprised 70%. Univariate analysis revealed the RS group had more males, lower PLMI and PLMAI and better SE than the non-RS group. Logistic regression revealed that male gender and SE were the only predictors of restful sleep (P values 0.047 and 0.025, respectively).
Conclusion: We found that male gender is associated with the perception of more RS after adjusting for baseline characteristics and severity of sleep apnea. Core polysomnography parameters such as AHI, or BMI were not independent predictors. Our findings are limited by the retrospective design and potential selection bias. A larger prospective study is necessary to substantiate this association between gender and the subjective quality of restful sleep after CPAP titration.

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SLEEP-RELATED BREATHING DISORDERS IN SICKLE CELL DISEASE

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Introduction: Nocturnal oxyhaemoglobin desaturation has been associated with complications of sickle cell disease but there are few data on prevalence or prediction of polysomnographic abnormality. We document the prevalence of nocturnal oxyhaemoglobin desaturation in a large series of unselected and referred patients with homozygous sickle cell disease (HbSS).

Methods: 91 unselected children in the East London cohort underwent home oximetry and 179 patients with HbSS underwent oximetry as inpatients in the sleep laboratory. Indications for inpatient sleep study were symptoms of upper airway obstruction (UAO, n=109), ongoing UAO symptoms despite adenotonsillectomy (n=13), frequent painful crises (n=4), stroke (n=24), transient ischemic attack (n=8), seizures (n=7), headache (n=6) or abnormal transcranial Doppler scan (n=8). 93 of the inpatients also had cardiorespiratory sleep studies with the ALICE4 and the 4% desaturation events per hour from the oximetry data was compared with the apnea-hypopnea index using logistic regression.
Results: In the 91 patients studied with home oximetry, median SpO2 was 95.4%, (range 84-99.7%). In those studied as inpatients, mean overnight SpO2 was a median of 94.4% (range 83.4 to 99.5%) while for >4% desaturations per hour, median was 4 (0-134). The number of desaturations was correlated with mean and minimum saturation (Spearman's rho -0.45 and -0.75, p=0.0001 and 0.0001 respectively). The desaturation index was associated with AHI in the 93 patients in whom both were undertaken (R2 0.1, p=0.002). Of 60 patients restudied after adenotonsillectomy, sleep studies remained abnormal in 47 (78%).
Conclusion: Low mean nocturnal oxygen saturation and frequent desaturations of at least 4% are common in unselected patients with sickle cell disease, as well as those referred with symptoms of UAO or SCD complications. Oximetry is commonly abnormal and varies greatly from the reference ranges ascertained in normal children.(1) Adenotonsillectomy as currently undertaken does not improve sleep disordered breathing in most SCD patients, in contrast to the improvement seen in the majority of patients without SCD.(2) Desaturation events per hour are associated with AHI but other indices, such as the delta 12 index,(3) may explain more of the variance.
Support (optional): 1. Urschitz MS. Chest. 2003; 123: 96-101. 2. Friedman BC. Sleep. 2003; 26: 999-1005. 3. Magalang UJ. Chest. 2003;124: 1694-701.

0734

INFLUENCE OF OBESITY BY ITSELF ON PHASE-SPECIFIC POLYSOMNOGRAPHIC VARIABLES

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Introduction: Obesity is amongst the most significant predisposing factors that leads to upper airway collapsibility and resulting obstructive sleep apnea (OSA). Few studies have studied the influence of obesity on phase-specific respiratory variables. Our hypothesis was that there would be crucial differences in PSG respiratory variables between obese and non-obese subjects with similar severity of OSA.
Methods: total of 1656 individuals who were referred for a sleep study and were enrolled into this study. Only persons diagnosed as having mild to moderate OSA if his AHI is ≥15 & < 25 were included in the analysis as we wished to study only moderate degree of OSA, severity of which would be equivalent in both groups. Obesity was defined as BMI > 30.
Results: 185 patients met inclusion criteria. Gender distribution was 77(42%) females, 108 males (58%). Mean age was 56.8 +/- 14.5 Mean BMI in the obese group was 37.8 +/- 6 and in the non-obese group was 26.9 +/- 2.3 Overall AHI between the two groups was identical (mean of 19.7 +/- 2.9 in both groups). Mean(SD) for REM AHI among obese was 33.3(21.3) while in non-obese mean(SD) was 22.9(18.8); p < 0.005. Mean (SD) for NREM AHI for obese and non-obese were 16.7(5.6) & 18.7(5.3) respectively, p < 0.05. AHI difference (REM AHI - NREM AHI) also varied significantly between obese and non-obese males - however no such difference was noted in females. Stratified by gender, REM AHI, and NREM AHI were not different between obese and non-obese females while a significant difference was found between obese and non-obese males.
Conclusion: Obesity significantly influences PSG variables as they relate to sleep apnea in patients with mild to moderate sleep disordered breathing. Crucial gender differences are also seen in this regard.

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HEART RATE VARIABILITY DOES NOT PREDICT PRESENCE OR SEVERITY OF SLEEP APNEA DURING AN ACUTE HEART FAILURE EXACERBATION

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Introduction: Heart rate variability (HRV) is an indirect measurement of cardiac autonomic tone. Decreased HRV is due to increased sympathetic activity and vagal withdrawal, previously shown to occur prior to acute heart failure exacerbations as well as in advanced chronic heart failure. In our previous presentations we have shown that Sleep disordered breathing is fairly common and severe in Acute Decompensated Heart Failure(ADHF). There is evidence that HRV may be decreased in patients with chronic sleep apnea. We attempted to evaluate the correlation of HRV with sleep apnea of Acute Heart Failure.
Methods: We evaluated 30 patients admitted with ADHF. All patients underwent evaluation with the Clear Path Sensor(Nexan Inc, Alpharetta, GA) within 24 hours of admission, which recorded patients EKG, respiratory impedance and sPO2 data. Data was then analyzed for apnea as well as for HRV.
Results: Patients who had an Apnea/Hypopnea index (AHI)of>15 events/hour (significant SDB) had a lower Heart Rate Variability(SDNN=54), but did not have a statistically significant difference in HRV compared to patients(SDNN=70) with an AHI<15 events/hour. In general, compared to historical controls(SDNN=141), HRV was decreased in patients with Acute Heart Failure Exacerbations(SDNN=67.6).
Conclusion: HRV is decreased during Acute Heart Failure Exacerbations. Sleep Disordered Breathing during these episodes does not alter HRV. HRV can be used as a surrogate identifier of Sleep Apnea in patients with Chronic Heart Failure, however this does not hold true for Acute Heart Failure. HRV cannot be used to identify SDB of Acute Heart Failure.

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FOR ACUTE HEART FAILURE, HEMODYNAMICS AND DEGREE OF LEFT VENTRICULAR DYSFUNCTION DO NOT PREDICT THE PRESENCE OR SEVERITY OF SLEEP APNEAS

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Introduction: Sleep disordered breathing (SDB) is commonly found in chronic ambulatory heart failure patients. We have shown in our previous work that up to 70% of patients with Acute Heart Failure can have SDB. This can lead to increased sympathetic nervous system discharge, surges in blood pressure and intermittent hypoxia and hypercarbia, which can worsen the failing heart.
Methods: A total of 42 consecutive ADHF patients were recruited to participate within 24 hours of admission. A validated overnight portable sleep diagnostic recorder with arrhythmia detection (Nexan Inc., Alpharetta GA) was applied overnight.
Results: Six patients were excluded from the analysis due to incomplete overnight recordings. The apnea hypopnea index (AHI=number of apnea/hypopnea events/ hr of quiet time) was calculated and patients were divided into <15 (n=19) or ≥15(N=17). There was no statistical difference in AHI of patients with a cardiac index of <2l/min/m.sq (AHI=30.5) when compared with pts with cardiac index 2-2.50l/min/m.sq (AHI=14.7) and pts with cardiac index >2.50l/min/m.sq (AHI=23.1). Similarly there was no statistical difference in AHI of patients with PCWP>15 mm (AHI=17.9)Hg and PCWP<15mm Hg (AHI=32). Simi-

larly, there was no difference in AHI of patients with PASP>30 or PASP <30, as well as Left Ventricular Ejection Fraction >30% or <30%.
Conclusion: None of the standard clinical and hemodynamic measures of ADHF are predictive of the presence or the severity of SDB in this population. This portable sleep test is almost mandatory to identify potentially treatable patients with SDB of Acute Heart Failure.

0737

EFFECTS OF THYROTROPIN-RELEASING HORMONE ANALOGS IN THE NARCOLEPTIC MODEL MOUSE

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Introduction: Thyrotropin releasing hormone (TRH) is a tripeptidic hormone originally extracted from the hypothalamus. Besides its effect on pituitary TSH and prolactin release, TRH has been shown to have CNS stimulating (wake-promoting and antidepressant) and neurotropic effects. We have shown that TRH and its stable analogs enhance sleep and reduce cataplexy in hypocretin receptor 2 mutated narcoleptic canines. Although the detailed mechanisms of wake-promoting mechanism of TRH are still controversial, a recent report in vitro suggests that direct activation of hypocretin (Hcrt) neurons is one of the mechanisms of wake-promoting effects of TRH. In the current study, we investigated the effect of TRH analogs, CG3703 and CG3509, on sleep using orexin/ataxn-3 transgenic (TG) narcoleptic and Hcrt-KO mice to evaluate if the Hcrt system is essential for mediating the wake-promoting effect of TRH.
Methods: TG, Hcrt-KO, and wild-type (WT) mice (n=7 for each group) were used. The mice were surgically prepared for sleep-polygraph recordings. Three drug doses (4,16, and 64mg/kg p.o.) of CG3703 and CG3509 and a vehicle administration during light period (ZT2) were performed. CG3703 administration during dark period (ZT14) was also performed. Data were analyzed for the six hours following drug administration, and each 10-second epoch was scored visually as wake, REM, NREM sleep, or direct transition from wake to REM sleep (DREM) during dark period.
Results: Both CG3703 and CG3509 increased wake and reduced NREM sleep in TG, Hcrt-KO, and WT mice in a dose-dependent manner. Wake promoting potency of CG3703 was larger than that of CG3509. Both narcoleptic (TG and Hcrt KO) and WT mice responded similarly to the TRH analogs, and similar amounts of wake enhancement were observed. Changes in the amount of REM sleep were not statistically significant. However, CG3703 reduced DREM significantly.
Conclusion: Our pharmacological experiment demonstrates that hypocretin system is not essential to mediate wake-promoting effect of TRH analogs. The result in TG mice suggested that substances, such as glutamate or dynorphin that colocalize in the hypocretin neurons are also not essential for mediating wake-promoting effects of TRH analogs. Our results also substantiate the possibility of clinical application of TRH analogs for the treatments of narcolepsy with both wake-promoting and anticataplectic effects expected.

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ACTIVITY OF PONTINE NEURONS DURING SLEEP AND CATAPLEXY IN OREXIN KNOCKOUT MICE

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Introduction: Cataplexy, which is a sudden loss of muscle activity during waking, is an important diagnostic symptom of narcolepsy. In humans and canines with narcolepsy, cataplexy is considered to be a separate and distinct behavioral state. On the other hand, in the mice model it is not known if such attacks represent quick transitions into REM sleep since all of the cardinal signs of REM sleep are also present during these attacks. To resolve this issue we monitored the activity of individual neurons in the rostral pons of orexin knockout mice. We find that as in humans and canines with narcolepsy, the cataplectic state in orexin knockout mice is separate and distinct from REM sleep.
Methods: Orexin-ko mice were implanted with EEG/EMG electrodes (under 2% isofluorane anesthesia) for sleep recording. In addition, unit recordings were done using microwire electrodes directed at the rostral pons that included the ventral lateral periaquaductal gray area (vlPAG). The microwire assembly included bundle of six microwires (25μ) passed through the cannula attached to a miniature microdrive that could be advanced at small increments. After post-surgery recovery and habituation, a well isolated signal-to-noise ratio(3:1) single neuronal activity were recorded over a multiple cycle of sleep-wake REM sleep and cataplexy episodes. The sites of neuronal recording were histologically identified. Cataplexy was verified by simultaneous EEG and video (infra red) recordings.
Results: A total of 44 neurons were recorded in the vlPAG. Most (40/44) of these were wake-active or wake-REM active. Interestingly, four neurons (4/44) were selectively active during REM sleep. All recorded neurons were less active during cataplexy compared to REM sleep. No neurons anticipated beginning or end of cataplexy.
Conclusion: Both cataplexy and REM sleep states in the orexin-ko mice are characterized by the absence of muscle tone, and theta EEG frequency (4-8 Hz), and yet neurons in the vlPAG were significantly less active in cataplexy compared to REM sleep. From this we conclude that cataplexy is a distinct state in the HCRT knockout mice separate from wake, non-REM sleep and REM sleep. It is important to record neurons in other brain regions, especially the tuberomammillary nucleus, locus coeruleus, dorsal raphe and medial medulla in an effort to determine generality of the findings between murine and canine cataplexy.
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GENE EXPRESSION PROFILING OF HYPOCRETIN/OREXIN-PRODUCING NEURONS BY MRNA TAGGING

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Introduction: Hypocretin/orexin (hcrt/orx) neurons play a major role in sleep and wakefulness. Deficiency in this system has been linked to narcolepsy in animals and humans. Despite the strong interest in the hcrt/orx system, the intra-cellular regulatory elements involved in the response of these neurons to different environmental cues, are not resolved. The aim of this work is to investigate the transcriptome of hcrt/orx to gain insight into the molecular machinery of these neurons and their functional correlates.
Methods: We generated BAC-based transgenic mice by replacing the hcrt/orx gene sequence by a flag-tagged Poly(A) binding protein (PABP) followed by IRES and eGFP sequences. As the PABP binds poly(A) tails of mRNAs, affinity-purification of flag-tagged PABP-mRNAs using a monoclonal antibody against the flag allows to co-precipitate all mRNAs from hcrt/orx neurons.
Results: The specific expression of our construct in transgenic mice was demonstrated at both RNA and protein levels. The specificity of the mRNA tagging process was revealed by a 20-fold relative enrichment of hcrt/orx mRNA as compared to MCH mRNA after immunoprecipitation (IP). Microarray expression profiling between IP-mRNA (n=9) and total brain RNA (n=9) indicated that 4323 probe sets were enriched at least 2 fold in IP samples. Many of the probe sets with high fold enrichment turned out to be non-annotated and hit several genomic localizations. However, the probe set 1447461_at was enriched 30 folds and hits a expressed sequence (LOC100048678) with high homology with Spindlins. Over-expression of Spendlin1 was recently found to induce cellular senescence, multinucleation and apoptosis. Another probe set (1420300_at) was also enriched 16.5 fold and hits Gabra2. To extract the most specific genes expressed in hcrt/orx-producing neurons, we have sought for those probe sets that were called present only in IP-mRNA hybridized chips. 71 probe sets were identified amongst which,

the genes with the highest fold change, are of functional importance and might be involved in abnormal functioning of hcrt/orx neurons, for instance in narcolepsy.
Conclusion: Our mouse model will allow for detailed analysis of hcrt/orx neurons in health and disease.

0740

THE NARCOLEPSY THERAPEUTIC GAMMA-HYDROXYBUTYRATE MODIFIES BEHAVIOR AND GABAERGIC AND CATECHOLAMINERGIC SIGNALING SYSTEMS IN A NARCOLEPTIC MOUSE MODEL

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Introduction: Gamma hydroxybutyrate (GHB) is a sedating GABAergic compound that ameliorates daytime symptoms of narcolepsy (cataplexy and sleep attacks) when administered chronically to human narcoleptics on a nightly basis. The orexin/ataxin-3 transgene causes degeneration of hypocretin-synthesizing cells of the hypothalamus. Mice harboring this transgene exhibit a syndrome similar to narcolepsy. Using these mice, we sought to develop an experimental model for studies on the neurobiology of GHB.
Methods: Male hypocretin/ataxin-3 mice were used in experiments beginning at age 6-8 weeks. Mice were subjected to video-based scoring of behavioral arrests, either simultaneous to EEG/EMG-based sleep data collection in a validation study, or alone in studies involving GHB.
Results: Simultaneous video- and EEG/EMG-based sleep scoring in hypocretin-ataxin transgenic mice demonstrated a high correlation between these two measures across two-hour intervals ($R = 0.94$, $P < 0.01$). When administered twice daily during the inactive phase of the LD12:12 cycle (2 hrs and 6 hrs after lights-on), GHB resulted in a gradual decrease, over two weeks, in the occurrence of behavioral quiescence during the active phase (from lights-off to two hours later). Chronic GHB administration resulted in a decrease in the expression of the $GABA_{B1a}$ subunit of the $GABA_B$ receptor in the hypothalamus. The $GABA_B$ antagonist CGP52432 ameliorated the narcolepsy phenotype when administered acutely to drug naïve animals during the nightly active phase, further indicating a role for the $GABA_B$ receptor in modulating the narcolepsy phenotype. In addition, GHB activated the catecholaminergic noradrenergic cells of the locus coeruleus, as indicated by FOS expression in those cells.
Conclusion: It is proposed that down regulation of $GABA_{B1a}$ receptors, and a resulting increase in neuronal excitability, is in part responsible for the gradual emergence of therapeutic efficacy for GHB in narcolepsy. $GABA_B$ antagonism may be a useful adjunct to GHB therapy.
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SCALE OF WAKE ABILITY AND FATIGUE: A NEW SCALE WITH HIGH INTERNAL CONSISTENCY, CONVERGENT AND DISCRIMINANT VALIDITY, AND TEST-RETEST RELIABILITY

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Introduction: Tests of sleepiness (MSLT, MWT, ESS), although correlated, measure different abilities. In terms of disability, fatigue and difficulty staying awake when needed may matter more than ability to fall asleep. The ESS queries neither. A scale for wake ability and fatigue is needed.
Methods: A 12-item questionnaire (Scale of Wake Ability and Fatigue or SWAF, with 6 items each querying wake ability, and fatigue/tiredness/lack of energy) was administered to 407 adults recruited randomly. They also gave other relevant information and completed the ESS. Subjects with incomplete questionnaires (44), on CNS-active medicines (55), with CNS disorders (3), getting >9 hours (27) or <=6 hours (44) in bed, with untreated depression (9), observed/perceived apneic episodes in sleep (22), BMI >=40 (10), or admitting to sleepiness/fatigue (64) were excluded in that order. This left 129 normal subjects (49 male, 80 female, mean age 39.2, SD 18). Of the 407 subjects, 94 retook the SWAF and ESS a month later. Upon excluding all but sleepy/fatigued and normal subjects, 33 remained.
Results: Cronbach's alpha (internal consistency) was 0.83 for SWAF, 0.76 for ESS. Factor analysis with varimax rotation revealed 3 SWAF factors: Factor 1 (37% of variance) included 4 items (three driving related); factor 2 (16%) included the remaining 5 fatigue items, factor 3 (9%) included the remaining 3 wake ability items. ESS and SWAF were correlated ($r=0.50$, $p<0.001$, convergent validity). Factor analysis combining SWAF and ESS revealed 5 factors. Factor 1 (30% of variance) remained unchanged. 5 of ESS items loaded by themselves on Factor 2, with minimal overlap with SWAF items on any factor. The 129 normal subjects differed from the 64 sleepy/fatigued subjects ($p<0.05$) in SWAF, ESS, SWAF factors 1, 2, and 3 (discriminant validity). They also differed from the 22 sleep apnea subjects ($p<0.05$) in SWAF, ESS, SWAF factors 1 and 2 (but not 3) (discriminant validity). Upon retest, the intraclass correlation coefficient for SWAF was 0.71; for ESS 0.86; for Factor 1 (driving wake ability and fatigue) 0.67; for Factor 2 (fatigue) 0.74; for Factor 3 (wake ability) 0.68 (all $p<0.002$). Using t-tests for paired samples, there were no significant differences between the test and re-test sums of scores for SWAF, ESS, and Factors 1, 2 and 3.
Conclusion: The SWAF, a new test of wake ability and fatigue, has high internal consistency, convergent and discriminant validity, and test-retest reliability. The SWAF and ESS measure different factors.

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CLINICAL AND GENETIC CHARACTERISTICS OF OBSTRUCTIVE SLEEP APNEA SYNDROME AND NARCOLEPSY IN KOREAN PATIENTS

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Introduction: Obstructive sleep apnea syndrome and narcolepsy both manifest as excessive daytime sleepiness. We evaluated and compared clinical, polysomnographic, and genetic characteristics of obstructive sleep apnea syndrome and narcolepsy in Korean patients.
Methods: 226 subjects complaining of daytime sleepiness were diagnosed as 1) Obstructive sleep apnea syndrome (OSAS), 2) Narcolepsy, and 3) Dual diagnosis of OSAS and narcolepsy using the revised ICSD-2 diagnostic criteria. Clinical evaluation, nocturnal polysomnography (NPSG) followed by multiple sleep latency test(MSLT), HLA typing, and cerebrospinal fluid(CSF) hypocretin-1 levels were assessed.
Results: All patients complained of excessive daytime sleepiness, as reported by Epworth Sleepiness Scale(ESS) and clinical interviews. ESS of patients with OSAS or narcolepsy did not differ from each other. Although dual diagnosis patients had higher ESS scores than patients with OSAS or narcolepsy, this finding was not significant. On NPSG, Patients with OSAS showed more stage 2 sleep, and less stage 3 and 4 sleep. On MSLT, patients with OSAS had longer mean sleep latency (SL), and less sleep-onset REM periods (SOREMPs) than patients with narcolepsy or dual diagnosis. On HLA typing, HLA DQB1*0602 frequencies were lowest in patients with OSAS than in narcoleptic or dual diagnosis patients. However, this value remained higher than that of the general population.
Conclusion: Nighttime sleep quality is worse in OSAS than in narcolepsy. OSAS manifests longer sleep latency and less SOREMP on MSLT. HLA-DQB1*0602 frequencies are lower in OSAS than in narcolepsy, but are higher than in healthy controls. Our findings further clarify the

different characteristics of OSAS and narcolepsy, which both present as pathologic daytime sleepiness.

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NOCTURNAL POLYSOMNOGRAPHIC CHARACTERISTICS OF PEDIATRIC NARCOLEPSY

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Introduction: The aim of this study was to describe the polysomnographic features of childhood-onset narcolepsy because there is little available information on this topic.
Methods: A retrospective review was carried out of all patients with narcolepsy with and without cataplexy who were below age 18 years at diagnosis. The study period was 1997-2008. The polysomnogram findings were compared with those of age matched controls without narcolepsy. Patients on REM-suppressant medications were excluded. Twenty-three narcolepsy subjects and 10 control subjects with other sleep diagnoses who underwent polysomnography and multiple sleep latency testing (MSLT) were identified.
Results: The mean age of subjects with narcolepsy was 13.5 years (range 6 - 17) while the mean age of the controls was 13.9 years (range 6 - 17). Ten of 23 (43%) narcolepsy subjects and 7/10 (70%) control subjects were female. The median nocturnal REM latency in narcolepsy subjects was 58 minutes, while in the control subjects it was 77 minutes (p=0.05). The narcolepsy subjects had a mean initial sleep latency of 10.9 minutes versus 20.4 minutes in control subjects (p=0.03), narcoleptic subjects had a mean sleep efficiency of 91.0%. The mean REM sleep percentage in narcoleptics was 24.6% compared to 19.7% seen in controls (p=0.02).
Conclusion: This study suggests that in patients with the clinical and neurophysiologic MSLT features of narcolepsy, there is a trend towards an abbreviated initial sleep latency and REM latency on nocturnal polysomnography.

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IDIOPATHIC HYPERSOMNIA WITH AND WITHOUT LONG SLEEP TIME: A CONTROLLED SERIES OF 75 PATIENTS

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Introduction: Objective: To characterize the clinical, psychological, and sleep pattern of idiopathic hypersomnia with and without long sleep time, and provide normative values for 24-hour polysomnography. Setting: University Hospital Design: Controlled, prospective cohort
Methods: Participants: 75 consecutive patients (aged 34±12 y) with idiopathic hypersomnia and 30 healthy matched controls. Intervention: Patients and controls underwent during 48 hours a face-to face interview, questionnaires, human leukocyte antigen genotype, a night polysomnography multiple sleep latency test (MSLT), followed by 24-hour ad libitum sleep monitoring.
Results: Hypersomniacs had more fatigue, higher anxiety and depression scores, and more frequent hypnagogic hallucinations (24%), sleep paralysis (28%), sleep drunkenness (36%) and un-refreshing naps (46%) than controls. They were more frequently evening types. DQB1*0602 genotype was similarly found in hypersomniacs (24.2%) and controls (19.2%). Hypersomniacs had more frequent slow wave sleep after 6 AM than controls. During 24-hour polysomnography, the 95% confidence interval for total sleep time was 493-558 min in controls, vs 672-718 min in hypersomniacs. There were 40 hypersomniacs with and 35 hypersomniacs without long (>600 min) sleep time. The hypersomniacs with long sleep time were younger (29±10 vs 40±13 y, P=0.0002), slimmer (body mass index: 26±5 vs 23±4 kg/m2; P=0.005), and had lower Horne-Ostberg scores and higher sleep efficiencies than those without long sleep time. MSLT latencies were normal (>8 min) in 71% hypersomniacs with long sleep time.
Conclusion: Hypersomnia, especially with long sleep time, is frequently associated with evening chronotype and young age. It is poorly diagnosed using MSLT.

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SUBJECTIVE EXCESSIVE DAYTIME SLEEPINESS IN A COMMUNITY-BASED SAMPLE: FREQUENCY AND ASSOCIATED FACTORS

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Introduction: Despite the fact that excessive daytime sleepiness is commonly reported and has been linked to several negative outcomes such as traffic accidents, epidemiological data on this subject are scarce. This study aimed at investigating the frequency of occurrence and associated factors of self-reported excessive daytime sleepiness in a community-based sample.
Methods: Participants were French-speaking adult residents of the province of Quebec (Canada) who took part in an epidemiological study examining the longitudinal course of insomnia in the general population. Data used in the current project are derived from the fifth annual postal follow-up, which assessed sleep/sleepiness, psychological and health variables, and was completed by 633 (aged 21-87 years old, mean = 49.7; 63.8% women) of the 997 participants who were initially included in the longitudinal study. Excessive daytime sleepiness (EDS) was defined as an Epworth Sleepiness Scale (ESS) score greater than 10. Pearson chi-square tests were computed to examine associations between EDS and several sociodemographic, life habits and health-related variables.
Results: Mean ESS score was 8.3 ± 4.3, and 28.1% of the sample had a score higher than 10. Chi-square tests revealed that the presence of EDS was significantly associated ($p < .05$) with a sleep duration shorter than 7 hours, the use of two or more caffeinated beverages per day, as well as the presence of chronic pain. Nearly significant associations ($.05 <= p < .09$) were found between EDS and a body mass index greater or equal to 30, a frequency of physical activity lower than once per week, as well as the presence of headaches/migraines, moderate/severe depression symptoms, and moderate/severe insomnia symptoms.
Conclusion: The frequency of self-reported EDS was relatively high in this sample compared to other epidemiological investigations. Several variables were associated with the presence of EDS, including sleep-related variables as well as the presence of specific chronic health conditions. Future analyses should investigate additional factors (e.g., use of medication) potentially associated with EDS.
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0746

NARCOLEPSY WITH LONG SLEEP TIME: A SPECIFIC ENTITY?

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Introduction: Background: The classical narcolepsy patient typically reports intense feelings of sleepiness (with/out cataplexy), normal or disrupted night-time sleep, and often takes short and restorative naps. However, with long-term monitoring, we identified some narcoleptics resembling patients with idiopathic hypersomnia. Objective: To isolate and describe a new subtype of narcolepsy with long sleep time (total sleep time greater than 660 min).
Methods: Setting: University Hospital Design: Controlled, prospective cohort Participants: Out of 160 consecutive narcoleptics newly diagnosed within the past 3 years, 29 (18%) had a long sleep time. We compared narcoleptics with (n=23) and without (n=23) long sleep time to 23 hypersomniacs with long sleep time as well as to 20 healthy subjects.

Intervention: Patients and controls underwent face-to face interviews, questionnaires, human leukocyte antigen genotype (HLA), an overnight polysomnography, multiple sleep latency test, and 24-hour ad libitum sleep monitoring.
Results: Narcoleptics with long sleep time had a similar disease course, and evidenced similar frequencies of cataplexy, sleep paralysis, multiple sleep onset in REM periods and HLA DQB1*0602 positivity as patients with classical narcolepsy did. However, they had less frequent hypnagogic hallucinations, shorter sleep latencies (4.9±0.5 vs 6.9±0.8 min, $P<0.05$), longer sleep time during 24 hours, and higher sleep efficiency. Eighty percent of them suffered un-refreshing naps.
Conclusion: The subgroup of narcoleptics with a long sleep time comprises 18% of narcoleptics and their symptoms combine the disabilities of both narcolepsy (severe sleepiness) and idiopathic hypersomnia (long sleep time and un-refreshing naps). Thus, they may constitute a group with multiple arousal system dysfunctions.

0747

NARCOLEPSY IN CHILDHOOD AND ADULTHOOD: CLINICAL STUDY OF THE DISEASE COURSE AND SEVERITY

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Introduction: The aim of the present study is to compare the course and severity of narcolepsy in relation to different age at the disease onset, and to find out if childhood narcolepsy has a more severe course than narcolepsy beginning in adulthood.
Methods: Clinical interview with the completion of the Stanford questionnaire, Epworth Sleepiness Scale (ESS) and MSLT were evaluated in 105 patients (44 males, 61 females, mean age 45.4±19.2, BMI 29.2±5.8) suffering from narcolepsy (87 cases narcolepsy with cataplexy, 18 patients narcolepsy without cataplexy). Statistical analysis was carried out using ANOVA, the two-sample t-test, chi-square test, correlation coefficient, univariate and multivariate linear regression, and logarithmic transformation.
Results: Most patients estimated the maximum severity by the frequency of imperative sleepiness and cataplectic attacks right from the disease onset. No relations with the age at onset and clinical tetrad were found; however, smoking statistically increased the number of hypnagogic hallucinations ($p=0.01$). There was no relation between the number of sleep and cataplectic attacks and the age at onset, nor did subjective ESS show any significant dependence. However, the younger the age at onset, the shorter the MSLT mean latency ($r=0.23$, $p<0.05$), but no differences were found in the mean number of SOREMP. ESS increased linearly ($r=0.266$, $p<0.01$) with age and with the disease duration. A significant correlation was also found between the BMI and age ($r=0.363$, $p<0.01$), the former growing in proportion to latter. A correlation was also found between BMI and MSLT. The higher the patients BMI, the shorter values were found ($r=-0.247$, $p<0.05$).
Conclusion: The clinical severity of narcolepsy does not depend on the age at onset; a shorter MSLT-rated mean sleep was the only parameter corresponding with the age at onset.
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0748

SELF-MANAGEMENT TECHNIQUES FOR EDS IN NARCOLEPSY

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Introduction: Sleepy patients experiment with tactics to manage symptoms, especially prior to diagnosis of a specific sleep disorder. Even after diagnosis, some patients employ self-management techniques to augment other therapies.
Methods: Participants at the 2008 national Narcolepsy Network meeting in Milwaukee, WI, completed a survey with a menu of 16 self-management techniques used for EDS developed by the authors Respondents rated the effectiveness of listed techniques and wrote in additional tactics.
Results: The 23 respondents, 71% female, had a mean age of 48. Cataplexy was present in 75% of the respondents. Narcoleptic symptoms started on average at age 21 and narcolepsy was diagnosed at age 33. On a 0-10 scale, the effectiveness of prescription medications for narcolepsy was 6.9 and usefulness of self-management techniques was 4.7. Scheduled naps were the most preferred technique by a significant margin. A cluster of tactics were ranked next: walking around, eating food, caffeinated beverages, and hot baths. Ranked subsequently were unscheduled naps, drinking non-caffeinated beverages, working out, listening to music, talking to another person, fidgeting, and a blast of cold air. The three respondents who endorsed nicotine use all ranked this highly. Caffeine pills and smokeless tobacco were not identified as widely used tools. When asked whether physicians had ever encouraged attempts of any self-management strategies (0-10 scale), the responses ranged from 0 (never) to 9 (many times) with a mean of 3.4.
Conclusion: Narcoleptic patients clearly view scheduled naps as the most effective self-management technique to manage EDS. Several other tactics are viewed as having therapeutic value as adjunctive to prescription medications. Subsequent studies measuring the efficacy of highly rated tactics would allow a better understanding of the role of these tools in a comprehensive treatment plan for EDS.

0749

HYPNAGOGIC HALLUCINATIONS AND "PSYCHOTIC" SYMPTOMS IN NARCOLEPSY: A COMPARISON WITH CONTROL SUBJECTS AND SCHIZOPHRENIC PATIENTS

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Introduction: Patients with narcolepsy often experience pervasive hypnagogic hallucinations, sometimes even leading to confusion with schizophrenia. We aimed to provide a detailed qualitative description of hypnagogic hallucinations and other "psychotic" symptoms in patients with narcolepsy and contrast these with schizophrenia patients and healthy controls. We also compared the prevalence of formal psychotic disorders between narcolepsy patients and controls.
Methods: We used SCAN 2.1 interviews to compare "psychotic" symptoms between 60 patients with narcolepsy, 102 with schizophrenia, and 120 matched population controls. In addition, qualitative data was collected to enable a detailed description of hypnagogic hallucinations in narcolepsy.
Results: There were clear differences in the pattern of hallucinatory experiences in narcolepsy versus schizophrenia patients. Narcoleptics reported multisensory "holistic" hallucinations rather than the predominantly verbal- auditory sensory mode of schizophrenia patients. Other psychotic symptoms such as delusions were not more frequent in narcolepsy compared to population controls. In addition, the prevalence of formal psychotic disorders was not increased in patients with narcolepsy. Almost half of narcoleptics reported moderate interference with functioning due to hallucinations, mostly due to related anxiety.
Conclusion: Although hypnagogic hallucinations in narcolepsy are frequent and pervasive, we did not find a higher frequency of psychotic

disorders compared to population controls, which points to a relatively healthy insight. Hypnagogic hallucinations are different on a phenomenological level (form and type) from hallucinations of schizophrenic patients.

0750

ARMODAFINIL IMPROVES WAKEFULNESS THROUGHOUT THE DAY IN PATIENTS WITH EXCESSIVE SLEEPINESS ASSOCIATED WITH NARCOLEPSY

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Introduction: Excessive sleepiness is a cardinal symptom of narcolepsy. Armodafinil (NUVIGIL®), the *R*- and longer-lasting isomer of modafinil, is a non-amphetamine, wakefulness-promoting medication that is efficacious and generally well tolerated in patients with excessive sleepiness associated with obstructive sleep apnea, shift work disorder, and narcolepsy. Compared to modafinil, on a mg-to-mg basis, armodafinil produces higher plasma concentrations later in the day, which may obviate the need to split, administer higher doses of modafinil, or both to maintain wakefulness throughout the day.
Methods: A post-hoc analysis was undertaken of data from the full analysis set of a 12-week, double-blind, placebo-controlled, multicenter study of 196 randomized patients with excessive sleepiness associated with narcolepsy. The objective was to compare effects of once daily armodafinil, 150 mg or 250 mg, versus placebo in sustaining wakefulness throughout the day (0900-1900 hours) and later in the day (1300-1900 hours) as assessed by mean sleep latency on the 20 minute Maintenance of Wakefulness Test (MWT). Efficacy of armodafinil in a subgroup of patients with a MWT latency <20 min at baseline (n=149) was determined. Tolerability was assessed.
Results: At final 12-week visit, mean changes from baseline on MWT latency across all 6 tests were 1.2 min (armodafinil 150 mg), 1.9 min (armodafinil 250 mg), and -1.6 min (placebo; all $P<0.05$). Comparable change scores for 1300-1900 tests were 1.5 min, 2.0 min, and -1.4 min (all $P<0.05$). In patients with mean baseline MWT scores < 20 min, respective findings across all 6 tests were 2.0 min, 2.3 min, and -1.1 min (all $P<0.01$). Headache was reported by 19% of patients and no other adverse event occurred in more than 7% of patients.
Conclusion: In patients with excessive sleepiness associated with narcolepsy, once daily armodafinil (150 or 250 mg) significantly improved wakefulness throughout the day, compared with placebo. Similar improvements in wakefulness were apparent even when subtests most proximal to dosing were excluded. Armodafinil was generally well tolerated.
Support (optional): Study sponsored by Cephalon, Inc.

0751

DECREASED CEREBRAL WHITE MATTER INTEGRITY IN YOUNG NARCOLEPTIC PATIENTS: A DIFFUSION TENSOR IMAGING STUDY

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Introduction: Structural brain changes of hypothalamus, where the hypocretin-producing neurons are located, have been hypothesized as playing a key role from prior brain imaging studies in narcoleptics. Most prior studies were on cerebral gray matter regions and the results are frequently inconsistent. The objective of the current study was to assess fractional anisotropy, a reliable indicator of white matter integrity, in order to evaluate white matter abnormalities in young narcoleptics by analyzing diffusion tensor images.
Methods: Twenty narcoleptics (12 men; 24.6 ± 5.1 years) and 20 healthy comparisons (12 men; 25.3 ± 4.3 years) were recruited. Inclusion criteria for narcoleptics included the presence of cataplexy, HLA allele DQB1 *0602, and two or more episodes of sleep-onset rapid eye movement (REM) sleep in MSLT Clinical severity of narcolepsy was assessed using polysomnography, the Ullanlinna narcolepsy scale and Epworth sleepiness scale. Statistical parametric mapping (SPM) was used to evaluate differences in global cerebral FA values between the two groups. Neuropsychological tests were performed.
Results: Narcoleptic patients had lower FA values in multiple brain regions including the right precentral gyrus, the right superior frontal gyrus, the left middle frontal gyrus, the left anterior cingulate, the left cingulate gyrus, the right insula, the right superior temporal gyrus and the left inferior parietal lobule (all corrected $p<0.05$) relative to healthy comparison subjects. The narcoleptic group had a lower rate of correct responses in the Digit Symbol test relative to the healthy comparison (beta= -0.39, p=0.01). FA values of the left anterior cingulate region inversely correlated with scores of the Epworth Sleepiness scale and subjective severity scores of the measurement of Excessive Daytime Sleepiness (r=-0.62, p=0.03; r=-0.50, p=0.01, respectively). FA values of the right superior frontal gyrus inversely correlated with subjective severity scores of Excessive Daytime Sleepiness (r=-0.55, p=0.02). FA values of the right temporal superior temporal gyrus positively correlated with scores of the Digit Symbol test (r=0.53, p=0.03).
Conclusion: We report decreased white matter integrity in multiple brain areas including frontal and limbic brain regions in narcoleptic patients. Decreased white matter integrity was associated with the extent of sleepiness and attention deficits. These results suggest the possibility of white matter abnormalities of young narcoleptic patients.

0752

ENVIRONMENTAL FACTORS IN THE KLEINE-LEVIN SYNDROME

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Introduction: Kleine-Levin syndrome (KLS) is rare disorder characterized by recurrent episodes of hypersomnia, cognitive disturbances, compulsive eating and hyper sexuality. Increased Jewish predisposition was observed in one study. The clinical profile of Israeli KLS cases was previously found to be very similar to the clinical presentation of KLS world-wide. The aim of the study was to investigate environmental variables that may be involved in the onset of KLS.
Methods: Thirty-three KLS patients (82% male) were recruited; clinical profile was previously described (APSS 2007). Ethnic and gender matched controls defined by grandparents' origin were also recruited. All patients, their parents and matched controls completed a detailed questionnaire containing 84 questions on environmental factors, way of life and development aspects during childhood.
Results: The following variables were found to distinguish KLS cases prior to onset compared to controls: living in an agricultural versus urban environment (p=0.006), living at altitude below 500 meters ($p< 0.0001$), lower rate of completed vaccination schedule ($p< 0.001$), higher rate of living environment changes (p=0.01) and sleep habits changes (p=0.01), more frequent recent initiation of the first intimate relationships (p=0.01), higher rate of discharge from military service (p=0.01), higher rate of recent change in economic status (p=0.003), higher rate of recent spouse

pregnancy (p=0.001), higher rate of recent child birth (p=0.001), and a lower rate of normal development, a higher rate of learning difficulties (p = 0.01) and a lower rate of appropriate gestational age at birth.
Conclusion: These findings suggest that specific environmental factors contribute to KLS onset.

0753

TIME UNDERESTIMATION IN A BEDSIDE EXAMINATION IS RELATED TO MWT-DEFINED ALERTNESS IN PARKINSONIAN PATIENTS

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Introduction: Parkinsonism is associated with daytime sleepiness and sleep onset REM periods. Apart from obvious psychomotor impairments, selective cognitive deficits involving presumed dorsolateral prefrontal dysfunction, often characterized as inability to shift set, also have been described. We employed a non-motor dependent, bedside-administered exam immediately prior to MWT to determine the relationship between these phenomena.
Methods: 15 Parkinsonian (X age = 66; 5 W, 10 M) pts underwent a 48-hr study with 2 nts PSG and 2 days MWT (4-nap/day, 40 min). Prior to each MWT, pts underwent a 3-trial, bedside, 30-sec time estimation task with accuracy feedback provided after each trial. We examined the % of trials (24 trials per pt over 48 hrs) where time estimates were less than 30 seconds.
Results: MWT-defined sleep latency was stable across the 2-day protocol (rho = .90, $p < .0001$). Two-day mean MWTs varied widely across individuals (range 0.25 - 40.0; X = 13.3 minutes). REM sleep occurred in MWTs of 8 of the 15 patients (range 1 to 8 naps). Pts with REM were significantly sleepier than those without (2.2 vs 26.1, $t = 4.65$, $p < .005$). Pts with higher proportions of short time estimates (< 30 sec) were significantly more alert on the MWT (rho = .47; $p < .08$)
Conclusion: These data confirm the existence of a narcoleptic phenotype in Parkinsonism. They also suggest that pts' characteristic level of alertness may be detectable in a simple bedside verbal exam involving time estimation that does not require intact motor function. The aberration of this short-term, internal time-keeping system in Parkinsonism may represent a window on cortical/subcortical "loop" dysfunction readily accessible to the physician.
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0754

HLA GENE EXPRESSION IN WHITE BLOOD CELLS OF NARCOLEPSY

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Introduction: The human leukocyte antigen (HLA)-DQB1*0602 is tightly associated with narcolepsy and proved to be one of the susceptible genes for narcolepsy. But the functional contribution of this HLA allele to narcolepsy has not been clarified. It is reported that the HLA-DR molecule density on the lymphocyte cell surface showed upregulation of the disease-associated HLA alleles in the rheumatoid arthritis patients. We hypothesized that HLA expression level shows disease specific alteration in narcolepsy patients.
Methods: RNA was purified from 5milliliters of blood by PAXgene system and used for single-stranded cDNA synthesis. Comparison of HLA-DRA, DRB1 total and DQB1*0602 expressions in white blood cells were performed by quantitative reverse-transcriptase polymerase chain reaction (RT-PCR), using normalization factors calculated by 3 stable housekeeping gene expressions (β-actin, glyceraldehyde-3-phosphate dehydrogenase and peptidylprolyl isomerase B). Samples from 44 narcolepsy patients, 34 age, sex-matched controls with HLA-DQB1*0602 allele and 24 age, sex-matched controls without this HLA allele were examined. Questionnaire relating to sleep was obtained at the time of blood collection and used for analysis. Mann-Whitney U test and SPSS 15.0 software were used for statistical analysis.
Results: HLA-DRA and DRB1 total gene expressions were significantly upregulated in subjects carrying HLA-DQB1*0602 allele ($P < 0.001$), but no differences in DRA, DRB1 total and DQB1*0602 expressions were observed between narcolepsy and HLA matched controls.
Conclusion: Our hypothesis that HLA molecule shows narcolepsy specific expressional regulation was not supported. Significantly higher expression of HLA molecules in subjects carrying HLA-DQB1*0602 might partly explain the HLA allele related susceptibility of narcolepsy. Further studies are required and on going to see whether HLA gene expressions altered according to the change in clinical state of narcolepsy patients or not.
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0755

MIS-DIAGNOSIS OF NARCOLEPSY/HYPERSOMNIA OVER AN EIGHT YEAR SPAN

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Introduction: Narcolepsy/hypersomnia are commonly misdiagnosed diseases. This could be attributed, in part, to the problem that their clinical presentation manifests much in the same way as numerous other disorders. Sleep medicine is a relatively new/accepted discipline that patients and general practitioners alike tend to seek help/treat familiar disorders before investigating the possible diagnosis of narcolepsy/hypersomnolence. We hypothesize that as sleep medicine has become more widely recognized; we should see a trend of patients and doctors coming to a sleep clinic as a first line of treatment.
Methods: A stratified sample of Multiple Sleep Latency Test (MSLT) patients was taken spanning the years 2000-2008. Patients attended a full night polysomnography (PSG) followed by a series of four naps, two hours apart, the next day. Yearly MSLTs were sub-divided into groups (2000-'01; '02-'03; '04-'06; '07-'08), six patients were randomly selected from each group (n=24). Further investigation was performed to determine which patients had previously sought treatment elsewhere, or initially attend a sleep clinic. Analysis of variance (ANOVA) was executed to determine if the differences were significant.
Results: For the years 2000 -'01; '02-'03; '04-'06, and '07- present, 33%, 66%, 50% and 83% of the sample groups sought treatment initially at the sleep clinic for narcolepsy/hypersomnolence, respectively. The F-ratio was calculated to be 3.332 (F-critical 3.4668, $\alpha=0.05$, p-value=0.083).
Conclusion: A general trend was seen in the number of patients initially attending the sleep clinic increasing over the years. Analysis of the data failed to show the difference over the years to be significant. We conclude patients are still seeking help elsewhere before coming to the sleep clinic, failing to support our hypothesis. Further education and acceptance of sleep medicine is still required.

0756

SEASONALITY OF MONTH-OF-BIRTH IN JAPANESE NARCOLEPSY-CATAPLEXY PATIENTS

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Introduction: Seasonality of birth in narcolepsy was recently reported as an environmental risk factor of narcolepsy, however there is little evidence for the Japanese.

Methods: The data of birth was obtained from our medical records of 883 narcolepsy-cataplexy patients, who were born from 1904 to 1986 in Japan and clinically diagnosed by narcolepsy specialists (coauthor YH) at the University of Tokyo Hospital and Seiwa Hospital, Tokyo, Japan. First, we examined the difference in monthly birth distributions between the observed and the expected among the patients. Second, we checked, using Rogers' test, the seasonality of birth as a sine function with a period of 12 months among the patients. Third, for each month, we compared the observed number of births of the patients with the expected, based on the proportion of births per each month to a total in the pooled general live births between 1904 and 1986, adjusted for the birth year of the patients. Of 883 patients, we excluded 105, born in 1944-1946, due to an absence of the general birth statistics of the Statistics Bureau, the Ministry of Internal Affairs and Communications, Japan. Therefore, the data of 778 patients were used for this study.
Results: Narcolepsy-cataplexy patients showed a significant difference in month-of-birth distribution, a peak in January-February and a trough in May-July ($\chi 2$=67.80, df=11, P<0.001; R=37.51, df=2, P<0.001). The significant decrease in May (OR: 0.73, 95% CI=0.52-0.99, P<0.05) and increase in February (OR: 1.24, 95%CI=0.99-1.52, P<0.05) were observed in the patients compared to the general population, respectively.
Conclusion: Narcolepsy-cataplexy has a significant seasonality of birth in Japan. Further investigation regarding the differences in the seasonal patterns in other places and ethnic groups may lead to find out environmental factors influencing the development of the disease.
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0757

SYMPTOMATIC NARCOLEPSY IN MS AND NMO PATIENTS

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Introduction: We have reported that several symptomatic narcolepsy cases are due to hypothalamic lesions with multiple sclerosis (MS) and low hypocretin levels. The brain MRI lesions of these cases were not typical of classical MS. These cases showed very rare locations and shapes of lesions, such as extremely localized hypothalamic and periaqueductal lesions. The reason for these shapes has been totally unknown. Neuromyelitis optica (NMO) is one type of MS typically manifesting transverse myelitis and bilateral optic neuritis. NMO-IgG, a disease specific autoantibody, was discovered in several patients, and the target antigen of NMO-IgG was recently identified as the aquaporin-4 (AQP4) water channel protein (Pittock2006). Brain lesions of NMO are identified and have been reported that they are often seen in the hypothalamic region. Since no cases have been reported about the relationship between the symptomatic narcolepsy and anti-AQP4 antibodies, we measured the anti-AQP4 antibodies in six cases with symptomatic narcolepsy due to hypothalamic lesions of MS.
Methods: Serums obtained from cases with symptomatic narcolepsy due to hypothalamic lesions were tested for anti-AQP4 antibodies by a sensitive detection method. CSF hypocretins were also measured by RIA.
Results: Three out of seven patients had serum anti-AQP4 antibodies. All six cases presented hypersomnia, symmetrical hypothalamic lesions on MRI, and decreased CSF hypocretin levels, all of which improved simultaneously after steroid treatment.
Conclusion: It has been demonstrated that in some MS patients who are seropositive for anti-AQP4 antibodies, hypothalamic and periaqueductal lesions correspond to brain regions where high AQP4 expression is observed. We considered that the hypothalamic lesions of our 3 cases with symptomatic narcolepsy could be caused by the immune reactivity of anti-AQP4 antibodies. This may be the reason for the rareness of the locations and shapes of the lesions. We propose to measure anti-AQP4 antibodies in patients in which symmetrical hypothalamic lesions and hypersomnia were observed.

0758

THE ASSOCIATION BETWEEN HLA DQB1*0602 AND THE EPWORTH SLEEPINESS SCALE IN PATIENTS WITH POSSIBLE NARCOLEPSY

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Introduction: Excessive Daytime Sleepiness (EDS) associated with Narcolepsy can be evaluated subjectively and objectively. Subjective tools include scales such as the Epworth Sleepiness Scale (ESS). Objective tests include the Multiple Sleep Latency Test (MSLT) and the HLA markers.
Methods: We retrospectively analyzed 55 consecutive patients with symptoms suggestive of Narcolepsy without Cataplexy. After a complete history and physical exam, only 50 of these patients agreed to have MSLT following an over-night Polysomnogram. Fifty-two patients were tested for HLA and 3 deferred this test.
Results: In this case series of 55 patients, the mean age was 45 (+/- 27) year-old, 30 (54.5%) were females, 25 (45.5%) were males, and all of them (100%) presented with EDS. The mean ESS score was 15 (+/- 9) in the 52 patients who were tested for the HLA. Only 26 (50%) of these 52 patients had an ESS score of 14 or more. Out of these 26 patients, 18 (69.2%) showed a positive result for the DQB1*0602 HLA marker. Out of these 52 patients, 35 (67.3%) showed positive results for the DQB1*0602 HLA marker. And 17 of these 35 patients (48.5%) had an ESS score of 14 or more.
Conclusion: This data suggest that there is no significant correlation between the objective HLA DQB1*0602 marker and the subjective ESS scores in patients with possible Narcolepsy. The ESS scores did not differentiate between DQB1*0602 positive and negative subjects, and the positive HLA DQB1*0602 marker did not correlate with the higher ESS scores. Clinicians should be aware that making a diagnosis of Narcolepsy, particularly without Cataplexy, is multi-factorial and can be challenging. More studies are needed to further correlate the different tools utilized to confirm the diagnosis of Narcolepsy, with or without Cataplexy.

0759

WHAT DOES THE INTERMEDIATE VALUE OF CSF OREXIN IN HYPRSOMNIA PATIENTS SUGGEST ?

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Introduction: The pathological condition of narcolepsy is becoming better understood, and more cases of CSF orexin measurements are being performed in confirming a diagnosis of narcolepsy. In some of these cases, the CSF orexin level shows an intermediate value. In this study, we evaluated patients who have hypersomnia symptoms but whose CSF orexin shows an intermediate value (110-200pg/ml).
Methods: The subjects were 6 patients (4 male, 2 female) who had been referred to our clinic for a close examination of narcoleptic symptoms. They were hospitalized and underwent various examinations. From these results we conducted evaluations on the sleep log, PSG, MSLT, and CSF orexin level.

Results: From each evaluation, the following characteristics were observed in patients with an intermediate CSF orexin value (123-162 pg/ml). The sleep log showed a longer daily sleeptime. The hypnogram by PSG showed a light sleep. MSLT showed that the sleep latency was either normal or slightly short.
Conclusion: These results suggest that orexin is related not only to narcolepsy but other hypersomniac disorders as well. We would like to evaluate more cases and further discuss the meaning of intermediate orexin levels.

0760

METABOLIC ALTERATIONS IN NARCOLEPSY WITH CATAPLEXY

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Introduction: Several studies have already shown an increased body weight and altered metabolic parameters in patients affected by Narcolepsy with Cataplexy (NC). Our aim is to explore metabolic alterations in hypocretin-1 deficient NC subjects, in comparison with subjects affected by Idiopathic Hypersomnia without long sleep period (IH), another central hypersomnia without lack of hypocretin-1. A second aim is to verify if the metabolic alterations satisfy the criteria for the diagnosis of a clear-cut metabolic syndrome.
Methods: Fourteen NC male patients and 14 IH male patients have been enrolled. In NC group, non ambiguous cataplexy, CSF hypocretin-1 deficiency (<110pg/ml), HLA DQB1*0602 aplotype have been additionally verified. The two groups were age-matched. In all patients BMI, waist circumference, arterial blood pressure, and plasmatic glucose and lipid profiles have been measured. The daily calorie intake was obtained as daily average of a three day food diary.
Results: Respect to IH, NC patients showed higher weight [P=0.019], BMI [P=0.012], waist circumference [P<0.001], and diastolic blood pressure [P=0.043]. Moreover, they showed significant reduced plasmatic levels of HDL cholesterol [P=0.004], and of GLU/IRI ratio [P<0.012], together with higher total cholesterol [P=0.016], triglycerides [P=0.008], and fasting insulin [P<0.047]. After BMI correction, NC patients still showed a significant increase in waist circumference [P=0.001] and a significant reduction of plasma HDL cholesterol [P=0.049] and GLU/IRI ratio [P=0.04]. NC patients showed also hypophagia [P=0.027]. Seven NC vs none of IH patients displayed the metabolic syndrome.
Conclusion: The striking prevalence of definite BMI independent metabolic alterations in NC patients, together with a lower daily calorie intake, confirm the hypothesis of a metabolic dysregulation intrinsic to NC, probably hypocretin-1 dependent. Moreover, these results provide an accurate metabolic phenotype of NC patients and stress the utility of a clinical metabolic assessment for the important cardiovascular risk linked to the metabolic syndrome.

0761

SLEEP DISORDERS, SLEEPINESS AT THE WHEEL AND DRIVING ACCIDENT RISK

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Introduction: Sleepiness at the wheel is a major risk factor for traffic accidents, but the respective role of each sleep disorders in the occurrence of accidents is poorly known.
Methods: An internet-linked survey was sent to 350,000 highway users in 2007. 35,004 drivers responded to the questionnaire.
Results: Responders were mainly male drivers (73%). 16% of the population was aged from 18 to 30 years, 48% from 31 to 50 years, 31% from 51 to 65 years and 5% was over 65 years old. 11.3% of drivers (n=3950) reported suffering from insomnia, 6.7% from obstructive sleep apnea syndrome (n=2340), 3.2% from restless leg syndrome (n=1106) and 0.1% from narcolepsy or hypersomnia (n=47). In the past year, 76% of narcoleptic patients, 65% of apneic patients, 58.8% of restless leg syndrome patients and 58.7% of insomnia patients reported at least one severe episode of sleepiness at the wheel (i.e. requiring to stop driving). 38.3% of narcoleptic patients, 35.9% of restless leg syndrome patients, 33.6% of apneic patients and 30.8% of insomniac patients reported at least one near-miss accident during the previous year (i.e. inappropriate line crossings) versus 29% of drivers free of sleep disorders. 21% of narcoleptic drivers, 6.3% of insomniac drivers, 6% of apneic drivers and 5.6% of restless leg syndrome patients reported at least one accident in the past year versus 7% of drivers free of sleep disorders. Sleep related accidents accounted for 20% of total accidents in narcoleptic drivers, 12% in apneic drivers, 7.9% in insomniac drivers, 7.1% in restless leg syndrome drivers, versus 4.2% in drivers free of sleep disorders. Only patients suffering from narcolepsy or hypersomnia present more sleep-related accidents than controls (P<.001).
Conclusion: Narcoleptic or hypersomnia drivers are more exposed to sleepiness at the wheel and sleep-related accidents than those suffering from other sleep disorders.

0762

GENOME-WIDE ASSOCIATION STUDY IDENTIFIES NEW NARCOLEPSY SUSCEPTIBILITY GENES

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Withdrawn

0763

IDIOPATHIC HYPERSOMNIA: A DOPAMINERGIC DISORDER ?

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Introduction: Idiopathic hypersomnia is a disorder of unknown origin characterized by excessive daytime sleepiness and prolonged non-refreshing sleep. Dopaminergic transmission is implicated in variety of brain functions including reward and sleep-wake regulation.
Methods: Untreated patients with IH diagnosed according to international criteria were studied. Dopamine transmission was assessed using positron emission tomography in two sessions (PET). Postsynaptic transmission was studied with a ligand for D2 dopamine receptors (Raclopride). Presynaptic uptake was studied with 18-Fluorodopa. Ratio of

the distribution of volumes in striatum to that in occipital cortex was calculated. The results were compared to a normative data set of healthy controls.

Results: There were 7 pts with a mean age of 34 years. All patients had an Epworth score > 10 (mean of 16), a high sleep efficiency (94%), a short sleep latency (11 minutes) and high amounts of slow wave sleep (17%). Hypocretin-1 levels in the cerebrospinal fluid were normal in all patients. On MSLT the mean sleep latency was 5.4 minutes. Dopamine-receptor availability was increased in the putamen (z-scores: left 3.2, SD 1.3; right 2.9, SD 0.9) and N. caudatus (left: 2.5, SD 0.7; right: 1.9, SD 0.5). Dopamine uptake was also increased in the putamen (left: 3.5, SD 0.2; right: 3.9, SD 0.6) but not in the N. caudatus (left: 1.9, SD 3.9; right: 0.6, SD 3.4). Mean sleep latencies on MSLT correlated with the increase in dopamine-receptor availability (Spearman's rho: 0.65, p=0.01) and the N. caudatus (0.56, p=0.04).

Conclusion: Preliminary results of this ongoing study suggest the existence of a dysfunctional dopaminergic transmission as biological marker of IH. The association of postsynaptic increased D2 receptor availability and increased presynaptic dopamine uptake may be due to a deficient synaptic release of dopamine.

0764

AMYGDALA ACTIVITY DURING AVERSIVE CONDITIONING IN HUMAN NARCOLEPSY

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Introduction: Human narcolepsy with cataplexy is caused by a depletion of hypothalamic hypocretins. Recent animal research has suggested that hypocretins may not only promote the consolidation of wakefulness but also influence neural plasticity in emotional contexts.

Methods: Fourteen unmedicated patients with narcolepsy and 14 healthy matched controls were studied by functional brain MRI during three successive fear conditioning ("acquisition") runs and two extinction runs. On each trial of the acquisition runs, one triangle was displayed at the center of screen and the subjects had to indicate whether the triangle was pointing to the left or to the right side. Triangles could be colored either in blue or in yellow. One color (CS+) signaled a possible upcoming aversive unconditioned stimulus (US), which was a brief painful electrical stimulation delivered on one finger on half of the CS+ trials (i.e., partial reinforcement). The other color was never associated with any other stimulation (CS-). The acquisition phase comprised three runs each including 6 CS+ paired with the US, 10 CS+ alone, and 10 CS-. The acquisition was immediately followed by two extinction runs with 13 CS+ (not paired with the US) and 13 CS-.

Results: During scanning, NC patients and controls did not differ in reaction times nor in accuracy on the triangle-orientation task. In both NC patients and controls, the painful stimulation activated the so-called "pain-matrix", known to be recruited during noxious stimuli perception. By directly comparing both groups for regions showing more activation during the CS+ alone (unpaired to the US) than during the CS-, the right amygdala was found to be more activated in controls. A connectivity analysis testing for changes in the functional coupling between the amygdala and any other brain region during the processing of CS+ trials revealed an increased negative coupling between the right amygdala and the medial prefrontal cortex in controls (but not in narcoleptics).

Conclusion: These findings document an impaired acquired fear response in the amygdala of narcoleptic patients.

0765

COGNITIVE FATIGUE MAY CONTRIBUTE TO THE BURDEN OF EXCESSIVE SLEEPINESS IN POOR DRIVING SIMULATOR PERFORMANCE

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Introduction: Not all patients with objective sleepiness measured by the multiple sleep latency test (MSLT) have poor driving simulator (DS) performance. We hypothesized that subjective sleepiness per the Epworth Sleepiness Scale (ESS), is necessary for poor performance.

Methods: 140 consecutive first-night patients complaining of daytime sleepiness completed nocturnal polysomnography, a next day 4-5 nap MSLT, and afternoon DS testing. We excluded patients completing split-night studies. Patients were in one of four groups per MSLT and ESS: 1) Pathological MSLT (MSLT ≤5 minutes) and Severe ESS (ESS>15). 2) Pathological MSLT and Non-severe ESS. 3) Non-pathological MSLT and Severe ESS. 4) Non-pathological MSLT and Non-severe ESS. We compared groups on DS lane position variability (LPV) using a 2 (MSLT) by 2 (ESS) ANOVA.

Results: The MSLT ($F(1,136)=6.85$, $p=0.010$), and ESS ($F(1,136)=5.73$, $p=0.018$ predicted LPV. Mean LPV (±SD ft) were: 1) Pathological MSLT sleepiness and Severe ESS sleepiness=1.6±0.27, n=23; 2) Pathological MSLT sleepiness and Non-severe ESS sleepiness=1.3±0.17, n=16; 3) Non-pathological MSLT sleepiness and Severe ESS sleepiness=1.3±0.35, n=33; 4) Non-pathological MSLT sleepiness and Non-severe ESS sleepiness=1.3±0.39, n=68. (Although we did not recruit a healthy control group, normal participants in our other studies typically have LPV of 0.8-1.1 feet.)

Conclusion: Together pathological sleepiness measured by MSLT and severe subjective sleepiness measured by ESS predicted the highest LPV. Although there is a correlation between the ESS and the Fatigue Severity Scale (Kirisoglu, 2004), others have reported that fatigue and subjective sleepiness are independent factors (Hossian, et al 2005). We hypothesize that in addition to sleepiness, the ESS measures a component of cognitive fatigue. During the DS task, those with cognitive fatigue and increased sleep pressure exert insufficient effort to stabilize vehicular position. Thus, fatigue may be the component of subjective sleepiness that contributes to poor performance in those with severe sleepiness.

0766

PRE-VERSUS POST-PUBERTAL NARCOLEPSY IN CHILDREN

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Introduction: Little is known regarding childhood narcolepsy, especially prior to puberty. In the last 8 years, 51 children (58% male, all <18 years old) were evaluated at the Stanford Narcolepsy Center, referred locally or from elsewhere in the US.

Methods: Evaluation included nocturnal polysomnography followed by MSLT, completing the Stanford Sleep Inventory, HLA-DQB1*0602 typing (all positive), CSF hypocretin-1 measurements (14 subjects, all hypocretin deficient) and clinical evaluation. Patients were separated into 4 groups: with prepubertal onset, studied prior to puberty (16), with onset and evaluation while undergoing puberty (6), with postpubertal onset, studied after puberty (12) and others (17). Clinical characteristics were compared.

Results: Delay between onset and evaluation was 2 years and did not differ with puberty. Onset of cataplexy and sleepiness were within the same year in 67%; others reported cataplexy as much as 3 years prior (1)

and up to 5 years later (1). Subjective sleepiness was present at similar severity levels. The frequency of napping, the severity of hypnagogic hallucinations, and the occurrence and severity of sleep paralysis increased at puberty. A similar percent of subjects from each group had cataplexy at evaluation (92-100%), with similar severity. Laughter was the most common trigger in all while anger was infrequent as a trigger in prepubertal children. A higher percentage of prepubertal children were African Americans (31% of 16) versus all other groups (6% of 35). Mean sleep latency on the MSLT was significantly higher in prepubertal (4.3±1.3) versus postpubertal onset subjects (1.3.±0.3) with a similar mean number of SOREMPs.

Conclusion: This study documents differences in symptomatology across subjects with childhood narcolepsy with onset prior to, during and after puberty. Most notably, prepubertal subjects were more frequently African Americans, were less sleepy objectively, reported less naps, and had less ancillary symptoms such as sleep paralysis and hypnagogic hallucinations.

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0767

EXCESSIVE DAYTIME SLEEPINESS IN THE AMERICAN GENERAL POPULATION

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Introduction: Generally speaking, surveys that investigate hypersomnia symptoms in the general population can be divided into two categories: those measuring excessive quantity of sleep and those assessing sleep propensity during wakefulness (excessive daytime sleepiness - EDS). Usually, studies that have assessed whether individuals were getting too much sleep only inquired about the subjective evaluation of sleep quantity. Studies that assessed EDS limited their assessment to a single question. Few studies have attempted to assess how these different measures are associated together.

Methods: The representative sample consisted of 8,937 non-institutionalized individuals aged 18 or over living in Texas, New York and California states. The telephone interviews included sleeping habits, health, sleep and mental disorders. Nocturnal awakenings were evaluated according to their frequency per week and per night, their duration and the motive(s) for the awakenings.

Results: Overall, 19.5% of the sample reported moderate EDS and 11.1% reported severe EDS. 3.5% of the sample estimated their sleep as being too long and 2.3% of the subjects were sleeping 9h30 or more per day. These three measures were more frequent among subjects younger than 35 years but only EDS was more frequent among women. Fewer than 20% of individuals claiming they were getting too much sleep slept nine hours or more per 24-hour period. Severe fatigue, as measure by the Fatigue Severity Scale, was associated with the three measures of sleepiness but more strongly with EDS.

Conclusion: Uniform operational definition of excessive sleepiness is needed. Our results show that severity of the consequences and associated factors greatly vary according to the definition used.

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0768

REDUCED BRAIN GABA IN PRIMARY INSOMNIA: PRELIMINARY DATA FROM 4T PROTON MAGNETIC RESONANCE SPECTROSCOPY (1H-MRS)

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Introduction: Both basic and clinical data suggest a potential significant role for GABA in the etiology and maintenance of primary insomnia (PI). Proton magnetic resonance spectroscopy (1H-MRS) can non-invasively determine GABA levels in human brain. Our objective was to assess GABA levels in unmedicated individuals with PI, using 1H-MRS.
Methods: This is a matched-groups, cross-sectional study conducted at two university-based hospitals. Participants were sixteen non-medicated individuals (8 women) with PI (mean age = 37.3 +/- 8.1) and 16 (7 women) well-screened normal sleepers (mean age = 37.6 +/- 4.5). PI was established with an unstructured clinical interview, a Structured Clinical Interview for DSM-IV (SCID), sleep diary, actigraphy and polysomnography (PSG). None of the subjects had a mood, substance abuse/dependence, or anxiety disorder, and none were taking hypnotic medication. 1H-MRS data were collected on a Varian 4 Tesla magnetic resonance imaging/spectroscopy scanner. Global brain GABA levels were averaged from samples in the basal ganglia, thalamus, and temporal, parietal, and occipital white-matter and cortex.
Results: Average GABA levels from sampled brain regions were reduced by nearly 30% in patients with primary insomnia compared to controls (PI = 0.18 +/- 0.06; controls = 0.25 +/- 0.11, t = 2.16, p = 0.039). No significant effects of age, gender, or BMI on GABA levels were observed. GABA levels were negatively correlated with wake after sleep onset (WASO) on two independent PSGs (r = -0.71, p = 0.0024 and -0.70, p = 0.0048). In the PI group assessed alone, neither the PSQI or ISI global scores or global sleep quality correlated with GABA levels, though self-reported sleep duration from the PSQI was correlated with GABA levels (r = -0.59, p = 0.0158).
Conclusion: Our preliminary finding of a global reduction in GABA in non-medicated individuals with PI is the first demonstration of a neurochemical difference in the brains of those with PI compared to normal sleeping controls. The high inverse correlations between GABA levels and PSG-derived WASO in PI provide further confidence in the value of our GABA measures. 1H-MRS is a valuable tool to assess GABA in vivo, and may provide a means to shed further light on the neurobiology of insomnia.
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0769

DOES CBT FOR INSOMNIA ALTER SLEEP MISPERCEPTIONS?

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Introduction: Individuals with insomnia tend to overestimate the severity of their sleep disturbances and to underestimate total sleep time (TST) relative to polysomnographic (PSG) recordings. Cognitive behavioral therapy (CBT) for insomnia, by addressing distorted beliefs and perceptions about sleep and insomnia symptoms, may indirectly reduce the discrepancy between subjective and PSG measures of total sleep time. This secondary analysis of data from an insomnia treatment trial aimed at investigating the impact of CBT for insomnia on sleep misperception.
Methods: A total of 160 individuals with chronic insomnia (mean age = 50.3 years, 60.6% women) were randomized to CBT alone or CBT combined with hypnotic medication. CBT consisted of six weekly group sessions including standard behavioral (stimulus control, sleep restriction) and cognitive procedures. Pre- and post-treatment assessments included sleep diaries, questionnaires, and PSG recordings (three baseline and two post-treatment nights). Participants completed morning questionnaires estimating several sleep-wake variables after each PSG recording. Percentage of accurate estimation of TST was computed from PSG data as : (estimated TST - objective TST)/objective TST X 100 (a negative score means an underestimation of TST). Values from the second and third baseline nights and the two post-treatment nights were averaged for each participant and analyzed using repeated-measures ANOVA.
Results: Overall, TST was underestimated by 17.5% (SD = 21.9, median = -13.7%) at baseline and underestimated by 7% (SD = 15.4, median = -6%) at post-treatment, which translates into an average underestimation of 67 and 23 minutes, respectively, compared to PSG recordings. There was a significant time effect suggesting an overall reduction of the magnitude of sleep underestimation. A significant group X time interaction effect indicated that the combined group had a larger reduction in sleep misperception than the CBT alone group. Exploratory analysis suggested that the improvement of sleep perception was positively associated with improvement reported on sleep diary measures, but not on the other questionnaires.
Conclusion: Results suggest that CBT for insomnia helps reduce sleep misperception in individuals with chronic insomnia, despite the fact that this issue was not directly addressed in the course of treatment. Larger reduction of sleep misperception in the combined group may reflect a drug-induced improvement of sleep perception.
Support (optional): National Institute of Mental Health (MH060413)

0770

A NON-PHARMACOLOGICAL ALTERNATIVE FOR THE TREATMENT OF INSOMNIA -INSTRUMENTAL CONDITIONING OF BRAIN OSCILLATIONS

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Introduction: Electroencephalographic recordings over the sensorimotor cortex show a very distinctive oscillatory pattern in a frequency range between 12-15Hz termed sensorimotor rhythm (SMR). SMR appears to be dominant during quiet but alert wakefulness, and synchronizes by the inhibition of motor behavior. This frequency range is also known to be abundant during light non-rapid eye movement sleep, and is overlapping with the sleep spindle band. Given our recent findings (Hoedlmoser et al., SLEEP, 2008) indicating that an increased SMR activity by instrumental conditioning (IC) was also expressed during subsequent sleep by eliciting positive changes in various sleep parameters like sleep spindle number or sleep onset latency, we aimed at changing sleep quality in humans suffering from primary insomnia by using SMR-IC.
Methods: 12 subjects suffering from primary insomnia (11 women; M=29.33; SD=10.56) attended the sleep laboratory 19 times (4 nights, 10 x SMR-IC, 5 x placebo-IC). A counterbalanced within subjects design was used. During SMR-IC subjects trained to enhance the amplitude of their SMR-frequency range whereas during placebo-IC a randomized-frequency-conditioning program (i.e., every session a different 3Hz frequency bin between 7 and 20Hz) was used. Before and after these IC blocks subjects had to spend one night in the sleep laboratory and additionally performed several questionnaires as well as a declarative memory task.
Results: Results confirmed the increase of 12-15Hz activity over the course of the ten SMR-IC training sessions (p=0.027) but not over the course of the placebo-IC training sessions. Interestingly, the increased SMR activity was associated with the enhancement of subjective sleep quality measured by the Pittsburgh Sleep Quality Index (p=0.001). Fur-

thermore sleep onset latency was tendentially reduced after SMR-IC (p=0.056) but not after placebo-IC.
Conclusion: Therefore we could show that people suffering from primary insomnia benefit from SMR-IC as indicated by improved measures of subjective and objective sleep quality. Relative SMR amplitude increased over 10 SMR-IC sessions and this 'shaping of one's own brain activity' improved subsequent quality of sleep.

0771

PD 0200390, A NOVEL ALPHA-2-DELTA LIGAND, FOR THE TREATMENT OF NON-RESTORATIVE SLEEP: A PILOT STUDY

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Withdrawn

0772

IMPACT OF CBT FOR INSOMNIA AND CBT COMBINED WITH MEDICATIONS ON DAYTIME FUNCTIONING

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Introduction: This study examined the effects of CBT for insomnia delivered alone to CBT combined with hypnotic medications (CBT+Med) on daytime functioning variables. A second objective was to compare the effects of different extended treatment strategies on daytime functioning.
Methods: One hundred and sixty individuals (61% women; mean age: 50.3 years) with persistent insomnia were randomized either to a CBT alone or CBT+Med condition. After initial treatment, patients treated with CBT alone were then randomized either to extended CBT (6 months) or to "no additional treatment". Those treated with CBT+Med were randomized to CBT combined with intermittent medication use or CBT with medication taper. Daytime functioning variables included fatigue (Multidimensional Fatigue Inventory; MFI), anxiety (Beck Anxiety Inventory; BAI), depression (Beck Depression Inventory; BDI), health perception (SF-36) and beliefs about sleep (Dysfunctional Beliefs about Sleep, DBAS-16).
Results: In the CBT alone group, significant pre-post improvements were observed on all measures but two SF-36 subscales, while in the CBT+Med group, significant changes were observed only on the DBAS-16 scores. After the extended phase, further improvements on the DBAS-16, MFI and SF-36's Vitality subscale scores were observed in the CBT alone group while in the "no additional treatment" group, SF-36's Mental Health and Physical Functioning subscale scores showed significant worsening. In the CBT+Med group who continued receiving medication, significant positive changes were observed on most measures, while in the medication tapering group, significant positive changes were observed only on the MFI and SF-36's Social Functioning and Vitality subscales.
Conclusion: Results suggest that CBT for insomnia has some positive effects on daytime functioning. However, adding medication to this therapy may hinder its positive effects in the initial treatment phase. Nevertheless, benefits associated with intermittent medication use seemed to appear in the extended treatment phase. Further research is needed to examine ideal combinations of CBT and medication, especially in those who benefit less from either approach alone.
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0773

ARE THE EFFECTS OF INSOMNIA TREATMENT ON DAYTIME MEASURES CLINICALLY IMPORTANT?

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Introduction: Clinical significance of treatment outcomes is seldom reported in insomnia studies. This study assessed if change experienced by individuals on daytime variables after CBT for insomnia was clinically meaningful. An additional goal was to evaluate if adding medication to CBT may enhance the proportion of participants experiencing a meaningful impairment reduction.
Methods: One hundred and sixty individuals (61% women; mean age: 50.3 years) with persistent insomnia were randomized to one of two 6-week insomnia treatment conditions, CBT alone or CBT plus medication (CBT+Med; zolpidem). Daytime variables assessed included fatigue (Multidimensional Fatigue Inventory; MFI), anxiety (Beck Anxiety Inventory; BAI), depression (Beck Depression Inventory; BDI), health perception (SF-36) and beliefs about sleep (Dysfunctional Beliefs about Sleep, DBAS-16). Participants were classified as "dysfunctional" or not on each measure at baseline based on descriptive data from normative or insomnia-free samples. At post treatment, participants were reclassified as recovered, improved, unimproved or deteriorated on each of the measures. Proportions of participants experiencing meaningful impairment reduction, i.e. recovered or improved, in each treatment condition were then compared.
Results: Depending on the daytime measure considered, the proportion of recovered participants ranged from 31.2% to 83.3% in the CBT alone condition and from 9.4% to 71.0% in the CBT+ Med condition. CBT alone yielded significantly higher proportions of improved and recovered subjects on the following variables: Depression ($\chi 21=3.62$, $p=.05$), SF-36 Vitality scale ($\chi 21=6$, $p<.05$), SF-36 Social functioning scale ($\chi 21=4.7$, $p<.05$) and SF-36 Role-Emotional scale ($\chi 21=4.5$, $p<.05$).
Conclusion: Unlike statistical significance testing, clinical significance analyses provide information regarding the standing of treated and untreated individuals relative to healthy controls. These findings suggest that some daytime deficits associated with insomnia may remit and return to normative levels with treatment. The results provide further evidence that CBT alone may be more effective than CBT+Med at ameliorating some of these daytime deficits.
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0774

THE OREXIN ANTAGONIST SB-649868 PROMOTES AND MAINTAINS SLEEP IN HEALTHY VOLUNTEERS AND IN PATIENTS WITH PRIMARY INSOMNIA

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Introduction: The orexin system appears to play an important role in the control of the sleep/wake cycle. Compounds which antagonize orexin receptors provide a novel therapeutic mechanism for the treatment of insomnia. SB-649868 is a potent orexin antagonist which has shown to have hypnotic properties in multiple preclinical models.
Methods: The hypnotic effects of SB-649868 were assessed in two randomized, double-blind, placebo-control cross-over studies. Study

1 assessed the polysomnographic (PSG) effects of SB-649868 in 20 healthy male volunteers. Study 2 assessed PSG effects of SB-649868 in 52 male subjects with a diagnosis of primary insomnia. In both studies, SB-649868 was administered after dinner 90 minutes before bed time, for a single night in study 1 and for two consecutive nights in study 2. Doses of 30 and 60 mg were administered in both studies while the 10 mg dose was tested only in Study 2. Next day residual effects were assessed in both studies.

Results: SB-649868 significantly reduced Latency to Persistent Sleep (LPS) and Wake After Sleep Onset (WASO) and increased Total Sleep Time (TST) compared to placebo in both studies. The PSG effects of 30 and 60 mg were similar in the healthy volunteers, while a dose-dependent effect was observed in males with primary insomnia. A dose-dependent increase in REM sleep was observed mainly at the 60 mg dose. SB-649868 was well tolerated with no evidence of next day residual effects.

Conclusion: These data demonstrate the sleep-promoting properties of the orexin antagonist SB-649868 in both healthy volunteers and male patients with insomnia.

Support (optional): The studies were sponsored by GlaxoSmithKline.

0775

CRH TYPE I RECEPTOR (CRHR1) POLYMORPHISMS AND RISK FOR PRIMARY INSOMNIA

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Introduction: We have hypothesized that abnormally increased activity of central corticotropin releasing hormone (CRH) is involved in the pathogenesis of primary insomnia (PI). Evidence that PI is familial implies that genetic factors may predispose to CRH hyperactivity. Recently, polymorphisms of the CRH Type I receptor (CRHR1) were shown to modulate depression risk in individuals with a history of childhood abuse. We examined whether this same polymorphism also alters the risk of PI.

Methods: 76 subjects with well-characterized PI (40f; avg. age 30.8y) and 80 normal sleepers (33f; avg. age 31.9y) were genotyped for polymorphisms at 3 SNP loci (rs7209436 C/T, rs110402 G/A and rs242924 G/T) within the CRHR1 gene using two-stage PCR and commercial (SNaPshot) sequence detection. The 3 SNPs were selected from among 10 with significant minor allele frequencies spanning the CRHR1 gene as having previously demonstrated the greatest gene x environment association with depression. Posterior haplotype-pair probabilities were estimated from genotypes using SNPHAP software. Age- and sex-adjusted nominal logistic regression models were used to examine the association of CRHR1 haplotype and PI diagnosis.

Results: Genotype and haplotype frequencies were comparable to previous reports; CGG 64%; TAT 34%. The absence of the TAT haplotype increased the risk of patient-reported PI (AOR: 1.45; 95% CI 1.05-2.09; $p < .02$). Unlike previous work with depression, the protective effect of the TAT haplotype was not greater in homozygotes. The effect was also present when the definition of PI included objective sleep disturbance (2nd night sleep lat >30 min. and/or SE < 85%). The absence of the protective TAT haplotype significantly increased the risk of objective PI (AOR 3.33; 1.16-9.5; $p<.02$).

Conclusion: Polymorphisms of the CRH Type I receptor are associated with significant variation in the probability of primary insomnia. This is consistent with our previous work suggesting abnormal HPA activity in PI, and supports the hypothesis that central HPA deregulation is involved in the pathogenesis of PI.

0776

IDENTIFYING PREDICTORS OF COMPLIANCE TO BEHAVIORAL RECOMMENDATIONS IN CBT FOR INSOMNIA

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Introduction: Previous studies have demonstrated that treatment compliance is associated with the positive outcomes of CBT-I, but few studies have identified predictors of compliance. The aim of the present study was to examine the role of insomnia severity and dysfunctional beliefs about sleep in predicting compliance with behavioral recommendations as part of a multi-component CBT-I intervention.

Methods: 30 participants (60% female, average age = 36.4 years) participated in a six-week treatment program of stimulus control, sleep restriction, sleep hygiene, and mindfulness meditation conducted in groups of 7-8 participants. Participants completed the Insomnia Severity Index (ISI) and the Dysfunctional Beliefs about Sleep (DBAS) scale at baseline, and daily sleep diaries throughout treatment. Compliance measures were derived from these diaries, including the total number of days in compliance with time in bed (TIB) recommendations, days in compliance with time out of bed (TOB) recommendations, and measures of deviation in TIB and TOB.

Results: Overall, compliance with TIB and TOB recommendations was 66% and 81% of nights, respectively. Results from stepwise linear regression analyses indicated that higher DBAS scores were independently associated with fewer days in compliance with TIB ($p < .03$) and TOB ($p < .01$) recommendations. Furthermore, there was a significant interaction between ISI and DBAS scores associated with both days in compliance with TIB ($p < .02$) and TOB ($p < .04$). For those with high insomnia severity, high DBAS scores were associated with poorer compliance; however, for those with low insomnia severity, high DBAS scores were associated with greater compliance. There were similar, but non-significant findings for deviation in TIB and TOB measures of compliance.

Conclusion: These preliminary results suggest that greater baseline maladaptive beliefs about sleep may predict poorer compliance with behavioral recommendations in CBT-I. Furthermore, this relationship may be moderated by ratings of insomnia severity at baseline.

0777

THE RELATION BETWEEN QUANTITATIVE MEASURES OF NIGHTTIME INSOMNIA SYMPTOMS AND DAYTIME IMPAIRMENT

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Introduction: The diagnosis of insomnia requires one or more symptoms of difficulty falling asleep, staying asleep, or non-restorative sleep. Cutpoints for these symptoms have been suggested, but the clinical significance of these cutpoints remains unknown. The present study used symptoms of daytime impairment to determine the clinical significance of levels of sleep disturbance.

Methods: 330 subjects were surveyed (mean age=44.4; 63% female). Qualitative (i.e., difficulty falling asleep, staying asleep, and non-restorative sleep) and quantitative (i.e., total sleep time [TST], minutes to fall asleep, number of awakenings, duration of awakening, and weekly frequency) insomnia symptoms were assessed. Symptoms of daytime impairment were based on Research Diagnostic Criteria (# of impairments). Bivariate correlations and multiple regression were used to determine significant and independent predictors of impairment. Finally, quantitative sleep measures were used to estimate at what levels of sleep

disturbance daytime impairment reached 1) significant levels and 2) asymptotic levels.

Results: Insomnia symptoms were significantly associated with number of impairments with correlations ranging between r=.27 to r=.54, p < .05. Multiple regression indicated that the strongest independent predictor of daytime impairment was the frequency of symptoms per week (b = .44, p<.001). Among the nocturnal symptoms, TST was the only independent predictor (b = -.13, p<.05). Analyses of quartiles indicated that with a symptom frequency of ≥3 times per week and TST of ≤6 hours there was an asymptote in impairment, while the largest increments occurred at a symptom frequency of ≥ 2 times per week and TST of ≤ 6 hours.

Conclusion: These findings demonstrate the relation between quantitative measures of sleep disturbance and daytime impairment. Reported TST and frequency of sleep symptoms are strong and independent predictors of daytime impairment with TST ≤ 6 hours per night and ≥ 3 awakenings per night having clinical significance.

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0778

CLINICAL OUTCOMES OF GROUP COGNITIVE-BEHAVIORAL THERAPY FOR INSOMNIA (CBT-I)

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Introduction: Chronic insomnia is common in sleep clinic patients and it is associated with high degree of psychiatric and/or medical comorbidities. CBT-I, a multi-component treatment that include cognitive restructuring, stimulus control, sleep restriction and education, is now recognized as a first line treatment for chronic insomnia. As clinicians who are trained to deliver CBT-I are still limited, group format is a cost-effective approach. We report changes of sleep and daytime symptoms following CBT-I in sleep clinic patients.

Methods: 175 consecutive patients (98 female, 77 male; mean age 41.8±12.3 years) received 8-week, 7-session group CBT-I delivered by a behavioral sleep medicine psychologist. Patients completed sleep log daily from baseline (BL; 1 week before Session 1) through the end of treatment (ET). Questionnaires included ISI, POMS-37, BDI, Beliefs and Attitudes about Sleep (BAS), Glasgow Sleep Effort Scale, ESS, and treatment satisfactions that were completed at BL and ET.

Results: Significant (p<0.05) improvement were observed for all measures on the sleep logs and all questionnaires from BL to ET. Effect sizes (ES) were 0.47 (16min) for SOL, 0.55 (36min) for WASO, 0.65 (10%) for SE, 0.15 (13min) for TST, and 0.73 for Sleep Quality. ES for measures of mood ranged from 0.54 on POMS to 0.74 on BDI. All components of BAS significantly improved with ES ranging from 0.22 to 1.4. 79.4% of patients were taking sleep medications at BL and 22.3% of them completely discontinued medication at ET.

Conclusion: In a sample of sleep clinic patients with heterogeneous sleep medication use and co-existing psychiatric and medical conditions, CBT-I is associated with significant improvement of sleep as well as mood and daytime symptoms. Emotional distress reduction and perception of sleep become more predicable were the most improved outcomes. Group CBT-I is an effective mechanism of treatment delivery, and produces clinically meaningful improvement with high patient satisfaction.

0779

INSOMNIA PATIENTS SHOW INCREASED CEREBRAL ACTIVATION WHEN COMPARED TO GOOD SLEEPERS DURING AN NBACK WORKING MEMORY TASK

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Introduction: Recent studies report that individuals undergoing total sleep deprivation show increased brain activation on working memory tasks. This increased activation has been interpreted as compensatory neurophysiologic change which helps the individual maintain performance when sleep deprived. Here, we hypothesized patients with Primary Insomnia (PI), relative to good sleepers (GS), would show similar increased activation on an NBack working memory task and that this "compensatory" activation would result in equivalent behavioral performance between groups.

Methods: 12 PIs (6F, age=39.4±9.6 yrs) were compared to 9 matched GS (4F, age=35.7±7.4 yrs) on an NBack working memory task. Functional MRI (fMRI) BOLD activation during the 3-back condition was compared between groups with a t-test. Regions of significant differences in cerebral activation were selected based on whole-brain alpha <.01. Behavioral performance was measured by reaction time for correct responses, number of correct responses, and number of errors committed.

Results: PIs showed increased BOLD activation, relative to GSs, in right middle frontal gyrus (BA 8/9) and anterior right middle frontal gyrus (BA10). PIs also showed decreased activation, relative to GSs, in right middle occipital gyrus (BA18) and fusiform gyrus (BA19) as well as left motor cingulate (BA24) and postcentral gyrus. Behaviorally, PIs showed significantly faster reaction times for correct responses (p=.001), but no differences were found for hits (p=.129) or errors (p=.670).

Conclusion: As expected, PIs showed increased activation relative to GS during this working memory task, particularly in areas responsible for visual-spatial attention and coordination of cognitive processes. This activation is consistent with the compensatory model and may explain PIs ability to maintain performance on this task. Unexpectedly, however PIs were observed to show decreased activation in visual and motor areas. These findings may suggest PIs have higher brain activation in these regions at baseline relative to GSs and/or GSs subjects required greater sensory input on this task.

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0780

SLEEP HOMEOSTASIS AND HYPERAROUSAL IN PRIMARY INSOMNIA: A PILOT STUDY WITH A SLEEP DEPRIVATION CHALLENGE BEFORE AND AFTER CBT-I

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Introduction: Both sleep homeostasis dysregulation and hyperarousal are putative causes of insomnia, which CBT-I purports to address via sleep restriction for sleep homeostasis and cognitive and/or relaxation therapies for hyperarousal. This pilot study assessed whether either mechanism is dysregulate in subjects with primary insomnia (PIs) compared to good sleepers (GSs) and if they respond to CBT-I.

Methods: 6 PIs and 5 GSs matched on age, gender and BMI completed Phase I, which included an adaptation PSG followed by 72 hrs of continuous monitoring: 8 hr nocturnal PSG(N2)-MSLT-full sleep deprivation(N3)-MSLT-10hr recovery PSG(N4)-MSLT. Sleep homeostasis was assessed via N2 SWS minutes; N2-N4 SWS increase; and mean MSLT following N2. Hyperarousal was assessed via assay of salivary cortisol samples taken 15 times per 24 hrs with samples every 30 minutes from 7-11pm; and Beta EEG activity. After 8 wk CBT-I (PIs only), all subjects repeated the above protocol (2 PIs withdrew prior to this phase - final groups remained matched on age and BMI; there were 2 men in the GS group). A priori analytic strategy was to compute effects sizes (Cohen's d).
Results: Small/no differences were observed in N2 SWS [PI: 37.6(31.2) vs. GS: 33.4(44.7); d=.12]; N2-N4 SWS increase [PI: 32.6(48.7) vs. GS: 37.5(29.8); d=.13]; Mean MSLT [12.3(3.6) vs. 14.6(2.2); d = .13]; and differences in delta activity were similarly small. The PI group had higher N2 cortisol concentrations levels 7-11 pm (d = 1.13); and modest elevations in Beta activity (d=.41). After CBT-I, PIs had subjective improvements in sleep exceeding published norms [e.g. mean Insomnia Severity Index 15.5(4.6) at baseline vs. 5.0(4.6) after TX]. After TX and compared to GSs, PIs had more N2 SWS, N2-N4 SWS increase, and pre-post N2-N4 SWS increases (d = .80, .47 and .78 respectively) with smaller differences in delta activity (d = .12 to .22), but N2 cortisol and Beta activity remained largely unchanged in each group. Subjective measures (not reported due to space) mirrored the above findings.
Conclusion: While limited by sample size, the findings suggest that PIs were hyperaroused, but did not appear to have objective sleep homeostasis differences at baseline. Given the improvements on sleep homeostasis measures following CBT-I, it remains possible that these PIs were not optimally homeostatically regulated. The lack of improvement in hyperarousal measures may be due to the form of CBT-I delivered, which was more focused on sleep restriction than other TX components.
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0781

GENETIC AND ENVIRONMENTAL RELATIONS BETWEEN INSOMNIA AND INTRUSIVE THINKING: THE CONTRIBUTION OF SLEEP REACTIVITY TO STRESS

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Introduction: Sleep reactivity to stress may explain some of the relationship between the experience of intrusive thoughts/ rumination and insomnia. The aim of this study was to specify the genetic and environmental structure of the relations among insomnia, sleep reactivity to stress, and intrusive thinking.
Methods: Participants were 1399 individual twins (854 female, 545 male), aged 18-30 (M=22.5, SD=2.7) from the Colorado Longitudinal Twin and Community Twin Studies who completed an online sleep survey. Genetic analyses included 536 complete twin pairs (281 MZ, 255 DZ). The survey included the 9-item Ford Insomnia Response to Stress Test (FIRST), 14 items from the White Bear Suppression Inventory and the Thought Control Ability Questionnaire, and questions about the frequency of three insomnia symptoms (difficulty falling asleep, staying asleep, and non-refreshing sleep), their duration, and impairment.
Results: The FIRST, intrusive thinking, and insomnia each had significant (p<.05) genetic (~35-45%), no shared environmental, and significant non-shared environmental (~55-65%) influences. Multivariate genetic models indicated that their phenotypic correlations (rs=~.40-.50) reflected shared genetic and environmental influences. The FIRST's genetic and environmental variances predicted both intrusive thoughts and insomnia; once these relations were partialled out, the remaining environmental variance in intrusive thinking still predicted insomnia, but the remaining genetic variance did not. Insomnia also had genetic and environmental influences independent of the FIRST and intrusive thoughts.
Conclusion: Genetic variance in intrusive thoughts no longer significantly predicts insomnia once genetic influences of sleep reactivity are partialled out, consistent with the hypothesis that sleep reactivity may mediate the genetic relation between intrusive thinking and insomnia. Environmental relationships between intrusive thoughts and insomnia are partially independent of sleep reactivity. These findings emphasize the importance of elucidating the influences of sleep reactivity in future studies of how intrusive thinking and ruminative tendencies can lead to insomnia.
Support (optional): Henry Ford Hospital Sleep Center.

0782

CAN AN INSOMNIA THERAPY TREAT SLEEP MAINTENANCE WITHOUT SUPPRESSING AROUSABILITY: EFFECTS OF DOXEPIN 1, 3, AND 6 MG ACROSS PHASE 3 TRIALS

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Introduction: This report reviews the sleep maintenance (SM) efficacy from three Phase 3 trials evaluating doxepin (DXP 1, 3, 6 mg), a selective H1 antagonist at the doses studied, in adult and elderly populations with either primary or transient insomnia.
Methods: SM endpoints from three double-blind placebo-controlled trials are reported. In two trials, patients meeting DSM-IV-TR criteria for primary insomnia were randomized for up to 12 wks of treatment. Study A was a 12-wk trial of elderly patients (N=240; DXP 1 and 3 mg vs. placebo (PBO)); Study B was a 5-wk trial of adults patients (N=221; DXP 3 and 6 mg vs. PBO). Study C was a single-night trial that used a model of transient insomnia to simulate sleep disturbance in healthy adults (N=565; DXP 6 mg vs. PBO). Efficacy was evaluated with polysomnography. SM endpoints included wake after sleep onset (WASO) and number of awakenings (NAW). Data from the first and final night (N; Study A=N85; Study B=N29) of the study are reported.
Results: DXP 1 mg (Study A; p<0.01), 3 mg (Study A and B; p<0.0001) and 6 mg (Study B and C; p<0.0001) significantly improved WASO on N1 of all three trials, with improvements vs. PBO ranging from 17 (Study A, 1 mg) to 40 minutes (Study C, 6 mg). These significant improvements were maintained at the final timepoint. NAW were not improved vs. PBO at any dose or timepoint in any trial.
Conclusion: DXP 1, 3 and 6 mg demonstrated significant improvement in WASO across three Phase 3 trials that was maintained at the final timepoint. Interestingly, SM efficacy was not accompanied by reductions in NAW, a finding inconsistent with the existing literature involving GABA-mediated hypnotic medication. These data suggest DXP is effective at treating SM insomnia in both transient and chronic insomnia populations, and in adult and elderly populations. Additionally, these data suggest that DXP 1, 3 and 6 mg may reduce time spent awake after nighttime arousals without suppressing arousability, though further evaluation is necessary.
Support (optional): This study was funded by Somaxon Pharmaceuticals.

0783

FREQUENCY OF NOCTURNAL AWAKENINGS AND ITS CONSEQUENCES

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Introduction: Sometimes encompassed under the general label of difficulty maintaining sleep, other times coined as disrupted sleep or middle of the night insomnia, nocturnal awakenings are the most frequent insomnia complaint in the general population reaching up to 65% among older individuals. However, it is unlikely that all these individuals experience daytime impairment or suffer from diagnosable sleep or mental disorder. This issue is particularly important when it comes to the experience of nocturnal awakenings since it affects a large segment of the general population especially elderly people.
Methods: The representative sample consisted of 8,937 non-institutionalized individuals aged 18 or over living in Texas, New York and California states. The telephone interviews included sleeping habits, health, sleep and mental disorders. Nocturnal awakenings were evaluated according to their frequency per week and per night, their duration and the motive(s) for the awakenings.
Results: Nocturnal awakenings occurring at least 3 nights per week were reported by 35.5% of the sample. More specifically, 23% woke up every night; 5% 5 or 6 nights/week and 8% 3 or 4 nights/week. When examining the number of awakenings within the same night, it was found that 49% woke up 1 or 2 times; 8% woke up at least 3 times and another 43% reported difficulty resuming sleep (DRS) once awaken. Daytime consequences were reported by 77.5% of subjects having DRS; 65,1% of those who woke up at least 3 times within the same night and 48.1% of those waking up 1 or 2 times in the same night ($p<.0001$). Severe daytime sleepiness was more frequently reported by individuals with DRS (22.1%) followed by those who woke up at 3 times/night (19.8%) compared to 11.4% for subjects waking up 1 or 2 times/night ($p<.0001$). Poor health quality was reported more frequently by DRS subjects (21.2%) and individuals with at least 3 times in the same night (21.6%) than by those who woke up 1 or 2 times in the same night (13.9%; $p<.0001$).
Conclusion: Our results show that the mere presence of nocturnal awakenings 3 nights per week is insufficient to define the symptom. Numbers of awakenings within the same night or difficulty resuming sleep are associated with greater daytime impairment and more frequently with health problems.
Support (optional): NIH grant # NS44199

0784

MEAN SEGMENT DURATION OF SLEEP EEG SPECTRAL DOMAINS: EXAMINING THE PHARMACODYNAMIC RESPONSE TO THERAPY IN PRIMARY INSOMNIA

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Introduction: Spectral analysis of PSG recordings in sleep provides insights into insomnia disease states. The current study compares signal processing outcomes using adaptive segmentation with traditional sleep parameters in adults identified with primary insomnia. Morpheus® is a system that performs automated analysis of sleep staging using a multidimensional mathematical analysis of EEG applying adaptive segmentation and fuzzy logic with Markov models enabling multiple spectral power EEG measurements.
Methods: 40 adults were selected with a diagnosis of primary insomnia. A post-hoc analysis compared R&K analysis to adaptive segmentation studying the first night in the sleep lab using a cross-over design with 4 compounds. Each patient received 3 different medications or placebo denoted by A, B, C and P (placebo). This represents first night analysis. Sleep efficiency (SE), latency to persistent sleep (LPS), slow wave sleep% (SWS), and REM sleep%. Analysis of mean segment duration was analyzed for each group and compared with the placebo group including % of high frequency activity(HF), % low-voltage mixed frequency activity(MFLE), % of high-voltage mixed frequency activity(MFHE), and % of low frequency activity(LF).
Results: Means and standard deviations are: SE%: P=75(16); A=86(9); B=86(7); C=83(11); LPS min.: P=49(52); A=43(25); B=18(14); and C=42(35); SWS%: P=14(7); A=21(7); B=18(7); and C=16(8). REM% was not different in all groups. T-tests of SE, LPS, SWS comparing placebo with groups A, B, C were significant at $p<0.05$ level except LPS comparing placebo to group A,C. Mean segment duration is: d(HF): P=1.07(0.2); A=0.93(0.14); B=1.04(0.16); C=1(0.16); d(MFHE): P=2.91(0.37); A=3.47(0.36); B=3(0.27); and C=3.19(0.38); d(LF): P=3.99(0.74); A=4.81(0.62); B=4.35(0.54); and C=4.46(0.55); d(MFLE): P=3.04(0.63); A= 3.83(0.74); B=3.21(0.58); and C=3.31(0.58). Results of t-tests of mean segment duration: d(HF): A/P=0.004; B/P=0.45; C/P=0.08. For d(MFHE): A/P=0.00001; B/P=0.003; and C/P=0.00001. For d(LF): A/P=0.00001; B=0.07; and C/P=0.01. For d(MFLE):A/P= 0.00001; B/P=0.09; and C/P=0.02.
Conclusion: There is a pharmacodynamic response seen in frequency domains using spectral analysis quantitatively different from R&K. Sleep state assessment in insomnia patients may be enhanced by spectral analysis.

0785

WHERE DOES THE SLEEP DISRUPTION OF SPOUSALLY BEREAVED SENIORS PLACE ON THE CONTINUUM BETWEEN GOOD SLEEPER CONTROLS AND OLDER ADULTS WITH INSOMNIA?

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Introduction: There are approximately 800,000 new widow(er)s every year in America, and many of them complain of sleep disruption. The objective of this study was to characterize the sleep of Spousally Bereaved (SB) seniors (60y+), comparing them to non-widowed Good Sleeper Controls (GSC) and non-widowed Older Adults with Insomnia (OAI).
Methods: Subjective and objective sleep measures were obtained in 47 SB (38f, 9m), 33 GSC (25f, 8m), and 47 OAI (38f, 9m), all with the same mean age (72y). SB subjects had lost a spouse/partner within 4-19mos. prior to evaluation; OAI subjects passed formal diagnostic criteria for primary or co-morbid insomnia; GSC subjects had no diagnosis of insomnia. At baseline (pre-treatment), all subjects were given the Pittsburgh Sleep Quality Index (PSQI), and completed a detailed sleep diary and wore a wrist actigraph for 2 consecutive weeks.
Results: Significant (p<0.001) group effects appeared in both PSQI (GSC: 2.4, SB: 6.7, OAI: 10.5; pair-wise Effect Sizes [ES] = 1.41, 1.12) and diary measures. In diary measures, for Total Sleep Time, Sleep Efficiency and Wake After Sleep Onset, SB were better than OAI and worse than GSC (0.47<ES<1.19). For Sleep Latency, SB was worse than GSC (ES=0.57), but similar to OAI. However, actigraphy results indicated no significant differences in any of the sleep measures considered for SB vs. GSC, or SB vs. OAI comparisons.
Conclusion: The sleep disruption of bereaved seniors appears to be intermediate between GSC and OAI, as reported either retrospectively using the PSQI, or prospectively using a sleep diary. Only in diary sleep latency, were SB and OAI values similar. This pattern was not, however, observed when parallel actigraphic measures were considered. Subjective poor sleep quality leads to distress and may increase the risk of adverse health outcomes. SB seniors may benefit from behavioral interventions to improve their sleep.
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0786

IMPACT OF NIGHTTIME AWAKENINGS ON WORKER PRODUCTIVITY AND PERFORMANCE

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Introduction: Waking up during the night is the most common complaint of people with insomnia. Previous studies have reported prevalence between 25-35% of people waking up at least three nights per week. The purpose of this study was to determine the impact of nighttime awakenings on daytime functioning in a sample of employed individuals.
Methods: Individuals in four US-based companies completed an anonymous, 55 - item, online survey. The survey questions related to health status, sleep, performance, and safety at work. Worker productivity was assessed using the Work Limitations Questionnaire (WLQ). Nighttime awakenings were reported for an average sleep period. Differences in productivity measures were examined with analyses of variance tests.
Results: A total of 4,188 respondents completed the survey (40+/-11.21 years, 53% male), with 11% (n=464) having 0, 57% (n=2,373) having 1-2, 24% (n=984) with 3-4, and 7% (n=289) with 5 or greater nighttime awakenings during an average sleep period. Women more frequently than men reported waking up 3-4 times (27% vs. 21%, p<.001) and >5 times (8% vs. 6%, p<.001) in the night compared to men. Medical or psychological comorbid condition was statistically (p<.001) greater in respondents that had 3-4 (22% and 10%) or >5 times (23% and 14%) nighttime awakenings. Compared to respondents with zero or 1-2 nighttime awakenings, respondents with 3-4 and 5 or greater nighttime awakenings had the greatest impairment (p<.001) in time-management, physical demands, mental demands, and output, as measured by WLQ. Similar results were observed in work performance across dimensions related to communication, coordination, decision making, energy, judgment, learning, memory, and motivation, with the greatest (p<.05) impairments in the groups reporting 3-4 and 5 nighttime awakenings compared to those reporting zero or 1-2.
Conclusion: Overall across all dimensions, respondents that had greater number of nighttime awakenings had poorer productivity and performance at work.
Support (optional): sanofi-aventis, U.S.

0787

RISK OF FRACTURES IN ADULT AND ELDERLY HYPNOTIC USERS VS. CONTROLS

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Introduction: In the United States, 10% of adult population receives prescriptions for sedative hypnotics, the primary agents used in the short-term management of insomnia. The objective of this study was to determine the risk of fractures among adult hypnotic users vs. controls.
Methods: A retrospective cohort study was designed using data from a large national managed care commercial claims database. Naïve hypnotic-users were identified using pharmacy claims during the index period (01/01/06-12/31/06). Two controls (non-hypnotic-user/diagnoses of insomnia) to each hypnotic-user were identified and matched on gender, region, payer, and age. An index-date for a control was randomly assigned and matched to the month of the hypnotic-users' index date. Fractures were captured using ICD-9-CM codes from medical claims and included: fracture of hip, upper/lower limbs, pelvis, vertebral column, face, or skull. Descriptive and multivariate analyses were conducted to estimate risk and economic burden of falls.
Results: A total of 42,040 hypnotic-users and 84,080 controls met the inclusion criteria. At baseline, hypnotic-users and controls were similar in age and proportion of females (p>.05). Overall hypnotic-users at baseline had a higher comorbidity as measured by the Charlson comorbidity index compared to controls (1.06 vs. 0.60, p<.001). Hypnotic-users had significantly (p<.001) greater proportion of fractures (4.44%) compared to controls (2.57%), and were 10.31% and 4.30% among elderly, and non-elderly hypnotic-users, respectively. AR% of fractures due to hypnotic-use was 42.0% in the entire study sample, and 45.4% and 41.8% in elderly and non-elderly sub-samples, respectively. After adjusting for all baseline differences including conditions that may place an individual at a higher risk for falls like balance disorders such as Parkinson's, relative-risk of fractures for hypnotic-users was 1.58 (95%CI:1.48-1.69) in the entire sample; 1.63 (95%CI:1.25-2.12) in elderly; and 1.58 (95%CI:1.48-1.69) in non-elderly.
Conclusion: Elderly and adult hypnotic users have a higher proportion and risk of fractures compared to non-users.
Support (optional): sanofi-aventis, U.S.

0788

RISK OF FALLS IN ADULT AND ELDERLY HYPNOTIC USERS VS. CONTROLS

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Introduction: A well-known adverse effect of many currently available hypnotics is psychomotor impairment. The objective of this study was to determine the risk of falls among adult hypnotic users vs. controls.
Methods: A retrospective cohort study was designed using data from a large national managed care commercial claims database. Naïve hypnotic-users were identified using pharmacy claims during the index period (01/01/06-12/31/06). Two controls (non-hypnotic-user/diagnoses of insomnia) to each hypnotic-user were identified and matched on gender, region, payer, and age. An index-date for a control was randomly assigned and matched to the month of the hypnotic-users' index date. Falls were captured using E-codes and included: falls on/from stairs or steps, ladders, from slipping, tripping, or stumbling. Descriptive and multivariate analyses were conducted to estimate risk and economic burden of falls.
Results: A total of 42,040 hypnotic-users and 84,080 controls met the inclusion criteria. At baseline, hypnotic-users and controls were similar in age and proportion of females (p>.05). Overall hypnotic-users at baseline had a higher comorbidity as measured by the Charlson comorbidity index compared to controls (1.06 vs. 0.60, p<.001). Hypnotic-users had a significantly (p<.001) greater proportion of falls (1.40%) compared to controls (1.01%), and were 5.21% and 1.31% among elderly, and non-elderly hypnotic-users, respectively. Attributable risk-percentage of falls due to hypnotic-use was 28.0% in the entire study sample, and 40.0% and 26.7% in elderly and non-elderly sub-samples, respectively. After adjusting for all baseline differences including conditions that may place an individual at a higher risk for falls like balance disorders such as Parkinson's, relative-risk of falls for hypnotic-users was 1.36 (95%CI:1.22-1.52) in the entire sample; 1.58 (95%CI:1.09-2.29) in elderly; and 1.34 (95%CI: 1.20-1.50) in non-elderly.
Conclusion: Elderly and adult hypnotic users have a higher proportion and risk of falls compared to non-users.
Support (optional): sanofi-aventis, U.S.

0789

IS PRE-SLEEP COGNITIVE AROUSAL STRICTLY A PRE-SLEEP PHENOMENON?

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Introduction: The Cognitive subscale of the Pre-Sleep Arousal Scale (PSAS-C) was developed to assess self-reported cognitive arousal in the immediate pre-sleep period, and was validated on those with sleep onset insomnia only. It is possible that those endorsing high pre-sleep cognitive arousal may have more general arousal problems that pervade across the 24-hour period. If this were true, other more general measures of cognitive arousal might relate to maintenance insomnia. This study evaluated the relation between pre-sleep and general cognitive arousal and wakefulness in the initial versus middle sleep period.
Methods: Adults with DSM-IV-TR insomnia diagnoses (N=174) completed two-weeks of sleep logs, PSAS-C and more global cognitive arousal measures: the Symptom-Focused Ruminations scale (SYM) and Penn State Worry Questionnaire (PSWQ). Using a 30 minute cutoff on mean sleep log data, participants were classified as having sleep onset problems only (SOI), sleep maintenance problems only (SMI), or having both types of insomnia (BOTH). A multivariate analysis of variance tested whether these groups differed on the PSAS-C, SYM or PSWQ. Two separate regression analyses tested whether the PSAS-C, SYM and PSWQ significantly predicted: 1) mean sleep onset latency or 2) mean middle WASO.
Results: The MANOVA was significant (p = .01) and follow-up ANOVAs revealed a main effect for group on PSAS-C only, such that those with SOI-only had higher PSAS-C scores than those with SMI-only (p=.001). None of the cognitive arousal measures significantly predicted MWASO on the regression analysis; however PSAS-C alone significantly predicted mean SOL (beta=.324).
Conclusion: These data would suggest that the PSAS-C is relevant to cognitive arousal in the pre-sleep period only, as PSAS-C most strongly relates to sleep onset latency. While cognitive arousal could be a factor in some maintenance insomnias the measures evaluated in this study do not relate to wakefulness in the middle of the night.
Support (optional): Pickwick Fellowship Award, National Sleep Foundation and the National Institute of Mental Health Grant # R01, MH067057.

0790

RUMINATION AND WORRY IN THOSE WITH CLINICAL INSOMNIA: "IT'S LIKE DAY AND NIGHT"

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Introduction: Worry and rumination are important perpetuating factors in insomnia (Harvey, 2002) but little is known about the relation between these similar processes. Teasdale (2001) has suggested that the shared process may be repetitive information-processing but the content of the repeating thoughts may differ. Ruminative content tends to be focused on attributing current states to past negative events and the relevant mood state is dysphoria. The content in worry is concerned with future consequences (e.g., poor daytime performance) of the current state (arousal/anxiety). If this conceptualization is true, rumination may predominate during the day as it would occur in response to dysphoric symptoms like fatigue and the attribution for the fatigue would be a past event; that is, the previous night's sleep. Worry may occur with nighttime arousal and thoughts about the impending consequences of poor sleep.
Methods: Adults (N=195) with DSM-IV-TR insomnia diagnoses (18-81 yrs) completed the Fatigue Severity Scale (FSS), Beck Depression Inventory II (BDI-II), Beck Anxiety Scale (BAI), Penn-State Worry Questionnaire (PSWQ) Pre-Sleep Arousal Scale (PSAS), Dysfunctional Beliefs and about Sleep Scale (DBAS-16), and Symptom-Focused Rumination (SYM). Two regression analyses evaluated predictors of: a daytime symptom (fatigue - FSS), and a nighttime symptom (PSAS-Cognitive). Each analysis entered the following predictors: PSWQ, BAI, BDI-II, SYM and DBAS-16.
Results: Regression analyses confirmed that rumination, not worry, predicted daytime fatigue. In combination with sleep beliefs, rumination accounted for 37% of the variance. Rumination did not predict pre-sleep arousal; worry, anxiety and sleep beliefs were predictors of pre-sleep arousal (40% of the variance).
Conclusion: The predictions were confirmed: rumination related to fatigue whereas worry predicted bedtime arousal. This both confirms and refines Harvey's (2002) model as it suggests that both factors are important in the 24-hour period but rumination may occur with daytime fatigue complaints whilst worry may occur predominantly with bedtime arousal.
Support (optional): Pickwick Fellowship Award, National Sleep Foundation and the National Institute of Mental Health Grant # R01, MH067057.

0791

HEALTHCARE UTILIZATION AND WELL-BEING AMONG INSOMNIA PATIENTS SEEKING TREATMENT AT A TERTIARY SLEEP CLINIC

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Introduction: Previous research suggests that chronic insomnia is a prevalent condition that affects roughly 10% of the general population and is associated with increased utilization of healthcare resources as well as poor self-perceived health. The aim of this study was to investigate perceptions of and patterns of health care use as demonstrated by a sample of insomniacs attending a cognitive behavioral therapy group for insomnia (CBT-I).
Methods: The sample consisted of 49 patients (38.8 % female) diagnosed with psychophysiologic insomnia who completed a baseline questionnaire that inquired about utilization of a variety of healthcare resources and perceptions of emotional and physical health. All consented to participate in the study. Healthcare utilization patterns were also correlated to insomnia severity as measured by the Insomnia Severity Index.
Results: In the two months prior to treatment, patients reported an average of 6.1 visits to any type health care provider with a breakdown of visits as follows: 29% of visits were made to primary care physicians; 8% of visits were made to psychiatrists; 32% of visits were made to psychologists; 29% of visits were made to other practitioners (e.g. acupuncturists, chiropractors, massage therapists, homeopathic practitioners, herbalists, physical therapists); 2% of visits were made to hospitals or ERs. Overall, 43% perceived that they were not in good physical health, and 69% perceived that they were not in good emotional health. 86% of participants had discussed their insomnia with their primary care doctor. The number of health care visits was not significantly correlated with insomnia severity.
Conclusion: If the results from this small study are replicable, they indicate that most people with insomnia presenting to a tertiary sleep clinic perceive that they are not in good emotional or physical health. Interestingly the number of health care visits was independent of the severity of insomnia.

0792

A COMPUTER MODEL OF CHRONIC PRIMARY INSOMNIA (CPI) AS RAPIDLY CYCLING DELAYED SLEEP PHASE

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Introduction: The prevalence of Chronic Insomnia is estimated at 9% to 17%. Patients with Primary Insomnia have insomnia without medical or psychiatric illness. These patients have complaints and performance deficits similar to sleep deprivation. The most effective long term treatments are similar to those for Delayed Sleep Phase (DSP). Pharmacologic intervention is as ineffective as in DSP. Positive PSG findings are elusive in CPI. The hyperarousal theory is complex and difficult to prove. This tests whether a Rapidly Cycling DSP models CPI .
Methods: The model uses 1000 hypothetical subjects. A subject is assigned a random sleep need (normal distribution, mean 8 hrs). Each "night" a subject receives a random "night's" sleep (normal distribution, mean 7 hrs). A subject's sleep deprivation (SD) = sleep need - sleep + previous SD (on night 1 all previous SD = 0). If SD $\geq$ 2 then SD is set to 0, implying sleep deprivation caused a full night's sleep, no insomnia. The model simulates a random number of "nights" (uniform distribution, 183 to 364). The model generates the number of subjects with insomnia, SD $\leq$ .5 hrs, possible insomnia, .5 hrs < SD $\leq$1.5 hrs, and no insomnia, SD > 1.5 hrs: representing a subject's next night PSG results.
Results: The model was run fifty times. The numbers of "nights" in a given run did not effect the results, the distribution of subjects into the three categories. The results of all 50 runs are combined. The model predicts that a PSG would not show insomnia in 20%, might show insomnia in 43%, and show insomnia in 37%.
Conclusion: This closely mirrors the PSG results seen by those studying insomnia especially in pharmacological trials. This model suggests Rapidly Cycling DSP possibly explains Chronic Primary Insomnia.

0793

IS PHASE ADVANCE SLEEP AN ADEQUATE MODEL FOR SLEEP ONSET INSOMNIA?

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Introduction: Phase advancing young, normal sleepers to produce longer sleep latency is a common model used to test hypnotics for efficacy. However, no comparison has been done to compare phase-advanced sleep in normals to sleep in sleep-onset insomnia patients to determine whether this model actually produces similar sleep to that found in the patient population.
Methods: Fourteen patients with a complaint of sleep onset insomnia verified by polysomnography were compared with a group of twelve verified normal sleepers who were re-evaluated after a phase advance of 3 hours in their normal bedtime. Both groups were free from any other sleep disorder and did not differ on age (26 years in insomnia patients and 22 in normals).
Results: As expected from history and study design, both insomnia patients and phase-advance Ss had extended sleep latency (54 + 27 min vs 46 + 25 min, NS). However, examination of sleep profiles from the two groups showed that the true insomnia patients also had significant decrements in many other sleep variables not seen in phase shifted normals: decreased total sleep time (367 vs 399 min), increased stage 1% (14 vs 6%), decreased stage 2% (42 vs 53%), decreased sleep efficiency (86 vs 92%), and decreased REM in the first third of the night (5 vs 12 min).
Conclusion: The data suggest that advance of sleep time increases sleep latency in normal young adults but has less effect on sleep efficiency, stage 1, stage 2 and REM than is seen in true insomnia patients. Inability of the phase advance to produce other sleep deficits similar in magnitude to those seen in true patients suggests that medications shown efficacious in such a model may not demonstrate similar efficacy in true insomnia patients.
Support (optional): Supported by the Dayton Department of Veterans Affairs Medical Center, Wright State University School of Medicine, and the Sleep-Wake Disorders Research Institute.

0794

USING THE ITSAT-Q TO EVALUATE PATIENTS WITH AND WITHOUT ANXIETY OR DEPRESSION: A MULTI-GROUP ANALYSIS

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Introduction: Anxiety and depression are reported to occur concomitantly with insomnia and to increase the risk for developing insomnia. In this study, confirmatory factor analysis was used to determine if the underlying structure of the measurement model was equivalent (valid) for insomnia patients with and without anxiety or depression.
Methods: Patients were recruited through the Sleep Research Project in Tuscaloosa, Alabama. Development of the Insomnia Treatment Satisfaction questionnaire (ITSAT-Q) followed a standard psychometric approach using focus groups, pre-testing, with final model development (factors = expectations, convenience, effectiveness, value and treatment satisfaction) based on 298 patients. The 34 questionnaire items were rated from not important at all to extremely important on a 5-point scale for treatment satisfaction.
Results: Average age of the 298 participants was 50.8 (SD=12.4) years. Females comprised 69.5% of the sample. Patients with anxiety or depression comprised 56% of the sample. All coefficients were significant ($p< 0.01$). For insomnia patients with (n= 167) and without (n=131) anxiety, the validity of the underlying factor structure of measurement model was confirmed $\chi2 = 123.3$, df = 106, p = 0.120, CFI = 0.988, TLI = 0.982. To compare groups, additional constraints were placed on the measurement model with model fit assessed at each level including the factor loadings, structural variances and covariances, and measurement residuals. Although invariance for the five-factor structure (measurement weights) was supported (delta-$\chi2 = 14.4$, df = 8, p = 0.072, delta-TLI = 0.005), results for the structural covariances (p = 0.015) and measurement residuals (p = 0.006) were significant. Patients without anxiety or depression perceived a stronger relationship between treatment satisfaction and value compared to patients with anxiety or depression.
Conclusion: The five-factor structure was supported with multi-group analysis. However, the relationship among factors differed for insomnia patients with and without anxiety or depression.
Support (optional): Unrestricted grant provided from Takeda Pharmaceuticals North America Inc.

0795

EPIDEMIOLOGY OF INSOMNIA: POLYSOMNOGRAPHIC AND CLINICAL FINDINGS

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Introduction: There are no studies evaluating the prevalence of insomnia in association to polysomnography (PSG) and clinical data. This study aimed in assessing the prevalence of insomnia for the adult population of Sao Paulo city in Brazil, and in analyzing potential PSG and clinical associated factors.
Methods: A population-based survey was conducted on a 3-stage probabilistic cluster sample, in order to be representative, according to gender, age (20-80), and socioeconomic status. Participants were interviewed,

completing multiple questionnaires (demographic/psychological/physical/sleep), and underwent full in-lab PSG. We determined 3 main categories for insomnia: IS-insomnia syndrome, using DSM-IV criteria; IC-insomnia complaints (difficulty initiating, maintaining sleep or early-morning awakenings at least 3 times a week); and NI-non-insomnia (no complaint of insomnia).
Results: A total of 1.042 subjects underwent PSG. 53.3% were women. The prevalence of IS was 13.5%, while IC was 34.5%. Mean age was: NI:38.8[37.3-40.3], IC:46.1[43.5-48.5], IS:41.8[38.9-44.9], and 47%, 55%, 72% were women, respectively. Scores for depression, anxiety, fatigue, and insomnia-severity were higher among insomnia subgroups (IS>IC>NI; p<0.01); scores for sleep quality and quality of life lower (IS < IC < NI; p<0.01). IS had lowest arousal (IS < NI < IC; p<0.01), and respiratory arousal index (IS>NI=IC; p<0.05). IC had highest oxyhemoglobin-desaturation (IC>NI=IS; p<0.01). Insomnia subgroups were more likely to be divorced/separated/widowed (IS:OR=3.24[1.26-8.35];IC:OR=2.03[1.09-3.76]), to take sleep promoters (IS:OR=3.71[2.28-6.00];IC:OR=2.43[1.73-3.41]), and to present fatigue (IS:OR=4.88[3.07-7.77];IC:OR=1.55[1.09-2.19]). IS was associated to moderate-severe anxiety symptomatology (OR=3.33[1.58-7.03]), and AHI between 5 and 15 (OR=1.92[1.07-3.42]). IC was associated to low socioeconomic status (OR=1.81[1.04-3.20]), being 50 years or older (OR=2.03[1.22-3.40]), and sleep efficiency <85% (OR=1.63[1.20-2.21]).
Conclusion: We found a slightly higher prevalence of insomnia among the adult population of Sao Paulo city compared to other studies. IS exhibited worsened psychological and physical status, while IC was older and presented characteristics of sleep fragmentation.
Support (optional): AFIP/FAPESP/CNPq.

0796

EFFECTS OF RAMELTEON 8 MG ON LATENCY TO PERSISTENT SLEEP IN ADULTS WITH CHRONIC INSOMNIA CHARACTERIZED BY SEVERE BASELINE SLEEP LATENCY: POOLED ANALYSIS OF 4 CLINICAL TRIALS

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Introduction: Ramelteon is an MT1/MT2 melatonin receptor agonist indicated for the treatment of insomnia characterized by difficulty with sleep onset. A pooled analysis of adults with chronic insomnia determined that ramelteon 8 mg reduced latency to persistent sleep (LPS) on Nights 1 and 2 by approximately 13 minutes. The current analysis is a follow-up to the previous study and evaluated the mean reduction in LPS at Nights 1 and 2 in a subset of subjects with severe baseline sleep latency (LPS>=60 min).
Methods: Adults (18-82 years) with chronic insomnia who took ramelteon 8 mg or placebo were included in this pooled analysis of 4 randomized, double-blind, placebo-controlled clinical trials. The primary endpoint of each trial was LPS, measured by polysomnography. Mean LPS from Nights 1 and 2 was evaluated in subjects with chronic insomnia and a baseline LPS>=60 min.
Results: Subjects who took ramelteon 8 mg (n=286, mean age 43.2 years) and placebo (n=269, mean age 44.9 years) were included in the analysis. Mean LPS at baseline was 97.2 min in the placebo group and 96.1 min in the ramelteon 8 mg group. Mean LPS at Nights 1 and 2 was 39.5 min in the ramelteon 8 mg group and 56.8 min in the placebo group. The LS mean difference from placebo was -17.2 min (P<0.0001).
Conclusion: In the current analysis of adults with chronic insomnia characterized by severe baseline sleep latency, ramelteon 8 mg significantly reduced mean LPS on Nights 1 and 2 by approximately 17 minutes compared with placebo.
Support (optional): This study was supported by funding from the Takeda Pharmaceuticals Company, Ltd.

0797

COGNITIVE REFOCUSING TREATMENT FOR INSOMNIA: AN OPEN-LABEL PILOT STUDY

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Introduction: This ongoing investigation assessed a treatment that targets the content and style of pre-sleep cognitions to improve sleep quality in people with insomnia. The treatment focuses exclusively on enhancing cognitive distraction immediately before and during the sleep period. In brief, the treatment provider worked with the participant in identifying 3 different 'categories of thought' compelling enough to maintain his or her attention at bedtime. The chosen categories were to be interesting, engaging, and at the same time, non-arousing.
Methods: An open label within group design was used. Individuals with primary insomnia met for 4 weekly individual treatment sessions. Participants were recruited from provider referrals from the Buffalo and Philadelphia Veterans Medical Centers. Participants (N = 7) completed the Pittsburgh Sleep Quality Index (PSQI) and Epworth Sleepiness Scale (ESS) at baseline and post treatment (3 individuals completed a one-month follow up). A total sleep quality score, average total sleep time, and average sleep onset latency during the previous month were assessed using the PSQI.
Results: Paired t-tests revealed significant increases in total sleep quality, $t(6) = 4.3$, $p < .01$ and total sleep time, $t(6) = 3.2$, $p < .05$ at post treatment. T-tests revealed trends toward decreased sleep onset latency, $t(6) = 2.3$, $p = .057$ and ESS score, $t(6) = 2.3$, $p = .056$. Effect sizes for all outcome variables fell in the large range. For those completing one month follow-ups improvements were maintained.
Conclusion: These data show preliminary evidence for cognitive refocusing treatment for insomnia. These results suggest that purposeful cognitive refocusing may be used to treat insomnia. It is hypothesized that this exercise allows the person with insomnia to distract themselves from unwanted pre-sleep cognitions, resulting in decreased arousal.
Support (optional): This work was supported by pilot grants from the Department of Veterans Affairs Mental Illness Research Education and Clinical Center and from the Department of Veterans Affairs Center for Integrated Healthcare.

0798

LACK OF HIPPOCAMPAL VOLUME DIFFERENCES IN PRIMARY INSOMNIA AND NORMAL SLEEPING CONTROLS: AN MRI VOLUMETRIC STUDY AT 3 TESLA

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Introduction: A recent pilot study reported that hippocampal volumes were reduced in patients with primary insomnia (PI) relative to normal sleepers. If confirmed, loss of hippocampal volume in PI might be attributed to chronic hyperarousal and/or chronic sleep debt and could have potential effects on neurocognitive performance. We performed hippocampal volumetric analysis employing rigorous screening criteria of community recruits with PI.
Methods: This cross-sectional design included community recruits meeting DSM-IV criteria for PI (n=20, 10 males, mean age 39.3 ±8.7) and normal sleepers (n=15, 9 males, mean age 38.8 ±5.3). All subjects were non-medicated and without comorbid psychiatric and medical illness. PI subjects were symptomatic at least 6 months, kept two weeks of sleep diaries and actigraphy, and underwent overnight PSG to screen for primary sleep disorders. Hippocampal and whole brain volumes were derived by a Siemens/Trio MRI scanner operating at 3 Tesla.

Results: The Pittsburgh Sleep Quality Index global score averaged 2.0 ±1.24 for the normal sleepers and 12.11 ± 3.05 for the PI group. Mean hippocampal volumes were 4322.0 ±299.7 mm3 for the normal sleepers and 4601.55 ± 537.4 mm3 for the PI group. The dependent variable, hippocampal volume, was analyzed by ANCOVA. Main effects were diagnosis and gender; whole brain volume served as the covariate. Although the overall model was significant (F=6.3 p=.001), the main effects of diagnosis (F=2.14) and gender (F=0.04) were not significant. The covariate of whole brain volume was significant (F=5.74, p=.023) as was the interaction of diagnosis with gender (F=10.22, p=.003), with male insomniacs having larger hippocampal volumes than male controls.
Conclusion: The study failed to confirm the hypothesis that hippocampal volumes are reduced in subjects diagnosed with PI relative to normal-sleeping controls. Differences between this study and the recent Riemann pilot study include: sample size, age of subjects, clinical vs community recruitment, length of medication-free period, method of correction for whole brain size, and magnet strength of the MRI scanner.
Support (optional): Supported by a research grant from Sepracor, GCRC grant M01-RR02635, and NIH grant MH58681.

0799

ETHNIC DIFFERENCES IN INSOMNIA AND DEPRESSION/ ANXIETY IN HISPANICS OF MEXICAN DESCENT AND NON-HISPANIC WHITES IN SAN DIEGO COUNTY

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Introduction: The association between insomnia and depression/anxiety is well known; however, it has not been extensively studied among Hispanics. We investigated this association in Hispanics of Mexican Descent (HMD) and Non Hispanic-Whites (NHW).
Methods: We performed a population-based telephone survey using random digit dialing. Insomnia was defined using three questions from the Sleep Heart Health Study Sleep Habits Questionnaire: How often do you experience trouble falling sleep; waking up during the night and have difficulty getting back to sleep; or waking up too early in the morning and unable to getting back to sleep The Hospital Anxiety and Depression Scale (HADS) was administered to assess depression and/or anxiety. Data on demographics, alcohol, tobacco and coffee use were collected.
Results: We surveyed 2336 subjects (54.6% HMD, 45.4% NHW, gender ration 1:1). HMD were younger (41.0±15.7 vs. 54.5±17.3 years, p=0.001) and reported having insomnia less often (41.7% vs 47.1 %. p<0.001). There were no difference in the prevalence of sleep onset insomnia (30.8% vs 32.5% for HMD and NHW respectively, p=0.4). NHW reported more sleep maintenance insomnia (33.1 % vs. 25%, p<0.001). There were no differences for early awakening insomnia (23.6% vs. 24.7% p=0.53). HMD were more frequently depressed (HADS-depression global score >7; 21.1% vs. 15.4%, p< 0.001). There was no difference in anxiety (HADS-anxiety global score >7; 24% vs 20.8%, p=0.08). Logistic regression indicated that being depressed (p=0.001), anxious (p<0.001) and older (p=0.004) were predictors for insomnia in both groups. Smoking (p=0.01) was an independent predictor for insomnia only in HMD.
Conclusion: HMD had a higher prevalence of depression while NHW reported insomnia more frequently. However, in both groups, anxiety and depression were independent predictors of having insomnia. The use of tobacco was an independent predictor of insomnia only in HMD.
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0800

THE EFFECTS OF A MINDFULNESS- BASED STRESS MANAGEMENT PROGRAM ON PRE-SLEEP AROUSAL AND INSOMNIA SYMPTOMS

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Introduction: Cognitive behavioral treatment for insomnia (CBT-I) is hypothesized to work by addressing factors that perpetuate the insomnia, not ongoing precipitating factors, such as stress. As such, there is an interest in examining the benefit impact of stress management interventions on sleep. One such intervention, mindfulness based stress reduction (MBSR), has been shown to decrease somatic and cognitive arousal as well as stress; factors elevated in patients with insomnia. This report describes the effects of an ongoing MBSR on insomnia severity, pre-sleep arousal, mindfulness, and mood.
Methods: Participants of an 8 week MBSR program at the University of Pennsylvania Penn Program for Stress Management (PPSM) (n=22) took part in this study. The sample was 54.5% female (mean(SD) age=48.0(14.5)). The program consists of 8 weekly sessions, each 2.5 hours long, and one 7-hour silent retreat. Participants were assessed pre and post intervention with the Pre- Sleep Arousal Scale (PSAS), the Insomnia Severity Index (ISI), and the Cognitive and Affective Mindfulness Scale- Revised (CAMS-R). Paired t-tests were used to compare pre- and post-treatment scores.
Results: The intervention was shown to lead to statistically significant reductions on the ISI (pre=9.9(5.7), post=7.4(5.0); p<.001), PSAS cognitive subscale (pre= 23.0(4.7), post=18.9(3.9); p<.001), and PSAS somatic subscale (pre= 17.6(5.9), post=13.5(4.5); p<.001). There was a significant increase in CAMS-R scores (pre= 29.0(5.7), post=32.9(5.1); p<.004).
Conclusion: The stress management intervention led to significant improvements in sleep and pre-sleep arousal, even though the intervention did not specifically target sleep. These results suggest that further study of MBSR as an intervention for insomnia is justified.

0801

THE EFFECTIVENESS OF L-TRYPTOPHAN IN THE TREATMENT OF CHRONIC PRIMARY INSOMNIA: A SYSTEMATIC REVIEW

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Introduction: Insomnia is the most common of all sleep disorders. Chronic primary insomnia (CPI) is characterized by a reduction of total sleep time (TST) associate with difficulties of sleep initiation (SI), sleep maintenance, or early morning awakening; with subsequent daytime functional impairment, and duration greater than 1 month. CPI prevalence is estimated to be between 1.5-5% of the general population. Prior to its 1989 FDA ban L-tryptophan, an amino acid and Serotonin precursor, had been used extensively in the treatment of CPI. Since its FDA reinstatement in 1994, it is once again being used in the treatment of CPI. The objective of this systematic review was to assess the effectiveness of L-tryptophan among adult CPI patients.

Methods: A comprehensive search for randomized trials or clinical trials of L-tryptophan for CPI included, but was not limited to, the following electronic databases: MEDLINE, EMBASE, PubMed, and PsycINFO; without language or publication restrictions. For completeness, references of relevant papers were hand searched and authors, and pharmaceutical companies, were contacted. Abstracts were searched from potentially relevant conferences. Studies involving subjects with comorbid physical or psychiatric pathologies, or those using concurrent sleeping medications, were excluded. Outcomes of interest included: changes in TST or sleep onset latency (SOL). Information on adverse effects was collected. Analysis of results used fixed and random effects methods.
Results: Six trials comparing pharmaceutical grade L-tryptophan to placebo were reviewed. Findings were statistically significant for SOL. Lower doses (250mg) provided greater increase in TST than higher doses ($p > 0.05$). There was no statistically significant risk differences associated with the use of L-tryptophan.
Conclusion: L-tryptophan did not have any statistically significant effect on TST. Dosages greater than 1000mg were no more beneficial than those dosages less than, or equal to, 1000mg. L-tryptophan effectiveness may be limited to those patients suffering specifically from SI difficulties of a transient nature.

0802

ARE INSOMNIA SYMPTOMS STABLE OVER TIME? A 5-YEAR PROSPECTIVE STUDY IN THE GENERAL POPULATION

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Introduction: Whether sleep onset, maintenance or mixed insomnia represent changing manifestations or distinct stable subtypes of insomnia remains unclear. The aim of this study was to examine the stability of insomnia subtypes across time.
Methods: Data are derived from an epidemiological study examining the longitudinal course of insomnia in the general population. Participants were contacted annually on six occasions covering a 5-year period and completed several questionnaires sent by mail, including the Pittsburgh Sleep Quality Index (PSQI). The subset used in this project includes those who reported symptoms of insomnia on at least two of the six assessments (N = 459; age range = 17 - 83, mean = 43.6; 63.8 % women). At each assessment period, participants who had symptoms of insomnia were classified as having either sleep onset, maintenance or mixed insomnia, or other types of insomnia (e.g., non-restorative sleep) according to their answers on selected items of the PSQI.
Results: Overall, 52.7% (n = 242) of participants remained classified within the same insomnia subtype over the 5-year period, with 1.7 % (n = 8) having sleep onset insomnia, 46.2% (n = 220) having maintenance insomnia and 4.8% (n = 22) having mixed insomnia. Within the remaining 47.3% (n = 217) of participants for whom the nature of symptoms changed over time, 36.9% (n = 80) did not experience a predominant insomnia subtype, 7.4% (n = 16) had predominant sleep onset insomnia, 38.71% (n = 84) had predominant maintenance insomnia and 17.1% (n = 37) had predominant mixed insomnia. For individuals classified as having sleep onset insomnia at a given assessment period, the probability of having sleep onset insomnia the next time they had insomnia symptoms was 32.3% (95% CI = 23.1 - 41.5). For those classified as having maintenance insomnia, the probability of remaining with maintenance insomnia the next time they experienced insomnia symptoms was 82.1% (95% CI = 79.4 - 84.8). Finally, for individuals classified as having mixed insomnia, the probability of having mixed insomnia again the next time they experienced insomnia symptoms was 49.8% (95% CI = 43.9 - 55.7).
Conclusion: The stability of insomnia subtypes varies among individuals with insomnia and also seems to differ depending on the nature of the subtype. While maintenance insomnia appears relatively stable across time, sleep onset and mixed insomnia seem more volatile. The correlates of stable and unstable insomnia subtypes should be further investigated.
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0803

HLA DQB1*0602 IS ASSOCIATED WITH SLEEP PERCEPTION IN OLDER INDIVIDUALS WITH INSOMNIA

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Introduction: A prominent aspect of insomnia is the dichotomy between subjectively and objectively assessed sleep quality. This may be due to measurement issues (i.e., are we measuring physiologic variables that accurately represent "quality") or it may be due to differences in the biology of individuals with insomnia, hypothesized to be within REM sleep. These differences may be under genetic control. A gene that may be involved is HLA DQB1*0602, which is present in ~25% of the general population, but is found in most individuals with hypocretin-deficient narcolepsy. Both narcolepsy and DQB1*0602 positivity in non-narcoleptics is associated with shortened REM latency. It is possible that non-pathological phenotypic variations in REM sleep and, by extension, perception of diminished sleep quality, may result from changes in hypocretin function that are mediated through DQB1*0602.
Methods: Two weeks of at-home sleep recordings with actigraphy and sleep-wake logs in a group of older individuals (n=46) with primary insomnia. DQB1*0602 genotype was determined using standard single specific primer-polymerase chain reaction procedures on blood-extracted DNA.
Results: Baseline demographics, night time and daytime sleep were mostly similar between DQB1*0602 positive (n=11, 24%) and negative (n=35). However, DQB1*0602 positive reported waking 3.1±1.1 times per night compared to 1.9±0.83 times per night in DQB1*0602 negative ($p<0.001$). DQB1*0602 positive also reported that they were significantly less well-rested (3.2 ± 0.86) than DQB1*0602 negative (3.94±1.0, $p<0.05$). When reporting sleeping less than 70% of the night, DQB1*0602 positive indicated a lower subjective restedness rating than DQB1*0602 negative given the same sleep efficiency. When sleeping at sleep efficiencies greater than 57%, DQB1*0602 positive consistently reported sleeping less than was indicated by wrist actigraphy. There was, however, no similar relationship between objective and subjective calculations of sleep efficiency ($r=0.097$, $p=0.13$) in DQB1*0602 negative.
Conclusion: The presence of the DQB1*0602 allele appears to explain some of the variability in self-reported sleep quality in older individuals with insomnia.
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0804

SPECIFICITY AND SENSITIVITY TO DIFFERENT INSOMNIA SYMPTOMS OF ONLINE COGNITIVE BEHAVIORAL THERAPY

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Introduction: CBT for insomnia (CBT-I) is an effective treatment for chronic insomnia. Recently, CBT-I has also been offered by means of internet-based consultation. The treatment consists of 8 sessions offering

sleep hygiene, sleep restriction, stimulus control and cognitive therapy. The efficacy of internet based treatment was shown to be equivalent to reports of face to face treatments. Insomnia patients have either one dominant symptom (problems of sleep initiation, sleep maintenance, early morning awakening) or a combination of symptoms. This paper reports results on the specificity and sensitivity of the treatment for the various symptom groups.

Methods: 70 Patients reported their symptoms by means of a Symptom Checklist before enrollment. All patients were enrolled in the same treatment protocol. Based on a weekly sleep diary and on additional information a personalized treatment was given through the internet. Sleep efficiency, sleep onset, total sleep time, wake after sleep onset (WASO) and the subjective sleep quality on a five point rating scale were computed from the sleep diary. The patients were divided in 3 groups based on their initial insomnia complaints: sleep initiation (30.6%), sleep maintenance (27.5%) and a combination of complaints (41.9%). The early morning awakening group was too small to use. The improvement in the various sleep parameters from the 1st (baseline) to the 7th consult was compared between the 3 symptom groups by means of the Wilcoxon signed rank test.

Results: Across all insomnia symptoms, all sleep parameters improved significantly ($p<0.002$) between baseline and the 7th treatment session. Sleep efficiency improved significantly in all 3 symptom groups ($p<0.001$). However, the highest improvement in sleep latency (37.4%) was found in the sleep initiating group ($p<0.0002$), whereas the decrease in WASO was highest in the sleep maintenance group (43.4%, $p<0.0008$). The improvement in Total Sleep Time was significant only for the combined symptoms group ($p<0.003$) and showed a trend for the sleep maintenance group ($p<0.01$). The improvement in subjective sleep quality and in feelings in the morning were significant only in the combination group ($p<0.0003$, $p<0.007$ respectively).

Conclusion: Somnio online CBT-I is effective for all types of insomnia complaints and the amount of improvement in the various sleep parameters is specific for the original sleep complaint.

0805

COMPARATIVE VALIDITY OF THE DSM-IV-TR AND ICSD-2 INSOMNIA NOSOLOGIES: HOW MANY WAYS SHOULD WE SLICE THE INSOMNIA PIE?

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Introduction: DSM-IV-TR and ICSD-2 provide discordant schemes for insomnia classification. DSM-IV-TR "lumps" insomnia disorders into a few general categories, whereas ICSD-2 "splits" them into many specific subtypes. This study evaluated and compared the validities of these insomnia nosologies.

Methods: To date, 333 (67% women; MAge= 46.8±14.5 yrs.) adults who met Research Diagnostic Criteria for insomnia enrolled across two study sites. Six sleep specialists interviewed each patient enrolled at their respective study site. Two clinicians conducted solely a structured sleep interview. Another pair conducted a standard clinical interview (CI) and reviewed patients' sleep history questionnaires (SHQ) and sleep diaries (SD). The third pair formulated impressions from CI SHQ, SD and PSG. All then rated how well (0 = "doesn't fit at all"; 100 = "fits extremely well") each of 10 DSM-IV-TR and 37 ICSD-2 insomnia diagnoses "fit" the patient. We computed mean diagnostic ratings within each clinician dyad for each patient and then computed inter-dyad Spearman correlations of these mean ratings across patients. Resultant averaged correlations across the 2 study sites were placed into multi-trait/multi-method matrices to examine the convergent validity (i.e., "hetereomethod-monotrait" correlation) of the DSM-IV-TR and ICSD-2 insomnia diagnoses.

Results: Results showed moderately good validity indices for DSM-IV-TR alcohol-induced insomnia (rs=.42-.55), insomnia related to mental (rs=.65-.68) and medical (rs=.53-.61) disorders, breathing-related sleep disorder (rs=.37-.68) and circadian rhythm sleep disorder (rs=.44-.54). Best supported ICSD-2 diagnoses included insomnia related to mental (rs=.66-.68) and medical (rs=.53-.62) disorders, restless legs syndrome (rs=.49-.63), idiopathic insomnia (rs=.50-.57), delayed sleep phase syndrome (rs=.44-.54), and obstructive sleep apnea (rs=.34-.64). Least supported DSM-IV-TR diagnoses were primary insomnia (rs=.25-.32), dyssomnia NOS (rs=.22-.25) and "other" insomnia (rs=.09-.18). The ICSD-2 diagnosis receiving least support was paradoxical insomnia (rs=.15-.22). Many ICSD-2 categories were seldom or never chosen.

Conclusion: Results supported the validity of some but not all DSM-IV-TR and ICSD-2 insomnia diagnoses. The DSM-IV-TR seemingly includes too few diagnoses, whereas the ICSD-2 has too many diagnoses for optimal insomnia classification. Future classification efforts should consider an insomnia nosology that lies somewhere between these two systems.

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0806

INSOMNIA IN AFRICAN AMERICAN AND CAUCASIAN OLDER ADULTS

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Introduction: Epidemiological studies assessing sleep often ask respondents to confirm or deny the presence of insomnia, but collect little additional sleep data. Thus, detailed data on sleep characteristics are often unavailable. The present study randomly sampled a metropolitan community and collected 14 days of sleep diaries and daytime functioning questionnaires to study normal and disordered sleep. The current study focuses on insomnia in African American (AA) and Caucasian (CA) older adults.

Methods: We used random-digit dialing to solicit participation from 772 participants: at least 50 men and 50 women in each decade from age 20 to 80 and older. Volunteers were paid between $15 and $200 (older adults were paid more). This paper will focus on the sleep diaries of the AA (N = 16) and CA (N = 72) insomnia subset with minimum age cutoff of 50.

Results: AA with insomnia slept worse that CA with insomnia on 6 of 7 sleep variables and this difference was significant for 4 variables-WASO (AA M = 87 min, SD = 64 and CA M = 52, SD = 30; t [adjusted 17] = 2.2, $p < .05$), TST (AA M = 340 min, SD = 88 and CA M = 396, SD = 71; t [86] = 2.7, $p < .01$), SE (AA M = 66 percent, SD = 11 and CA M = 76, SD = 8; t [86] = 4.0, $p < .001$), and NAP (AA M = 39 min, SD = 26 and CA M = 23, SD = 25; t [86] = 2.4, $p < .05$). SOL, NWAK and rated sleep quality were not significantly different.

Conclusion: Based upon self-reported sleep derived from 14 days of sleep diaries, we conclude that insomnia is more severe in AA than in CA older adults.

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0807

ARE SLEEP-ONSET PROBLEMS STABLE OVER THE COURSE OF DEVELOPMENT?

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Introduction: Sleep-onset problems are associated with the development of a variety of physical and psychological problems. Despite this, there is little research on the long-term stability of sleep-onset problems.
Methods: Data from a longitudinal, birth to midlife, population study is used to investigate the stability of sleep-onset problems from childhood through midlife. Participants were born from April 1955 to April 1958 in a suburb of Stockholm, Sweden. The resulting sample was 212 children, 122 boys and 90 girls. Sleep-onset was measured by parent-reports ages 6 through 16, as well as by self-reports ages 15 through 17, 25, and 35. Stepwise multiple regressions were used to predict sleep-onset problems in later years, from those in previous years.
Results: Frequencies for parent-reported sleep-onset problems were 31% ages 6 through 8, 34% ages 9 through 11, 33% ages 12 through 14, 47% ages 15 through 16. Frequencies for self-reported sleep-onset problems were 10% ages 15 through 17, and 15% at ages 25 and 35. We found sleep-onset problems to be stable from childhood to midlife. Parent-reported sleep-onset problems ages 6 through 8 predicted sleep-onset problems ages 9 through 11 ($\beta = .71$, $p < .001$); 9 through 11 predicted sleep-onset problems ages 12 through 14 ($\beta = .68$, $p < .001$); 12 through 14 predicted sleep-onset problems ages 15 through 16 ($\beta = .70$, $p < .001$). Self-reported sleep-onset problems ages 15 through 17 predicted sleep-onset problems at age 25 ($\beta = .39$, $p < .001$); age 25 predicted sleep-onset problems at age 35 ($\beta = .25$, $p < .01$).
Conclusion: Sleep-onset problems appear to be characterized by chronicity. Prevention programs, early identification and intervention may be warranted due to the potential risk sleep-onset problems pose for health and psychological problems.

0808

HERITABILITY OF INSOMNIA IN ADOLESCENTS: HOW MUCH IS JUST DEPRESSION AND ANXIETY?

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Introduction: Despite great strides in our understanding of the genetics of sleep disorders, little is known about the genetics of insomnia. A few studies have examined heritability of one or more questions on insomnia symptoms. This report describes the first attempt to establish the heritability of insomnia based on diagnostic criteria and to determine the extent of overlap with major depression and generalized anxiety in children and adolescents.
Methods: The Virginia Twin Study of Adolescent Behavioral Development is a sequential cohort study of twins aged 8-17 and their parents. The first wave sample contained 749 MZ and 687 DZ twin pairs (mean age=11.99 (2.58)). Trained interviewers administered the Child and Adolescent Psychiatric Assessment (CAPA) to each child and to at least one parent about each child. On the CAPA, ratings of insomnia, depression, and overanxious disorder were obtained based on DSM-III-R criteria. Structural equation modeling with the statistical program Mx was used to 1) estimate the heritability of insomnia, 2) test for gender differences in the variance components, and 3) determine whether a single common genetic factor could account for the overlap among insomnia, depression, and anxiety.
Results: Criteria for insomnia were met by 19.5% of the sample. Additive genetic effects accounted for 23.9% of the variance. There were no significant gender effects in the relative role of genes and environment. In a multivariate model controlling for depression and anxiety, there were no trait specific genetic effects unique to insomnia.
Conclusion: Insomnia as a diagnosis has a moderate heritability in 8-16 year olds, which is consistent with past studies of insomnia symptoms in adults. There were significant genetic effects shared with depression and anxiety, suggesting that overlapping genetic mechanisms underlie these disorders. This may explain, in part, the high prevalence of insomnia in patients with depression and anxiety.

0809

SHOULD DSM-IV-TR PRIMARY INSOMNIA BE DIVIDED INTO SPECIFIC SUBTYPES?

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Introduction: DSM-IV-TR indicates primary insomnia (PI) is assigned when insomnia complaints occur independent of psychiatric, medical, or substance-related causes. PI is, thus, established by a process of exclusion rather than by ascertaining specific defining features. In the ICSD-2, various diagnostic subtypes that would be subsumed within the more global DSM-IV-TR PI label are defined by the presence of specific, discriminating criteria (e.g., conditioned arousal, childhood onset, etc.). This study compared the validity of DSM-IV-TR primary insomnia with the more specific related ICSD-2 subtypes.
Methods: Participants included 333 (67% women; 59.4% Caucasians; MAge= 46.8±14.5 yrs.) insomnia sufferers enrolled across two study sites (Duke & Rush University Medical Centers). Six sleep specialists interviewed each patient enrolled at their respective study site. Two specialists conducted solely a structured sleep interview. Another pair conducted a standard clinical interview and reviewed patients' sleep history questionnaires (SHQ) and sleep diaries (SD). The third pair formulated impressions from an interview, SHQ, SD and polysomnography. Clinicians then rated how well (0 = "doesn't fit at all"; 100 = "fits extremely well") each of 10 DSM-IV-TR and 37 ICSD-2 insomnia diagnoses "fit" the patient. We computed mean diagnostic ratings within each clinician dyad for each patient and then computed inter-dyad Spearman correlations of these mean ratings across patients. Resultant averaged correlations across the 2 study sites were placed into multi-trait/multi-method matrices to examine the convergent validity (i.e., "heteroemethod-monotrait" correlation) of DSM-IV-TR primary insomnia and 5 related ICSD-2 insomnia subtypes.
Results: ICSD-2 categories of idiopathic insomnia (rs=.50-.57), psychophysiological insomnia (rs=.29-.47), environmental sleep disorder (rs=.31-.36) and inadequate sleep hygiene (rs=.30-.34) had more favorable validity indices than did primary insomnia (rs=.25-.32). However, ICSD-2 paradoxical insomnia (rs=.15-.22) was not well supported.
Conclusion: Specific defining features as outlined in their diagnostic criteria sets may enhance the validity of several ICSD-2 PI subtypes relative to the more global and less well defined DSM-IV-TR PI category. Perhaps a criteria set with more specific, defining features for PI will enhance validity of this diagnosis.

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0810

RELIABILITY AND VALIDITY OF THE DUKE STRUCTURED INTERVIEW FOR SLEEP DISORDERS FOR INSOMNIA SCREENING

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Introduction: Sleep research has long needed a validated structured sleep interview for subject screening/sample selection. This study tested the inter-rater reliability and validity of the Duke Structured Interview for Sleep Disorders (DSISD) with insomnia sufferers.
Methods: To date, 333 (67% women; MAge= 46.8±14.5 yrs.) participants enrolled at two study sites. Six clinicians interviewed each enrollee at their respective site. One clinician pair (Dyad-1) used only the DSISD; a second pair (Dyad-2) conducted a standard clinical interview (CI) and reviewed patients' sleep history questionnaires (SHQ) and sleep diaries (SD); the third pair (Dyad-3) derived diagnoses based on CI, SHQ, SD, and PSG. They then rated how well (0 = "doesn't fit at all"; 100 = "fits extremely well") each of 10 DSM-IV-TR and 37 ICSD-2 insomnia diagnoses "fit" the patient. We computed mean Spearman correlations between raters using the DSISD across sites to assess inter-rater agreement. To assess DSISD validity, we computed mean ratings within each dyad for each patient and then computed inter-dyad Spearman correlations of these means across patients for 10 DSM-IV-TR and 13 common ICSD-2 diagnoses. Ratings of Dyad-3 at each site served as "gold standards" for testing validity of DSISD ratings (Dyad-1) relative to those derived from standard assessment (Dyad-2).
Results: Inter-rater agreement was acceptable for DSM-IV-TR breathing-related sleep disorder (r=.56), circadian rhythm disorder (r=.46), and insomnias related to mental (r=.55) and medical (r=.41); and for ICSD-2 psychophysiological insomnia (r=.42), idiopathic insomnia (r=.63), obstructive sleep apnea (r=.63), RLS (r=.54), periodic limb movement disorder (r=.57), delayed sleep phase syndrome (r=.45), and insomnias due to mental (r=.56) and medical (r=.45) disorders. Relative to Dyad-2, clinicians using the DSISD derived diagnoses more closely related to "gold standard" diagnoses for DSM-IV-TR primary insomnia, breathing-related sleep disorder, circadian rhythm disorder, substance-induced insomnia, and insomnia related to a medical disorder; and for ICSD-2 delayed sleep phase syndrome, insomnia due to a medical disorder, and obstructive sleep apnea.
Conclusion: Findings support the reliability/validity of the DSISD. Future studies should test if reliability/validity of DSISD diagnoses can be improved by special training or access to additional diagnostic information (e.g., SCID results).
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0811

BAROREFLEX FUNCTION DURING SLEEP AND WAKEFULNESS IN PRIMARY INSOMNIA: PRELIMINARY RESULTS

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Introduction: The arterial baroreflex is an important mechanism implicated in the short term regulation of blood pressure (BP). We assessed baroreflex function (BR) during pre-sleep wakefulness and across sleep stages in subjects with chronic primary insomnia compared to good sleepers.
Methods: We studied 11 subjects with chronic primary insomnia (7 women; 43±7 years) and 11 sex and age matched good sleepers. Subjects were free of any medical or psychiatric co-morbidity and other sleep disorders. Subjects underwent 2 week sleep diary and 3 night polysomnography (PSG) including non-invasive beat-to-beat BP recordings. BR was assessed during pre-sleep wakefulness, stage 2 non-REM and REM sleep of night 3 by calculating: 1) the total slope of the regression line between R-R interval and systolic BP changes occurring spontaneously (sequence method) and 2) the α-coefficient index in the low frequency band (αLF), high frequency (α HF) and the αlumped ((αLF + αHF)/2), obtained by cross analysis of R-R interval and systolic BP variability. Between groups comparison was performed by unpaired t-test or by Mann-Whitney U-test. Pearson correlation coefficients were calculated between BR measures and sleep measures.
Results: Total slope, αLF and αlumped were highly similar between insomniacs and good sleepers during wakefulness and sleep. However, these measures of BR during stage 2 tended to be lower in insomniacs with impaired sleep efficiency (SE) at PSG (SE<85%, N=6 subjects) versus those with preserved SE (≥85%, N=5 subjects). Values were respectively: total slope 10.3±5.7 vs 19.5±9 ms/mmHg, p=0.06; αLF 7.2±3.9 vs 12.6±4.4 ms/mmHg; p=0.1; and αlumped 10.2±6.3 vs 18.8±8.6 ms/mmHg; p=0.1. αLF was positively associated with sleep efficiency among insomniacs (R=0.56, p=0.07).
Conclusion: Our preliminary results suggest that baroreflex mechanisms are preserved in subjects complaining of insomnia. Nevertheless, certain impairment may occur in insomniacs as a function of objective measures of poor sleep.

0812

AMERICAN INSOMNIA SURVEY: METHODOLOGY

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Introduction: The prevalence of insomnia is not well described. We know little about the nature, number of symptoms, their severity, or chronicity. Most epidemiologic studies of insomnia have failed to study

subtypes [onset, maintenance insomnia (nighttime wakening and waking too early), non-restorative sleep] in sufficient detail or to document their relative or joint effects on daytime functioning. The relative burden of primary insomnia versus comorbid insomnias is also poorly defined.
Methods: The American Insomnia Survey (AIS) is a landmark survey designed to examine the prevalence and impairments associated with insomnia and insomnia subtypes in the U.S. The phone survey (approximately 40 minutes) is administered to a representative sample of an anticipated 15,000 subscribers to the nation's largest health plan, Wellpoint, allowing us to link survey data with medical and pharmacy claims data. We plan to investigate a wide range of consequences of insomnia, including daytime impairment, accidents, injuries, lost productivity and health care utilization. We will also examine prevalence and burden of insomnia in sub-samples defined by presence of important comorbidities. The latter are identified by ICD-9 codes from WellPoint medical records, including COPD, osteoarthritis, hypertension, obstructive sleep apnea, neuropathic pain, diabetes, and GERD.
Results: In each case, we evaluate prevalence and incremental predictive effects of insomnia on functioning in comorbid disorders controlling for disorder severity. We describe planned analyses, including diagnostic threshold examination for clinically relevant insomnia based upon symptom clustering, severity, in addition to correlates with daytime impairment and consequences. We are also carrying out special analyses of respondents aged 65+. The AIS is currently in the field enrolling participants with broad geographic and socio-demographic representation.
Conclusion: This presentation describes AIS methods, including instrument development and rationale for choice of scales within the instrument, validation against clinician diagnostic clinical interviews, as well as planned analyses.
Support (optional): sanofi-aventis

0813

INSOMNIA SUBTYPES AND IMPROVEMENT FROM NONPHARMACOLOGICAL THERAPY

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Introduction: Insomnia subtypes of having sleep onset, sleep maintenance, or both sleep problems are examined for how they relate to improvement in response to nonpharmacological therapy.
Methods: Seventy-seven participants (females 48; age 23 to 89, M = 54.18) who were enrolled at one site of a multi-site study were randomly assigned to either a group therapy for insomnia (CBT-I) or a self-paced booklet. In prior analyses (Cousins, et al, 2007), CBT-I outperformed the booklet on a number of sleep variables, although both treatments produced improvement. Participants were eligible for current analyses if they had problems with sleep initiation (n = 15), sleep maintenance (n = 29), or both, "mixed" (n = 33) based on pretreatment diary sleep-onset latency (SOL) and wake after sleep onset (WASO) with means greater than 30 minutes.
Results: Although the mixed group did not have significantly greater baseline SOL or WASO than the initiation or maintenance-problem groups, the mixed group had significantly higher scores than the maintenance group on the Insomnia Severity Index and the Pittsburgh Sleep Quality Index. When comparing individuals from the initiation only with the mixed group on SOL, both reported equivalent improvement ($F = 66.14$, $p < .001$). When comparing participants in the maintenance with the mixed group on WASO, the mixed group (M = 42.07 minutes) reported significantly greater improvement ($F = 11.47$, $p < .001$) than the maintenance only group (M = 17.84 minutes).
Conclusion: Participants with both sleep problems improved significantly more on WASO than those with only sleep maintenance problems despite reporting more severe sleep disturbance. Perhaps having both sleep problems resulted in increased commitment to general, omnibus treatments as studied here. Individualized treatments may be beneficial for those with only sleep maintenance problems.
Support (optional): This research was supported by NIH/NINR grant NR05075.

0814

PHARMACODYNAMIC PROFILE OF THREE NOVEL FORMULATIONS OF ZALEPLON VERSUS PLACEBO AND MARKETED ZALEPLON MEASURED BY ELECTROENCEPHALOGRAPHY IN HEALTHY VOLUNTEERS

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Introduction: Zaleplon is commercially available for sleep induction, but its short half-life has made it less useful for patients with middle-of-the-night awakenings. Three novel formulations of zaleplon were studied in healthy volunteers to determine pharmacodynamic (PD) profile over a 12-hour period post-dosing.
Methods: Non-elderly adults were enrolled in this crossover, double-blind trial. Objective measures of PD were obtained by 4-lead (F4-T4, F3-T3, T4-O2, T3-O1) electroencephalography (EEG) and the Karolinska Drowsiness Test (KDT). EEG and KDT were obtained 1 hour pre-dose (baseline), and at each hour post-dose after receiving a single oral dose of each formulation (A, B, C) of zaleplon (15mg), placebo, or marketed zaleplon (10mg). EEG parameters were calculated on the median of the 4 leads for the standard EEG and for each 3 derivations (Fz-Cz, Cz-Pz, Pz-Oz) for the KDT during eyes-open and eyes-closed sessions. Results for EEG and KDT at each time point were expressed as change from baseline. Drug plasma levels were obtained at the same times.
Results: Eighteen subjects (12 females, 6 males; ages 21-46) had available data. Alpha-Slow-wave Index (ASI), absolute power in the alpha band, and total absolute power varied significantly as a function of treatment ($p<0.001$, $p<0.001$, $p=0.008$, respectively). Formulations A, B and C globally decreased these parameters 3, 4 and 5 hours after administration compared to placebo and marketed zaleplon. KDT parameters correlated with EEG with the greatest sleepiness generally noted at the same periods of time. Results for EEG and KDT corresponded to drug plasma levels, which peaked between 3.9 and 4.9 hours post-dose for the three 15mg formulations and 1.5 hours for zaleplon 10mg. EEG and KDT parameters were comparable to placebo 8 hours post-dosing.
Conclusion: Zaleplon in a novel formulation provided maximum sedation 3 to 5 hours post-administration with no residual effects 8 hours post-dosing.
Support (optional): Study supported by Somnus Therapeutics, Inc.

0815

A RESPONDER ANALYSIS USING THE INSOMNIA SEVERITY INDEX IN OLDER ADULTS TREATED FOR 12 WEEKS WITH ESZOPICLONE 2 MG OR PLACEBO

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Introduction: The Insomnia Severity Index (ISI) measures patient perceptions of insomnia symptom severity and impairments of daytime functioning. The items capture the main symptom-based diagnostic criteria for insomnia and are therefore sensitive to detect changes related to treatment. This abstract presents the results from an individual ISI responder analysis of data collected in a clinical trial of older adults with primary insomnia (PI) treated with eszopiclone 2 mg or placebo.

Methods: Participants (65-85 years) in this double-blind, placebo-controlled trial met DSM-IV-TR criteria for PI and their self-reported sleep was characterized by total sleep times (TST) of ≤6 hr and wake times after sleep onset (WASO) of ≥45 min. Patients were randomized to receive eszopiclone 2 mg (n=194) or placebo (n=194) for 12 weeks. Treatment response was defined as a reduction of ≥6 points from the ISI baseline score to each assessment at Weeks 3, 6, 9, and 12. This criterion was based on prior analyses that identified the minimal clinically important difference to detect changes in various domains of daytime functioning (i.e., work limitations, fatigue, and quality of life).
Results: At all timepoints, the proportion of patients in the eszopiclone 2 mg group who had a treatment response on the ISI was significantly greater than the proportion in the placebo group (all p-values ≤0.001). At each respective week, the proportion of eszopiclone-treated responders was 42.1%, 44.2%, 46.3%, and 48.9% versus 25.5%, 26.6%, 28.6%, and 32.3% of placebo-treated responders. The percentage of patients in both treatment groups with a response increased over 12 weeks of treatment.
Conclusion: In this trial, a significantly greater proportion of eszopiclone-treated older adults with PI achieved a clinically meaningful reduction in ISI scores over the course of 12 weeks of treatment relative to placebo-treated patients.
Support (optional): Support for this study provided by Sepracor Inc.

0816

PHARMACODYNAMIC PROFILE OF THREE NOVEL FORMULATIONS OF ZALEPLON IN NORMAL VOLUNTEERS AS EVALUATED BY THE MULTIPLE SLEEP LATENCY TEST

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Introduction: This Phase I trial was conducted to compare the pharmacokinetics and pharmacodynamics (PD) of three novel formulations of zaleplon with marketed zaleplon and placebo. The multiple sleep latency test (MSLT) was used pre- and post-dose to describe PD over time.
Methods: Nineteen healthy volunteers (13 female, 6 male; ages 21-46) were enrolled in this 5-arm (zaleplon 15mg in formulations A, B, C; placebo; marketed zaleplon (10mg), single-dose, crossover trial with each treatment arm separated by a 4-7 day washout period. In this study, subjects had three assessments pre-dose (-20, -12, -1 hours; mean = baseline) and each hour for 12 assessments post-dose; plasma drug concentrations were also measured at the post-dose time points. Study drug was administered at 09:00; post-dose differences between each formulation and placebo or zaleplon were described with a mixed model on change from baseline.
Results: MSLT changes with placebo administration followed the known circadian time course of shortest MSLT 5 hours post-dose (14:00), with MSLT increasing thereafter, peaking 11 hours post-dose (20:00). Significant treatment differences versus placebo ($p \leq 0.05$) were noted for A (hours 2-4), B (hours 2-4), and C (hours 1-3) versus placebo. Shorter sleep latencies versus zaleplon 10 mg were significant for formulations A ($p<0.01$) and B ($p<0.05$) 4 hours postdose. Sleep latencies decreased from 5-12 hours postdose and were comparable among all treatments. Changes in MSLT paralleled plasma drug concentrations.
Conclusion: Zaleplon 15mg in three novel formulations resulted in significantly decreased MSLT versus placebo and versus marketed zaleplon which indicates differing time courses of sleep-promoting activity and which correspond with plasma drug levels.
Support (optional): Study supported by Somnus Therapeutics, Inc.

0817

PHARMACOKINETIC PROFILE OF SINGLE ORAL DOSES OF ZALEPLON IN THREE NOVEL FORMULATIONS IN NORMAL VOLUNTEERS

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Introduction: Zaleplon is an effective sleep agent with a short half-life. This profile may be advantageous for preventing middle-of-the-night awakening if exposure to zaleplon could be controlled after initiation of natural sleep.
Methods: This was a phase I, double-blind crossover study of single oral doses of zaleplon 15mg in three formulations (A, B, C) with different release characteristics; placebo, and an open comparator arm (marketed zaleplon, 10mg). Nineteen healthy volunteers (13 female, 6 male; ages 21-46) received treatments separated by a 4- to 7-day washout period. Blood samples were drawn predose and at 13 time points up to 12 hours postdose. Noncompartmental analysis was performed to calculate pharmacokinetics (peak plasma concentration [Cmax], time from administration to Cmax [Tmax], lag time [time from administration to drug release], elimination half-life [T1/2], and area under the plasma concentration-time curve to the time of last quantifiable concentration [AUC]).
Results: Relative bioavailability for A, B, and C were 98%, 97%, and 93%, respectively. Lag times for A, B, and C (hours ±SD) were 3.1 ±0.3, 1.9 ±0.3, and 1.2 ±0.5, respectively; Tmax (hours +SD) was 4.9 ±1.0, 4.1 ±0.7, and 3.9 ±0.9 respectively. Marketed zaleplon had no lag time and a short Tmax of 1.5 ±0.8 hours. Plasma concentrations declined after Tmax with a T1/2 (hours ±SD) of 1.5 ±0.3, 1.4 ±0.4, 1.8 ±0.4, and 1.2 ±0.2 for A, B, C, and marketed zaleplon, respectively. AUC (ng●h/mL +SD) was 83.2 ±53.0, 83.1 ±45.7, 79.5 ±57.0, and 56.8 ±26.0 for A, B, C, and marketed zaleplon, respectively. No differences were noted between males and females.
Conclusion: The three novel formulations of zaleplon provided consistent active drug concentrations at different time points after administration with rapid decline after Tmax. Pharmacokinetic profiles differed between formulations and the active comparator, but were similar within treatment arms.
Support (optional): Study was supported by Somnus Therapeutics, Inc.

0818

USE OF THE ADDICTION RESEARCH CENTER INVENTORY (SEDATION SUBSCALE) AND THE KAROLINSKA SLEEPINESS SCALE TO EVALUATE SUBJECTIVE ALERTNESS AFTER SINGLE ORAL DOSES OF ZALEPLON IN THREE NOVEL FORMULATIONS

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Introduction: Different assessment methods are used in clinical trials to evaluate subjective effects of drugs. In this phase I trial, the Addiction Research Center Inventory (ARCI-49) and the Karolinska Sleepiness Scale (KSS) were administered in order to measure changes in subject-perceived alertness after administration of three novel formulations of zaleplon.
Methods: This was a double-blind, crossover, placebo and marketed zaleplon (10mg) controlled study, which compared three novel formulations (A, B, C) of zaleplon (15mg) in healthy volunteers. 19 subjects (13 women, 6 men aged between 21 and 46 years) were enrolled. The ARCI-49, a self-rating 49-item true-false questionnaire, measures subjective effects of drugs with diverse pharmacological actions. Sedation subscale data are presented here. The KSS, a nine-point self-rating Likert scale (1 = very alert and 9 = very sleepy) was also done. Both scales were presented one hour before administration (baseline). ARCI-49 was

administered 1, 3, 5, and 8 hours postdose; KSS was administered every hour for 12 hours postdose.
Results: ARCI-49: Subjects felt significantly more sedated 1 hour after receiving control zaleplon compared with A ($p=0.0048$), B ($p<0.001$), or C ($p=0.012$). KSS: A, B, and C formulations increased subjective sleepiness ($p<0.001$, $p=0.0197$ and $p=0.0261$, respectively) vs placebo; the time course and amplitude of the effect were different between formulations. Compared to zaleplon, all three formulations led to greater subjective feelings of sleepiness at later time points following administration.
Conclusion: Both subjective scales led to the same observation. A significant increase in subjective sedation and sleepiness feelings was noticed under all three formulations. Compared to marketed zaleplon, these increases occurred later with the new formulations of zaleplon.
Support (optional): Study supported by Somnus Therapeutics, Inc.

0819

EPIDEMIOLOGY OF INSOMNIA IN A POPULATION-BASED SAMPLE

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Introduction: The goals of the present study were to estimate the prevalence of insomnia symptoms and syndrome in the general population and to describe the types of products used to promote sleep.
Methods: A telephone survey was conducted in the spring of 2007. The target population consisted of all Canadians aged 18 years and older. A representative sample was obtained using a random digit dialing method programmed to generate geographically stratified phone numbers. Of the 4 869 persons contacted, 2000 (41%) completed the telephone interview. Participants' mean age was 48.6 years old (range 18-99 years) and 60.5% were women. For the purpose of another study, the province of Quebec was over-sampled compared to the other Canadian regions (60% of the sample). Data were weighted to adjust for differences between gender and region representation in the sample and that of the last national census.
Results: Of the total sample, 39.9% presented at least one insomnia symptom (i.e., initial, middle, late insomnia) for a minimum of three nights per week and 36.5% reported non-restorative sleep. Conversely, 54.9% of the sample was satisfied with their sleep and reported no insomnia symptoms. When looking at the DSM-IV-TR and ICD-10 diagnostic criteria, 10.9% of the sample met the criteria for an insomnia syndrome. Regarding consultations for sleep problems specifically, 13.1% of the overall sample and 23.5% of the individuals with an insomnia syndrome reported having consulted once in their lifetime for sleep difficulties. Moreover, 9.9% of the total sample and 28.9% of the subsample of individuals with insomnia reported having used prescribed medications in the year preceding the survey, while 43% reported not having used any sleep promoting products despite their difficulties.
Conclusion: These results confirm the high prevalence of insomnia in the Canadian general population and the low level of consultation and treatment-seeking for this condition.
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0820

RELATIONSHIP OF SUBJECTIVE AND OBJECTIVE ENDPOINTS FOR OUTCOMES OF A PHASE I TRIAL OF A POTENTIAL NEW SLEEP AGENT

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Introduction: A phase I placebo-controlled, crossover double-blind study employed objective and subjective parameters to investigate the pharmacodynamic (PD) central nervous system (CNS) profile of three novel formulations of Zaleplon 15mg. This analysis examines the correlation between these parameters in accurately defining PD profile.
Methods: Nineteen healthy volunteers (13 females, 6 males; ages 21-46) were enrolled and received 5 study treatments: Zaleplon 15mg in formulations A, B, and C; placebo; marketed Zaleplon 10mg, each treatment separated by a 4-7 day washout period. Objective endpoints were changes from baseline in electroencephalography (EEG) calculated on the median of 4 leads for the standard EEG and for each 3 derivations (Fz-Cz, Cz-Pz, Pz-Oz) for the Karolinska Drowsiness Test (KDT) during eyes-open and eyes-closed sessions. Subjective endpoints included changes from baseline for the multiple sleep latency test (MSLT) and the Karolinska Sleepiness Scale (KSS). Each test was given -20, -12, and -1 hour predose to establish baseline, and each hour for 12 hours postdose. PD CNS effects were analyzed through a 2-way mixed-model ANOVA with treatment as a 5-level between groups factor, and as a 12-level within group factor.
Results: There was a significant treatment effect for most PD endpoints. Between treatment contrasts indicated that A, B, and C significantly ($p<0.001$, $p\leq0.01$, $p\leq0.05$, respectively) differentiated from placebo for objective and subjective evaluations of sleepiness. Treatment over timed interactions was observed for the KSS and two EEG parameters (alpha slow wave index and alpha 2 absolute power). A, B, and C had a greater delayed and prolonged time course compared to marketed Zaleplon as demonstrated by all endpoints. A positive relationship between Zaleplon plasma concentration and drug-related PD effects was noted with peak activity 4-5 hours postdose.
Conclusion: PD profile of three novel formulations of Zaleplon was consistent as defined by objective and subjective evaluations.
Support (optional): The study was supported by Somnus Therapeutics, Inc.

0821

EFFECTIVENESS OF A COGNITIVE-BEHAVIORAL TREATMENT PROGRAM FOR CHRONIC INSOMNIA

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Introduction: Over the past several decades, numerous studies have been published supporting the efficacy of multi-component cognitive-behavioral treatment strategies for insomnia (CBT-I). However, few have evaluated the effectiveness of CBT-I in a clinical setting. The present study reports treatment outcomes for an insomnia treatment program in an independent sleep disorders center.
Methods: A chart review of patients seen in our Insomnia Treatment Program and Behavioral Sleep Medicine Clinic was undertaken. Patients referred for evaluation and treatment, with a presenting complaint of chronic sleep onset insomnia (SOI), sleep maintenance insomnia (SMI), or both sleep onset and sleep maintenance insomnia (SOMI) were included. Patients completed between 2 and 10 treatment sessions, and sleep was monitored prospectively using sleep diaries.

Results: 115 cases with prolonged (≥30 minutes) sleep onset latency (SOL) and/or wake after sleep onset (WASO) and who attended at least 2 treatment sessions were evaluated. Of these, 45 (39.1%) experienced only SOI, 20 (17.4%) only SMI, and 50 (43.5%) with SOMI. Those with SOI showed significant improvement in SOL, mean difference was 58.4 minutes, t(44)=7.385, p<0.0001. Those with SMI showed significant improvement on WASO, mean difference was 30.7 minutes, t(19)=4.676, p<0.0002. Those with SOMI showed significant improvement on both SOL (mean difference was 40.4 minutes, t(49)=6.186, p<0.0001) and WASO (mean difference was 41.6 minutes, t(49)=6.260, p<0.001). Corresponding effect sizes(Cohen's *d*) were 1.10 for SOI, 1.05 for SMI, and .87, .89 on SOL, WASO for SOMI. Among the 64 patients who completed 5 or more treatment sessions, there were significant improvements (p<.001) on the presenting complaint(s), as well as other outcomes measures including sleep efficiency (SE), average nightly awakenings (NOA), total sleep time (TST), and average nights of sleep medication use/week (SMU). Corresponding effect sizes were 1.29 for SE, .34 for NOA, .54 for TST and .62 for SMU.
Conclusion: Clinically meaningful treatment effects were found for both the primary complaint, as well as other sleep parameters, with effect sizes comparable to those found in controlled clinical trials and meta-analyses of CBT-I. CBT-I appears to be an effective treatment approach for various types of chronic insomnia when applied in a "real world" clinical setting.

0822

INSOMNIA AS A RISK FACTOR FOR HEALTH PROBLEMS: A LONGITUDINAL STUDY

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Introduction: Longitudinal studies indicate that health problems are associated with a higher incidence of insomnia suggesting that they may represent a risk factor. Little research, however, has addressed if insomnia is itself a risk factor for developing health problems. Therefore, the aim of the present study was to investigate the role of insomnia in the development of health problems.
Methods: Participants (n = 997 adults, mean age = 45.0 years, 51.7% women) completed a questionnaire assessing sleep, physical and mental health, lifestyle habits, personality and demographics at baseline, and at 6- and 18-month follow ups. They were divided into two groups: (a) insomnia symptoms or syndrome (n = 358) and (b) good sleepers (n = 482) according to baseline sleep. The main dependent variable was self-reported current health problems.
Results: Among participants without health problems at baseline, insomniacs did not show a significant increased risk of developing health problems 18 months later compared to good sleepers. However, good sleepers who had developed insomnia had a significantly higher risk of developing at least one health problem compared to those who remained good sleepers (OR = 2.04). Also, participants whose insomnia persisted both at 6 and 18 months after baseline exhibited a significantly greater risk of developing at least one health problem by the last follow up, compared to those who remained good sleepers for the same interval (OR = 2.14).
Conclusion: The results suggest that the incidence of insomnia is associated with the development of health problems, but the direction of that link remains unclear as insomnia could either constitute a risk factor or a consequence of health problems. However, the persistence of insomnia seems a risk factor for the subsequent development of health problems.
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0823

EMOTIONAL RESPONSES TO SYMPTOMS-RELATED STIMULI IN POOR SLEEPERS AND IN CONTROL PARTICIPANTS: PRELIMINARY RESULTS

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Introduction: An attentional bias for sleep-related information is suggested to be a maintaining factor for primary insomnia (e.g. Espie et al., 2006). It has been discussed that different emotional reactions could be strongly associated with this effect. Emotions can be described as the result of two dimensions: Valence and Arousal. This study examined whether the emotional valence predicts different psychophysiological responses to stimuli related and not related to the symptoms in poor sleepers and in control participants.
Methods: Up to now, 22 university female students took part to the study. Participants were assigned to three groups: people referring only symptoms of insomnia (PI; N=9), people referring both symptoms of insomnia and symptoms of eating disorders (MG; N=7), people referring no sleep or eating problems (CG; N=6). Participants were shown 5 blocks of 10 pictures each, which differed in the content and in the emotional valence: neutral stimuli (N), sleep-related positive (S+) and negative (S-) stimuli, eating/body shape-related positive (B+) and negative (B-) stimuli. Facial electromyography activity over the corrugator and the zygomatic muscles, heart rate (HR) and skin conductance (SC) were recorded during the pictures viewing.
Results: Analyses of the variance (ANOVAs) conducted to compare the 3 groups in the 5 conditions showed: an increase of the SC (F(4,76)=4.89; p=0.001) in response to negative stimuli (both S- and B-); only in the PI a decrease of activity over the corrugator muscle in response to B- and an increase of activity of this muscle in response to S- (F(8,76)=2.10; p=0.046).
Conclusion: Findings suggest that people with insomnia present an altered emotional response to negative symptoms-relevant stimuli compared to controls participants. The valence dimension differentiates people with insomnia and controls in the emotional responses to stimuli related with the symptoms. These preliminary results have to be confirmed in a larger sample.

0824

SLEEPLESS IN SWEDEN: EFFECTS OF COGNITIVE THERAPY ON YOUTHS WITH PRIMARY INSOMNIA

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Introduction: Sleeping difficulties are an increasing problem for youths, but there is a lack of treatment research for this age group. The aim of this study was to investigate the effects of Cognitive Therapy (CT-I), on youths with primary insomnia. Treatment was based on current cognitive theories about psychological maintaining factors of insomnia, and had never been tested on youth before.
Methods: The study was conducted according to a Single-Case AB Phase design with pre- and posttests. Three youths between the ages of 16 to 18 (2 male) were recruited through school health care, and participated in a seven week long treatment, after 1-2 weeks of baseline measures. All met diagnostic criteria for primary insomnia and one met the criteria for co-morbid depression. A sleep diary was used throughout the treatment. A follow-up measure including one week of sleep diary was conducted three months later. Visual inspection and statistical effect size measures were used to analyze outcome.
Results: None of the participants fulfilled the diagnostic criteria for insomnia, nor depression, after treatment. Daytime functioning had in-

creased, and individual treatment goals, such as decreased sleep onset latency, were met to a large extent. Daily measures showed that changes in sleep related symptoms and daytime symptoms, like tiredness and concentration difficulties, varied among the participants, with larger improvements for those who had elevated scores during baseline. The degree of maintaining cognitive processes (as worry and excessive monitoring of sleep related threats) had decreased. These results were maintained at the follow-up measure.
Conclusion: CT-I is a promising treatment for youths with insomnia and the treatment should be tested further in randomized controlled studies.

0825

RELATIONSHIPS BETWEEN SUBJECTIVE AND OBJECTIVE SLEEP MEASURES AND THE DENSITY OF SPONTANEOUS K-COMPLEXES AND SLEEP SPINDLES IN INSOMNIA INDIVIDUALS AND GOOD SLEEPERS

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Introduction: Recently, our group has shown that the density of spontaneous K-Complexes and spindles in stage 2 were similar in insomnia individuals and good sleepers while between groups quality of sleep varied. This study aims at investigating if subjective and objective sleep measures are related to the density of both phasic events in each group.
Methods: The sample included 16 psychophysiological insomnia sufferers (INS; Mage = 43.4 years) and 14 good sleepers (GS; Mage = 38.1 years). From the second (N2) and third night (N3) of a four consecutive PSG recordings nights protocol, subjective (S) and objective (O) sleep measures were derived (SOL, WASO, TST, SE). Spontaneous K-Complexes (KC) and spindles were scored at Cz in all night stage 2 further subdivided in early (2E) and late (2L).
Results: Significance level was set at $p<.05$. Between nights comparisons revealed longer SSOL [t(13)=2.28] and STST [t(13)=2.41] in GS on N2 than on N3. On the other hand, INS had longer OSOL on N2 than on N3 [t(14)=2.46]. No other significant differences were observed between N2 and N3 for subjective and objective sleep measures in either group. In GS, SSOL was negatively associated with KC density (r =-.54) and spindle density (r=-63) in 2E, but positively associated with spindle density in 2L (r=.66). In INS, SSOL was positively associated with KC density in 2L (r =.62). In GS, N2 OSOL correlated negatively with both KC (r =-.56) and spindle density in 2E (r =-.63).
Conclusion: In good sleepers, longer sleep latency was associated to decreased densities in both phasic events early in the night. These early night associations were not observed in insomnia sufferers. It is possible that objectively longer sleep latency disrupts normal sleep homeostasis which is then reflected through increased phasic activity at the end of the night, and this, only in good sleepers.
Support (optional): Research supported by the Canadian Institutes of Health Research (# 49500 and # 86571).

0826

RELATIONSHIPS BETWEEN THE FREQUENCY AND DENSITY OF SPONTANEOUS K-COMPLEXES AND SLEEP SPINDLES IN INSOMNIA INDIVIDUALS AND GOOD SLEEPERS

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Introduction: The spindle has been associated to sleep protection mechanisms. The role of the K-Complex remains equivocal: arousal, forerunner of delta waves or sleep protection. Recently, our group has shown that the frequency and density of K-Complexes and spindles were similar between insomnia individuals and good sleepers. However, the relationship between these two phasic events was not investigated. The present study aims at documenting the relationship between the density of spindles and K-Complexes in stage 2 sleep in insomnia individuals and good sleepers.
Methods: The sample included 16 psychophysiological insomnia individuals (INS; Mage = 43.4 years) and 14 good sleepers (GS; Mage = 38.1 years). Spontaneous K-Complexes and sleep spindles were scored at Cz in all night stage 2, further subdivided in early (2E) and late (2L), on two consecutive nights (N2 and N3) of a four night protocol.
Results: In all participants, many significant negative correlations between phasic events were found on N2 while none were observed on N3. Correlations between the frequency of K-Complexes and the frequency of spindles in total stage 2 (r =-.68) as well as between the frequency of K-Complexes in 2E and the frequency of spindles in 2L (r =-.80) were observed on N2.
Conclusion: In all sleepers, as the frequency of K-Complexes increased, the frequency of sleep spindles usually decreased, and vice-versa. These results suggest that both events may play similar role or/and may share similar physiological regulation mechanisms distributed along a continuum (ex. cortico-thalamic polarization). As such, low polarization would be associated with greater spindle frequency while high polarization (hyperpolarization) would be associated with greater K-Complex frequency. In addition, these results highlight that K-Complexes and spindles may be markers of sleep recovery on a second night of PSG recordings after a possible first night effect due to laboratory settings.
Support (optional): Research supported by the Canadian Institutes of Health Research (# 49500 and # 86571).

0827

COMPARING BEHAVIORAL THERAPY FOR INSOMNIA RESPONSE IN OLDER ADULTS WITH AND WITHOUT A HISTORY OF CHRONIC PAIN

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Introduction: When treating sleep disorders in older adults, comorbid medical conditions can raise concerns about efficacy of treatment. This may be particularly true in chronic pain. Previous research has shown that significant gains can be made when using Cognitive-Behavioral Therapy for insomnia with individuals with chronic pain. However, this research lacked a non-pain group. We hypothesize that individuals with insomnia and a history of chronic pain (HCP) who receive Behavioral Therapy for insomnia (BTi) will show significant improvements on the outcome measure, percent change in sleep efficiency (SE), but individuals without chronic pain will have greater improvements.
Methods: Older adults with insomnia (M_{age}=70.3,SD=7.86) completed baseline, 4-week BTi treatment (stimulus control, sleep restriction, relaxation) or control, post-treatment, and 3-month follow-up. Throughout the study individuals completed daily sleep diaries. A 2x2 repeated measures ANOVA compared SE percent change from baseline, [(Time2-Time1)/Time1]x100, at post treatment and follow-up. Between-groups factors were BTi versus control and presence/absence of HCP.
Results: Treatment(M=22.4%chg) resulted in a significant percent change compared to control(M=2.4%chg) in SE over baseline, [$F(2,42)=9.87, p<.001$, Roy'sTheta=.49] and was significant at post-treatment and follow-up. The treatment group had a significant difference between non-HCP (M=30.92%chg) and HCP (M=13.94%chg) [$F(1,39)=4.21, p<.05, \eta^2=.10$]. In the HCP group, there was no significant difference between control and treatment. Rates of clinically significant change (SE>85%) in non-HCP treatment group were 50% at post-treatment and 61.1% at follow-up, and those with HCP were 70.6% and 88.2%, respectively. The difference between these groups was not significant.
Conclusion: Our hypothesis that non-HCP participants would demonstrate greater improvement than those with a HCP was confirmed. However, both treatment groups achieved high rates of average SE in

the clinically significant range suggesting that BTi can be a brief but effective sleep intervention among individuals with a HCP. Analyses of a wider range of sleep variables will be included in the final presentation.
Support (optional): NIH/NIA (1 R21 AG024459-01 Christina S. McCrae, PhD, PI)

0828

ERP MEASURES DURING SLEEP IN PSYCHOPHYSIOLOGICAL AND PARADOXICAL INSOMNIA SUFFERERS

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Introduction: Using PSA, high cortical arousal has been reported during the night in psychophysiological insomnia sufferers (Psy-I), and even more so in paradoxical insomnia sufferers (Para-I). Although event-related potentials (ERPs) provide powerful indexes of arousal levels in sleep, studies using them are scarce. The objective of the present study is to use ERPs (N1 and P2) to document arousal levels in Psy-I, Para-I and good sleepers (GS) in stages 2, 3-4 and REM sleep.
Methods: Eight Psy-I (mean age = 40.4y), 9 Para-I (mean age = 43.1y) and 10 GS (mean age = 43.9y) underwent four consecutive nights of PSG (N1 to N4). ERPs N1 and P2 were recorded during the fourth night in stages 2, 3-4 and REM. Auditory stimuli consisted of 'standard' frequent (70 dB, 2000 Hz, .85 probability) and 'deviant' rare stimuli (90 dB, 1500 Hz, .15 probability).
Results: Mixed ANOVAs on N1 amplitude showed significant main effects of auditory stimuli $F(1, 24) = 12.99$, $p < .01$. Mixed ANOVAS on P2 amplitude resulted in significant effects for auditory stimuli ($F(1, 23) = 30.23$, $p = .00$). Furthermore, Recording Time × Auditory Stimuli ($F(2, 46) = 4.13$, $p = .04$) was also significant. Analyses on latency measures of N1 and P2 revealed no significant effects at all. No between groups differences were found.
Conclusion: These preliminary results suggest that the amplitude and latency of the different ERPs is similar during stages 2, 3-4 and REM sleep in insomnia sufferers and good sleepers. Hyperarousal, as measured with ERPs, might thus be limited to the awake and sleep-onset periods and not sleep in insomnia sufferers.
Support (optional): Research supported by the Canadian Institutes of Health Research (# 49500 and # 86571).

0829

NIGHTTIME CARDIAC ARRHYTHMIAS ARE NOT INCREASED IN APPARENTLY HEALTHY SUBJECTS WITH CHRONIC INSOMNIA: A RETROSPECTIVE ANALYSIS

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Introduction: Chronic insomnia has been linked to increased risk for cardiovascular morbidity and mortality. However, whether cardiac arrhythmias are more frequent in this condition has never been thoroughly investigated. We assessed presence and quantification of supraventricular and ventricular arrhythmias during sleep in subjects with chronic insomnia as compared to good sleepers.
Methods: We examined polysomnographic recordings (PSG) of 85 subjects (45 men, age 48±10 years) with chronic primary insomnia and 57 good sleepers (33 men, age 41±13 years). Subjects were free of major medical or psychiatric comorbidities and other sleep disorders, and were not taking medications potentially affecting the heart rhythm. Electrocardiographic recordings (ECG) were extracted from PSG and analyzed using Vision Premier© software to assess the occurrence of overnight premature ventricular complexes (PVCs) and premature supraventricular complexes (PSVCs). Overall and hourly incidence of PVCs and PSVCs were assessed. Average heart rate (HRavg), maximum heart rate (HRmax) and minimum heart rate (HRmin) were also measured. Independent-samples t-test and Mann-Whitney U-test were used for comparison. Pearson correlation coefficients were also calculated between ECG variables and sleep variables, which included: sleep efficiency, wake time after sleep onset, number of awakenings and micro arousal index.
Results: HRavg, HRmax and HRmin were similar between the two groups. Overall PVCs did not differ between insomniacs (4.5±24.9) and good sleepers (2.6±14.7) ($p=0.6$). None of the subjects had malignant ventricular arrhythmias. No differences were observed in PSVCs among insomniacs (20.4±88.2) when compared to good sleepers (13.9±80.5) ($p=0.7$). PVCs and PSVCs did not appear to be associated with any of the sleep variables considered.
Conclusion: Our data suggest that nighttime supraventricular and ventricular premature complexes are not increased in apparently healthy subjects with chronic insomnia and are not associated with objective indexes of poor sleep. Whether these findings can be extended to insomniacs with overt heart disease remains to be investigated.

0830

SLEEP IMPROVES IN PATIENTS DISCONTINUING MEDICATION USE WITH CBT-I

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Introduction: Although hypnotics are not a recommended treatment for chronic insomnia, many patients become long-term users. Patients who use hypnotics for an extended period may develop a tolerance or suffer withdrawal (e.g. rebound insomnia) following discontinuation. CBT-I has been shown to be efficacious in treating insomnia, but less is known about its effectiveness in assisting "real world" patients in discontinuing use of hypnotics. The present study reports rates of discontinuation in those participating in a CBT-I treatment program.
Methods: Sleep data was obtained from weekly sleep diaries completed by patients referred for evaluation and treatment of insomnia who completed at least four treatment sessions of CBT-I.
Results: Of patients (n=86) who attended at least four sessions of CBT-I, 46 patients used hypnotic medication 3 to 7 days per week at baseline. The mean medication use of this group was approximately 6 days per week. 78.3% discontinued hypnotic use completely during treatment. Hypnotic discontinuers (n=36) attended between 5 and 6 sessions on average. Despite eliminating use of medication, overall SOL was reduced by 49 minutes ($t(35)=5.01$, $p<.001$); WASO was reduced by 30 minutes ($t(30)=3.56$, $p=.001$); SE increased by 14% ($t(35)=4.53$, $p<.001$); and TST remained stable in patients treated with CBT-I. SOL and WASO both fell below 30 minutes at the final treatment session, reflecting clinically significant improvement. Sleep efficiency improved from 70% at baseline to 85% at the final treatment session and hypnotic discontinuers reported feeling better upon awakening following treatment ($t(34)=2.22$, $p=.03$).
Conclusion: Insomnia patients who discontinued medication use following treatment with CBT-I reported clinically meaningful effects of treatment on sleep onset latency, wake after sleep onset, and sleep efficiency as well as maintenance of total sleep time. CBT-I appears to be an effective treatment for insomnia in patients who wish to discontinue hypnotic use.

0831

PRELIMINARY EVALUATION OF THE INSOMNIA SEVERITY INDEX IN OPERATION ENDURING FREEDOM/ OPERATION IRAQI FREEDOM VETERANS

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Introduction: Sleep disturbance, including insomnia, is frequently reported by Operation Enduring Freedom/Operation Iraqi Freedom (OEF/OIF) veterans. A brief, psychometrically sound, self-report screening instrument is needed for the clinical evaluation of insomnia in returning veterans. The goals of this study were to determine the initial psychometric properties of the Insomnia Severity Index (ISI) and describe insomnia severity in OEF/OIF veterans.
Methods: A retrospective chart review was conducted. The ISI, a 7-item brief screen of perceived insomnia severity, was administered as part of the neuropsychological evaluation of OEF/OIF veterans. Demographic and clinical characteristics were extracted from the electronic health record.
Results: The 76 veterans (5 females) were 28.9 (SD=5.9) years of age. The majority of veterans had served in Iraq with an average service duration of 14.4 (SD=6.1) months. Fifty percent of the veterans had a PTSD diagnosis. Sleep medication was prescribed for 55.3% of the veterans and 22.4% had an insomnia diagnosis. The Cronbach's alpha coefficient of the ISI was .90 with item-total correlations ranging from .58 to .84. A principal axis factor revealed one extracted factor that explained 59.2% of the variance, had an Eigenvalue of 4.1, and demonstrated factor loadings from .60 to .91. The ISI mean score was 15.2 (SD=6.7). Moderate to severe insomnia was found in 57.9% of veterans.
Conclusion: Initial support was provided for the psychometric properties of the ISI in returning veterans. The ISI may be useful for clinical purposes in this population but further research is needed to evaluate its psychometric properties including validity, cut-off scores, sensitivity, and specificity. The substantial insomnia difficulty experienced by OEF/OIF veterans underscores the need to test evidence-based interventions in this population.

0832

SLEEP/WAKE COMPARISONS OF INSOMNIA SUFFERERS WITH/WITHOUT FIBROMYALGIA

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Introduction: Fibromyalgia (FM) patients often present with insomnia complaints that mimic the complaints of other insomnia sufferers and show some response to cognitive-behavioral intervention. However, optimizing FM treatment response may depend on fashioning therapy to the specific sleep/wake symptom topography of FM. The current study attempted to identify sleep and wake symptom differences between female insomnia sufferers and a group of women with FM and comorbid insomnia.
Methods: The sample comprised 46 female FM patients enrolled in an insomnia treatment study and a group of 134 women insomnia sufferers enrolled in a diagnostic reliability/validity study at the same academic medical center. All participants were between 21 and 65 years old and met Research Diagnostic Criteria for insomnia disorder to qualify for entry into their respective parent study. Participants completed several questionnaires including the Pittsburgh Sleep Quality Index (PSQI), Medical Outcomes Study Short Form (SF-36), Dysfunctional Beliefs and Attitudes Scale (DBAS), and Profile of Moods States (POMS). Questionnaire scores and common sleep diary measures were extracted and used to compare the two groups. Two-sample t-tests and Wilcoxon rank sum tests were used for group comparisons as appropriate to ascertain statistically significant group differences.
Results: Relative to the comparison group of mixed insomnia sufferers, those with FM had significantly lower diary measures of middle of the night wake time (34.2±22.5 min. vs. 47.7±34.3 minutes; $p < .03$) and SF-36 Physical Component scores (29.1±8.5 vs. 43.4±11.6; $p < .0001$). In contrast, the FM group had higher SF-36 Mental Component scores (47.2±10.1 vs. 42.7±12.4; $p < .03$). The groups did not differ significantly on most diary measures or in regard to their POMS, DBAS and PSQI scores.
Conclusion: Findings would imply that, in many respects, the insomnia disorders of FM patients resemble those displayed by other insomnia patients. However, optimal treatment of insomnia in FM may benefit by therapies that specifically target daytime physical sequelae of nighttime sleep difficulties and the FM disease in general to maximize treatment benefits.
Support (optional): National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) Grant Number R01AR052368-01A1

0833

PREVALENCE OF CO-EXISTING OBSTRUCTIVE SLEEP APNEA IN PATIENTS WITH CHRONIC INSOMNIA

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Introduction: The prevalence of obstructive sleep apnea (OSA), among patients whose chief complaint is chronic insomnia, has been reported to range from below 10% to above 50%. To further explore OSA prevalence in insomnia, we used a validated OSA questionnaire followed by polysomnography (PSG) in evaluating a sample of patients who responded to recruitment ads for an insomnia trial.
Methods: A total of 477 adults (253 female, 219 male, 5 gender not recorded; mean age 57.3±12.9 years, 57 age not recorded) responded to recruitment ads; among whom, 231 chose not to participate in preliminary phone screen. The remaining 246 were asked questions from the Berlin Questionnaire (BQ) to identify those at high risk for OSA. The BQ is a validated instrument with high predictability (≥2 positive categories indicates high risk) for sleep apnea. Persons with low risk underwent comprehensive medical history review and physical examination (H&P), and diagnostic laboratory PSG.
Results: Of 246 chronic (≥6 months) insomniacs screened by phone, 61 (31%; 29 women, 32 men; mean age 57.5±12.1 years) were identified as high risk for OSA with the BQ. Among 97 participants identified as low risk for OSA, another 7 were re-assigned as high-risk upon H&P by an experienced sleep physician and 13 others were found to exhibit OSA (AHI ≥ 10 by ASDA 1999 criteria) with PSG. Combined, 33% of chronic insomniacs met BQ or PSG criteria for clear OSA.
Conclusion: In a sample not necessarily representative of a local population, but also presumably not biased for presence of OSA, approximately 1/3 of individuals with chronic insomnia exhibited OSA based on BQ (high risk) or PSG (AHI ≥ 10, by traditional conservative criteria). These results, combined with those of previous studies, suggest a need for careful assessment of all patients complaining of chronic insomnia symptoms to recognize and address co-existing OSA.
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0834

BRIEF BEHAVIORAL TREATMENT FOR INSOMNIA IN MILITARY VETERANS: PRELIMINARY FINDINGS

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Introduction: Chronic comorbid insomnia is prevalent in military veterans. This pilot study aimed at adapting a brief treatment for insomnia

(BBTI) in combat-exposed military veterans (MV) and evaluating its credibility, acceptability, adherence, and possible therapeutic effects.
Methods: Twenty military veterans (19 men, Age: 54.3 ±4.7 years old) enrolled in this study. Visual analog scales were used to assess treatment credibility, acceptability and satisfaction with BBTI. Veterans completed the Insomnia Severity Index (ISI) and the Pittsburgh Sleep Quality (PSQI) pre- and post-BBTI. BBTI was delivered over 2 face-to-face sessions, and 2 brief telephone contacts over a period of 4 weeks. Session 1 focuses on education and on tailoring instructions for sleep restriction and stimulus control to each participant. On subsequent weeks, contacts focused on the review of progress and obstacles to adherence, using prospective sleep diary and actigraphy data.
Results: Eleven veterans initiated and completed BBTI. Nine were unable to start BBTI-MV due to family/work obligations. Chronic insomnia was comorbid with subthreshold or full criteria for posttraumatic stress disorder (n=6), other anxiety disorders (n=5), and/or depression (n=1). Pre-BBTI, treatment expectations reflected some skepticism, but were generally positive. Veterans attributed high credibility (70%±22%) to BBTI and high satisfaction (98%) with BBTI. Few barriers to adherence were encountered, and 98% of sessions were completed. Post-BBTI, 5 veterans showed a reduction ≥ 6 points on the ISI, and 8 showed a reduction by ≥ than 3 points on the PSQI. Four of the eleven veterans achieved ISI and PSQI scores below clinical thresholds post-BBTI.
Conclusion: These data suggest that BBTI may be associated with significant improvements in chronic insomnia in military veterans. BBTI is acceptable, credible, and associated with high levels of satisfaction. BBTI may be a helpful first-line adjunct intervention in returning veterans with insomnia comorbid who experience post-deployment adjustment difficulties.
Support (optional): US Department of Defense (W81XWH-06-1-0257), and the National Institutes of Health (AG00972; MH080696)

0835

SODIUM OXYBATE AND ZOLPIDEM IN THE TREATMENT OF CHRONIC INSOMNIA: A RANDOMIZED, DOUBLE-BLIND, DOUBLE-DUMMY, PLACEBO-CONTROLLED, 3-ARM, PARALLEL-GROUP STUDY

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Introduction: Sodium oxybate (SXB) is known to impart dose-dependent soporific effects in animals and humans, but has not been tested in a controlled fashion in patients with chronic insomnia. This 12-week trial compared the effects of nightly SXB to placebo (PBO). For reference, effects of zolpidem (ZOL) were assessed, in parallel.
Methods: 32 women and 17 men (age 53.2±12.3 years, range 20-76) with insomnia ≥6 months received double-dummy, randomized, blinded SXB+PBO, ZOL+PBO, or PBO nightly, with blinded flexible-dose titration weeks 1-4 (target dose: 6-9g/night for SXB and 5-10mg/night for ZOL), and fixed-doses weeks 5-12. Measures included PSG and questionnaires at baseline and end of weeks 4 and 12. ANOVA was performed to compare change scores from baseline.
Results: Mean doses were 4.29±1.60g/night for SXB and 9.17±1.92mg/night for ZOL. A significant treatment effect was not seen for TST, SE, SOL, or WASO; however, all groups had a significant improvement from baseline to week 12 for Insomnia Severity Index, Epworth Sleepiness Scale (ESS), and Pittsburgh Sleep Quality Index. Significant ($p<0.05$) improvement in overall insomnia was observed with CGI ratings for both active treatments. SXB reduced S1 shifts and awakenings compared to PBO ($p<0.05$), and increased SWS% compared to PBO and ZOL ($p<0.05$). On the POMS fatigue measure, SXB and ZOL produced a decrease from baseline to week 4, and from weeks 4 to 12, SXB showed a further decrease in fatigue while ZOL returned to baseline. SXB produced significantly ($p<0.05$) greater reductions in ESS compared with PBO. The most common adverse events (AEs) were dizziness (67%) and nausea (60%) for SXB and grogginess (50%) and headaches (39%) for ZOL. There were no severe AEs.
Conclusion: SXB may benefit both sleep and daytime symptoms in patients with chronic insomnia. Insufficient power for most parameters was a planned limitation of study; replication with a larger sample is needed.
Support (optional): Work funded, in part, by Jazz Pharmaceuticals, Sanofi-Aventis, and Cephalon, Inc.

0836

THE CORRELATION BETWEEN OUT OF POCKET EXPENSE AND ATTENDANCE FOR INSOMNIA GROUP TREATMENT

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Introduction: Group format has been shown to be a viable mode of delivery for cognitive behavioral therapy for insomnia (CBTI). As demonstrated in the literature, improvements seen after CBTI either in individual or group format are largely maintained at follow-up. With a limited number of practitioners trained to provide CBTI and a growing number of patients seeking this treatment, utilizing group format can be advantageous. Although CBTI is effective patients may be reluctant or unwilling to access treatment if their insurance does not cover the service or covers only a small percentage. The purpose of this study is to evaluate whether the out of pocket expense (OPE) is associated with attendance in group CBTI.
Methods: The sample consisted of 99 consecutive cases (68 females, 31 males; age 19-81 yrs, M= 45.97 ± 12.26 yrs) that were placed on a list to receive one of 5 insomnia group treatments over the course of a year. The cost of the treatment per session was 70 dollars. The CBTI group consists of 7 sessions spread over 9 weeks and each session is approximately 1 ½ hours. OPE was calculated as the amount the patient would need to pay out of pocket to attend each group session.
Results: An independent samples t-test showed significant difference in OPE ($t= 3.56$, $p < .001$) between those that did not attend any of the group sessions (N= 65; M= 47.93 ± 23.82) and those that attended at least 1 session (N= 34; M= 30.19 ± 23.04). A Pearson correlation revealed no significant correlation between OPE and number of sessions attended ($r= .258$, $p= .140$).
Conclusion: Patients that attended treatment paid 17 dollars less out of pocket than those who did not attend. The results suggest that out of pocket expense hinders access to a cost effective treatment of insomnia.

0837

THE ASSOCIATION BETWEEN SELECTIVE ATTENTION FOR SLEEP-RELATED CUES AND POLYSOMNOGRAPHICALLY MEASURED SLEEP IN PRIMARY INSOMNIA

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Introduction: Although attentional preference for sleep-related cues has been shown to be evident in primary insomnia (PI), the association with objectively measured sleep has not been investigated.
Methods: Thirty patients with PI and thirty healthy controls were studied using a visual dot probe task (VDP) and an emotional Stroop task (EST). Polysomnography (PSG) was carried out in a sub-sample (n=22) of patients in the subsequent night.
Results: PI patients revealed a significant sleep-related attentional bias in the EST and a trend towards significance in the VDP, when compared with the control group. VDP attentional bias scores were positively correlated with total sleep time, sleep efficiency and the amount of slow wave sleep in the subsequent night. EST attentional bias scores were

positively correlated with the duration of PI but not with subsequent PSG parameters. No correlation has been observed between the two tasks.
Conclusion: VDP and EST seem to measure different aspects of sleep-related attentional bias. We suggest that the pictorial VDP is more likely to be influenced by a motivational state (sleep pressure), while the verbal EST predominantly measures trait aspects of primary insomnia.

0838

THE EFFECT OF DYSFUNCTIONAL BELIEFS, SELF EFFICACY AND DECISION BALANCE ON HYPNOTIC TAPERING IN PATIENTS WITH PRIMARY INSOMNIA

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Introduction: Gradual dose tapering is a common practice applied to reduce the use of hypnotics in clinical settings. Previous researches have been conducted to assess the predictability of some pharmacological factors on the successfulness of hypnotic tapering. Less attention was paid to the psychological factors that may be associated with drug tapering. The current study is to investigate the association between cognitive factors and hypnotic tapering, with the hypothesis that dysfunctional beliefs may affect hypnotic tapering through the mediation of self efficacy and decision balance.
Methods: Thirty-seven patients with primary insomnia were recruited from a general hospital to participate in a 10-week hypnotic tapering program. All participants had to complete a set of questionnaires including the Dysfunctional Beliefs and Attitudes about Sleep Questionnaire (DBAS), a decision balance questionnaire assessing the perceived pros and cons of hypnotic tapering and a single-item self-efficacy rating scale before and after administration of a hypnotic tapering plan. During the 10-week tapering period, each participant was required to keep a sleep diary to evaluate the changes in sleep parameters and the status of drug use.
Results: The correlation between dysfunctional beliefs and the amount of drug tapering did not reach significance, indicating no direct association between dysfunctional beliefs and tapering behavior. However, decision balance ($r=.358$, $p<.05$) and self efficiency ($r=.632$, $p<.001$) significantly correlated with tapering behavior. Hierarchical multiple regression further showed that dysfunctional beliefs, decision balance, and self-efficacy can explain the variation in the amount of drug reduction up to 64.7 %.
Conclusion: The higher self efficacy and the more positive evaluation of drug discontinuation a patient has, the more reduction of hypnotic dose can be obtained following a graduate tapering program. It implies that psychological factors could be important in the evaluation and intervention for drug reduction in clinical patients.

0839

ANXIETY AND PERCEIVED ACTIVITY LEVEL AS SIGNIFICANT PREDICTORS OF INSOMNIA IN OLDER ADULTS

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Introduction: The prevalence of insomnia increases throughout older adulthood. The number of medications used and co-occurring medical conditions have previously been identified as prominent correlates with this trend. However, the causes and correlates of insomnia in older adults remain poorly understood. The current study examined the independent contribution of anxiety and perceived activity level on insomnia severity.
Methods: Three self-report measures (Beck Anxiety Inventory, Geriatric Depression Scale - Short Form, and Insomnia Severity Index) were administered in a structured interview format to 71 older adults in assisted living communities. Demographic information including gender, education, exercise, perceived activity level, medication use, and medical diagnoses were also gathered. Hierarchal regressions were conducted to determine the independent influence of these variables on insomnia severity.
Results: Anxiety accounted for 8% of variance ($r = .28$, $p < .05$) over and above variance accounted for by depression and demographic variables. Of the demographic variables, perceived activity level ($\beta = -0.43$, $p < .01$) was also a significant predictor of insomnia. Based on these findings, a subsequent hierarchal regression revealed that perceived activity level also accounted for 8% of the variance ($r = .28$, $p < .05$) over and above what is accounted for by anxiety, depression and other demographic variables. In this model anxiety ($\beta = .38$, $p < .01$) was also a significant predictor of insomnia.
Conclusion: Anxiety and perceived activity level are each significant independent predictors of insomnia severity in older adults living in assisted living communities. Assessing for anxiety and perceived activity level is important when determining the etiology of insomnia and appropriate treatment in this population. Anxiety and low activity levels may represent meaningful targets in the treatment of insomnia in this population.

0840

CORRELATES OF FATIGUE AND DAYTIME IMPAIRMENT IN OLDER ADULTS WITH PRIMARY INSOMNIA

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Introduction: The objective of this analysis was to determine the clinical and polysomnographic correlates associated with fatigue and daytime dysfunction in a sample of older adults with the diagnosis of chronic primary insomnia.
Methods: Male and female subjects ages 55 years and older were screened for the diagnosis of chronic primary insomnia. Those meeting the diagnosis via DSM-IV-TR criteria in addition to reporting threshold determinations on sleep diaries for sleep latency of >30 minutes, wake time after sleep onset (WASO) of >30 minutes, and sleep efficiency <85% underwent overnight polysomnography (PSG). Subjects with PSG evidence of sleep related breathing or movement disorders were excluded from the study. The remaining subjects who met inclusion criteria (n=50) were evaluated using multivariate analysis to determine what clinical and objective sleep correlates, if any, associated those who experienced fatigue that negatively impacted daytime functioning. Data reported from Fatigue Severity Index (FSI) reports as well as survey questions specifically related to the impact of fatigue on daytime dysfunction were used as the dependent variable.
Results: Of the demographic, clinical, and PSG data collected, four correlates reached statistical significance. Younger age ($p=.013$), absence of marriage or cohabitation ($p=.040$), Multi-Dimensional Fatigue Symptom Inventory score ($p=.000$), and wake after sleep onset ($p=.001$) all were significantly correlated with increased reports of fatigue's impact on daytime dysfunction in the sample subjects.
Conclusion: These observations suggest that subjects with chronic insomnia differ in the nature and severity of objective sleep disturbance, and that awakenings throughout the night uniquely contribute to daytime dysfunction. Treatments that target maintenance of sleep in chronic insomnia have the potential to improve functioning with decreases in daytime fatigue and clinical impairments.

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0841

CAN PSYCHO-EDUCATIONAL INSOMNIA WORKSHOPS REACH AND HELP MEMBERS OF THE PUBLIC?

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Introduction: Whilst effective psychological treatments such as CBT-I have been developed for insomnia, access has been difficult given the limited awareness of them amongst referrers and the limited capacity of services offering CBT-I. To increase access, a CBT-I program was adapted into a one-day workshop format, with each workshop able to take up to 30 participants. A small pilot study using this approach and where participants could self-refer, had obtained promising results.
Methods: An RCT design is being used to evaluate the clinical and health economic aspects of these CBT-I workshops. Self-referring participants will be randomly allocated to 2 experimental and 2 control group workshops. Scores of the experimental group participants taken 3 months after their workshops will be compared with the scores of the control group participants 3 months after the baseline measures are taken and before their workshops. Assessment measures used include the Insomnia Severity Index (ISI), the Beck Depression Inventory (BDI), the Client Service Receipt Inventory (CSRI) and the Euroqol. Workshops are being held on Sundays in non-mental health settings.
Results: These workshops have attracted a large number of enquiries and 128 people have agreed to participate in the study. Of these, 49.2% have never consulted their GPs for their insomnia problems, the average age is 57 years and just under 70% of participants are female. In terms of scores on the ISI, participants most commonly reported moderately severe clinical insomnia (54.7%), subthreshold insomnia (26.6%) and severe clinical insomnia (14.1%). In terms of depression scores on the BDI, responses most commonly fall into the mild-moderate depression (43%) and moderate-severe depression (20.3%) categories.
Conclusion: The proposed talk/poster will present the clinical and health economic results of this study, which will be available in March 2009.
Support (optional): This study has been supported by the National Institute of Health Research (NIHR) Biomedical Research centre

0842

PATIENTS WITH PRIMARY INSOMNIA EXPERIENCE MORE SPONTANOUS PAIN AND HYPERALGESIA

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Introduction: The development and augmentation of spontaneous pain and hyperalgesia under experimental conditions of sleep deprivation, restriction, or fragmentation has been well documented. Do patients suffering from primary insomnia experience enhanced spontaneous pain and hyperalgesia when compared to participants with good quantity/quality sleep? Preliminary data of an ongoing study will be presented.
Methods: Ten participants with good quantity/quality sleep and five participants with primary insomnia (mean age 25+/-7 yrs, BMI 24+/-4 m2/kg, groups did not differ with respect to age, BMI, sex ratio), underwent a 2-week actigraphy and sleep log recording period, in order to assess sleep-wake patterns and daily ratings of emotional and physical well-being (100mm visual analog scales). Following the sleep log and actigraphy recording phase, participants were invited to come to the Clinical Research Center to carry out fasted blood and urine collection and blood pressure measures. Experimental pain testing started at 1pm, one hour after lunch, and consisted of measures of pain thresholds to heat (HPT) and pressure (PPT), supra-thresholds, and measures of central sensitization (temporal summation, TS) and pain-inhibitory capacity (defuse noxious inhibitory control, DNIC).
Results: Participants suffering from primary insomnia trended to experience twice as much spontaneous pain as compared to good sleepers, as averaged across two weeks of diary recording (21+/-17 vs. 10+/-8%, $p<0.10$). HTP trended to be lower in insomniacs compared to controls (43.6 vs. 46.2 degree C, $p<0.10$). In addition, HTP and supra-thresholds (HTP+4 degree C) were experienced as more intense in insomniacs compared to controls (93 vs. 70% for supra-thresholds, $p=0.08$). Maximal tolerable temperature during a temporal summation sequence of 10 heat pulses trended to be lower in insomniacs compared to controls (47.6 vs. 49.0 degree C, $p=0.06$). No systematic differences were found for indices of central pain-modulatory mechanisms (TS, DNIC) in this very preliminary data set.
Conclusion: The current preliminary findings suggest that study participants suffering from primary insomnia experience enhanced spontaneous pain and hyperalgesia. Improving sleep homeostasis should be considered as a priority in those suffering from inadequate sleep quantity and quality, in order to prevent the development or augmentation of pain and hyperalgesia, which is likely a consequence of insomnia.
Support (optional): Sepracor Inc.

0843

MOTIVATIONAL INTERVIEWING IN INSOMNIA TREATMENT: A RANDOMIZED CONTROL PILOT STUDY

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Introduction: Cognitive Behavioral Treatment for Insomnia (CBT-I) is effective for chronic insomnia when provided both in individual and group formats. Group CBT-I is both clinically effective and cost effective; however, it typically necessitates a longer wait-time for patients as compared to individual psychotherapy. Wait-time leads to attrition before the group begins. The current study is an initial investigation of the utility of Motivational Interviewing (MI) techniques for reducing pretreatment attrition and increasing attendance in group CBT-I.
Methods: This study was a randomized control pilot design conducted in a tertiary clinic setting. Eighteen participants were randomized with equal probability to receive a single-session MI intervention or a control interview, delivered via telephone to participants on a waitlist to begin group CBT-I.
Results: Five of ten participants who received MI, but only one of eight in the control group, attended at least one group session of CBT-I. Use of hypnotic medications did not differ between those who did and did not attend the group. Exploratory qualitative analyses revealed that participants who made a greater number of statements reflecting "disadvantages of the status quo" had greater rates of attendance in the CBT-I group to a statistically significant degree. The most important issues raised by patients during the MI interview were questions about the group logistics and about the content and effectiveness of the group.
Conclusion: This preliminary finding suggests that Motivational Interviewing might have a role in reducing pretreatment attrition and enhancing attendance in group CBT for insomnia. An abbreviated interview that utilizes MI principles and focuses on answering patients' questions regarding the group logistics and how the group is going to help them

may be the most effective approach. However this assertion awaits further empirical testing.

0844

WHAT'S KEEPING COLLEGE STUDENTS WITH INSOMNIA UP AT NIGHT?

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Introduction: Sleep onset insomnia is one of the most commonly cited sleep disturbances among college students. To better understand what to target in developing college-specific insomnia interventions, we examined what factors they identified when asked what was most likely to keep them up at night. Second, we explored if variables known to correlate with chronic primary insomnia in adult populations would similarly be, not only elevated, but also correlated, with longer latencies to sleep onset [SOL] among college students with insomnia.
Methods: As part of a larger data set from a study examining the effects of a narrative exercise on pre-sleep arousal, we extracted baseline data (N= 64) and narrative data from undergraduates with insomnia in the writing condition (N= 32) who wrote about what was likely to keep them awake. We also compared our college student sample's ratings of dysfunctional beliefs and attitudes about sleep [DBAS], pre-sleep arousal [PSAS], sleep related beliefs [SRBQ], and pain [McGill Pain] to normative samples and correlated these measures with SOL.
Results: On a sample weekday night, the stressors that college students wrote about primarily involved academic (61.1%) and pain (35.9%) problems. T-tests revealed higher elevations of insomnia related symptoms compared to other adult healthy sleepers on the DBAS, PSAS, McGill Pain, and SRBQ, all p's <.05. However, only cognitive and somatic arousal were significantly correlated with longer SOLs ($r=0.43$, $p<0.001$ and $r=0.28$, $p=0.02$, respectively).
Conclusion: Similar to adult samples, college students with insomnia showed elevated scores on arousal, dysfunctional beliefs, pain, and safety behaviors, though only arousal scores were correlated with SOL. Based on our sample, it appears that stress about academics and pain are what is keeping college students with insomnia up at night. A discussion about how this compared to general adult samples with chronic primary insomnia will ensue.

0845

IS NON-DRUG TREATMENT OF INSOMNIA IMPAIRED BY THE PRESENCE OF CO-MORBID OSA?

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Introduction: Research indicates a considerable degree of overlap between insomnia and obstructive sleep apnea (OSA) that may have etiological importance and treatment consequences. The presence of co-morbid OSA may impair the treatment of insomnia. The aim of the study was to determine the impact of this co-morbidity on the response to insomnia treatment.
Methods: Ninety-three patients (69% women) with primary insomnia were compared with 57 patients (65% women) with insomnia and co-morbid OSA (respiratory disturbance index (RDI) >15, indicative of at least mild OSA). They all attended an outpatient cognitive/behavioral treatment program for insomnia that included a full diagnostic PSG. Treatment response was determined from 7-day sleep/wake diaries and daytime sleepiness and fatigue measures at pre-treatment, 5 week and 3 month follow-up.
Results: To date, 38% of insomnia patients also presented with an RDI of at least 15. There were no significant differences between groups on depression or gender, however, the co-morbid group was significantly ($p<0.05$) older by 11 years and had greater BMI (26.2 vs 24.4). For the entire group as a whole there were significant improvements in sleep onset latency ($F(2,216)=48.2$), wake time after sleep onset ($F(2,204)=99.8$), total sleep time ($F(2,216)= 31.7$), and sleep efficiency ($F(2,206)=110.9$) with all $p<0.001$ and moderate to large effect sizes. Both groups showed significant but small increases of sleepiness at 5 weeks (ESS from 5 to 6) but comparable decreases at 3 month follow-up. Both groups showed significant ($F(2,184)=65.4$, $p<0.001$) decreases in fatigue with large effect size. All improvements in sleep and daytime functioning variables were similar in the two groups with no interaction effects between groups and time ($p>0.10$). When the co-morbid groups were further subdivided into mild and moderate to severe OSA (RDI>30), there were still no group by time significant interactions apart from a greater overall decrease of sleepiness with treatment in the more severe OSA group.
Conclusion: More than a third of patients referred for the treatment of insomnia had at least mild OSA. Following a non-drug treatment program for insomnia, those with co-morbid OSA (both mild and more severe) showed improvements in sleep and daytime functioning variables at least as great as those without OSA. The presence of co-morbid OSA did not impair the treatment of insomnia in this study.

0846

DEVELOPMENT OF THE CHINESE INSOMNIA SCREENING SCALE BASED ON ICSD-II CRITERIA: A PRELIMINARY STUDY

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Introduction: Although various instruments have been developed to evaluate individual's insomniac symptoms, none of them are based on International Classification of Sleep Disorder, 2nd ed., 2005 (ICSD-II). The purpose of this study is to develop a new scaling system, Insomnia Screening Scale (ISS) in Chinese based on ICSD-II to fit the new diagnostic criteria.
Methods: Chinese version of ISS is composed of 111 items and can be divided into 4 major subscales, including sleep environment (SE), sleep opportunity (SO), insomniac symptoms (IS) and daytime symptoms (DS). This study examined the internal consistency, construct validity and concurrent validity of the ISS in 48 participants: 32 insomniacs (71.88% female, mean age 41.97±14.54 years old) and 16 normal subjects (50.00% female, mean age 40.93±11.55 years old).
Results: The Cronbach's alpha of SE, SO, IS, DS were 0.93, 0.67, 0.97, and 0.95. Only the difference of IS scores between insomniacs and normal subjects confirmed the construct validity of this scale ($IS\ t=4.76$, $p<0.01$). The correlation between ISS and Pittsburgh Sleep Quality Index (SE $r=0.33$, $p=0.03$; SO $r=0.36$, $p=0.02$; IS $r=0.91$, $p<0.01$; DS $r=0.71$, $p<0.01$) and Insomnia Severity Scale (SE $r=0.29$,$p=0.05$; SO $r=0.28$, $p=0.054$; IS $r=0.83$, $p<0.01$; DS $r=0.66$, $p<0.01$) identified the concurrent validity.
Conclusion: The results demonstrated that the ICSD-II based ISS is a reliable and valid instrument to evaluate individual's insomniac symptoms. The major difference between ISS and the former instruments is that ISS not only targets on the subjective insomniac and daytime symptoms, but also examines sleep environment and sleep opportunity of participants.

0847

EFFECTS OF ANESTHESIA ON TREATMENT OF PATIENTS WITH CHRONIC PRIMARY INSOMNIA

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Introduction: Similarity in neurophysiology between sleeping and anesthetized states suggests that anesthesia may reverse the effect of sleep deprivation. To test the hypothesis that recovery from chronic pri-

mary insomnia occurs during anesthesia, we evaluated the effects of anesthesia on treatment of patients with chronic primary insomnia.
Methods: The patients with primary insomnia (n=83) were randomly divided into two groups. The treatment group (TG, n=42) were administered with single intravenous injection of midazolam (2.0 mg) and followed with intravenous infusion of propofol (3.0 μg/L, speed) with micro-injection pump for two h. The control group (CG, n=41) received identical administration with saline, but without midazolam. TG patients were maintained in light anesthetized state prior to sleep for consecutive five days. At days 6 and 90, they were evaluated with Leeds Sleep Evaluation Questionnaire (LSEQ) following an overnight polysomnographic sleep examination.
Results: At days 6 and 90, LSEQ evaluation revealed that TG group showed significant improvement in sleep onset, sleep quality, wakefulness after sleep onset and vigilance, compared to CG group. Overnight polysomnographic examination showed that TG patients exhibited increases in total sleep time and the percentages of S3, S4 and REM, and decreases in sleep latency, wakefulness time and wakefulness episodes after sleep onset, relative to CG patients.
Conclusion: The anesthesia prior to sleep with intravenous infusion of propofol for two h for consecutive five days is the valid method to treat the patients with chronic insomnia.

0848

THE RELATIONSHIP OF COPING AND INSOMNIA IN CHRONIC INSOMNIACS AND NORMAL SLEEPERS VULNERABLE TO STRESS-RELATED SLEEP DISTURBANCE

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Introduction: Transient insomnia is a common reaction to daily life stressors. Previous researches focused more on the relationship between coping style and sleep disturbances in chronic insomniacs. Less studies examined the characteristics of non-insomniacs who are vulnerable to stress-related transient sleep disturbance. The goals of this study are to examine (1) the psychological characteristics of the individuals who are vulnerable to transient insomnia, (2) the role of stress coping style in related to other etiological factors in both transient and persistent insomnia.
Methods: The subjects included 62 chronic insomnia patients (CI) and 144 individual without frequent sleep complaint. All subjects were asked to complete a set of questionnaires, including the Ford Insomnia Response to Stress Test(FIRST), the Insomnia Severity Index, the Pre-Sleep Arousal Scale, the Sleep-Related Behavior Questionnaire, the Dysfunctional Beliefs and Attitudes about Sleep questionnaire, COPE, the Center for Epidemiologic Studies Depression Scale, the Beck Anxiety Inventory and the Pittsburgh Sleep Quality Inventory. The non-insomnia participants were categorized into 75 good sleepers (GS) and 74 vulnerable sleepers (VS) based on their scores on the FIRST.
Results: ANOVA results showed that CI reported more dysfunctional beliefs and attitudes about sleep ($F=21.253$, $p<.001$), sleep related safety behaviors ($F=30.257$, $p<.001$) and pre-sleep arousals ($F=58.364$, $p<.001$) than the other groups. Also, VS reported more safety behaviors and pre-sleep arousals than GS. In addition, CI and VS used more coping styles of "problem solving, positive reinterpretation and acceptance" ($F=7.466$, $p<.05$), "social support, focus on and venting of emotions" ($F=5.641$, $p<.05$), and "avoidance" ($F=10.884$, $p<.001$) than GS. Furthermore, path analysis showed that the safety behaviors and arousal play an important mediating role between dysfunctional beliefs and attitudes about sleep and insomnia in CI (GFI= .92, SRMR= .067, RMSEA= .064, CFI = .98, NNFI= .91). Finally, avoidance coping could predict the frequency of sleep related safety behaviors in all groups.
Conclusion: More dysfunctional beliefs and attitudes about sleep, sleep-related safety behaviors and avoidance coping were found in CI than in GS and VS. VS showed higher sleep-related safety behaviors and avoidance coping than GS. The results imply that VS may have more avoidant coping style and engaging in more safety behaviors that may perpetuate them into persistent insomnia.

0849

IMPACT OF STRESS ON INSOMNIA DEVELOPMENT AMONG INDIVIDUALS ESCAPED FROM SHIDA KARTLI, GEORGIA

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Introduction: Individuals subjected to different kind of traumatic events report significant sleep difficulties even in the absence of a full-blown post-traumatic stress disorder (PTSD). Here we test whether the stress of escaping from a war zone may predispose individuals to insomnia.
Methods: Participants were 45 individuals (mean age 35.4, 60% woman) who were forced to escape from Shida Kartli during Russia-Georgia conflict, August 2008. They were interviewed regarding the main sleep-wake characteristics, physical health, and demographics after about 3 month from the war conflict. Measures of insomnia and stress reactivity were derived from Insomnia Severity Index (ISI) and posttraumatic stress diagnostic scale (PDS). The subtypes of insomnia based on symptoms (difficulty falling asleep, maintaining asleep and non-refreshing sleep) were also identified.
Results: Mean ISI score in this group of interviewed individuals were 11.33 (SD=0.89). 29 subjects (64.4%) met diagnostic criteria for insomnia (the cut-off score of 10), and 16 subjects (35.5%) insomnia were moderate to severe (score >15). Subjective data indicated that 11 subjects (24.4%) had none of insomnia symptoms, while 16 subjects (35.5%) had all 3 types of insomnia (onset, maintenance, terminal). We found significant difference by gender in the rate of insomnia reports. 78.5% of women vs 64.7% reported at least one type of insomnia. More than two thirds of participants were not satisfied with their current sleep and most of them were complaining about appearing of nightmares, as a disturbing factor of sleep.
Conclusion: These results suggest that individuals subjected to strong stress associated with experienced traumatic events are at high risk for developing of insomnia.
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0850

THE GLASGOW SLEEP IMPACT INDEX: A PATIENT GENERATED MEASURE FOR CAPTURING SLEEP-RELATED QUALITY OF LIFE

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Introduction: Historically, outcome studies in insomnia research have tended to focus on night-time sleep parameters. Only recently has there been emphasis on assessing aspects of functioning and health-related quality of life. Interestingly, there are mixed findings concerning whether improvements in sleep are actually accompanied by improvements in daily functioning. One potential reason for this is that current measurement techniques (predominantly pre-determined generic scale methods) may not be sensitive enough to fully capture the impact of insomnia. We report here the development of a new measure, the Glasgow Sleep Im-

pact Index (GSII), which takes a more idiographic approach to assessing sleep-related quality of life.
Methods: As part of an ongoing treatment protocol, 18 individuals (15 female; mean age = 39.1 yrs) meeting DSM-IV criteria for Primary Insomnia completed the GSII. The GSII asks participants to generate, using their own words, areas of their life that are most affected by their sleep. Subsequent ranking and rating then provide an indication of the relative importance of each item, and the extent to which it currently impacts the patient. Thus, the unique feature of the scale is the inclusion of personalized idiographic descriptors, which can then be quantified using scale methods and used for both within and between subject analyses. We report the range of generated daily life domains, and some preliminary sensitivity data, in a sub-sample of participants undergoing sleep restriction therapy.
Results: The GSII is a three item self-generated scale, with three additional stages of ranking and rating, and takes approximately 2-3 minutes to complete. Generated items spanned several areas of daily functioning, including mood/temperament, motivation/energy, appearance, neurocognitive ability, health, social, occupational, and family/relationship functioning. Ratings for each participant's number one, two and three, ranked areas (in terms of concern) were collapsed across the group and assessed pre-and post sleep restriction therapy. Statistically significant ($p<0.05$) improvements were found, post intervention, for the two most importantly ranked areas by participants.
Conclusion: The GSII looks to be a promising, sensitive measure, capturing individual sleep-related quality of life impairment, yet also permits quantification at the group level. Psychometric properties, including reliability and concurrent validity, are currently being assessed.

0851

TRAIT AND STATE EMOTIONALITY IN INSOMNIA

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Introduction: This study examined the relationship between emotionality and insomnia, in a population-based sample, through questionnaires which measure trait and state characteristics in a sample of British and Italian volunteers.
Methods: Participants were assigned to three groups: good sleep, subthreshold insomnia, clinically significant insomnia. Classification was based on criteria indicated by the Diagnostic and Statistical Manual of Mental Disorders, IV edition, Text Revision and the International Classification of Sleep Disorders, II edition. Participants (n=688; 439 F, 246 M, 3 did not reported gender information) completed questionnaires investigating symptoms of insomnia, trait emotionality and state emotionality related to the sleep-onset period of the best and of the worst nights of sleep experienced in the month preceding the completion of the questionnaires.
Results: Findings indicate that people who report a trait of heightened negative emotionality are more likely to report clinically significant insomnia ($F(2,651)=14.39$; $p<0.001$). On the other hand, good sleepers report stronger positive emotions compared to people with insomnia, but only in the British sample ($F(2,651)=2.55$; $p=0.038$). With respect to the state measures, people with insomnia associate heightened negative state emotionality to a bad night of sleep, compared to good sleepers ($F(2,645)=3.62$; $p=0.027$). No group difference was found with respect to the good night of sleep. Within the group with subthreshold insomnia, those who systematically associate diurnal consequences to sleep difficulties seem to be at risk to develop a chronic disorder and report high trait negative emotions.
Conclusion: Results indicate that insomnia is linked to heightened negative trait and state emotionality, which varies consistently with the quality of sleep across the nights. Psychological treatment of insomnia could benefit from increasing the patient's self-regulation of the emotional charge associated with the pre-sleep period.

0852

DOES 'ACCEPTANCE' HAVE A ROLE TO PLAY IN MANAGING IDIOPATHIC INSOMNIA? A GROUP COMPARISON OF BELIEFS, COPING STYLE AND TREATMENT ACCEPTANCE IN IDIOPATHIC INSOMNIA AND PSYCHOPHYSIOLOGICAL INSOMNIA

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Introduction: Although ICSD-2 distinguishes psychophysiological insomnia (PI), idiopathic insomnia (IdI) and paradoxical insomnia, treatment of such sub-types is seldom differentiated in practice. This study investigated patients' own conceptualization (in PI and IdI) of their sleep difficulties. In particular, it was hypothesized that IdI patients would perceive their insomnia to be more permanent/uncontrollable, and would be more accepting of their problem than adults with PI.
Methods: Cross sectional between-group comparison of PI [n=31: 24F, mean age 38.5(14.5)yr] and IdI [n=30; 24F, 34.6(15.7)yr] with a normal sleeper control group (NS:n=31: 18F, 29.6(8.3)yr], on the Illness Perception Questionnaire-Revised, Illness Cognition Questionnaire, Brief COPE, and Treatment Acceptability Scale, controlling for insomnia severity and other characteristics as required.
Results: PI and IdI had similar scores, in the clinical range, on the ISI, PSQI and DBAS, all measures being greater than NS controls ($p<.001$). Both PI and IdI rated behavioral therapy more acceptable than either a pharmacological or acceptance-based approach ($p<.01$), adults with IdI rated an acceptance-based approach as more acceptable than adults with PI ($p=.02$). The latter is consistent with IdI group perceiving their insomnia to be more permanent ($p=.03$). Relative to PI, IdI patients report greater use of humor ($p=.003$) and distraction ($p=.03$)in their coping style.
Conclusion: Patients with both PI and IdI would prefer a psychological treatment approach. CBT is the traditional form of intervention, but treatment based on an acceptance model be also be appropriate, particularly in IdI. Further work is required on the behavioral and cognitive phenotypes of insomnia and in relating these directly to treatment strategy.
Support (optional): Supported by the DR Mortimer & Theresa Sackler Foundation.

0853

PHARMACOKINETIC-PHARMACODYNAMIC MODEL OF SB-649868 IN INSOMNIA, PRECLINICAL AND CLINICAL CORRELATES

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Introduction: SB-649868 is a potent orexin antagonist which has demonstrated sleep-promoting properties in preclinical models and in humans. Data from preclinical and clinical experiments have been used to characterize the relationship between SB-649868 exposure and relevant polysomnographic (PSG) endpoints.
Methods: Pharmacokinetic (PK) and pharmacodynamic (PD) data were collected in different studies assessing the hypnotic effects of SB-649868 in rat and marmoset noise insomnia models, and in men with primary insomnia. A non-linear mixed effect modelling approach using individual PSG measurements was applied using NONMEM VI. The population

PK-PD modelling was conducted to formally test the hypothesis of a concentration-related effect and assess the SB-649868 population PK-PD parameters and between-subject variability.
Results: In the rat and marmoset model, a concentration dependent reduction in sleep latency, and an increase in time in deep sleep was observed. Plasma concentrations that provided 50% of the maximum predicted effect (EC50) were similar in both species and in the range of 800-1000 ng/ml. In insomniacs, PK-PD analysis demonstrated a consistent and highly statistically significant concentration-response relationship for latency to persistent sleep (LPS), total sleep time (TST), and wake time after sleep onset (WASO). EC50 for LPS, TST and WASO were 340, 560 and 1000 ng/ml respectively.
Conclusion: SB-649868 PSG effects were highly correlated to circulating levels both in preclinical models and in patients with primary insomnia. The EC50 related to the sleep maintenance effects of the drug was consistent across species.

0854

ON PINEAL CALCIFICATION, MELATONIN EXCRETION AND POLYSOMNOGRAPHIC SLEEP MEASURES IN PRIMARY INSOMNIC PATIENTS

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Introduction: Melatonin plays a key role in the proper functioning of the circadian timing system (CTS), and exogenous melatonin has been shown to be beneficial in cases of CTS and sleep disturbances. Nevertheless, the concept of "melatonin deficit" has yet to be defined. The aim of our study was thus to determine the relationship between degree of pineal calcification (DOC) and objective sleep parameters using polysomnography (PSG).
Methods: A total of 31 outpatients (17 women, 14 men, mean age 45.7 years; SD 14.4) with insomnia were included in our study. Following an adaptation night, a PSG recording night was performed. Urine samples were collected at predefined intervals over a 32-hour period that included both PSG nights in the sleep laboratory. 6-sulphatoxymelatonin (aMT6s) levels were determined using ELISA. DOC and Uncalcified pineal tissue (UPT) was estimated by means of cranial computed tomography.
Results: UPT was positively associated with aMT6s-production ($r = 0.569$; $P = 0.002$). Controlling for age, aMT6s parameters and UPT did not correlate with any of the PSG parameters evaluated. In contrast, DOC was negatively associated with REM-sleep percentage ($r=-0.567$, $P=0.001$), total sleep time ($r=-0.463$, $P=0.010$), and sleep efficiency ($r=-0.422$, $P=0.020$).
Conclusion: DOC appears to be superior to measurements of the absolute amount of melatonin in the circulation as an indicator of melatonin deficit. High DOC values indicate changes predominantly in those PSG parameters that are governed by the circadian timing system. As such, DOC may serve as a marker of CTS instability.

0855

VALIDATION OF A MISPERCEPTION INDEX TO MEASURE THE ERROR IN SLEEP ESTIMATION AND IDENTIFY PARADOXICAL INSOMNIACS

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Introduction: Sleep time estimation is often a difficult task for insomniacs, who usually tend to underestimate their total sleep time (TST). Paradoxical insomniacs show a "consistent marked mismatch" between objective and subjective self-reported or diary estimations. The aim of the present study was to validate statistically a new index, correlated positively with the magnitude of sleep misperception and able to indicate its direction. An attempt was also made to establish an eventual threshold value for sleep misperception in the diagnosis of paradoxical insomnia (PI).
Methods: Two-step retrospective (study 1) and prospective (study 2) validation study was carried out. The study 1 included 288 normal subjects (176 females and 112 males, mean age 58.5 years, SD 7.23). Study 2 included 159 patients (98 females and 61 males; mean age 49.1 years, SD 12.71) with primary insomnia. Participants underwent a full-night polysomnographic study, followed by a morning assessment of subjective sleep parameters. A Misperception Index (MI) was computed using the following formula: MI=[objective total sleep time (oTST)−subjective total sleep time (sTST)]/oTST.
Results: The Bland-Altman test in controls demonstrated the reliability of this index for values of oTST > 120 min. The statistical analysis of the distribution of MI in insomnia patients disclosed the presence of two subgroups, one with a moderate sleep misperception (132 patients) and another with high sleep misperception (27 patients). The latter presented MI values ≥0.9, exhibiting statistical properties different from those with MI <0.9 and from normal subjects.
Conclusion: This study demonstrates that the application of a standardized and statistically validated approach to the study of sleep misperception in primary insomnia is able to disclose a subgroup o patients with a probable true sleep misperception insomnia which might be as rare as reported in the current classification system.

0856

SLEEP DISTURBANCES IN A RACIALLY MIXED AND SOCIOECONOMICALLY DISADVANTAGED SAMPLE IN AN URBAN PRIMARY CARE SETTING

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Introduction: Health disparities due to both race and socioeconomic status (SES) have been observed in several health conditions, though little work has assessed whether similar disparities exist for sleep problems. The current study sought to characterize the severity of sleep disturbance in a diverse sample and to test whether income or race was associated with severity of these disturbances.
Methods: Patients aged 40 and above were recruited from an urban family medicine practice; 103 patients enrolled and the 92 who completed all study instruments included 77% women; 51% African American (AA), 43% White, and 6% other; 62% with annual income below $20k; and had a mean (sd) age of 51.9 (8.9) with 4.0 (3.1) chronic illnesses. Subjects completed the Pittsburgh Sleep Quality Index (PSQI), the Center for Epidemiologic Studies-Depression scale (CESD), and the Perceived Stress Scale (PSS). Sleep disturbance was assessed by the Global PSQI score, each of the 7 PSQI components, and the sleep efficiency (SE) and total sleep time (TST) items. For contingency analyses, a PSQI cutoff of >6 was used for clinical sleep disturbance (better published sensitivity/specificity for insomnia than a cutoff of 5), race was dichotomized as AA vs. other, and income as above or below $20k.
Results: The mean Global PSQI score was 10.0(4.9) with SE of 75.0%(20.1) and TST of 5.8 (1.8) hrs. All PSQI components were elevated compared to normative data and 70% had a PSQI >6. Mean CESD, PSS and chronic illness scores did not differ by income or race. Annual income <$20k was associated with higher mean PSQI ($p=.02$) and lower SE ($p=.07$), while being AA was associated with higher mean PSQI ($p=.07$), lower SE ($p=.03$), and lower TST ($p=.003$). In a multinomial logistic regression, depression and race, (but not income, age, gender, or chronic illness category) were significant predictors of PSQI >6. In bivariate logistic regressions AA race was associated with PSQI

>6 (OR: 3.15; 95% CI: 1.15-8.61; adjusting for CESD by quartiles) and remained significantly associated when also adjusted for income above/below $20k (2.69:1.03-7.01).
Conclusion: The mean global PSQI score demonstrates an elevated level of sleep disturbance in this older, ethnically diverse, and low SES sample, while the pattern of PSQI component and item scores suggests a high degree of insomnia. Moreover, the findings highlight a health disparity in sleep disturbances that is most robust with respect to AAs while controlling for depression and income.
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0857

CLINICAL AND PHYSIOLOGICAL CORRELATES OF CAFFEINE AND CAFFEINE METABOLITES IN PRIMARY INSOMNIA

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Introduction: Sleep hygiene recommendations routinely suggest that insomnia patients reduce caffeine consumption. However, little is actually known about the relationship between caffeine consumption/metabolism and sleep in the home environment. This study explored the relationship between plasma concentrations of caffeine and its metabolites and subjective and polysomnographic measures of sleep disturbance in both good sleepers (GS) and subjects with primary insomnia (PI). These analyses describe caffeine-related sleep disturbance in subjects in their natural state, consuming regular, dietary amounts of caffeine.
Methods: 65 PI subjects (mean age 36.5 + 9 years) and 29 GS (mean age 30 + 9 years) consuming less than four coffee cup equivalents of caffeine daily were recruited. Subjects completed a home study detailing sleep habits, physical and psychological well-being, alcohol and drug use, and caffeine consumption. A blood plasma sample was acquired immediately prior to a night of laboratory polysomnography, which included visual scoring and power spectral analyses. Concentrations of plasma caffeine, paraxanthine, and other methylated xanthines were determined by high performance liquid chromatography (HPLC) and spectrophotometry.
Results: Plasma xanthine concentrations and endorsed caffeine intake did not differ between GS and PI. Significant correlations were found between reported caffeine intake and plasma concentrations of caffeine and its metabolites ($r=.58$, $p<.05$). However, plasma caffeine concentrations were poorly correlated with subjective or polysomnographic sleep measures in either GS or PI. Caffeine concentration weakly correlated with Stage 1% ($r=.23$, $p<.05$), but not with other sleep continuity, sleep architecture, or quantitative EEG measures.
Conclusion: Plasma xanthine concentrations and endorsed caffeine intake were only weakly correlated with sleep disturbance in both groups when consumption is limited to less than four coffee cup equivalents per day. These data suggests that routine, moderate caffeine consumption is at most a minor determinant of sleep disturbance among good sleepers and insomniacs.
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0858

LOWER EDUCATIONAL ATTAINMENT IS RELATED TO MORE FREQUENT USE OF HYPNOTICS: RESULTS FROM A SWEDISH TELEPHONE POPULATION SURVEY

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Introduction: The prevalence of sleep related complaints in developed countries has been growing steadily. The self-reported complaint of "trouble with sleep" in the Swedish population currently exceeds 25%. The aim of this study was to examine sleep complaints and health care utilization with a particular focus on gender and educational attainment disparities in a representative population sample.
Methods: We used data from a SIFO (non-government supported research institute) survey (telephone interviews) of 1000 randomly selected households (aged 15+) with uniform geographic representation. The interview queried sleep duration and quality, excessive daytime somnolence (EDS), physician consultations and current use of "sleep" medications. Educational attainment was coded into primary, secondary and tertiary (college) levels. We used multivariate logistic regression to estimate the effects of education, gender and age on sleep complaints and treatment utilization.
Results: Short sleep duration, poor sleep quality and EDS was reported by 20/19, 18/24 and 7/13% of men/women. Short sleep duration and EDS but not dimensions reflecting poor quality of sleep were associated with lower educational level. In multivariate models male gender was associated with shorter sleep while poor quality of sleep and EDS were more common in women. Medication use (>2 times/week) by men was only half as likely than by women (OR 0.50, CI 0.34-0.74) after adjustment for age and education. Medication use was more than twice as likely in respondents without a college education (OR primary 2.02, CI 1.12-3.40, OR secondary 2.14, CI 1.29-3.54). The patterns of physician consultations mirrored hypnotic use.
Conclusion: Sleep related problems are frequent in the general population. Poor sleep quality and sleep disturbance are proportionally unaffected by educational level but treatment utilization is disproportionately high among non-college educated people.

0859

WEIGHT CHANGES IN PATIENTS WITH PRIMARY INSOMNIA FOLLOWING LONG-TERM ESZOPICLONE TREATMENT

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Introduction: An association has been demonstrated between sleep duration and obesity (as well as related conditions such as diabetes, metabolic syndrome, and heart disease), with a trend for higher body mass index (BMI) among patients with sleep duration ≤6 hours. Patients with primary insomnia (PI) have reduced sleep duration and, therefore, may be at risk of weight gain. Two studies examined the long-term efficacy of eszopiclone, a single-isomer, non-benzodiazepine GABA-A receptor modulator in patients with PI. A post hoc analysis of weight change over 6 months was conducted.
Methods: Data from two 6-month, double-blind, randomized, placebo-controlled studies were pooled to evaluate whether treating PI with eszopiclone had an effect on patients' weight during the studies. In the combined studies, patients received placebo (n=475) or eszopiclone 3 mg (n=1141) nightly. Weight was measured at baseline, and at 3 and 6 months.
Results: Most patients (53% overall) had a BMI ≥27 kg/m2 at baseline. The eszopiclone group showed a significantly greater decrease in weight than the placebo group both at Month 3 (mean [±SD] change from base-

line (kg): placebo -0.01 ±3.1, eszopiclone 0.57 ±2.9, p<0.01) and at Month 6 (placebo +0.21 ±4.7, eszopiclone -0.79 ±4.1, p<0.01). Analysis in groups stratified by baseline BMI showed a tendency for greater weight loss with higher BMI, particularly in the eszopiclone groups - BMI <22 kg/m2: placebo (n=43) +0.48 ±1.7, eszopiclone (n=80) -0.18 ±2.9, p=0.22; BMI 22 to <27 kg/m2: placebo (n=80) +0.57 ±2.8, eszopiclone (n=244) -0.46 ±3.4, p=0.02; ≥27 kg/m2: placebo (n=122) -0.12 ±6.2, eszopiclone (n=377) -1.11 ±4.6, p=0.06; BMI ≥30 kg/m2: placebo (n=77) -0.58 ±7.4, eszopiclone (n=247) -1.26 ±5.1, p=0.35.

Conclusion: In this post hoc analysis of data from two 6-month studies, placebo-treated patients demonstrated negligible weight gain. In comparison, eszopiclone-treated patients demonstrated a small but significant weight reduction.

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0860

AN INVESTIGATION OF HOME IMPLEMENTATION DURING ACUTE SLEEP RESTRICTION FOR INSOMNIA: A MULTI-METHOD APPROACH

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Introduction: Sleep restriction therapy (SRT) is arguably one of the most effective components of the cognitive behavioral package for insomnia. However, little is know about the patient's experience of implementing sleep restriction instructions, the mechanisms that help explain SRT gains, or indeed the impact of SRT on daytime functioning. We sought to better understand the acute implementation of a dedicated SRT intervention, as well the longer term effects associated with treatment benefit, using both quantitative and qualitative methodologies.

Methods: Twelve individuals (9f; mean age = 38.8 yrs), meeting DSM-IV criteria for primary insomnia completed the sleep restriction protocol. Therapy involved weekly sessions over a 4 week period - two initial group sessions, and two subsequent individual phone calls. Pre- and post-intervention data were collected on sleep parameters and measures of daytime functioning. Participants kept a prospective audio-diary (Olympus Dictaphone) for the first week of the intervention, recording entries twice per day on the process of implementing new threshold and rising times, and if/how the program impacted on daily functioning. On completion of therapy, semi-structured interviews were conducted probing changes in sleep, adherence to therapy instructions, credibility of treatment, and impact on functioning and well-being. Data were transcribed verbatim and submitted to a thorough qualitative analysis.

Results: Qualitative analysis of 134 diary entries revealed interesting data on the obstacles participants encounter during SRT, as well as experienced 'side-effects', particularly in the early stages of the program. Post-intervention interviews indicated substantial improvements in sleep and daily functioning, coupled with shifts in sleep-related cognitions.

Conclusion: Our novel use of qualitative methodologies sheds light on the patient experience of SRT. Such data help understand the mechanisms underpinning SRT gains, inform on potential ways to improve adherence to behavioral instructions, and reveal simultaneous improvements in both sleep and daytime functioning parameters, after only a brief behavioral intervention.

0861

TRANSCRANEAL MAGNETIC STIMULATION AS THERAPEUTIC OPTION IN PATIENTS WITH INSOMNIA AND ANXIETY SYMPTOMS

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Introduction: Insomnia is defined as the incapability to initiate or maintain sleep. In some cases, insomnia cannot be attributed to a medical or to a sleep disorder. In clinical practice, polysomnographic (PSG) study is not part of the usual patient management. On the other hand, insomniac patients with additional symptoms of anxiety, frequently show evidences of focal and/or generalized abnormalities in electroencephalographic (EEG) activity. This data indicates a pathophysiological substrate that generates EEG hiperexcitability. On the other hand, Repetitive Transcraneal Magnetic Stimulation (rTMS) is considered as a therapeutic option in some disorders that course with EEG hiperexcitability, as in some psychiatric or neurological disorders. In this study rTMS was assessed as a possible therapeutic option for insomniac patients, showing additional symptoms of anxiety.

Methods: 10/20 EEG and PSG study was performed in 20 patients with insomnia and additional symptoms of anxiety. Thereafter, patients were submitted to Low Frequency rTMS (<1 Hz) sessions, during 15 minutes, daily during ten days. Finally, a second 10/20 EEG/PSG was performed.

Results: In the first study, eight patients showed EEG abnormalities. After rTMS, reduction of sleep latency (p = 0.04), increment in total sleep time (p = 0.019) as well as an increase of sleep efficiency were observed. There were no changes in the sleep pattern. All the patients reported subjective improvement.

Conclusion: In patients with insomnia accompanied with symptoms of anxiety, the recording of EEG is a valuable diagnostic tool. Furthermore, rTMS seems to be effective as a therapeutic option for this particular type of insomnia. Nowadays, no treatment has been found for insomnia that reinstates the normal sleep pattern. Therefore, treatment with rTMS in these patients deserves further observations to verify the present results.

0862

INSOMNIA WITH OBJECTIVE SHORT SLEEP DURATION IS ASSOCIATED WITH DEFICITS IN NEUROCOGNITIVE PERFORMANCE

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Introduction: Because chronic insomnia with objective short sleep duration is associated with significant medical morbidity (e.g. hypertension) and with a hyperactivity of the hypothalamic-pituitary-adrenal axis which may affect memory and other neurocognitive functions, we examined the joint effects of chronic insomnia and short sleep duration on neuropsychological functioning in a general population random sample.

Methods: "Insomnia" was defined as complaint of insomnia with a duration of ≥ 1 year and the absence of sleep-disordered breathing (SDB). We classified polysomnographic sleep duration into two categories: ≥ 6 hours of sleep and <6 hours of sleep. We controlled for age, race, gender, education, BMI, and depression in a MANOVA model.

Results: Compared to the normal sleeping group (n=343), the insomnia with < 6 hour sleep duration group (n=51) showed poorer cognitive performance in the domains of information processing speed [SDMT

(51.22 ± 0.48 vs. 46.92 ± 1.30; p<0.05); BVRT omissions (0.37 ± 0.05 vs. 0.71 ± 0.12; p<0.05)], complex focused attention [TMT B (73.66 ± 1.93 vs. 84.72 ± 5.09; p<0.05); BVRT errors (4.61 ± 0.14 vs. 5.60 ± 0.37; p<0.05)], and set-shifting attentional abilities [TMT B-A (42.71 ± 1.68 vs. 52.51 ± 4.44; p<0.05)]. The insomnia with ≥ 6 hour sleep duration group (n=65) showed no significant differences in terms of neuropsychological functioning when compared to the normal sleeping group.
Conclusion: Insomnia with objective short sleep duration is associated with deficits in neurocognitive functioning, and to some degree comparable to that of other common sleep-disordered conditions, i.e., SDB. The neurocognitive profile suggested deficits in the "executive control of attention", a higher cognitive function that involves the lateral prefrontal cortex and the anterior cingulated cortex. Objective short sleep duration may be a useful marker of the severity of chronic insomnia.
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0863

EFFICACY OF BRIEF BEHAVIORAL TREATMENT FOR INSOMNIA (BBTI) IN OLDER ADULTS WITH INSOMNIA: FINAL RESULTS

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Introduction: Behavioral and psychological treatments for insomnia have proven efficacy, but their use in clinical practice may be limited by their length and complexity, their administration by highly-trained therapists, and the use of highly-screened subjects in previous studies. We report on final short-term outcomes from a randomized trial of BBTI versus an Information Control (IC) condition in older adults with insomnia and typical comorbidities.
Methods: Subjects included 79 older adults (68%F, mean age 72 years) who met DSM-IV criteria for insomnia disorder, recruited from medical practices and the community. Subjects with untreated current psychiatric or sleep disorders were excluded; those with medications, treated depression, and other medical disorders were included. After baseline clinical, sleep diary, and home polysomnographic assessments, subjects were randomly assigned to BBTI (n=39) or IC (n=40). BBTI included an initial session focusing on sleep restriction and stimulus control techniques, with one "booster" session after two weeks. IC included printed pamphlets on sleep, aging, and insomnia. Categorical and continuous outcome measures were assessed after four weeks.
Results: BBTI and IC subjects had no clinical or sleep differences between at baseline. A higher percentage of responders/remitters was observed in BBTI than IC (67% vs. 10%, p=.0004). BBTI was also associated with significantly greater improvement on general clinical and sleep measures (e.g., PSQI, SF-36 general health, Hamilton depression ratings); sleep diary outcomes of sleep continuity and quality; and actigraphy outcomes of sleep continuity (MANOVA group-time interaction for each category p<.004). BBTI and IC did not differ on polysomnographic outcomes.
Conclusion: BBTI was associated with significantly better short-term outcomes than IC in older adults with comorbid and primary insomnia. The magnitude of effects was similar to that observed for traditional behavioral and psychological treatments for insomnia. BBTI may be useful for treating insomnia in primary and specialty care settings
Support (optional): AG020677, RR024153

0864

AS-NEEDED TREATMENT OF INSOMNIA FOLLOWING MOTN AWAKENING: CLINICAL EFFICACY OF LOW-DOSE ZOLPIDEM TARTRATE SUBLINGUAL LOZENGE

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Introduction: A binary buffer-containing low-dose zolpidem tartrate sublingual lozenge (ZSL; Intermezzo®) is being developed for "as-needed" (prn) treatment of insomnia when a middle-of-the-night (MOTN) awakening is followed by difficulty returning to sleep. Previous studies have demonstrated rapid absorption and decreased latency to sleep onset post MOTN awakening. This study evaluated ZSL 3.5 mg in an outpatient setting for an extended period of time using prn dosing.
Methods: Adults (18 to 64 years, N=295) with DSM-IV primary insomnia characterized by MOTN awakenings were randomized to 4 weeks of prn double-blind treatment with either ZSL 3.5 mg or placebo, after a 2-week single-blind placebo screening. Subjects had to demonstrate at least 2 MOTN awakenings >30 minutes and 1 MOTN awakening >60 minutes per week to be eligible. Subjects called IVRS following an MOTN awakening and, if they had been awake > 10 minutes and had > 4 hours remaining in bed, were instructed to take study medication at that time.
Results: Compared to placebo, 3.5 mg ZSL significantly reduced latency to sleep onset after MOTN awakenings and improved sleep quality and next-day alertness ratings throughout the treatment period. Furthermore, ZSL significantly improved the post-MOTN sleep maintenance parameters of wake after sleep onset and number of awakenings versus placebo. ZSL also improved post-MOTN total sleep time, but the difference was statistically significant only at week 1 and 2. Mean weekly intake was similar for ZSL and placebo and decreased over time.
Conclusion: This study demonstrated the efficacy of ZSL for as-needed treatment of insomnia when a middle-of-the-night awakening is followed by difficulty returning to sleep. These patient reported outcomes complement the results of the previous polysomnography study.
Support (optional): Funded by Transcept Pharmaceuticals, Inc., Pt. Richmond, CA.

0865

ABSENCE OF REBOUND EFFECTS WITH LOW-DOSE ZOLPIDEM TARTRATE SUBLINGUAL LOZENGE 3.5 MG (ZSL) PRN USE: PRELIMINARY ANALYSIS

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Introduction: Insomnia characterized by difficulty returning to sleep after a middle of the night awakening (MOTN) is a common occurrence. Dosing only when needed at the time of the awakening decreases patients' overall exposure to hypnotics. It is not known, however, if as-needed MOTN dosing would result in rebound insomnia on nights medication was not taken. A low-dose (3.5 mg) zolpidem tartrate sublingual lozenge (ZSL; Intermezzo®) has been shown to be effective in treating difficulty returning to sleep following MOTN awakenings when used prn. This analysis evaluated sleep characteristics on non-dosing nights when ZSL or placebo was taken prn for the treatment of middle-of-the-night awakening and the pattern of prn use.
Methods: Adults (age 18 to 64, N=295) with prolonged awakenings were randomized to 4 weeks of prn double-blind treatment. During the 4 weeks of treatment, subjects called the Interactive Voice Response System at night after a MOTN awakening and every morning whether or not they took medication.

Results: Overall, 76.7% of the patients in the ZSL group and 79.7% of the patients taking placebo did not take medication nightly. On nights when medication was not taken, no rebound effects were seen, as determined by TST (355 min placebo, 369 min active, 373 min active baseline), sleep latency (51 min placebo, 47 min active, 46 min active baseline) or sleep quality (9 point rating: 5.1 placebo, 5.3 active, 5.0 active baseline). Drug use decreased during the 4-week period in both groups. Subjects took medication on approximately 5 nights during week 1 and 4 nights during week 4. The decrease in use in the two treatment groups was similar.
Conclusion: These data show that use of sublingual zolpidem tartrate 3.5 mg, taken only when needed, is not associated with rebound insomnia.
Support (optional): Funded by Transcept Pharmaceuticals, Inc., Pt. Richmond, CA.

0866

INSOMNIA WITH OBJECTIVE SHORT SLEEP DURATION IS ASSOCIATED WITH DIABETES

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Introduction: It has been shown that insomnia with objective short sleep duration is associated with higher autonomic activation, hypercortisolemia, and hypertension, all of which may lead to cardiometabolic disorders. In this study we examined the joint effects of insomnia and objective short sleep duration on diabetes.
Methods: 1,741 men and women randomly selected from Central Pennsylvania were studied in the sleep laboratory. "Insomnia" was defined by a complaint of insomnia with a duration of ≥ 1 year while "poor sleep" was defined as a complaint of difficulty falling asleep, staying asleep, or early final awakening. Polysomnographic sleep duration was classified into three categories: ≥ 6 hours of sleep (top 50% of the sample); 5-6 hours (approximately third quartile of the sample); and ≤ 5 hours (approximately the bottom quartile of the sample). Diabetes was defined either based on a fasting blood sugar > 126 or treatment. Logistic regression was used to calculate odds ratio and 95% CI of diabetes associated with insomnia and sleep duration, simultaneously controlling for age, race, sex, body mass index, smoking, alcohol use, depression, sleep disordered breathing (SDB), and sampling weight.
Results: Compared to the normal sleeping and ≥ 6 hour sleep duration group, the highest risk of diabetes was in individuals with insomnia and ≤ 5 hour sleep duration group [OR (95% CI) 2.95 (1.2 - 7.0)], and in insomniacs who slept 5-6 hours [OR (95% CI) 2.07 (0.68 - 6.4)]. The risk for diabetes was not significantly higher in "poor sleepers" with short sleep duration.
Conclusion: Insomnia with short sleep duration is associated with increased risk of diabetes, to a degree comparable to that of other common sleep disorders, i.e., SDB. Objective sleep duration may predict the medical severity of chronic insomnia, a prevalent condition whose medical impact has been apparently underestimated.
Support (optional): NIH grants RO1 51931, RO1 40916 and RO1 64415.

0867

ELEVATED MSLTS IN INSOMNIACS COMPARED TO POPULATION CONTROLS

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Introduction: It is hypothesized that chronic insomnia is characterized as a state of hyperarousal. Hyperarousal has been shown on various physiological measures including MSLT. This study compared MSLT scores in primary insomniacs to a population-based sample of non insomniacs and assessed the relation of sleep to MSLT in insomniacs versus controls.
Methods: Primary insomniacs (N= 57) meeting DSM-IV criteria, ages 23-70, without psychiatric disease or drug dependency and in good general health were recruited. Insomniacs had no other primary sleep disorders and a screening sleep efficiency of <85% on a NPSG. Age-matched non insomniacs, ages 23 to 61, were selected from the Southeastern Michigan Sleep Survey database containing a random population sample of the Metropolitan Detroit area. Population normals reported no psychiatric diseases, drug dependency or sleep complaints and were not taking any prescription medications. All participants had a standard NPSG and MSLT the following day at 1000, 1200, 1400, and 1600 hrs.
Results: Insomniacs had significantly higher MSLT scores in comparison to the population normals, mean daily latency of 12.849 vs. 10.463 min (p=0.007). When comparing the MSLT distributions of insomniacs and controls, there were significantly more insomniacs having MSLT scores greater than 10 min (74% vs. 47%), (X2 =8.73; p=0.003). Evaluating the relation of sleep and MSLT, the normals with high TSTs (based on a median split) had lower MSLTs than those with low TSTs (9.2 + 4.8 vs 11.8+4.6 mins; t=2.9, p<.04), In contrast, there was no difference in MSLT between insomniacs with low and high TSTs (12.8 + 4.5 vs 13.2+4.6 mins).
Conclusion: Primary insomniacs had higher MSLT scores compared to a control sample from the population. Importantly, unlike normals among primary insomniacs there is no relation between nocturnal sleep and level of daytime sleepiness.
Support (optional): NIDA grant#: R01DA17355 awarded to Dr. Roehrs.

0868

INSOMNIA WITH OBJECTIVE SHORT SLEEP DURATION IS ASSOCIATED WITH INCREASED MORTALITY IN MEN

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Introduction: It has been shown that insomnia with objective short sleep duration is associated with higher autonomic activation and hypercortisolemia and hypertension, conditions associated with increased risk for cardiovascular morbidity. The goal of this study was to examine the joint effects of insomnia and objective short sleep duration on mortality.
Methods: We examined this question in 1,741 men and women randomly selected from Central Pennsylvania who were studied in the sleep laboratory and were followed-up for 14 years (men) and 10 years (women). "Insomnia" was defined by a complaint of insomnia with a duration of ≥ 1 year while "poor sleep" was defined as a complaint of difficulty falling asleep, staying asleep, or early final awakening. Polysomnographic sleep duration was classified into three categories: ≥ 6 hours of sleep (top 50% of the sample); 5-6 hours (approximately third quartile of the sample); and ≤ 5 hours (approximately the bottom quartile of the sample). We controlled for age, race, sex, body mass index, smoking, and sampling weight.

Results: The mortality rate was 19.6% (145/741) for men and 10.3% (103/1,000) for women. Compared to the normal sleeping and ≥ 6 hour sleep duration group, the highest risk of dying was in men with insomnia and ≤ 5 hour sleep duration group [OR (95% CI) 4.51 (1.4 - 18.6)], and in men with insomnia who slept 5-6 hours [OR (95% CI) 5.0 (0.67 - 37.1)]. Controlling further for depression or sleep-disordered breathing did not change the pattern. The mortality risk was increased, but not significantly, in women with insomnia and short sleep duration.
Conclusion: Insomnia with short sleep duration in men is associated with increased mortality. Objective sleep duration may predict the medical severity of chronic insomnia a prevalent condition whose morbidity and mortality risks have been apparently underestimated.
Support (optional): Support: NIH grants RO1 51931, RO1 40916 and RO1 64415.

0869

EFFECT OF A PERIOD 3 (*PER3*) GENE POLYMORPHISM ON RESPONSE TO TASIMELTEON TREATMENT IN A PHASE ADVANCE MODEL OF TRANSIENT INSOMNIA

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Introduction: A polymorphism in the Period 3 gene (*PER3*), consisting of 4 or 5 repeats encoding a 18 amino acid motif, has been associated with diurnal preference, delayed-sleep phase syndrome and cognitive performance following sleep loss. The role of this gene in the etiology of transient insomnia is unknown. Here, we examined the effect of the *PER3* 4-5 polymorphism in improving sleep initiation and maintenance in individuals with phase advance induced transient insomnia in response to treatment with placebo or tasimelteon, a novel melatonin receptor agonist.
Methods: Transient insomnia was induced in healthy subjects through a 5-hour phase advance protocol and a "first night effect". Polysomnographic sleep parameters analyzed for genotyped individuals (N=288) included sleep efficiency (SE), total sleep time (TST), latency to persistent sleep (LPS), wake after sleep onset (WASO), rapid eye movement (REM) and non-REM (NREM) sleep. Statistical analysis of variance within and between treatment and placebo groups per genotype was performed using a generalized linear model.
Results: In the placebo group, individuals with the *PER3* non-5/5 genotype (N=67) had statistically significant lower SE than 5/5 individuals (N=9). Non-5/5 individuals treated with tasimelteon (N=190) showed statistically significant improvement in SE throughout the night, TST, LPS and WASO compared to placebo (N=22) ($p<0.05$). Significantly faster accumulation of REM and NREM sleep was also seen in non-5/5 individuals following tasimelteon treatment compared to placebo ($p<0.05$).
Conclusion: *PER3* non-5/5 individuals treated with placebo were more disrupted in their sleep by phase advance induced transient insomnia than placebo-treated 5/5 individuals. Tasimelteon treatment resulted in significant sleep improvement compared to placebo for non-5/5 individuals. A circadian phase-shifting drug such as tasimelteon, which is able to improve sleep latency and maintenance, may be beneficial, particularly to PER3 non-5/5 individuals (frequency ~90%), in treating transient insomnia associated with jet lag or circadian rhythm sleep disorders.

0870

CLASSIFICATION OF INSOMNIA SUFFERERS BASED ON LABORATORY PSG RECORDINGS AND SUBJECTIVE SLEEP REPORTS

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Introduction: Classification of chronic insomnia sufferers (INS) as psychophysiological (PsyI) or paradoxical (ParI) subtypes usually depends on objective sleep variables and sleep perception. PsyI present below normative PSG values and an accurate perception of their sleep while ParI show normal PSG values and an underestimation of sleep. The objective of this study is to describe the distribution of INS's PSG sleep parameters and accuracy of sleep perception in order to test the validity of the actual PsyI/ParI classification.
Methods: Forty-six chronic INS (Mage = 42.4 years) underwent four consecutive PSG recording nights while completing sleep diaries each morning. From nights 2 and 3, subjective (S) and objective (O) sleep measures were computed (TST, SE) as well as difference scores (O-S; diffTST, diffSE). K-Means cluster analyses were performed with 2, 3 and 4 clusters using OTST, OSE, diffTST and diffSE as variables.
Results: Based on cluster size, the 2-cluster model was retained. INS were classified on the basis of sleep perception: accurate (n=31; diffTST≤82.0min, diffSE≤18.2%) or overestimation of sleep difficulties (n=15; diffTST≥102.7min, diffSE≥22.0%). Between groups ANOVAs revealed significant differences in diffTST and diffSE ($p<.001$), but similar OTST and OSE ($p>.05$). It is noteworthy that the 3 and 4-cluster models both generated a small group (n=3) of poor sleepers (OTST =363.5min, OSE=75.7%) greatly overestimating their sleep difficulties (diffTST=279.0min, diffSE=59.7%).
Conclusion: These results suggest that chronic insomnia sufferers who accurately perceive their sleep and those who show large objective-subjective differences might belong to different insomnia subtypes. Contrary to our expectations, this classification is obtained regardless of objective sleep difficulties. However, according to the 3 or 4-cluster models, some individuals, having objectively poor sleep and considerably underestimating their sleep time, may represent another, although rare, subtype of chronic insomnia. Further research shall be conducted to validate this classification (ex. using cortical activation).
Support (optional): Research supported by the Canadian Institutes of Health Research (# 49500 and # 86571).

0871

ITI-007/ITI-722: A NEW APPROACH FOR THE TREATMENT OF SLEEP MAINTENANCE INSOMNIA AND SLEEP DISORDERS ASSOCIATED WITH PSYCHIATRIC AND NEUROLOGICAL DISEASES

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Introduction: ITI-007/ITI-722 is an investigational new drug with a unique pharmacological profile. At low doses, ITI-722 is primarily a serotonin 5-HT2A antagonist. At higher doses, ITI-007 also acts as a pre-synaptic partial agonist, post-synaptic antagonist at D2 dopamine receptors and inhibits the serotonin transporter. The present study evaluated a range of doses of ITI-007/ITI-722 in patients with sleep maintenance insomnia (SMI). The main objectives of this study were to determine if ITI-007/ITI-722 decreases wake time after sleep onset (WASO) as a measure of sleep maintenance efficacy and if ITI-007/ITI-722 increases slow wave sleep (SWS) as a biomarker for 5-HT2A brain receptor occupancy.
Methods: The study was a randomized, double-blind, complete crossover design. Eighteen patients experiencing SMI, aged 18 to 65, were included in the efficacy analysis. All subjects received three single doses of ITI-007/ITI-722 and placebo, administered the evening before overnight PSG recordings with one week washout between doses. SWS, WASO, other PSG measures, and safety were analyzed.
Results: ITI-007/ITI-722 dose-dependently decreased WASO ($p = 0.032$) and increased SWS ($p = 0.002$). ITI-007/ITI-722 preserved normal sleep architecture over the course of the night. ITI-007/ITI-722 was safe and well tolerated.
Conclusion: ITI-007/ITI-722 dose-dependently and robustly decreased WASO in patients with SMI, suggesting efficacy for improved sleep maintenance. The magnitude of effect on WASO at the highest tested dose suggests that the unique pharmacological profile of ITI-007 is use-

ful in maintaining sleep above and beyond that provided by 5-HT2A antagonism. In addition, increases in SWS sleep suggest that significant occupancy of brain 5-HT2A receptors is occurring. These data will be used to direct further study of ITI-007/ITI-722 in patients with SMI and for the treatment of sleep disorders associated with psychiatric and neurological diseases.

0872

INSOMNIA PATIENTS SHOW DECREASED CEREBRAL RESPONSE RELATIVE TO GOOD SLEEPERS DURING A VERBAL ENCODING TASK

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Introduction: Recent research has demonstrated that insomnia patients, in the absence of behavioral deficits, show decreased brain activation on verbal fluency tasks. In this study we hypothesized that relative to good sleepers (GS), patients with Primary Insomnia (PI) would demonstrate similar hypo activation on a verbal encoding task despite equivalent behavioral performance.
Methods: 12 PIs (6F 39.4 +/-9.6 yrs) were compared to 9 GS (4F 35.7 +/-7.4 yrs) on a verbal encoding task. Functional MRI BOLD activation was examined during memorization of words and FMRI analyses focused on task-specific regions of interest. Behavioral performance was measured by immediate free recall and delayed recognition memory (d-prime).
Results: As expected, there were no significant differences between the groups in memory performance (free recall: p=.523, d': p=.609). On FMRI, PIs showed decreased BOLD activation in the bilateral inferior frontal gyrus (BA 45/47) and the right inferior parietal lobe (BA 40), as compared to GS.
Conclusion: PIs showed smaller BOLD responses in task-related regions, relative to GSs, during a verbal encoding task. This finding is consistent with the only other published manuscript using FMRI to study cognition in PI. One possible interpretation of both findings is that PIs show differential vulnerability to language tasks, a vulnerability that might lead to difficulties in performance with longer or harder tasks. An alternative explanation is that PIs have higher levels of brain activation at baseline relative to good sleepers, activation which may be associated with particular cognitive features of insomnia (e.g., rumination). Given the BOLD signal is a relative measure (activation during memorization minus a baseline), such increased cognition during baseline would produce reduced BOLD signal measurements ascribed, in this case, to memorization. Future studies will be needed to examine these potential differences in activation using measures of cerebral blood flow, which can separately examine activation during baseline and memorization.
Support (optional): IMH NSRA-F31 MH077411-01A1, UCSD GCRC M01 RR00827

0873

TROUBLE FALLING ASLEEP IS ASSOCIATED WITH REDUCED ACTIVATION OF DORSOLATERAL PREFRONTAL CORTEX DURING A SIMPLE ATTENTION TASK

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Introduction: Insomnia has been associated with hyperarousal of wake-promoting brain regions during attempts to sleep. Furthermore, during periods of normal waking, insomnia patients show reduced activity of prefrontal cortical regions compared to healthy subjects. Such findings are consistent with brain imaging data showing that sleep deprivation reduces prefrontal glucose metabolism. It remains unclear whether subjective ratings of sleep onset problems are associated with prefrontal hypoactivation in healthy (i.e., non-clinical) subjects.
Methods: Sixteen healthy adults (8 male; 8 female) ranging from 40 to 57 years (M = 47.3, SD = 5.4) were assessed and scanned using fMRI (3-Tesla) while viewing a series of complex color photographs depicting either low-interest baseline pictures of leaves, flowers, and rocks, or slightly more interesting pictures of colorful dining-related utensils including decorative plates, dinnerware, and table place-settings. The paradigm was 150 seconds in duration, and comprised 5 alternating 30-second periods. Each block consisted of ten photographs (2500 msec stimulus presentation and a 500 msec inter-stimulus interval). Subjects also rated their typical sleep onset on a 10-point scale from "fall asleep easily" to "difficulty falling asleep or can't sleep at all." Scores on this scale were entered into a linear regression analysis in SPM99 to predict cerebral responses to the high-interest utensil blocks.
Results: Whole brain analysis revealed three clusters ($k \geq 25$) of activation that were negatively correlated with greater difficulty falling asleep ($p < .01$, FDR corrected), including the inferior frontal gyrus bilaterally and right inferior operculum. No regions were positively correlated with difficulty falling asleep.
Conclusion: In healthy adults engaged in a simple visual attention task, greater self-reported difficulty falling asleep was correlated with lower waking activation within bilateral regions of the inferior dorsolateral prefrontal cortex, regions that are critically involved in executive functions. Findings are consistent with evidence suggesting that poor sleep is associated with reduced prefrontal functioning.

0874

EFFECTS OF MEDITATION ON SLEEP IN INDIVIDUALS WITH CHRONIC INSOMNIA

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Introduction: Insomnia is viewed by most clinicians as a night time problem and treated with medications and behavioral methods which target night time symptoms. However, insomnia is conceptualized to be a 24 hour problem of hyperarousal and elevated measures of arousal are seen throughout the day. This study looks at the effects of daytime meditation on sleep in individuals with chronic primary insomnia.
Methods: Meditation is a state of focused internalized attention, and has been shown to reduce measures of arousal. Kriya yoga is a type of meditation which is a synthesis of different yogic techniques. 11 healthy subjects between the ages of 25-45 with chronic primary insomnia were randomized to Kriya Yoga (N-7) or Health Education (N-4) group for 2 months. Both groups received sleep hygiene education. Measures of sleep (sleep logs, Pittsburgh Sleep Quality Index) and depression (Beck Depression Inventory) were collected at baseline and post-intervention. The data was analyzed using repeated measure ANOVA and paired t-test.
Results: Measures of sleep [Sleep Latency (p=.02), Total Sleep Time (p<.001), Total Wake Time (p=.04), Wake After Sleep Onset (p=.02), Sleep Efficiency (p=.004)], sleep quality [PSQI (p<.001)] and depression [BDI (p=.004)] improved over time in both groups. There were no significant group or time by group interactions but the effect sizes were large for PSQI (p= .263, partial eta squared=.174) and TWT (p=.275, partial eta squared= .168). In separate pre-post comparisons of each group, significant improvements were seen in sleep [SL (p=.001), TST (p=.004), TWT (p=.002), WASO (p=.002), SE (p=.002)], sleep quality [PSQI (p=.001)] and depression [BDI (p=.02)] in the meditation group,

whereas the control group demonstrated improvements in TST (p=.013) only.
Conclusion: Results of this small pilot study indicate that meditation may be an effective behavioral intervention in the treatment of insomnia as seen by improvement in subjective sleep quality and sleep diary parameters with meditation. Future research is needed to test these effects with a larger sample size.

0875

TOTAL KNEE REPLACEMENT SURGERY AND POST-OPERATIVE INSOMNIA

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Introduction: Total knee replacement (TKR) is one of the most common orthopedic operations in the United States. Anecdotal reports by orthopedic surgeons describe insomnia as a common post-operative complaint following TKR surgery; conversely they report much less trouble with sleep in their patients who have undergone total hip replacement (THR). While post-operative sleep disruption from joint pain and other pain after surgery has been recognized in previous separate studies of TKR and THR, no studies to our knowledge have explored whether post-operative insomnia is more likely in TKR patients than THR patients. We hypothesize that TKR patients have significant post-operative insomnia compared to their own baseline sleep and THR subjects.
Methods: Questionnaires were given to post-operative hip and knee replacement surgery patients at their first post-operative follow-up visits. This questionnaire assessed their sleep quality and habits before and after their procedure.
Results: 48.7% of TKR subjects and 23.1% of THR subjects reported decreased sleep quality post-operatively, although this difference was not significant ($P < 0.200$). Post-operative pain in TKR subjects was significantly worse than in THR subjects (4.6 vs. 2.9 on 1-10 scale, $P< 0.007$). TKR subjects (n=39) were not significantly more likely to develop post-operative insomnia than THR subjects (n=34), although trends indicate that TKR subjects slept more poorly than THR subjects.
Conclusion: These findings demonstrate that TKR subjects have more post-operative pain than THR subjects. Although TKR subjects were not more likely to develop insomnia, there was a suggestion that sleep quality was worse. Further evaluation of sleep in TKR and THR is warranted.

0876

DEMOGRAPHIC VARIABLES AND INSOMNIA COMPLAINTS

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Introduction: In clinical practice, insomnia diagnoses are often based on a client's subjective complaints. However, it is unclear what factors influence people's perceptions of their sleep and lead them to register an insomnia complaint. We evaluated whether demographic factors, in addition to sleep and daytime functioning variables, may be related to insomnia complaints.
Methods: We used epidemiological data on sleep and daytime functioning, collected in Shelby County, Tennessee. Individuals who complained of insomnia lasting longer than six months (n=234) and those who reported no sleep problems (n=490) were compared. A hierarchical regression model with four sets was used to identify factors related to complaints. Set 1 included three sleep diary pattern variables, averaged over a two-week period. Set 2 included measures of daytime symptoms associated with poor sleep, the Fatigue Severity Scale and the Epworth Sleepiness Scale. Set 3 included the Beck Depression Inventory and the State-Trait Anxiety Inventory. Age, gender, and ethnicity were tested in Set 4.
Results: The influence of sets included later in the model was tested after controlling for the variance explained by earlier sets. Set 1 was significantly related to insomnia complaints ($R2=.23$, $F[3,730]=71.31$, $p < .001$). Set 2 ($\Delta R2=.04$, $F[5,781]=53.38$, $p<.001$) and Set 3 ($\Delta R2=.04$, $F[7,716] = 45.59$, $p < .001$) produced a significant change in the amount of explained variance in insomnia complaints. The demographic variables in Set 4 produced a significant increase in the variance explained by the model ($\Delta R2=.3$, $F[10,713]=36.27$, $p<.001$). We found a relation between race and insomnia complaint ($\beta=.13$, $t=4.11$, $p<.001$), indicating that African Americans were more likely to complain compared to Caucasian Americans, and age was related to complaints ($\beta=.16$, $t=3.01$, $p<.001$), with older individuals more likely to complain. Gender was not significantly related to insomnia complaints.
Conclusion: After controlling for seven sleep and daytime impairment variables, ethnicity and age added to explained variance in insomnia complaints. This study could not determine the salient dimensions of ethnicity and age related to insomnia complaints.
Support (optional): Research supported by National Institute on Aging grants AG12136 and AG14738.

0877

RELATIONSHIP BETWEEN SLOW WAVE SLEEP AND CIRCADIAN LEPTIN AMPLITUDE IN OLDER ADULTS WITH INSOMNIA

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Introduction: Sleep deprivation and suppression of slow wave sleep (SWS) have been shown to alter metabolic function. Considering the age-related decline in SWS it is important to determine the relationship between SWS and metabolism in older adults with insomnia. Leptin is a lipostatic signal modulating feeding behavior and energy expenditure, and age-related metabolic dysfunctions. The aim of this study is to determine the association between SWS and leptin profile in older adults with insomnia.
Methods: Fourteen sedentary healthy older adults (mean aged 63.4 ±6.2 , 13 female) with primary insomnia were recruited. Insomnia was defined as a complaint of difficulty falling asleep, staying asleep, or inadequate sleep duration on most days for at least 3 months and a reported total sleep time less than 6.5 hours. Subjects completed extensive screening and a 4 day inpatient study with 3 nights of polysomnography and serial blood sampling for 24 hours at 30 minutes intervals. Leptin amplitude (difference between nadir and acrophase) and the percentage of SWS were calculated.
Results: There was a significant correlation between leptin amplitude and SWS% ($r=0.57$, $p=0.035$), and adjusting for BMI did not change the relationship ($r=0.68$, $p=0.052$). However, there was no significant association between fasting leptin levels and SWS% ($p=0.21$), or between 24hours mean leptin and SWS% ($p=0.11$).
Conclusion: Our data indicate that higher levels of SWS are associated with heightened diurnal amplitude of leptin in older adults with insomnia. Lower levels of SWS may contribute to older people's increased susceptibility to metabolic disorders, especially those involving leptin signaling. These findings provide a possible mechanism linking insomnia and metabolic health in older adults.
Support (optional): Supported by National Institutes of Health grant#: P01 AG11412,T32 AG020506-02 and, in part, by M01 RR-00048 from the National Center for Research Resources

0878

SLEEP PATTERNS IN SLEEP-DISTURBED LONG EVANS RATS TREATED WITH ESZOPICLONE: A PRELIMINARY REPORT

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Introduction: Eszopiclone (ESZ) is prescribed for insomnia. We used a unique sleep-disturbance system in rats to simulate human sleep dysregulation, approximating the characteristics of sleep initiation- and maintenance insomnia with different schedules of planned arousals in the course of the 12/12 hr light-dark cycle. Our working hypothesis was that eszopiclone would promote normal sleep amounts in the sleep-disturbed (SD) rats.
Methods: Sleep in Long-Evans rats was repeatedly interrupted by a computer-controlled system, inducing rapid horizontal rotations of the housing cages for 1.0-1.5 secs after onset of every slow wave sleep (SWS) bout. During the active (dark) phase, arousals were triggered after 10 secs of continuous SWS, whereas in the light (rest) phase animals were allowed 180 sec of SWS before shaking was instituted. Animals were implanted with standard sleep recording electrodes and allowed six days of recovery. Then an osmotic mini-pump containing ESZ (equivalent of 10mg/kg/day in acetate buffer solution, infused at 2.5 µl/hr, IP) was implanted in each animal. ESZ delivery was initiated four days later at the onset of the SD protocol. The "sleep-perturbation" condition was then enforced for three days in the expectation of establishing a partial insomnia (n=4). Control (NS) rats (n=4) were treated similarly to SD animals but were allowed to sleep without disturbance. The last 24 hrs of each digitized 72 hr ECoG and EMG recording was visually scored, assigning one of three state-scores (REMS, SWS, Wake) to the predominant state in every 15-sec epoch. A fourth category, Mixed, was assigned to epochs lacking a majority stage.
Results: Independent t-tests indicate no differences in total sleep amounts in the SD and control groups. However, sleep patterns over 24 hr were significantly different (repeated measures ANOVA, hourly stage quantities as a repeated measure within stages and groups, $F(69,391) = 6.85$, $p < 0.0001$). Rats in the SD group were much more active in the light phase and spent more time asleep in the dark in contrast to control rats that were more active in the dark and slept more during the light. Inspection of bout frequency and number data suggests greater sleep fragmentation in the SD rats.
Conclusion: These preliminary data indicate that SD animals had more disturbed, i.e., abnormal, sleep patterns compared to NS rats despite achieving nearly equivalent total amounts of sleep and wake over 24 hours.
Support (optional): Work supported by an investigator initiated research grant from Sepracor Inc.

0879

INSOMNIA SUFFERERS' EXPERIENCES WITH EHEALTH AND DOCTOR-PATIENT INTERACTIONS

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Withdrawn

0880

INVOLVEMENT OF SEROTONERGIC SYSTEM IN POTENTIATING PENTOBARBITAL-INDUCED SLEEP OF SINI SAN LYOPHILIZED POWDER

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Introduction: Sini San is an often used prescription to treat primary insomnia in the practice of Chinese medicine clinic. It contains four herbs, including Radix Bupleuri, Radix Paeoniae Alba, Radix Et Rhizoma Glycyrrhizae and Fructus Aurantii Immaturus. It is the established method to use synergism with pentobarbital as an index to simply screen potential sleep promotion agents in mice. We previously demonstrated that Sini San can increase total sleep time in the experiment of synergism with pentobarbital in mice. In this work, we examined involvement of the serotonergic system in potentiating pentobarbital-induced sleep of Sini San lyophilized powder.
Methods: After injection of pentobarbital (50 mg/kg, IP), the time spent from loss of righting reflex to the recovery were considered as total sleep time. Six groups of mice were used in the experiment. Groups 1 and 2 received water (20ml/kg) and Sinia San lyophilized power (2.5 g/kg) via gavage for consecutive 9 days, respectively. Groups 3 and 4 received p-chlorophenylalanine (PCPA, inhibitor of tryptophan hydroxylase, 300mg/kg) and 5-hydroxytryptophan (5-HTP, 5-hydroxytryptamine precursor, 2.5mg/kg) via IP injection. Groups 5 and 6 received PCPA plus Sini San or 5-HTP plus Sini San, respectively. Afterwards, total sleep time were measured with injection of pentobarbital.
Results: The comparison between groups revealed that group 2 had significantly increased total sleep time compared to group 1. Relative to group 4, group 6 exhibited enhanced total sleep time whereas group 5 did not show significant changes compared to group 3.
Conclusion: The results suggest that serotonergic system may play important role in the sleep promotion of Sini San.

0881

FRONTAL CEREBRAL HYPOTHERMIA: A NEW APPROACH TO THE TREATMENT OF INSOMNIA

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Introduction: Insomnia is associated with increased frontal cerebral metabolism during NREM sleep. Cerebral hypothermia has been observed to reduce cerebral metabolism in other medical conditions, but its effects in insomnia are unknown. The current study aimed to determine if frontal cerebral hypothermia reduced frontal cerebral metabolism and core body temperature in insomnia patients.
Methods: 148 subjects were screened, 12 met DSM-IV criteria for Primary Insomnia, and 8 completed the study. Subjects wore a medical device on the scalp overlying the frontal cortex. The device delivered either a neutral temperature control or a mild hypothermic stimulus for 60 minutes before bedtime and during the first NREM cycle of sleep. Presentation of conditions was randomized and separated by a night of sleep. NREM sleep [18F]-FDG PET scans and core body temperature were assessed. Statistics included paired t-tests and ANCOVA.
Results: Relative to control, the frontal hypothermic condition was associated with a relative reduction in metabolism in the underlying frontal and cingulate cortex ($T = 8.2$; corrected $p < .005$; 3802 voxels). Five of eight insomnia patients showed reductions in whole brain metabolism in the frontal hypothermic condition in relation to the control. In relation to the control, the frontal hypothermic condition was associated with an accelerated drop in core body temperature around the sleep onset period (group $F = 3.68$, one-tailed $p = .03$, time $F = 53.6$, $p < .0001$; group x time $F = 1.7$, one-tailed $p = .10$). 75% of subjects subjectively reported ben-

efits of the device, such as decreased distracting thoughts, facilitation of sleep maintenance and/or refreshing sleep.
Conclusion: Frontal cerebral hypothermia reduced brain metabolism during sleep especially in the frontal cortex in insomnia patients. Frontal cerebral hypothermia also facilitated the reduction in core body temperature at sleep onset in insomnia patients. Further clinical trials are warranted to determine the efficacy of this intervention for chronic insomnia.
Support (optional): Respironics Foundation; MH66227; MH061566; AG20677; MH24652; RR000056

0882

THE RELATIONSHIP BETWEEN MSLT NAP ONSET LATENCY AND THE EFFECT OF VESTIBULAR STIMULATION ON TRANSIENT INSOMNIA

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Introduction: A series of studies suggest links between the vestibular system and sleep. This study was carried out to determine if vestibular stimulation is an effective therapy for transient insomnia in a sleep phase advance model.
Methods: This was a multi-site, double-blind, randomized, parallel-group, sham-controlled trial carried out at 6 sites in the United States. Subjects were 198 healthy normal sleepers who were randomized to receive vestibular stimulation vs sham stimulation on a night where they underwent a 4 hour sleep phase advance. Vestibular stimulation consisted of bi-lateral electrical stimulation of the vestibular apparatus of the inner ear via electrodes on the skin of the mastoid process. Multiple Sleep Latency Testing (MSLT) was carried out in all subjects during pre-treatment assessment.
Results: We did not find a significant effect of treatment on our primary outcome variable, latency to persistent sleep onset (LPS). However, our planned analysis identified that MSLT nap latency was a significant covariate. A significant effect of treatment on LPS was found in those subjects with mean MSLT sleep onset latency > 14 minutes. Vestibular stimulation was well-tolerated. All adverse effects were transient and the only adverse effects occurring in more than one individual were headache and dizziness.
Conclusion: This study provides preliminary evidence that vestibular stimulation may have a therapeutic effect in the treatment of transient insomnia in those with longer MSLT nap onset latency.
Support (optional): This study was funded by Respironics.

0883

NEW DIRECTIONS IN THE TREATMENT OF INSOMNIA: THE EFFECTS OF SELECTIVE HISTAMINE ANTAGONISM IN THE BRAIN

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Introduction: Histamine (H1) is a neurotransmitter that is activated in the latter part of the night (very early morning) to promote wakefulness. Doxepin (DXP), a potent H1 antagonist, decreases wakefulness and has demonstrated improvements in sleep onset, sleep maintenance, and early morning awakenings in insomnia patients at doses 12- to 300-fold below the established antidepressant dose range, without the expected side effects associated with H1 antagonism based on previous research. Though the sleep-promoting effects of H1 antagonists are well known, existing tricyclic and OTC sleep medications have significant receptor effects other than H1 and little systematic research has been conducted on their binding affinities.
Methods: This report evaluates the affinity of DXP at CNS targets, with an emphasis on exploring the mechanism for its sleep-promoting effects. The antihistamine sleep aids diphenhydramine and doxylamine, and the sedating antidepressant trazodone were also examined as comparators.
Results: DXP had high affinity and potency as an antagonist at the H1 receptor and substantially lower affinity for various adrenergic, muscarinic and serotonergic sites. Diphenhydramine and doxylamine also had affinity for H1, though substantially lower (20-50-fold) than DXP. Trazodone had low affinity for all sites except the 5-HT2A and α1B receptors.
Conclusion: The high affinity of DXP as an H1 antagonist represents the likely mechanism for its sleep-promoting effects and may provide an explanation for its efficacy at very low doses of 1, 3, and 6 mg. Additionally, doxepin's high selectivity for the H1 receptor may account for the absence of adverse events typically observed with tricyclic antidepressants, OTC antihistamines and sleep aids, and higher doses of doxepin. These results further suggest that selective H1 antagonism represents a promising new mechanism for the treatment of insomnia.
Support (optional): This study was funded by Somaxon Pharmaceuticals.

0884

NIGHT 1/WEEK 1 EFFECTS OF DOXEPIN 1, 3, AND 6 MG ON SLEEP ONSET ACROSS PHASE 3 TRIALS OF TRANSIENT AND CHRONIC INSOMNIA

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Introduction: This report reviews sleep onset efficacy from four Phase 3 trials evaluating doxepin (DXP 1, 3, 6 mg), a selective H1 antagonist at the doses studied, in adult and elderly patient populations with either primary or transient insomnia.
Methods: Sleep onset endpoints from four randomized, double-blind, placebo-controlled trials are reported. In three trials, patients meeting DSM-IV-TR criteria for primary insomnia were randomized for up to 12 weeks of treatment. Study A was a 12-week polysomnography (PSG) trial of elderly patients (N=240; DXP 1 and 3 mg vs. placebo (PBO)); Study B was a 4-week outpatient trial also with elderly patients (N=255; DXP 6 mg vs. PBO); Study C was a 5-week PSG trial of adult patients (N=221; DXP 3 and 6mg vs. PBO). The fourth trial (Study D) used a model of transient insomnia to simulate sleep onset disturbance in healthy adults (N=565; DXP 6 mg vs. PBO). Efficacy was evaluated with PSG and patient reports. Endpoints of sleep onset included sleep efficiency (SE) in hour 1 (Studies A, C and D), latency to persistent sleep (LPS; Studies A, C and D), and patient-reported latency to sleep onset (LSO; Study A and B). Data from the first assessment point are reported; this corresponds to night 1 for all LPS measurements; week 1 for LSO in Study A; night 1 for LSO in Study B.
Results: In Study A, DXP 3 mg significantly improved SE at hour 1 and LSO. In Study B, DXP 6 mg significantly improved LSO. In Study C, DXP 3 mg significantly improved SE in hour 1 and LPS; DXP 6mg significantly improved LPS. In Study D, DXP 6 mg significantly improved all onset variables.
Conclusion: DXP 3 and 6 mg significantly improved the majority of objective and subjective sleep onset parameters across four Phase 3 trials. These data suggest that DXP 3 and 6 mg are effective at treating insomnia characterized by sleep onset difficulty in both transient and chronic insomnia populations, in both adult and elderly patient populations.
Support (optional): This study was funded by Somaxon Pharmaceuticals.

0885

EFFECTS OF DOXEPIN 1 AND 3 MG ON EARLY MORNING AWAKENINGS IN ELDERLY ADULTS WITH PRIMARY INSOMNIA

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Introduction: Early morning awakenings (EMA), waking too early and being unable to fall back to sleep, is often a key symptom of many with chronic insomnia. Though it is a core symptom of DSM-IV diagnosed insomnia, it is seldom addressed in clinical trials examining medication effects on sleep parameters. The present analysis examined the impact of doxepin (DXP 1, 3 mg), a selective H1 antagonist at the doses studied, on EMA in an elderly population with primary insomnia.
Methods: Selected endpoints from a randomized, double-blind, placebo-controlled study of elderly adults with DSM-IV-TR defined primary insomnia are reported. Patients were randomized to 12 weeks of DXP 1 mg (N=77), 3 mg (N=82), or placebo (PBO; N=81). Efficacy was evaluated with polysomnography (PSG) data from the first and last time points of the study, nights 1 (N1) and 85 (N85). PSG endpoints of early morning awakenings included sleep efficiency (SE) in the last third-of-the-night (SE-LTN), SE last quarter-of-the-night (SE-LQN), and SE in hours 7 and 8. Next-day residual effects were assessed using the Digit Symbol Substitution Test (DSST), Symbol Copying Test (SCT), and a Visual Analog Scale (VAS) for sleepiness.
Results: On N1, DXP 1 and 3 mg significantly improved SE-LTN ($p \leq 0.0007$), SE-LQN ($p \leq 0.0011$) and SE in hours 7 ($p \leq 0.0028$) and 8 ($p \leq 0.0211$), when respectively compared with PBO. These improvements were sustained at N85, with significance versus PBO maintained for 3 mg on all parameters except SE in hour 8 ($p=0.06$). There were no significant group differences in the DSST, SCT, or VAS at any timepoint during the trial.
Conclusion: In adults with chronic insomnia, DXP 1 and 3mg significantly improved PSG parameters associated with EMA, a prevalent, bothersome, but neglected symptom. These improvements were sustained through the final hour of the night with no observed next-day residual effects. These data suggest that DXP 1 and 3 mg are effective at treating early morning awakenings without causing next-day residual effects.
Support (optional): This study was funded by Somaxon Pharmaceuticals.

0886

EFFECTS OF DOXEPIN 1, 3, AND 6 MG ON SLEEP EFFICIENCY BY HOUR FROM TWO LONG-TERM TRIALS OF CHRONIC INSOMNIA

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Introduction: Currently approved insomnia medications that act as GABA modulators have not demonstrated efficacy lasting into the final hours of the night without significant next-day residual effects. This report reviews time spent asleep by hour and residual effects data from two long-term polysomnography (PSG) trials evaluating doxepin (DXP), a selective H1 antagonist at the doses studied (1, 3, 6 mg), for the treatment of insomnia.
Methods: Time asleep was evaluated in two double-blind, placebo-controlled trials; a 12-week trial of elderly patients (Study A; N=240; DXP 1 and 3 mg vs. placebo (PBO)) and a 5-week trial of adult patients (Study B; N=221; DXP 3 and 6 mg vs. PBO). Total sleep time (TST) was analyzed globally, in each of the 8 hours of PSG assessment, and in the final third and quarter of the night. Next-day residual effects were assessed using the Digit Symbol Substitution Test (DSST) and the Symbol Copying Test (SCT). Data from Night 1 (N1) are reported.
Results: DXP 1 mg (Study A), 3 mg (Study A and B) and 6 mg (Study B) significantly improved overall TST in both trials compared with PBO. Significant improvements in the % of time asleep in the final third and quarter of the night, in the final hour, and in the majority of other hours across the night were also observed. In terms of next-day residual effects, there were no significant differences in the DSST or SCT at any dose in either trial.
Conclusion: In adult and elderly patients with chronic insomnia, DXP 1, 3 and 6 mg significantly improved the % of time asleep both globally and at most hours throughout the night, with the strongest effect in the last part of the night. Importantly, though low-dose DXP increased the amount of time asleep through the final hour of assessment (hour 8), efficacy was not accompanied by evidence of next-day residual sedation at hour 9. These data suggest histamine may be an integral part of a gating mechanism in the arousal system that allows transition from sleep to wake without residual sedation.
Support (optional): This study was funded by Somaxon Pharmaceuticals.

0887

THE EFFECT OF VESTIBULAR STIMULATION ON TRANSIENT INSOMNIA INDUCED BY A FIVE-HOUR SLEEP PHASE ADVANCE

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Introduction: A series of studies suggest links between the vestibular system and sleep. In a prior study we found that vestibular stimulation improved latency to persistent sleep in a four-hour phase advance model in transient insomnia patients who had a multiple sleep latency test (MSLT) average nap latency of > 14 minutes. This study was intended to build on that study and evaluate the effectiveness of vestibular stimulation for transient insomnia in a five-hour phase advance model.
Methods: This was a multi-site, double-blind, randomized, parallel-group, sham-controlled trial carried out at 7 sites in the United States. Subjects were 282 healthy normal sleepers who had an MSLT average nap onset latency of > 14 minutes. These subjects were randomized to receive vestibular stimulation vs sham stimulation on a night where they underwent a 5 hour sleep phase advance. Vestibular stimulation occurred during the first 60 minutes of the night and consisted of bi-lateral electrical stimulation of the vestibular apparatus of the inner ear via electrodes on the skin of the mastoid process
Results: Vestibular stimulation was associated with a significantly shorter latency to persistent sleep (LPS) compared with the sham therapy (mean difference 18.9 minutes; $p<0.04$). There were no other significant effects on sleep variables. Vestibular stimulation was well tolerated. The most common adverse effects were skin irritation and headache.
Conclusion: These results are consistent with the findings of our prior study and suggest that vestibular stimulation may have a therapeutic effect in the treatment of transient insomnia.
Support (optional): This study was funded by Respironics.

0888

POPULATION-BASED INVESTIGATION OF HLA STATUS AND SLEEP COMPLAINTS IN A CONTROL POPULATION

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Introduction: Human leukocyte antigen (HLA) DQB1*0602 is known to be associated with narcolepsy. Few studies have examined the association between HLA status and sleep phenotypes in the general population. We conducted a population-based investigation of this association in a sample of individuals from King County, Washington.
Methods: As part of the parent study, a registry was created of all prevalent cases of physician-diagnosed narcolepsy residing in King County. A control group was identified using random-digit dialing between August 2002 and March 2005. Controls were 18-50 year old residents of King County without narcolepsy (n=448). After consenting, controls were interviewed and 443 provided buccal specimens for DNA analysis: 348 (78.6%) had no HLA DQB1*0602 alleles, 81 (18.3%) had one and 14 (3.2%) had two. Fisher exact tests were performed to examine the association between the number of HLA alleles and sleep characteristics. Parasomnia was defined by controls as endorsing sleepwalking, dream enactment or violent nocturnal movements.
Results: Controls were 70.9% women, 82.1% Caucasian, with a mean age of 35.0 years (SD=9.3). Parasomnia symptoms were significantly associated with HLA DQB1*0602 allele frequency ($p<0.05$). Among those claiming to have parasomnia symptoms "often" or "always", 9 (2.6%) had no alleles, 0 had one and 2 (14.3%) had two. Among those claiming "rare" or "occasional" parasomnia symptoms, 73 (21.0%) had no alleles, 22 (27.2%) had one and 4 (28.6%) had two. Lastly, among those claiming "never" having parasomnia symptoms, 266 (76.4%) had no alleles, 59 (72.8%) had one and 8 (57.1%) had two. No significant association was found between allele copy number and the Epworth Sleepiness Scale, sleep latency, total sleep time or presence of daytime sleepiness.
Conclusion: In this population, the reporting of parasomnia symptoms was significantly associated with an increased number of HLA DQB1*0602 alleles. Confirmation is needed given the number of comparisons examined.
Support (optional): The National Institute of Neurological Disorders and Stroke (NS038523).

0889

EXCESSIVE TONIC AND PHASIC MUSCULAR ACTIVITY DURING REM SLEEP INCREASES OVER TIME IN IDIOPATHIC REM SLEEP BEHAVIOR DISORDER

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Withdrawn

0890

WHAT IS NOCTURNAL GROANING (CATATHRENIA)? - ANALYSIS OF PSG DATA -

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Introduction: Sleep related groaning (catathrenia) is characterized by episodes of nocturnal groaning (NG) during sleep and is defined as a new parasomnia in the International Classification of Sleep Disorders 2nd edition. Recently, it is reported that some cases with catathrenia respond well to continuous positive airway pressure treatment, and it should be classified in the sleep-related breathing disorders category. We describe the polysomnography (PSG) characteristics of catathrenia patients with special emphasis on sleep stages that NG occur in and temporal relationship between NG and EEG arousal, and other events of data.
Methods: The subjects were consecutive 15,052 patients who presented with sleep and/or wake problems at our sleep center between April 1998 to October 2008. Diagnosis of catathrenia was based on ICSD-2 criteria
Results: We found out 25 cases (0.17%) with catathrenia. Eight of 25 cases who presented episodes of NG on video-PSG were studied. The mean age at presentation in 8 patients (4 men and 4 women) was 33.4±11.3 years. Number of NG events among patients during PSG varied from 8 to 3,490 episodes with event duration ranging from 1.0 to 55.2 seconds. In 2 cases out of 8, NG was exclusively or predominantly observed during REM sleep (REM sleep cluster), but the others showed groaning during stage 1and 2 (non- REM sleep cluster). The relationship between NG and EEG arousal was investigated. More than 50% of the NG episodes occurred after arousal in five of eight cases, but causes of arousal were varied.
Conclusion: Our findings suggest that catathrenia is unlikely to be caused by a single pathopysiology. Catathrenia may be divided into 'REM sleep cluster' catathrenia and 'non- REM sleep cluster' catathrenia. Detailed analysis of PSG data is important to relevant to the difference of two groups and clarify the pathophysiology of catathrenia.

0891

AMPLITUDE AND DENSITY OF SLOW WAVE OSCILLATIONS PRIOR TO SOMNAMBULISTIC EPISODES RECORDED FROM SLOW WAVE SLEEP

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Introduction: Although sleepwalking episodes can be facilitated or precipitated by various factors (e.g., sleep-disordered breathing), many episodes appear spontaneously in predisposed individuals. Some studies suggest that episodes are preceded by an increase in slow wave activity, including low delta power. The aim of this study was to quantify delta activity prior to somnambulistic episodes recorded from slow wave sleep (SWS).
Methods: Twenty-two sleepwalkers (11M, 11F; mean age: 28.4±7.4) underwent a 25hr sleep deprivation protocol followed by daytime recovery sleep. All experienced at least one episode during their first SWS period. Delta activity (1-4 Hz) as well as slow delta waves (0.5-1 Hz) were separately analyzed on Cz, Fz and Pz derivations prior to each subject's episode. The mean amplitude and density of slow wave oscillations was calculated during successive 4sec windows during the 200 seconds that immediately preceded each episode. Linear regressions were used to examine possible gains in delta and slow delta activity during various time intervals (from 8 to 200sec) preceding the episodes.
Results: There were no increases in delta or slow delta activity over the 200sec investigated. However, there was a linear increase in wave density, particularly in slow delta waves, over the 32sec immediately

prior to episode onset. Wilcoxon Signed Rank tests revealed no differences in signal amplitude between the 20sec prior to the episodes and the subsequent 3min. However, the density of both delta and slow delta waves was significantly higher during the last 20sec over frontal and central derivations.
Conclusion: There is no evidence for a steady build-up of slow oscillations during the 3min that precede somnambulistic episodes. However, there is a clear increase in the density of delta and slow delta waves observed during approximately the last 30sec prior to episode onset.
Support (optional): This research was supported by the Canadian Institutes of Health Research (CIHR).

0892

EXPERIMENTALLY INDUCED AWAKENINGS FROM AUDITORY STIMULI DURING SLEEP IN SLEEPWALKERS AND CONTROLS

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Introduction: It has been suggested that sleepwalkers are more difficult to fully awaken from sleep than controls. However, no quantified comparisons have been made between these two populations. The present study assessed the effects of auditory stimuli (AS) in sleepwalkers and controls during normal and recovery sleep.
Methods: Ten sleepwalkers (4M, 6W; mean age: 26.3±5.3) and ten normal controls (3M, 7W; mean age: 25.6±3.2) were investigated. Participants were presented with AS during slow-wave sleep (SWS), REM and stage 2 sleep either during normal or recovery sleep following 25hr of sleep deprivation. In the targeted sleep stage, 3sec AS were presented at 1min intervals in ascending intensities (40dB to 90dB) after at least 1min of stable EEG and EMG until an awakening, a somnambulistic episode or a maximum of 6 stimulations was reached.
Results: When compared to controls, sleepwalkers had a significantly lower mean percentage of AS that induced awakenings during normal REM sleep, a significantly higher mean intensity of AS (in dB) that induced awakenings during normal REM sleep, and a significantly higher mean percentage of AS that induced awakenings (including awakenings and/or sleepwalking) during recovery SWS. When compared to normal sleep, recovery sleep resulted in a significantly higher percentage of AS that induced awakenings in sleepwalkers during REM sleep, and a significantly higher percentage of AS that induced arousals in both groups. There were no other significant group or sleep period differences for the mean percentage of AS or mean intensity of AS (in dB) that induced awakenings.
Conclusion: The data suggest that during normal sleep, sleepwalkers have a higher auditory awakening threshold compared to controls, but only for REM sleep. The significant increase in the percentage of AS that induced awakenings during both groups' daytime recovery stage 2 sleep could be related to circadian effects.
Support (optional): Research supported by the Canadian Institutes of Health Research and the Natural Sciences and Engineering Research Council of Canada.

0893

THE EFFECT OF ORTHODONTIC EXPANSION TREATMENT ON SLEEP ARCHITECTURE IN HEALTHY YOUNG ADULTS

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Introduction: Narrow palate may contribute to malocclusion and also predisposes to sleep disordered breathing. Rapid maxillary expansion (RME) is commonly used treatment for correcting such an orthodontic problem and RME has also been found to be effective in improving respiration and sleep in patients with sleep disordered breathing. However, little is know how the surgical treatment affects the sleep architecture in non-apneic patients. The aim of this follow-up study was to determine whether RME has an effect on NREM sleep structure in healthy, non-apneic young adults.
Methods: Eighteen patients aged 15-25 years (10 males, mean age 17.3 ±3.0 years) presenting narrow palate at the orthodontic examination, were recruited into the study. All children underwent a standardized RME procedure (mean expansion 7.6±1.7 mm). Overnight polygraph recordings in the sleep laboratory were performed following one adaptation night before and after the RME. The mean follow-up time was 9.7±0.5 months.
Results: There was a significant increase from 101.0 minutes to 123.7 minutes (22.5%, P=0.004) in the duration of sleep stages 3 and 4 after the intervention. This was counterbalanced by the reduction of sleep stage 2, from 227.1 min to 207.7 min (8.5%, P=0.08). There were no significant differences in mean sleep duration, sleep efficacy or latency, snoring, awakenings or REM sleep duration between the baseline and follow-up recordings.
Conclusion: RME improves sleep architecture in non-apneic young adults by increasing the amount of sleep stages 3 and 4. Further analyses are still needed to evaluate the effect of the treatment on respiratory and EEG spectral parameters.
Support (optional): Canadian Institutes of Health Research operating and training grant in Applied Oral Health Research

0894

SLEEPWALKING IN PATIENTS WITH PARKINSON'S DISEASE

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Introduction: Sleepwalking (SW) corresponds to a complex sleep-associated behavior, which includes locomotion, mental confusion, and amnesia. SW is present in about 10% of children and 2-4% of adults, but only 0.6% of adults report SW "de novo". In a series of 165 consecutive patients with Parkinson's disease (PD) we found SW "de novo" in 6 (4%). The aim of the present study was to assess the frequency and the characteristics of SW in patients with PD.
Methods: A questionnaire including items on sleep quality, sleep disorders, in particular SW and REM sleep behavior disorder (RBD), PD characteristics and severity, was sent to the members of the national PD patients' organization in Switzerland.
Results: 420 questionnaires were received. Three patients had to be excluded for diagnoses other than idiopathic PD. 36/417 patients (9%) reported adult SW, of them 22 (5% of the population studied) had SW "de novo". Patients with SW had significantly longer disease duration (p=0.035), they reported more often hallucinations (p=0.004) and nightmares (p=0.003), their dream content was more variable (p=0.046) and they had higher scores, suggestive for RBD in a validated questionnaire (p=0.001). Patients with SW also had a trend for a higher Epworth sleepiness scale score (p=0.055).
Conclusion: Our results suggest that SW in PD patients is more common then in the general population. SW appears to be a late manifestation of PD. Most patients with SW also had questionnaire scores suggestive for RBD. The simultaneous occurrence of SW and RBD suggests a complex disturbance of arousal, locomotion and muscle tone during REM and NREM sleep in PD.
Support (optional): The national PD patients' organization in Switzerland helped us to send the questionnaire together with its monthly magazine.

0895

TREATMENT OF REM BEHAVIOR DISORDER WITH ACETYLCHOLINESTERASE INHIBITORS

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Introduction: The author previously reported 3 cases of REM sleep behavior disorder (RBD) that improved by Tx with acetylcholinesterase inhibitors (AI) (Neurology 2000 Sept. 26;55(6):870-1). Now a series of ten cases of RBD are presented that were similarly treated with AI's and all of whom also demonstrated improvement in parasomnias.
Methods: Patients ranged from 48 to 70 yrs old with an average age of 63.9 (5F / 5M). Treatment was with the AI donepezil or rivastigmine, typically used in the treatment of Alzheimer's disease. Patients that were also found to have OSA or PLMS were included in this study if they continued to exhibit REM parasomnias after Tx of the OSA and PLMS. Duration of Tx at the time of this assessment ranged from 4 to 18 months, average of 11.5 months. Responses to treatment were based on clinical follow-up, primarily from bed partners observations.
Results: All of the patients placed on AI's demonstrated a significant improvement in the magnitude of parasomnic events and/or frequency of observed events. Dosages of medications were as high as 20 mg for donepezil, and if side effects, such as diarrhea developed, then they were switched to rivastigmine and dosages went as high as 6 mg qhs (not bid). Of note many patients with RBD who were also found to have OSA and / or PLMS demonstrated drastic improvement in their parasomnias by treatment of the OSA / PLMS alone and further treatment was not necessary. Clonazepam was not initiated in any of our patients, but two came to our center already on clonazepam with persistent REM events. Clonazepam was not withdrawn in these patients but they demonstrated improvement with the addition of the AI.
Conclusion: This study provides additional evidence that RBD can be treated by enhancing cholinergic neurotransmission. There is considerable evidence that neurons located in the pedunculopontine nuclei play a major role in producing REM sleep and the related atonia. This region activates the glycine mediated reticulospinal tract post synaptic inhibition of motor neurons. GABA neurons also play a role in the muscle atonia of REM sleep but treatment to enhance this pathway with clonazepam is frequently accompanied by sedating side effects as well as all of the other long term negative effects on sleep associated with clonazepam. Therefore, it would be reasonable to consider the use of acetylcholinesterase inhibitors as a first line treatment in patients with RBD and then switching to clonazepam if adequate clinical response is not achieved.

0896

UPDRS ACTIVITIES OF DAILY LIVING AND REM BEHAVIOR DISORDER IN PATIENTS WITH PARKINSON'S DISEASE

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Introduction: It is estimated that 74-94% of Parkinson's disease (PD) patients have sleep disorders. REM Sleep Behavior Disorder (RBD) has an estimated occurrence of 15-47% within PD. PD functionality is assessed with the widely used Unified Parkinson's Disease Rating Scale (UPDRS) that is composed of three subscales: (1) mentation, behavior, and mood (MBM); (2) activities of daily living (ADL); and (3) motor examination. The ADL subscale addresses the impact of PD on daily functioning and has been suggested to be a more accurate measure of disease progression as it is impacted less by medication cycles and motor variability than other subscales. Sleep fragmentation resulting from RBD has been shown to have a negative impact on general functioning and quality of life, thus it can be hypothesized to have a positive correlation with UPDRS-ADL scores in PD patients.
Methods: As part of a larger study, 18 patients with mild-moderate PD were assessed with the UPDRS (greater score reflects greater impairment) and with the RBD Screening Questionnaire (RBDSQ; score of ≥5 meets criteria for RBD).
Results: A one-tailed Pearson correlation analysis demonstrated a significant positive correlation ($r=0.43$, $p=0.039$) between RBDSQ score and UPDRS-ADL score, with patients with more RBD symptoms endorsing more impairment of activities of daily living.
Conclusion: Although preliminary, the results suggest that in PD, patients with more RBD symptoms have greater impairment of activities of daily living, such as speech, walking, and dressing, than patients with fewer RBD symptoms. If one considers the ADL score as a marker of disease progression, the data may also suggest that RBD becomes increasingly likely with neurodegenerative progression. Further data collection will allow for continuing assessment and control of confounding variables.
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0897

BRAIN PERFUSION ABNORMALITIES IN PATIENTS WITH IDIOPATHIC REM SLEEP BEHAVIOR DISORDER

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Introduction: REM sleep behavior disorder (RBD) is characterized by intermittent loss of normal atonia during REM sleep and elaborated motor activity associated with dream mentation. A pilot study conducted in our laboratory on eight patients with idiopathic RBD has shown perfusion abnormalities (Mazza, Neurology, 2006). The aim of this study was to investigate the regional cerebral blood flow in a different and larger sample of patients with idiopathic RBD.
Methods: Twenty patients with polysomnographically confirmed RBD and 20 healthy controls matched for age and gender were studied by means of single photon emission computerized tomography (SPECT). The RBD group was made of 14 males and six females, with a mean age of 67.60±5.99 years and disease duration of 11.37±7.23 years. The control group included 15 males and five females with a mean age of 67.35±6.38 years. None of the controls or the patients have received a diagnosis of another neurological disorder or dementia. Two-sample t-tests were made using SPM2. Significance was set at 0.01 for at least 50 contiguous voxels.
Results: Compared to controls, RBD patients showed decreased perfusion in the dorsolateral prefrontal cortex bilaterally (Brodmann 9) and the right anterior prefrontal cortex (Brodmann 10). We also found hypoperfusion in posterior cortical areas, including the left occipito-parietal cortex (Brodmann 7, 19) and the left posterior cingular cortex. Increased perfusion was found in brainstem structures including medulla, pons and putamen. We also observed hyperperfusion in the parahippocampal cortex bilaterally (Brodman 36) and in the left temporal cortex (Brodmann 21, 22, 38).

Conclusion: This provides further evidences of brain perfusion abnormalities in idiopathic RBD. These results confirm and expand those of our previous study with decreased perfusion in several cortical regions and increased perfusion in the putamen and in the pons. A similar increased perfusion in the putamen was previously reported in early PD.

0898

A LOCUS FOR AUTOSOMAL DOMINANT SLEEPWALKING ON CHROMOSOME 20Q12-Q13.12

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Introduction: Sleepwalking is a disorder of arousal that occurs during non-rapid eye movement sleep; it is common among children and less common among adults. Genetic effects have been to shown to have a significant impact on the prevalence of sleepwalking but the genes or chromosomal localization of genes responsible for sleepwalking have not been identified. The goal of this study is to describe the inheritance pattern of sleepwalking in a four-generation family and to identify the chromosomal location of a gene responsible for sleepwalking in this family.
Methods: Nine affected and thirteen unaffected family members of a single large family were interviewed regarding a variety of different sleep disorders and DNA saliva samples were collected from them. Parametric linkage analysis was performed.
Results: The proband had a history of sleepwalking since age 6 and had an extensive family history of sleepwalking with 8 other family members affected. This family did not have other sleep disorders. Genetic testing demonstrated that sleepwalking was inherited as an autosomal dominant disorder with reduced penetrance in this family. Multipoint parametric logarithm of the odds (LOD) score analysis for sleepwalking revealed a maximum multipoint LOD of 3.44 on at chromosome 20q12-q13.12 between 55.6 and 61.4 cM.
Conclusion: Sleepwalking is transmitted as an autosomal dominant trait with reduced penetrance in some families. A potential gene responsible for increased risk of sleepwalking is located on chromosome 20q12-q13.12. The adenosine deaminase gene is the most likely candidate gene in this chromosomal interval because of its relationship to slow-wave sleep activity.

0899

CLINICAL AND POLYSOMNOGRAPHIC CHARACTERISTICS OF REM SLEEP WITHOUT ATONIA

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Introduction: RBD is characterized by the polysomnographic finding of REM sleep without atonia in association with a history of dream enactment behavior or evidence of such excessive motor behaviors during PSG. RBD is frequently associated with synucleinopathies. Occasionally patients have REM sleep without atonia without a clinical history or polysomnographic evidence of RBD. It is uncertain, if REM sleep without atonia represents a separate entity or if it clinically progresses to RBD. We describe the clinical and PSG characteristics of such patients in a pilot study of 10 consecutive patients seen at our sleep center.
Methods: Retrospective review of history, examination findings, comorbidities, medications and PSG findings of patients diagnosed with REM sleep without atonia.
Results: 10 consecutive patients with REM sleep without atonia were identified. No patient had a history of excessive nocturnal motor behaviors. 5/10 patients were female. Mean age was 44.7 (+/- 16.6) years. 7/10 patients reported excessive daytime sleepiness (mean ESS 9.1 (+/-4.4)). All patients had a normal neurologic examination. Brain MRI showed a left dorsal pontine curvilinear enhancing lesion in 1 patient, bilateral cerebral hemispheric white matter lesions in another. 4/10 had comorbid psychiatric conditions, and 6/10 were using antidepressants (4 SSRI, 1 SNRI, 2 TCA, 1dopamine-norepinephrine reuptake inhibitor) with some patients taking multiple medications. 3 patients reported NREM parasomnias (2 with concurrent nightmares; 1 prior history of somnambulism). Comorbid sleep diagnosis included OSA in 4, periodic limb movements in 7, alpha intrusion in 3, and primary snoring in 1 patient.
Conclusion: There appears to be no gender predominance in RWA. Patients tend to be younger than typically seen in RBD. Psychiatric comorbidities and antidepressant use were common as were comorbid sleep diagnoses. Structural brain lesions may be found. Long-term follow up studies will be needed to determine the natural progression.

0900

IMPULSE CONTROL DISORDERS WITH THE USE OF DOPAMINERGIC AGENTS IN RESTLESS LEGS SYNDROME: A CONTROLLED STUDY

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Introduction: An increased frequency of impulse control disorders (ICDs) has been recognized with the use of dopaminergic agents in Parkinson's disease (PD). The objective of this study was to determine the frequency of ICDs with the use of dopaminergic agents in restless legs syndrome (RLS), a common condition for which this class of medications is widely prescribed.

Methods: A screening questionnaire for ICDs was administered to: 1) 100 patients with RLS currently or previously treated with dopaminergic agents; 2) 275 obstructive sleep apnea (OSA) patients without RLS or exposure to dopaminergic agents; and 3) 52 RLS patients never treated with dopaminergic agents. Patients with PD were excluded. Using available diagnostic criteria, phone interviews were conducted for those meeting survey thresholds for ICDs in order to confirm the diagnoses.

Results: Based on the questionnaire, frequencies of ICDs for the RLS group treated with dopaminergic agents were 10% compulsive shopping (3% OSA controls; 2% RLS controls), 7% pathologic gambling (1% OSA controls; 2% RLS controls), 8% hypersexuality (5% OSA controls; 2% RLS controls), and 10% punding (6% OSA controls; 8% RLS controls). These values were significant when compared to the OSA group for compulsive shopping (p=0.004) and pathologic gambling (p=0.005). Based also on the phone interviews, the adjusted frequencies of ICDs for the RLS group treated with dopaminergic agents were 9% compulsive shopping (0.7% OSA controls; 0% RLS controls), 5% pathologic gambling (0.4% OSA controls; 2% RLS controls), 3% hypersexuality (0.4% OSA controls; 0% RLS controls), and 7% punding (1% OSA controls; 0% RLS controls). These values were significant when compared to the OSA group for compulsive shopping (p=0.0002), pathologic gambling (p=0.006), and punding (p=0.005), as well as for compulsive shopping (p=0.03) when compared to the group of RLS patients never treated with dopaminergic agents. There was no statistically significant dose effect in the group of RLS patients treated with dopaminergic agents. The mean duration of treatment before onset of ICDs was 9.5 months.

Conclusion: ICDs, especially compulsive shopping and pathologic gambling, are common with the use of dopaminergic agents for treatment of RLS, regardless of dose. Given the potentially devastating psychosocial consequences of these conditions, it is critical to actively screen for ICDs in this population.

0901

EFFECTIVE TREATMENT OF IDIOPATHIC RESTLESS LEGS SYNDROME WITH PREGABALIN: A TWELVE-WEEK, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY WITH CLINICAL AND POLYSOMNOGRAPHIC ASSESSMENT

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Introduction: Pregabalin is an alpha-2 delta receptor agonist that has been approved for the treatment of disorders such as epilepsy, neuropathic pain, generalized anxiety and fibromyalgia. No controlled investigations have been performed so far in Restless Legs Syndrome (RLS), although an open study suggested therapeutic effects in neuropathic RLS. We report here on the first controlled study on the efficacy of pregabalin in idiopathic RLS.

Methods: The study was designed as a double-blind, placebo-controlled, parallel treatment trial with pregabalin. Following a two-week placebo run-in, subjects with an improvement on the International RLS Severity Scale (IRLS) total score of more than 40% were excluded. Fifty eight patients diagnosed with idiopathic RLS were then randomized to receive either a 12-week flexible-dose treatment with pregabalin (n=30) or placebo (n=28). Polysomnographic studies were performed at baseline and at the end of treatment. Severity ratings and dose adjustments were performed every two weeks by means of the IRLSSG, CGI, RLS-6, and the MOS sleep subscale.

Results: During the twelve-week treatment period with pregabalin, the IRLS score improved significantly compared with placebo (mean +SD: 19.8±4.2 to 7.4±6.9 versus 21.5±3.8 to 12.8±8.6, p=0.02). The mean effective dose of pregabalin at the end of treatment was 322.50±98.77 mg/day. Similarly, statistically significant improvements were observed on the CGI, the RLS-6 scale, and the MOS sleep subscale (all p<0.01). Treatment with pregabalin also resulted in an improvement in the mean (+SD) periodic leg movement index from 31.25±24.9 to 13.79±14.4, while in the placebo group it worsened from 33.1±36.3 to 40.98±47.15 (p>0.001). Pregabalin generally well tolerated. The main side effects reported were headache, dizziness, postural instability, dry mouth and daytime sleepiness (all <5%).

Conclusion: These results suggest that pregabalin is effective for the treatment of idiopathic RLS and exerts significant therapeutic effects both on sensitive and motor symptoms. Pregabalin is a promising alternative to existing dopaminergic treatments for the long-term management of RLS, as it is unlikely to cause RLS augmentation.

Support (optional): This study was supported by a research grant from Pfizer Inc.

0902

DOUBLE-BLIND, PLACEBO-CONTROLLED MULTI-CENTER EVALUATION OF RESTLESS LEGS SYNDROME (RLS) TREATMENT WITH A 1,000 MG OF IV IRON (FERRIC CABOXYMALTOSE -FCM)

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Introduction: Brain iron deficiency has been well documented in RLS patients. IV iron treatment with iron dextran has been demonstrated in open label trials to dramatically reduce RLS symptoms but in one controlled trial IV iron sucrose showed little benefit. The controlled study reported here evaluated efficacy of a large IV dose of FCM.

Methods: Primary moderate-to-severe RLS patients free of any RLS medications were randomly assigned to either IV FCM treatment (n=24) with 500 mg on day 0 repeated on day 5 (total 1000 mg dose) or placebo (n=21) on the same days. IRLS, MOS sleep and RLS-Qol were obtained at baseline. These were repeated at days 14 and 28 for IRLS and MOS and at day 28 for RLS-QoL. The clinician's global impression of improvement (CGI-I) was obtained at days 14 and 28. Day 14 evaluations were obtained for 24 patients on FCM and 20 on placebo and day 28 obtained for 24 on FCM and 19 on placebo. Patients were evaluated for up to 168 days after IV FCM for length of time before needing added medication for the RLS.

Results: The evaluation at day 28 showed: IRLS for FCM treated vs. Placebo decreased from baseline by 8.9 vs 4.0 (p=0.04). The number of remitters (IRLS≤10) on day 28 was 7 (29%) for FCM compared to 1 (4.8%) for placebo (p=0.051). The day 28 IRLS score ≤ 5 occurred for 4 (17%) patients on FCM vs. none on placebo (p=0.11). Total MOS sleep scores improved from baseline for FCM vs. placebo by 24 vs. 19 (p=0.09) and for RLS-QoL by 23 vs. 18 (p=0.024) points. FCM vs. placebo CGI-I was much or very much improved for 58% vs 14% (p=0.005). Satisfactory treatment not requiring added medication after IV FCM was reported for 75% of the patients 1 month, 38% at 3 months and 25% at 168 days (5.5 months). No significant adverse events were

reported. An asymptomatic transient decrease in phosphorus generally occurred that returned to normal during follow up.
Conclusion: FCM IV iron provides safe and effective treatment for moderate to severe RLS with 25% reporting no need for additional RLS medications at 168 days after treatment.
Support (optional): Study supported by Luitpold Pharma.

0903

RESTLESS LEGS SYNDROME IN PREGNANCY: A PROSPECTIVE, SYSTEMATIC STUDY

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Introduction: Three retrospective studies suggested a high frequency (11-26%) of restless legs syndrome (RLS) in pregnancy. None of these studies used standardized methods for assessment of RLS and sleep. Characteristics and determinants of RLS during pregnancy are poorly known.
Methods: Women during (from the 2nd trimester, 1x/month) and after pregnancy (8 weeks post-partum) are prospectively studied. Assessment includes 1) interview about RLS-symptoms and sleep habits/disturbances: 2) standardized questionnaires (incl. the international RLS-scale (IRLSS), Epworth sleepiness scale (ESS), and Pittsburgh Sleep Quality Questionnaire (PSQI)); 3) blood tests (incl. hemoglobin, C- reactive protein and ferritin), 4) leg actigraphy (3rd trimester and post-partum).
Results: So far 233 women were included. RLS was diagnosed in 22 women (9.5%). 28% of them had a positive family history for RLS, 60% reported onset of RLS-symptoms before the 20th week, 60% had RLS-symptoms daily, 60% had an IRLSS>20, and 85% had a PSQI> 5. Anemia (defined as Hb <11 g/dl in pregnant women) was found in 10% of affected and unaffected women. Ferritin levels <50 were found in 88% of women. Women with (pRLS) and without RLS (nRLS) had similar values in hemoglobin CRP, and ferritin (mean Hb 11.8 mg/dl in pRLS, 12mg/dl in nRLS; Ferritin 19.1 µg/l in pRLS, 13.3 in nRLS).
Conclusion: Preliminary results of this ongoing study suggest that RLS in pregnancy: 1) is present in 10% of women; 2) frequently appears early in pregnancy; 3) is often severe/ frequent; 4) may not be related (only) to anemia/low ferritin levels; 5) has a significant impact on sleep quality.

0904

ARE PERIODIC LIMB MOVEMENTS IN SLEEP ASSOCIATED WITH COGNITIVE PERFORMANCE IN OLDER WOMEN?

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Introduction: The prevalence of periodic limb movements in sleep (PLMS) and cognitive impairment increase with age, yet we know little about the association between PLMS and cognition in elders. We determined this association in community-dwelling older women, and whether it differed in those with and without clinician-identified restless legs or PLMS.
Methods: We performed a cross-sectional study of 427 women (mean age = 82.8) who completed 1 night of polysomnography and reported whether a clinician had told them that they have "restless legs or periodic leg movements." Cognition was measured with the Mini-Mental State Exam (MMSE) and the Trailmaking Test, Part B (Trails-B). We conducted linear regression analyses with periodic limb movement index (PLMI) or PLMS with arousal index (PLMA) quartiles as predictors, and log-transformed cognitive test scores as the outcomes. We repeated analyses, stratifying by clinician-identified restless legs/PLMS.
Results: The highest PLM quartiles were PLMI ≥46.5 and PLMA ≥5.2 per hr. There were no significant associations between indices and cognition among all women combined. However, among women reporting clinician-identified symptoms (n = 31), those with PLMA ≥5.2 took 53.2% longer to complete Trails-B (percent difference = 53.2, 95% confidence interval (CI) 8.0, 117.5) than those in the lowest quartile (PLMA ≤0.14), adjusting for age, race, and antidepressant use. In women without clinician-identified symptoms (n = 396), this association was non-significant (percent difference = -7.6, 95% CI -16.9, 2.8; p for interaction = 0.002). We observed a similar, trend-level interaction between PLMI and clinician-identified symptoms for the Trails-B outcome, but no interactions for the MMSE.
Conclusion: Preliminary findings indicate that PLMS are associated with worse executive function in older women reporting provider-identified restless legs/PLMS. Clinician identification of these symptoms might reflect greater symptom severity or symptom-related distress. Further studies are needed to determine whether these factors account for our findings.

0905

PREVALENCE OF RESTLESS LEGS SYNDROME IN THE SAO PAULO EPIDEMIOLOGIC SLEEP STUDY

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Introduction: Prevalence of Restless Legs Syndrome (RLS) has been reported with a wide variation. However, there is no epidemiological study using questionnaires and polysomnography (PSG) to evaluate RLS. The aim of this study was to characterize the epidemiology of RLS in the adult general population from Sao Paulo, Brazil.
Methods: A population based survey adopting a probabilistic three-stage cluster sample of the Sao Paulo city was used to represent the population according to gender, age (20-80 years), and socioeconomic classes. International Restless Legs Scale, Chalder Fatigue Scale, Beck Anxiety Inventory, and WHOQOL-BREF quality of life assessment were face-to-face applied and in-lab full night PSG was performed.
Results: A total of 1101 volunteers were selected to represent the adult population from Sao Paulo city and 1042 underwent to PSG (refusal rate=5.4%). Mean age was 42±14 yrs, 55% were women, and 60% presented BMI>25 kg/m2. Prevalence of RLS was 23.02% in the general population, 17.72% in men, and 27.65% in women. RLS frequency increased with age (p <0.001). RLS was associated with higher sleep latency, fatigue, anxiety, and with worsening physical, psychological, and social quality of life (p <0.001). Periodic leg movements during sleep (index >5 mov/h) were found in 30% of patients with RLS.
Conclusion: The results suggest high prevalence of RLS in the adult population of Sao Paulo, Brazil. This condition was associated with physical and mental complains and may negatively impact sleep and quality of life.
Support (optional): AFIP, FAPESP, FADA, CNPQ.

0906

UTILITY OF OVERNIGHT OXIMETRY AS A SCREENING TOOL FOR PERIODIC LIMB MOVEMENT DISORDER

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Introduction: Over night oximetry is a widely used case finding tool in patients with suspected sleep apnea in the UK. The oximeter records two channels of physiologic data; however, in most instances, only the saturation trace is considered in making a diagnosis and changes in pulse rate are interpreted in the context of desaturation. Thus, the utility of overnight oximetry outside the setting of sleep apnea is limited. This study was undertaken in a group of patients with periodic limb movement disorder (PLMD) to assess whether pulse rate variability (PRV) in the absence of desaturation on overnight oximetry was an indicator of PLMD.
Methods: This was a retrospective study in which 70 sleepy patients with a polysomnographic diagnosis of PLMD were included. All patients had undergone initial oximetry followed by complete polysomnography (PSG). The oximetry tracings were analyzed by four independent observers for the presence of PRV without desaturation. Further, the association between PRV and periodic limb movements (PLM) was evaluated in the summary graph of the PSG.
Results: Out of 70 patients with PLMD, 57 (81.4%) had definite evidence of PRV without desaturation on initial oximetry, which was later confirmed to be due to PLM on PSG. Thirteen (18.6%) patients had no PRV on oximetry but had PLM on PSG. The inter-observer concordance in suspecting a diagnosis of PLMD based on the presence of PRV without desaturation on oximetry was 84.3%. Thirty five (50%) patients had co-existent sleep apnea and were already on nocturnal CPAP therapy. These patients underwent oximetry for evaluation of persistent sleepiness despite optimal CPAP therapy.
Conclusion: The presence of isolated pulse rate variability on overnight oximetry is a valuable tool in suspecting non-sleep apnea syndromes like PLMD.

0907

PREVALENCE AND RISK FACTORS OF SLEEP BRUXISM IN A SAO PAULO EPIDEMIOLOGIC SLEEP STUDY

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Introduction: Sleep bruxism (SB) is a prevalent clinical condition, but the estimate of the rate in a population design study and the risk factor associated are still unclear. The aim of this study was to estimate sleep bruxism and its risk factors in an adult population based on a sample from Sao Paulo city.
Methods: A population based survey adopting a probabilistic three-stage cluster sample of the Sao Paulo city was used to represent the population according to gender, age (20-80 years), and socioeconomic classes. Questionnaires and in lab full night polysomnography(PSG) were done. History of Sleep Bruxism were considered if there was: sleep tooth grinding at last twice a week and these were classified in two groups (ICSD, 2005): Group A: SB without orofacial pain and group B with orofacial pain or discomfort on awakening. Multivariate logistic regression model to analyze risk factors to SB was done considering: Beck Depression Inventory, Anxiety Beck Inventory, periodic leg movements(PLM), headache during last six months, awake at night or in morning with headache.
Results: Tooth grinding was reported by 11.8% of the volunteers and 1/3 of these (3.8% of the total) had orofacial pain or discomfort at awakening. Ratio of SB in the women and men was 1.2:1 and 4.8:1 in group A and B respectively. SB was higher in women between 20-29y in group B. The risk factor to SB in group A was anxiety (OR,1.68), however for group B the risk and concomitant factors were: anxiety (OR,3.43), depression (OR,3.04); headache during the last six months (OR,2.11); awake at morning with headache (OR,2.44) and awake during the night with headache (OR,3.66).
Conclusion: The prevalence of SB was high in the adult population of Sao Paulo city. The association with orofacial pain was higher in women and among subjects presenting anxiety, depression and headache.
Support (optional): AFIP, FAPESP and CNPq.

0908

PRAMIPEXOLE IS WELL-TOLERATED IN THE TREATMENT OF RESTLESS LEGS SYNDROME: POOLED RESULTS FROM TWO RECENT PLACEBO-CONTROLLED TRIALS

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Introduction: Pramipexole is indicated for treatment of moderate and severe restless legs syndrome (RLS). Patients with this level of disease often require daily treatment over a long-term period. Tolerability of the RLS treatment is crucial in this situation.
Methods: Data from 2 similar 12-week, randomized, double-blind trials were pooled. In both trials, patients were required to have moderate or severe RLS and received pramipexole (optimally titrated from 0.125 to 0.75 mg) or placebo 2-3 hours before bedtime. In one of these trials (N = 403), patients were required to have comorbid mood disturbance; there were no special requirements in the other trial (N = 369).
Results: The majority of the study population was white, female, and had not previously treated their RLS. The mean age was 56 years. Overall, 48.8% (189/387) of the placebo group reported an adverse event (AE) versus 59.7% (230/385) of the pramipexole group. Drug-related AE incidence was 22.7% for placebo and 36.4% for pramipexole. Nausea, headache, and fatigue were the most common drug-related AEs (4.9%, 5.4%, and 2.3% for placebo versus 13.2%, 6.2%, and 7.3% for pramipexole). Serious AEs were reported by 3 placebo-treated patients and 5 pramipexole-treated patients. Twenty-four percent of the placebo group withdrew from the study (7.0% AE-related; 13.7% from poor efficacy) versus 13.8% in the pramipexole group (6.8% AE-related; 3.1% from poor efficacy).
Conclusion: Pramipexole was well-tolerated in this pooled analysis of 772 RLS patients. Although the AE rate was somewhat higher in the pramipexole group, these events did not result in a higher study withdrawal rate. In fact, nearly twice as many placebo-treated patients did not complete the study. Efficacy-related withdrawals accounted for the disparity.
Support (optional): These studies were supported by Boehringer Ingelheim International GmbH.

0909

IS RESTLESS LEGS SYNDROME (RLS) ASSOCIATED WITH PROTON PUMP INHIBITOR (PPI) USE? A PRELIMINARY REPORT

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Introduction: Because RLS is associated with iron deficiency, and iron absorption requires acidic gastric pH, we questioned whether PPI use, which reduces gastric acidity, may be associated with increased frequency of RLS.

Methods: This is a prospective cross-sectional study of 400 consecutive adults undergoing upper endoscopy (EGD). Patients were interviewed before EGD and excluded if they had conditions predisposing to RLS (current pregnancy, end-stage renal disease, peripheral neuropathy); Conditions associated with iron deficiency (total/partial gastrectomy, recent GI neoplasm); And recent therapy known to improve RLS symptoms. RLS was diagnosed using the four criteria of the International Restless Legs Syndrome Study Group. For each patient, we documented PPI usage, Epworth Sleepiness Score, our 6 point Subjective Sleep Quality Score, and indication for EGD.
Results: Data from our first 110 of 400 anticipated participants (68 F, 42 M; average age 55 ± 17.7 y) showed a prevalence of RLS and PPI use of 14.5% (16/110) and 44.5% (49/110) respectively. RLS prevalence was higher among PPI users [20.4% (10/49)] compared with PPI non-users [9.8% (6/61)], but this difference lacked significance (P = 0.125). RLS was diagnosed in 27.0% (10/37) of patients with the EGD indication of abdominal pain/dyspepsia compared with 8.2% (6/73) without this complaint (P = 0.012). RLS was not associated with other EGD indications. Subjective Sleep Quality Score and Epworth Sleepiness Score did not differ significantly among those with and without RLS, PPI users and non-users, or patients with RLS regardless of their PPI usage.
Conclusion: RLS occurred frequently among patients undergoing EGD, particularly when abdominal pain/dyspepsia was the EGD indication. The trend for increased RLS prevalence among PPI users may have lacked significance due to true absence of association or insufficient power at this stage of the study.

0910

CLINICAL AND SLEEP LABORATORY CHARACTERISTICS IN PATIENTS WITH AND WITHOUT EXCESSIVE DAYTIME SOMNOLENCE

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Introduction: Epidemiological studies have shown that excessive daytime sleepiness (EDS) is present in up to 35% of patients with Restless legs Syndrome, but some studies have failed to observe differences in the Epworth Sleepiness Score (ESS) between patients and controls. Nevertheless, the prevalence of EDS in RLS is surprisingly low, considering the significant amount of sleep loss present in these patients, according to subjective reports or PSG studies. The objective of the present study was to investigate the clinical and sleep laboratory differences between RLS patients with (RLS+EDS) and without EDS (RLS-EDS).
Methods: Thirty five consecutive patients diagnosed with idiopathic RLS and fourteen controls underwent a clinical evaluation that included severity measurement by means of the International Restless Legs Scale (IRLS), Epworth Sleepiness Scale as well as a sleep laboratory by means of a polysomnography and a multiple sleep latency test. Patients were classified into two separate groups depending on their ESS score: RLS+EDS (≥9; n=16) vs- RLS-EDS (<9; n=19). Clinical and sleep laboratory characteristics were compared between groups. MSLT evaluation included an assessment of the PLM index during each nap.
Results: The mean±SD ESS total scores in both groups were 12.4±1.8and 4.4±2.9, respectively. No differences were seen between groups in age, gender, age of onset, ferritin plasma levels, or IRLS total score. RLS+EDS had a lower PLM-index than PLM-EDS (20.1±23.4 vs. 38.3±11.7, p<0.05). MSLT mean values were lower in RLS+EDS (10.6±2.3) than in RLS-EDS (15.2±3.1) or controls (16.3±.9) (p<0.05). During the MSLT, PLM-index during wakefulness (PLMW) was lower in RLS-EDS (18.1±10.1) than in RLS+EDS (38.4±12.5), particularly during the third, fourth and fifth nap (p<0.05).
Conclusion: Our results show that EDS in RLS is generally mild. However, the subgroup of patients with EDS showed lower sleep latencies and a greater PLMW during the MSLT. These results suggest that in these patients, the degree of daytime sleepiness might be related to the degree of motor dysfunction during the day.

0911

PRELIMINARY EVIDENCE OF ASSOCIATION BETWEEN SINGLE NUCLEOTIDE POLYMORPHISMS ASSOCIATED WITH PERIODIC LIMB MOVEMENTS OF SLEEP AND RESTLESS LEGS SYNDROME AND MORTALITY IN END-STAGE RENAL DISEASE

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Introduction: Several single nucleotide polymorphisms (SNPs) have been reported to be associated with periodic limb movements in sleep (PLMS) and restless legs syndrome (RLS). Both disorders are themselves associated with increased mortality in patients with end-stage renal disease (ESRD). This study examined the potential association between the PLMS/RLS associated SNPs and one year mortality in incident ESRD patients.
Methods: Demographic and dialysis-related characteristics, standard laboratory tests, and vital status at one year following initiation of dialysis were collected from subjects with ESRD (n=2493) from the Accelerated Mortality on Renal Replacement (ArMORR) cohort study. Seven identified risk alleles (rs12469063, rs1026732, rs3784709, rs3923809, rs2300478, rs6710341, rs12593813) for PLMS/RLS were examined. Unadjusted and adjusted (age, gender, BMI) analyses for association of each SNP with mortality were performed. Analyses were stratified by race.
Results: There were 358 (14.4%) incident one year mortality cases. The rs12593813 variant, in the MAP2K5 gene, was significantly associated with one year mortality (unadjusted OR: AA v. GG, 1.4, 95% CI: 1.1, 1.9, p=0.029). Bivariate analyses indicated independent effects of race, BMI, and age on mortality in the entire cohort. When stratified by race, the age and BMI-adjusted OR was 2.0 (95% CI: 0.95, 4.1, p = 0.065) among blacks (AA=9% of blacks), but was not significant among whites (OR: 1.1, 95% CI, 0.7, 1.6). Additionally, rs6710341 in the MEIS1 gene was significantly associated with mortality in whites (GG=3% of whites) (unadjusted OR: GG v. AA, 2.3, 95% CI, 1.2, 4.7, p=0.017) but not in blacks (OR: 0.5, 95% CI, 0.06, 3.7). After adjustment for age and BMI, the OR in whites for this variant was 2.7 (95% CI: 1.3, 5.5, p=0.009).
Conclusion: Preliminary evidence suggests an association between SNPs associated with PLMS/RLS and mortality in ESRD.
Support (optional): The Frank Gillis Fund and the Florence Petrlik Charitable Foundation

0912

GABAPENTIN ENACARBIL IMPROVES MOOD, QUALITY OF LIFE, AND FUNCTIONING IN SUBJECTS WITH PRIMARY RESTLESS LEGS SYNDROME

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Introduction: Gabapentin enacarbil (GEn) is a non-dopaminergic therapy under investigation for the treatment of Restless Legs Syndrome (RLS). RLS symptoms negatively impact subjects' mood and quality of life (QoL). We evaluated the effects of GEn 1200 mg once daily on RLS symptoms, mood, QoL and functioning in subjects with moderate-to-severe primary RLS.

Methods: XP052 was a 12-week, double-blind, placebo-controlled multicenter study that randomized subjects with moderate-to-severe primary RLS to GEn 1200 mg (n=114) or placebo (n=108) at 5 pm with food. Co-primary endpoints were mean change from baseline in International Restless Legs Scale (IRLS) total score and proportion of responders (rated 'very much' or 'much' improved) on the investigator-rated Clinical Global Impression-Improvement (CGI-I) scale. Mood, QoL, and functioning were assessed using the Profile Of Mood State (POMS), a Mood Assessment Question (MAQ), Johns Hopkins RLSQoL questionnaire, and item 2 (ability to function in the past week) of the Post-Sleep Questionnaire (PSQ). Tolerability was assessed using adverse events (AEs), electrocardiograms (ECGs) vital signs, and laboratory tests.
Results: GEn 1200 mg improved mean IRLS total score versus placebo at Week 12 last observation carried forward (LOCF) compared with baseline (adjusted mean treatment difference [AMTD] change from baseline: -4.0; 95% confidence interval [CI]: -6.2, -1.9; p=0.0003) and more subjects were CGI-I responders (76.1% vs 38.9%; adjusted odds ratio: 5.1; 95% CI: 2.8, 9.2; p<0.0001). GEn improved POMS total mood disturbance score from baseline (AMTD: -6.9; 95% CI: -11.1, -2.7; p=0.014), overall mood (MAQ; p=0.0008), mean overall RLSQoL life impact score (AMTD [standard error]: 7.8 [1.86]; p<0.0001), and functioning (PSQ, item 2; p=0.0002) versus placebo at Week 12 LOCF. The two most frequently reported AEs (GEn, placebo, respectively) were somnolence (27% vs 7%) and dizziness (19% vs 5%). No clinically significant changes in vital signs, ECGs, or laboratory parameters were observed. No serious AEs were reported in the GEn group; 1 subject in the placebo group reported a serious AE of appendicitis that was not considered related to study medication. AEs led to withdrawal in 8% and 3% of subjects in the GEn and placebo groups, respectively.
Conclusion: GEn 1200 mg once daily significantly improved RLS symptoms and overall mood, QoL, and functioning.

0913

EVIDENCE POINT TO SPINAL ORIGIN OF PERIODIC LEG MOVEMENTS IN SPINAL CORD INJURY

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Introduction: Periodic leg movements (PLM) are a sleep disorder characterized by repetitive stereotyped movements that occur mainly in legs and are frequently associated with restless legs syndrome (RLS). PLM is reported in patients with spinal cord injury (SCI), indicating a spinal component of the disorder.
Methods: Twenty-one individuals were evaluated. The SCI group (SCIG) was composed by 5 patients with 26±7,4 years of age (males) with ASIA A cervical or thoracic chronic spinal cord injury (3,9±1,6 years of injury). The control group (CG) was composed by 16 volunteers with 24,4±4,0 years of age (8 males/8 females). Patients were evaluated with the scales: ASIA and Frankel, Sleepiness evaluation with Epworth Sleepiness scale and International Restless Legs Syndrome Scale. Polysomnography was performed in both groups.
Results: In SCIG, 80% presented PLM (PLM index: 17,7±22,8)comparing to 31,3% in CG (PLM index: 6,0±11,9; p=0,06). Mild, moderate and severe PLM were found respectively in 75%, 0% and 25% of SCIG and in 80%, 20% and 0% of CG (p=1,0). According to Epworth Sleepiness Scale, 100% of SCIG and 75% of CG presented score < 10 (p=0,708). All SCI patients presented symptoms of RLS (12,4± 7,44) and 4 volunteers of the CG had RLS symptoms (12,67± 2,52; p=0,764).
Conclusion: The preliminary results suggest that PLM in spinal cord injury originate in a central pattern generator of the spinal cord, probably different from the origin of this sleep disorder in patients without SCI. Thus, PLM might represent a possibility for the study of neuroplasticity in SCI patients.

0914

PREVALENCE OF RESLTESS LEG SYNDROME IN PATIENTS WITH CONGESTIVE HEART FAILURE

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Introduction: Cardiovascular disease has been associated with Restless Legs Syndromes (RLS) and heart failure has been linked to prevalence of periodic limb movements in sleep (PLMS). However we do not know if congestive heart failure (CHF) patients are at greater risk for symptoms of RLS or if the prevalence of RLS increases with the progression of CHF.
Methods: We surveyed 30 heart failure patients seen at UNC Heart Failure Clinic using a questionnaire focused on symptoms of RLS and sleep difficulties Pearson Product Moment Correlations were used to correlate symptoms and cardiac features (p<0.05)
Results: Participants average ages were between 50-59 years and did not vary across NYHA class (20 Male). The distribution of NYHA classification was I - 5, II - 11, III - 13, IV - 1. We found 8/30 of individuals met the four criteria for RLS and 0 had at least three criteria and 3 had two criteria, 2 had one criteria and 16 had none. 6 of these 8 had NYHA class III or IV. Separately, 8/30 reported overall poor quality sleep and 7 of that 8 were NYHA class III or IV. We found a correlation of NYHA class to RLS symptoms r=0.414 and to poor sleep quality r=0.53. Patients also noted other sleep complaints including 12/29 experienced nocturnal respiratory difficulty and 27/29 nocturia and 17/30 had coughing or snoring interrupting their sleep.
Conclusion: Twenty six percent of our patients with advanced heart failure surveyed endorsed the symptoms of RLS. This is higher than the prevalence in the general population and raises interesting questions of mechanism. Patients demonstrated a bimodal distribution for presence or absence of RLS and NYHA was more associated than age. Clinicians should ask patients with heart failure regarding the presence of symptoms of RLS as well as other symptoms of sleep disturbance.

0915

PREVALENCE OF RESTLESS LEGS SYNDROME IN BLOOD DONORS

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Introduction: Restless legs syndrome (RLS) is a common movement disorder characterized by paresthesias in the legs and sometimes in the arms that predominate in the evening and at rest and are relieved with activity. The symptoms are coupled with an irresistible urge to move the affected extremities. Iron deficiency anemia has been linked to RLS. It has been reported that repeated blood donations may be associated with RLS. A recent study from Sweden found that 25% of the female donors were affected by RLS. However, this type of study has not been replicated in the United States.
Methods: All adults attending our blood donation unit for a period of two months were interviewed. To identify those with RLS, the RLS diagnostic index questionnaire by Benes et al was employed. Data collection also focused on the number of prior blood donations and hemoglobin level. The proportion of blood donors with RLS was estimated and the number of blood donations and the hemoglobin levels were compared to the RLS status.
Results: One hundred and fifty one patients consented out of 153 screened; Of this group, seven donated only platelets and were excluded leaving 144 patients for analysis. The average number of donation was 2 for the past year and 5 during the past 5 years. In total, there were 13 patients (9%) identified with RLS. Of these 7(5%) had possible RLS, 2(1%) had intermittent RLS, and 4(3%) had chronic RLS. There was no evidence of an association between RLS and the number of blood donations or the hemoglobin level.

Conclusion: In our population of blood donors, the overall prevalence of RLS was 9%. We could not demonstrate an association between RLS and the frequency of blood donation or hemoglobin level; however, power to detect such associations is low in this study due to the small number of patients with RLS.

0916

ETHNIC DIFFERENCES IN THE PREVALENCE AND PREDICTORS OF RESTLESS LEG SYNDROME BETWEEN NON-HISPANIC WHITES AND HISPANICS OF MEXICAN DESCENT

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Introduction: The prevalence of restless leg syndrome (RLS) varies between 5-15%. However, differences in RLS prevalence in specific ethnic groups has not been extensively studied. The aim of this study was to assess the prevalence and predictors of RLS in non-Hispanic Whites (NHW) and Hispanics of Mexican descent (HMD) living in San Diego County.
Methods: Subjects participated in a telephone questionnaire as part of the Sleep-Health and Knowledge in US Hispanics study. Participants were recruited through random digit dialing and a randomization procedure to recruit only one participant per household. The diagnosis of RLS was defined by the presence of all four essential criteria by the International Restless Legs Study Group. The prevalence and predictor of RLS and sleep-related parameters were compared between NHW and HMD using student t-test, chi-square test and logistic regression.
Results: A total of 2,330 adults (1,270 NHW and 1,060 HMD, gender ratio 1:1) participated in the study. NHW were significantly older (54.4 ± 17.4 vs. 41.0 ± 15.8, $p < 0.001$) and thinner (BMI 27.2 ± 5.7 vs. 28.3 ± 6.6, $p < 0.001$) than HMD. NHW had a higher prevalence of smoking and alcohol consumption than HMD ($p < 0.007$). The prevalence of RLS was significantly higher in NHW than in HMD (17.5% vs. 14.2% $p = 0.031$). Multivariate logistic regression showed that high Epworth Sleepiness Scale score (ESS) and reports of more than two nights of having trouble falling asleep were predictors for RLS. Ethnicity was not a predictor. In ethnic subgroup analyses, ESS score and difficulty falling asleep were predictors of RLS in both groups. Being female was a predictor of RLS only in HMD.
Conclusion: The prevalence of RLS was higher in NHW than HMD. The predictors of RLS may differ slightly between NHW and HMD.
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0917

GABAPENTIN ENACARBIL IMPROVES SLEEP IN SUBJECTS WITH MODERATE-TO-SEVERE PRIMARY RESTLESS LEGS SYNDROME

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Introduction: Sleep disturbance is the primary complaint of subjects seeking treatment for Restless Legs Syndrome (RLS). Gabapentin enacarbil (GEn) is a non-dopaminergic therapy under investigation for the treatment of primary RLS. We assessed sleep outcomes with GEn 1200 mg once daily in subjects with RLS.
Methods: XP052 was a 12-week, double-blind, multicenter study. Subjects with moderate-to-severe primary RLS were randomized to GEn 1200 mg (n=114) or placebo (n=108) at 5 pm with food. Co-primary endpoints were mean change from baseline in International Restless Legs Scale (IRLS) total score and proportion of responders (rated 'very much' or 'much' improved) on the investigator-rated Clinical Global Impression-Improvement (CGI-I) scale. Sleep disturbance was assessed using the Medical Outcomes Study (MOS) Sleep Scale, the Pittsburgh Sleep Diary (PghSD) and Post-Sleep Questionnaire (PSQ). Assessments of tolerability included adverse events, vital signs, electrocardiograms (ECGs), and laboratory tests.
Results: GEn improved mean IRLS total score versus placebo at Week 12 last observation carried forward (LOCF; adjusted mean treatment difference - change from baseline: -4.0; 95%CI: -6.2, -1.9; p=0.0003) and more subjects receiving GEn were CGI-I responders (76.1% vs 38.9%; adjusted odds ratio: 5.1; 95% CI: 2.8, 9.2; p<0.0001). GEn improved MOS Sleep Scale domain scores from baseline to Week 12 LOCF compared with placebo (daytime somnolence: -17.4 vs -9.6, p=0.0018; sleep quantity: 0.8 vs 0.4 hrs, p=0.0084; sleep adequacy: 27.7 vs 13.4, p<0.0001; sleep disturbance: -29.1 vs -15.5, p<0.0001). GEn also improved PghSD average daily wake time (-17.6 vs -11.8, p<0.0033). Subjects receiving GEn reported higher overall sleep quality, greater ability to function, and fewer nights with RLS symptoms, nighttime awakenings, and hours awake per night due to RLS symptoms compared with placebo at Week 12 LOCF (all items p<0.05, for distribution of responses on PSQ). The two most frequently reported AEs (GEn, placebo, respectively) were somnolence (27% vs 7%) and dizziness (19% vs 5%). No clinically significant changes in vital signs, ECGs, or laboratory parameters were observed.
Conclusion: In addition to significantly reducing RLS symptoms, GEn 1200 mg once daily significantly improves subjective sleep outcomes compared with placebo.

0918

GABAPENTIN ENACARBIL RELIEVES PAIN ASSOCIATED WITH RESTLESS LEGS SYNDROME

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Introduction: Approximately 60% of patients with Restless Legs Syndrome (RLS) report painful symptoms. Gabapentin enacarbil (GEn) is a non-dopaminergic treatment under investigation for moderate-to-severe primary RLS. We evaluated the effects of GEn on RLS symptoms and associated pain.
Methods: XP052, a 12-week, double-blind, multicenter study, randomized subjects with moderate-to-severe primary RLS to GEn 1200 mg (n=114) or placebo (n=108) at 5 pm with food. Co-primary endpoints: mean change from baseline in International Restless Legs Scale (IRLS) total score and proportion of responders (rated 'very much' or 'much' improved) on the investigator-rated Clinical Global Impression-Improvement (CGI-I) scale. Subjects recorded 'pain associated with RLS symptoms' in the last 24 hrs on an 11-point pain scale (0=no pain, 10=most intense pain imaginable) every morning for 7 days prior to baseline and at the end of Weeks 2, 4, 8, and 12.
Results: GEn 1200 mg significantly improved mean IRLS total scores versus placebo at Week 12 last observation carried forward (LOCF; adjusted mean treatment difference [AMTD]: -4.0; 95% CI: -6.2, -1.9; p=0.0003); significantly more subjects receiving GEn were CGI-I responders (76.1% vs 38.9%; adjusted odds ratio [AOR]: 5.1; 95% CI: 2.8, 9.2; p<0.0001). Overall, 89% and 51% of subjects reported baseline average daily RLS pain scores of >0 and ≥4, respectively. GEn significantly reduced mean (SD) pain scores versus placebo for subjects with baseline pain scores >0 (-2.5 [2.32] vs -1.3 [2.07]; AMTD:-1.1; 95% CI: -1.8, -0.6; p<0.0001) and ≥4 (-3.7 [2.18] vs -1.9 [2.36]; AMTD:-1.7; 95% CI: -2.6, -0.9; p<0.0001) at Week 12 LOCF. More GEn-treated subjects reported ≥30% reduction in daily pain scores versus placebo

with baseline pain scores >0 (66.7% vs 48.1%; AOR: 2.2; 95% CI: 1.2, 3.7; p=0.0063) and ≥4 (82.0% vs 52.9%; AOR: 4.6; 95% CI: 1.8, 11.3; p<0.0010; *post hoc*). Similarly, more GEn-treated subjects reported ≥50% reduction in daily pain scores versus placebo with baseline pain scores >0 (58.6% vs 35.2%; AOR: 2.6; 95% CI: 1.5, 4.5; p=0.0006) and ≥4 (75.4% vs 33.3%; AOR: 6.9; 95% CI: 2.9, 16.5; p<0.0001; *post hoc*). The two most frequently reported adverse events (GEn, placebo) were somnolence (27%, 7%) and dizziness (19%, 5%).
Conclusion: GEn 1200 mg once daily significantly improves RLS symptoms and reduces pain associated with RLS symptoms compared with placebo.

0919

EFFICACY AND TOLERABILITY OF GABAPENTIN ENACARBIL IN SUBJECTS WITH RESTLESS LEGS SYNDROME: A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY

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Introduction: Gabapentin enacarbil (GEn) is a non-dopaminergic treatment under investigation for Restless Legs Syndrome (RLS). The efficacy and tolerability of GEn 1200 mg and 600 mg compared with placebo were assessed in adults with moderate-to-severe primary RLS (PIVOT RLS II).
Methods: In this 12-week, double-blind, randomized, placebo-controlled study (XP053), subjects received GEn 1200 mg, 600 mg, or placebo (1:1:1), at 5 pm with food. Co-primary endpoints, GEn 1200 mg versus placebo: mean change from baseline in International Restless Legs Scale (IRLS) total score and proportion of responders ('much' or 'very much' improved) on the investigator-rated Clinical Global Impression-Improvement (CGI-I) scale at Week 12 last observation carried forward (LOCF). Secondary endpoints: GEn 600 mg versus placebo on the same efficacy measures and change from baseline in IRLS total score at Week 1 (GEn 1200 mg versus placebo). Tolerability assessments included adverse events (AEs).
Results: For the modified ITT population (n=321; GEn 1200 mg=111, 600 mg=114, placebo=96), GEn 1200 mg improved mean IRLS total score versus placebo at Week 12 LOCF (-13.0 vs -9.8; adjusted mean treatment difference [AMTD] for change from baseline: -3.5; 95% CI: -5.6, -1.3; p=0.0015); and at Week 1 LOCF (-8.7 vs -6.0; AMTD: -3.0; 95% CI: -4.8, -1.1; p=0.0017). In addition, more subjects taking GEn were CGI-I responders (77.5% vs 44.8%; adjusted odds ratio [AOR]: 4.3; 95% CI: 2.3, 7.9; p<0.0001). GEn 600 mg improved mean IRLS total score versus placebo (-13.8 vs -9.8; AMTD: -4.3; 95% CI: -6.4, -2.3; p<0.0001); and more subjects taking GEn were CGI-I responders (72.8% vs 44.8%; AOR: 3.3; 95% CI: 1.8, 6.0; p<0.0001). The two most commonly reported AEs (GEn 1200 mg, 600 mg, placebo, respectively), were dizziness (24%, 10%, 5%) and somnolence (18%, 22%, 2%). AEs led to withdrawal in 7.2%, 6.1%, and 6.3% of subjects.
Conclusion: GEn 1200 mg once daily significantly improves RLS symptoms compared with placebo. A treatment benefit is also seen with GEn 600 mg once daily. Both doses of GEn are generally well tolerated.

0920

A PHASE IV RANDOMIZED, PLACEBO-CONTROLLED 6-WEEK TRIAL OF ALTERNATIVE PRAMIPEXOLE-DOSE TITRATION STRATEGIES IN RESTLESS LEGS SYNDROME

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Introduction: Restless legs syndrome (RLS) is a sensorimotor disorder that disrupts sleep. In studies establishing the efficacy of pramipexole, the starting dosage was 0.125 mg/d, with up-titration as needed to ≤0.75 mg/d. However, the optimal initial dosage merits further investigation.
Methods: At baseline, patients met RLS criteria of the International RLS Study Group and scored >15 on the International RLS Rating Scale (IRLS). For 6 double-blind weeks, they received fixed-dose pramipexole (0.25 mg/d), titrated pramipexole (0.125 mg/d for week 1, then 0.25 mg/d), or placebo. Efficacy was assessed by change on IRLS (adjusted for baseline and center) and by responder rate (at least "much improved") on the Clinical Global Impression-Improvement scale (CGI-I; analyzed by Cochran-Mantel-Haenszel test stratified by center). Onset of symptom relief was a secondary endpoint. Safety was judged by adverse events (AEs).
Results: Among patients receiving randomized study medication, 132 received fixed-dose pramipexole, 137 titrated-dose pramipexole, and 132 placebo. At 6 weeks for patients with evaluable data, change on IRLS was -15.1 (P=.0165 vs placebo) vs -13.7 (P=.2587) vs -12.6, respectively. The CGI-I responder rate was 66.7% (P=.1185) vs 59.5% (P=.8559) vs 58.3%. AEs were generally mild or moderate in intensity and the most frequent were headache, nausea, and insomnia. The dropout rate due to AEs was 9.8% vs 3.6% vs 0.8%, and during week 1 was 6.1% vs 3.6% vs 0.0%.
Conclusion: The magnitude of response to pramipexole treatment was comparable to previous studies. However, the high placebo response led to statistical significance for only the change on IRLS for the fixed 0.25-mg dose vs placebo, which was associated with a higher rate of AEs than the titrated dose, particularly during the first week of treatment. Overall efficacy and tolerability results do not support a deviation from the approved treatment regimen starting with a 0.125-mg dose.
Support (optional): This study was supported by Boehringer Ingelheim.

0921

GAMBLING, SPENDING, AND BEING SEXY: AUGMENTATION SEVERITY AND IMPULSE CONTROL IN PATIENTS WITH RESTLESS LEGS SYNDROME (RLS)

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Introduction: Augmentation affects a subpopulation of RLS patients who have been treated with levodopa and dopamine agonists. Impulsivity has also been attributed to dopaminergic treatment in both Parkinson's disease and RLS. The spectrum of augmentation includes symptom extension beyond the legs and earlier onset and severity of symptoms. We hypothesized that impulsivity (gambling, hypersexuality, and excessive spending) might comprise part of the augmentation spectrum.
Methods: We administered the Augmentation Severity Rating Scale (ASRS) for RLS and the Minnesota Impulsiveness Disorders Interview (MIDI) to augmenting (N=22) and non-augmenting (N= 11) RLS patients. We analyzed the relationship of the ASRS to iron parameters, impulse control, gender, age, chronicity of RLS (yrs, and levodopa equivalent daily dosage (LEDD).
Results: The ASRS did not correlate to iron parameters, sex, age, chronicity of RLS (yrs), or LEDD. Patients experiencing impulsivity showed a trend towards higher scores on the ASRS than those with no history

of impulse control (13.1 vs. 9.2 t=1.80 p<0.08). Gender stratification showed that augmentation severity in men (N=15) correlated to higher LEDD (p=0.03)and lower ferritin values (p=0.04). In women (N=18), augmentation severity correlated to higher ferritin levels (p=0.004) but exhibited no relationship to LEDD.
Conclusion: The relationship between augmentation and impulse control in restless legs syndrome is unclear. There is a trend towards higher augmentation severity scores in patients with a positive history of impulsivity. The biological basis for differences between augmentation severity, ferritin, and LEDD in men and women need to be further elucidated.

0922

COMPARISON OF CLINICAL AND POLYSOMNOGRAPHIC FINDINGS IN PATIENTS WITH RESTLESS LEGS SYNDROME ACCORDING TO THE PRESENCE OF PERIODIC LIMB MOVEMENTS DURING SLEEP

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Introduction: Although it has been reported that periodic limb movements during sleep (PLMS) is present up to 80% in patients with restless legs syndrome (RLS), it is unclear that PLMS could influence on sleep quality and daytime function in patients with RLS. We hypothesize that presence of PLMS in patients with RLS might influence on sleep quality and daytime function. To investigate about this issue, we analyzed sleep quality and excessive daytime sleepiness in patients with RLS.
Methods: Sixty two RLS patients were included in this study. RLS was diagnosed according to IRLSSG criteria. Group I (n=35) consisted of RLS without PLMS patients. Group II (n=27) consisted of RLS with PLMS patients. The severity of RLS symptom was assessed using International RLS Study Group Rating Scale (IRLS). Subjective sleep quality was assessed by Pittsburgh Sleep Quality Index (PSQI), Athens Insomnia Scale (AIS), and Epworth Sleepiness Scale (ESS). Serum ferritin level and various polysomnographic parameters were also compared between both groups.
Results: Mean age, IRLS and serum ferritin level were not different between groups. ESS and AIS were not significantly different between them. However, Pittsburgh Sleep Quality Index (PSQI) was significantly higher in Group I (p<0.05). Among sleep parameters except PLM related variables, only Apnea-Hyponea index (AHI) was significantly higher in Group I. Covariate analysis showed AHI has no effect on PSQI. Age and PSQI were significantly higher in Group I (p<0.05) when patients without sleep apnea (AHI < 5) were analyzed.
Conclusion: Presence of PLMS in patients with RLS has no significant negative effect on sleep quality and daytime function.

0923

RESTLESS LEGS SYNDROME: A COMMUNITY-BASED CASE-CONTROL STUDY

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Introduction: Recently, we demonstrate a 7,7% prevalence of Restless Legs Syndrome (RLS) in Brazil. The purpose of this study is to evaluate de quality of sleep and the quality of life in RLS individuals.
Methods: Design: case-control study. Cases: we interviewed 1155 adults in Cássia dos Coqueiros, São Paulo, Brazil. Those who were diagnosticated with RLS were invited to participate in the case-control study. Among of 89 patients with RLS, 68 accepted. Controls: 68 individuals from the population were randomly selected and were stratified by sex and age. Protocol: the interview was done by a neurologist with sleep medicine expertise. We evaluated quality of life, by SF-36, and quality of sleep, by Pittsburgh Sleep Quality Index (PSQI).
Results: The global PSQI score was significantly higher in RLS individuals than in controls (7,09+3,95 vs 4,8+3,3; p<0,001). The components, sleep latency (1,68+1,11 vs 0,97+0,96; p <0,001; RLS and controls, respectively), sleep disturbances (1,34+0,54 vs 0,92+0,43; p<0,001; RLS and controls, respectively) and daytime dysfunction (1,12+0,84 vs 0,64+0,74; p<0,001; RLS and controls, respectively), showed significantly higher values in RLS individuals. There weren't differences in the others components. Regarding the SF-36 domains, the RLS individuals showed significantly lower values on the physical functioning (80+22 vs 87,1+17,4; p<0,02; RLS and controls, respectively), pain (65,96+23,97 vs 75,32+244; p<0,02; RLS and controls, respectively), general health perceptions (68,09+16,63 vs 74,33+15,97; p<0,03; RLS and controls, respectively), vitality (58,59+19,78 vs 66,17+19,47; p<0,03; RLS and controls, respectively), and social functioning (70,5+26,38 vs 79,96+24,82; p<0,02; RLS and controls, respectively). There weren't differences in the others components.
Conclusion: Comparison of the SF-36 and PSQI scores of the individuals with and without RLS suggests that the disorder has a significant impact on quality of life and sleep.
Support (optional): Capes/CNPQ and FAPESP 07/54326-3

0924

RESTLESS LEGS SYNDROME IN CHILDREN: A PREVALENCE STUDY AND ASSOCIATED FEATURES IN BRAZIL

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Introduction: Epidemiological studies of RLS in adults and children are scarce, especially those using the International RLS Study Group (IRLSSG) criteria. Our group determined the prevalence of 7.7% among adult population in Brazil. Recently, PEDS-REST study found a prevalence of 2% among children. Our purpose was to determine the prevalence and features of RLS in children
Methods: A cross-sectional study was performed. It was conducted in Cássia dos Coqueiros, São Paulo, Brazil. The aim of this study was to interview 431 children, aged 6 to 12, regularly matriculated on primary school. The interview consisted of "face-to-face" interview conducted by a neurologist with sleep medicine expertise. A semi-structure questionnaire was used. RLS was diagnosed if respondents answered affirmatively to all questions of the four essential National Institutes of Health/IRLSSG criteria for diagnosis of RLS in children.
Results: We interviewed 301 subjects (74% of participation rate), which 50.8% were males. The prevalence of RLS was 5.0 %. No difference between groups were found regarding ethnics. Girls were two fold more affected than boys and serum ferritin was below 50 ng/dl in 11/14 cases (p<0.003). The RLS children are older than those without RLS (p<0,05).
Conclusion: This is the first Brazilian population study on RLS in children. The prevalence of girls was higher than boys. There was correlation between low Ferritin and RLS diagnosis. Larger studies are warranted to better characterize RLS in children.

0925

ROLE OF THE SUBSTANTIA NIGRA IN THE CONTROL OF SLEEP AND MOTOR ACTIVITY IN SLEEP

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Introduction: Clinical studies and postmortem examination have shown iron insufficiency, hypoechogenicity, and a significant decrease in the area in the substantia nigra (SN) in restless legs syndrome (RLS) patients. More than 85% of RLS patients also have periodic leg movement (PLM) disorder. Our animal studies showed that neurotoxic lesions in the SN generated PLM in sleep in the cat. In this study, we showed that muscimol, a GABA-A receptor agonist infused into the SN pars compacta (SNC) and pars reticulata (SNR) generated periodic leg/neck movements in sleep in the rat.
Methods: Adult male Sprague-Dawley rats were implanted with EEG and EMG (neck and hind limb musculatures) electrodes, and a guide cannula targeting the SN. The rats were housed individually in sound-attenuated chambers in LD 12:12. Muscimol was delivered via microdialysis probes (CMA/11) at a rate of 2 μl/min. Each one-hour of muscimol infusion (ZT4 to ZT5 in the light period) was preceded by a 2-hour baseline period of artificial cerebrospinal fluid (aCSF) infusion and was followed by a 6-hour aCSF infusion.
Results: Muscimol (50, 100, 200 μM) infused into the SNR generated a dose-dependent decrease in sleep. Muscimol infused into the SNC produced a biphasic effect on sleep. Low doses (50, 100 μM) increased sleep and high doses (200 μM) decreased sleep. All 3 doses of muscimol microinfused into the SNC and SNR also increased both periodic and isolated motor activity in the leg and neck in slow wave sleep, with profound effect on neck musculatures.
Conclusion: Our results indicate that inactivation of neuronal activity by muscimol infusion in the ventral midbrain may participate in the generation of motor disorders in sleep.
Support (optional): This work is supported by NIH R01 grants, NS042566 (YYL) and HL041370 (JMS), and Department of Veterans Affairs, VAGLAHS Sepulveda.

0926

POLYSOMNOGRAPHICS STUDY IN SLEEP BRUXISM

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Introduction: Sleep bruxism (SB) is reported by 8% of the adult population and is mainly associated with rhythmic masticatory muscle activity (RMMA) characterized by repetitive jaw muscle contractions (3 bursts or more at a frequency of 1 Hz). The purpose of this study was to evaluate the nature of sleep bruxism and to discuss its consequences.
Methods: We prospectively studied 10 patients who were referred to the clinical sleep apnea laboratory for study. They underwent standard nocturnal polysomnographic examination; in addition, masticatory activity was measured with a masseter electromyogram. Patients slept in the supine and lateral decubitus positions.
Results: Nocturnal clenching was higher in patients with higher respiratory disturbance index. 9 among 10 patients were included in the criteria of obstructive sleep apnea; average respiratory disturbance index (RDI) was 24.5. 7 among 9 patients were included in the criteria of position related obstructive sleep apnea. 195 clenches demonstrated in all patients. 176 among 195 clenches were associated with the respiratory events related arousals. 164 among 195 clenches demonstrated while in supine position. All the patient had a special position without evidence of sleep bruxism.
Conclusion: We conclude that there is an association between sleep related breathing disorder and bruxisms that sleep position affects the incidence of both sleep disordered breathing and bruxisms, and that analysis of apneas and hypopneas and clenching events in both supine and lateral decubitus sleeping positions may be helpful.

0927

EXPERIENCE WITH PRAMIPEXOLE IN THE THERAPY OF THE SYMPTOMS OF RLS

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Introduction: Patients with RLS may present with symptoms of insomnia and excessive daytime sleepiness, that can significantly interfere with daytime personal and social activities, cause emotional disturbances. Dopamine receptor agonists are now considered the drugs of choice for the management of RLS. They improved the uncomfortable sensations, urge to move and other symptoms of RLS. Pramipexole has been reported to be effective in the treatment of RLS symptoms in the international literature. Treatment with pramipexole even in long-term studies was associated with mild augmentation, only, which, however, was easily controllable.
Methods: Twenty one patients with idiopathic RLS received pramipexole as monotherapy. The dose range was between 0.88 and 0,54 mg/day. Mean age of male patients (n=8) were aged 46,25(±9,18) years, whereas female participants (n=13) were aged 38,38 (±8,93) years on average. Two patients discontinued pramipexole owing to the lack of efficacy (n=2), the one discontinued because occurrence of side effects (n=1). No augmentation occurred. Therapeutic efficacy was monitored with the International RLS Study Group Rating Scale (IRLS), the Epworth sleepiness scale and the Insomnia Severity Index (ISI) at the beginning of the treatment and at 12 weeks. Changes associated with pramipexole treatment were presented using box and whiskers diagrams.
Results: As reflected by IRLS rating scale (24,9 SD 5,7 vs. 9,1 SD 2,3) and Epworth sleepiness scale (13,8 SD 3,1 vs. 6,1 SD 2,1) treatment with pramipexole accomplished a substantial improvement. Analyzing baseline vs. post-treatment mean values with Student's one-tailed t-test revealed a statistically significant difference (p:0,0023). Treatment with pramipexole was associated with an improvement of the Insomnia Severity Index (ISI).
Conclusion: In our study we measured the effect of pramipexole treatment on improving sleep and daytime sleepiness.

0928

PHASIC ELECTROMYOGRAPHIC ACTIVITY IN PARKINSON'S DISEASE (PD) DISTINGUISHES RIGID (RD) FROM TREMOROUS (TR) SUBTYPES

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Introduction: Motor features of PD are predictive of disease course, with RD subtypes progressing more rapidly than those with predominantly tremor (TR). We evaluated phasic EMG activity in sleep to discriminate between these subtypes.
Methods: 28 patients (X age = 61.3; 21 M, 7 F, X yrs with PD = 10.9) were evaluated by a blind rater using the Unified Parkinson's Disease Rating scale (UPDRS). Relative predominance of TR vs RD was calculated as the maximal 5-site UPDRS TR rating (bilateral upper/lower extremities plus face) (range 0 - 4) minus the maximal 5-site RD rating (bilateral upper/lower extremities plus neck) (range 0 - 4). Overall TR vs RD predominance was calculated similarly as the sum of the 5-site rating (range -20 to + 20). Phasic EMG activity (PEM) during sleep was quantified as previously described from both REM and NREM sleep in chin, bilateral anterior tibialis and brachioradialis (J Clin Neurophysiol 2006: 23: 59-67).
Results: RD subtype predominated (X UPDRS sum difference = -3.5; range -18 to + 20). Based on maximal motor impairment site, 5 pts were considered TR subtype. TR was significantly lower than RD for PEM for the following: chin NREM ($p = .006$); L arm NREM ($p = .097$); R arm REM ($p = .027$); R arm NREM ($p = .072$); chin REM and all leg values trended in the similar direction. RD PEM rates were approximately twice that of TR rates for all PEM variables.

Conclusion: PD patients with a preponderance of waking hyperkinesis (TR subtype) exhibited less motor activity during sleep than rigid patients. PEM activity in both REM and NREM sleep could represent indirect influences of the basal ganglia over brainstem pre-motor networks or primary brainstem pathology in RD as opposed to the corticothalamic circuits thought to subserve tremor.
Support (optional): NS-050595

0929

RESTLESS LEGS SYNDROME IN DIFFERENT SUBTYPES OF CHARCOT-MARIE-TOOTH DISEASE

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Introduction: Restless legs syndrome (RLS) exists in 7.2% to 11.5% of adults in western country and 7.5% in Korea, often associated with various medical conditions including peripheral neuropathy. Charcot-Marie-Tooth disease (CMT), one of the well-known inherited neuropathies, was reported higher incidence of RLS in type II CMT with axonal polyneuropathy, but not in type I with demyelinating polyneuropathy, but has not been examined precisely in other genetic subtypes. We investigated the prevalence of RLS in a large number of CMT patients, whose diagnosis was confirmed genetically, to show the possible relationship with genetic subtypes and the characteristics of specific phenotypes.
Methods: 155 patients with CMT (mean age, 35.6 years; 75 males and 80 females), diagnosed by clinical and neurophysiologic study, and confirmed by genetic study, were enrolled in this study. Genetic types of CMT patients were type I (81/154), type IIA (44/154), type X (19/154) and distal hereditary motor neuropathy (dHMN, 11/154). They underwent the telephone interview with the questionnaire about sleep-related complaints, including RLS, snoring, apnea, excessive daytime sleepiness or insomnia. The diagnosis of RLS was based on the standardized criteria of international RLS study group (IRLSSG), and the severity of RLS was evaluated as well. Among them, 10 patients with RLS underwent night polysomnogram (PSG).
Results: The overall prevalence of RLS in CMT patients was 10.3% (16/155) and the mean RLS severity score was 19.7±8.9. The prevalence of RLS in each subgroup was 8.5% in type I, 9.1% in type II, 11.1% in type X, and 27.3% in dHMN (p = 0.279). Other sleep-related symptoms were snoring (17%), witnessed apnea (7.8%), choking sensations (10.4%), excessive daytime sleepiness (23.4%), frequent awakening (30.3%), leg kicking during sleep (3.2%), insomnia (10.5%) and non-refreshing sleep (62.7%). Patients with dHMN complained of more prevalent frequent awakening during sleep than other groups (p= 0.016). Mean periodic limb movement index during sleep of 10 RLS patients was 5.1±7.3/hr and mean respiratory disturbance index was 14.6±9.0/hr in night PSG.
Conclusion: This study showed that dHMN showed higher prevalence of RLS, while no difference was found between in CMT type I, type II and type X CMT. These findings suggest there might be a different pathophysiology causing RLS other than abnormal sensory perception and axonal damage.

0930

A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED, DOSE-RESPONSE STUDY TO ASSESS THE PHARMACOKINETICS AND TOLERABILITY OF GABAPENTIN ENACARBIL IN SUBJECTS WITH RESTLESS LEGS SYNDROME

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Introduction: Gabapentin enacarbil (GEn), a non-dopaminergic therapy under investigation for the treatment of Restless Legs Syndrome (RLS), provides sustained, dose-proportional gabapentin exposure in healthy adults. We evaluated gabapentin exposure, efficacy, and tolerability across four doses of GEn in subjects with RLS.
Methods: During this 12-week, double-blind, placebo-controlled, parallel-group study (protocol XP081), subjects with moderate-to-severe primary RLS were randomized to GEn 600, 1200, 1800, or 2400 mg (extended-release tablets) or placebo once daily at 5 pm with food. Plasma gabapentin concentration was measured at Weeks 4 and 12 (0, 0.5, 1, 2, 3, 4, 5, 6, 8, 10, 12, 16, 20, and 24 hrs post-dose) using LC-MS/MS methods and analyzed by noncompartmental methods. Tolerability evaluation included treatment-emergent adverse events (AEs), laboratory values, vital signs, and electrocardiograms (ECGs). Efficacy was assessed with International Restless Legs Scale (IRLS) scores and investigator ratings of response, and will be presented separately.
Results: 217 subjects were randomized (GEn 600 mg, n=48; 1200 mg, n=45; 1800 mg, n=38; 2400 mg, n=45; placebo, n=41). The half-life of gabapentin (~6 hrs) was consistent across the dose range; time-to-peak plasma concentration was 7-9 hrs. Gabapentin exposures in plasma at steady state at Week 4 over the dose range studied were: mean $C_{ss,max}$ (μg/mL): GEn 600 mg=3.86, 1200 mg=7.14, 1800 mg=11.4, 2400 mg=14.0; mean $AUC_{ss,24}$ (μg*hr/mL): GEn 600 mg=49.3, 1200 mg=96.1, 1800 mg=141.0, 2400 mg=176.0; mean T_{max} (hr): GEn 600 mg=8.76, 1200 mg=8.57, 1800 mg=7.61, 2400 mg=8.01. Exposure was not significantly changed at Week 12: mean $C_{ss,max}$ (μg/mL): GEn 600 mg=4.14, 1200 mg=7.15, 1800 mg=12.0, 2400 mg=13.3; mean $AUC_{ss,24}$ (μg*hr/mL): GEn 600 mg=51.4, 1200 mg=95.7, 1800 mg=146.0, 2400 mg=173.0; mean T_{max} (hr): GEn 600 mg=6.96, 1200 mg=8.72, 1800 mg=8.00, 2400 mg=8.13. The most commonly reported AEs in each GEn group were somnolence and dizziness, which increased with dose, usually occurred during the first 2 weeks of treatment, and were mild or moderate in intensity. No clinically relevant safety concerns were identified from laboratory values, vital signs, or ECGs.
Conclusion: GEn once daily provides dose-proportional gabapentin exposure over the dose range of 600-2400 mg in subjects with moderate-to-severe primary RLS and is generally well tolerated.

0931

VALIDATION OF THE POST-SLEEP QUESTIONNAIRE (PSQ) FOR ASSESSMENT OF SLEEP IN SUBJECTS WITH RESTLESS LEGS SYNDROME (RLS)

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Introduction: The 5-item post-sleep questionnaire (PSQ) was developed specifically for RLS: it measures subjects' perception of sleep quality; ability to function; number of nights with RLS symptoms; number of awakenings per night; number of hours awake per night. To assess the psychometric validity and responsiveness of the PSQ in subjects with moderate-to-severe primary RLS.
Methods: Data from two similar US clinical trials (PIVOT RLS I and II) of gabapentin enacarbil (XP13512/GSK138262) versus placebo were

pooled for these analyses. Convergent validity was assessed by correlating PSQ scores with the following: International Restless Legs Scale (IRLS); Profile of Mood States (POMS); RLS Quality of Life (RLSQoL); Medical Outcome Study Sleep Scale (MOS). Divergent validity was assessed by correlating PSQ scores with demographic variables that were expected to be unrelated. Known-group validity was determined by assessing whether PSQ scores discriminated among subjects with varying RLS symptom severity based on IRLS total score. Responsiveness to change in clinical status, measured by investigator-rated individual Clinical Global Impression (CGI) scores, was assessed by the effect size of change from baseline PSQ scores.
Results: The analysis included 544 adults. All PSQ scores showed significant correlations with the IRLS total score (r= 0.25 to 0.49; P<0.0001 for all). Ability to function (PSQ item #2) showed significant correlation with POMS fatigue-inertia score (r= 0.48), RLSQoL (r= -0.57) and MOS daytime somnolence score (r= 0.43) (P<0.0001 for all reported). As expected, PSQ scores had low, non-significant associations with demographic variables. The PSQ was able to discriminate among IRLS-measured levels of symptom severity in this population (P<0.0001). For all PSQ scores, the magnitude of effect size among improved subjects ranged from moderate to large (Cohen's D 0.50 to 3.30).
Conclusion: The PSQ is a valid and responsive measure of RLS-associated sleep outcomes among subjects with moderate-to-severe primary RLS.

0932

DEVELOPING AND VALIDATING A PATIENT-REPORTED POST-SLEEP DIARY FOR RESTLESS LEGS SYNDROME (RLS)

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Introduction: Sleep improvement is an indicator of treatment success in RLS. Some sleep outcomes are best assessed by the patient. The FDA recommends that patient-reported outcome (PRO) instrument development starts with the patient perspective, with validity and reliability confirmed using measurement theory. Develop and validate a patient-reported diary that captures RLS-related sleep outcomes, following FDA guidance for PROs.
Methods: Patient focus groups and cognitive debriefing sessions were used to develop a subjective daily sleep diary. The resulting 12-question subjective post-sleep diary (SPSD) was then evaluated by psychometric testing in 181 subjects with physician-diagnosed RLS, using an Interactive Voice Response System (IVRS). The following assessments were completed: the SPSD (captured daily for a week); the International Restless Legs Syndrome rating scale (IRLS), Medical Outcomes Study sleep scale (MOS), Social Desirability Response Set survey (SDRS), and Patient Global Impression of Sleep (SGI) (all assessed on Day 7, adjusted to relate to the past week). Internal consistency, convergent validity, divergent validity, and known-groups validity were assessed for seven derived SPSD scores.
Results: These findings are based on 89 participants (49%) who completed the SPSD on seven consecutive mornings. SPSD-derived scores had moderate to large correlations with the IRLS (range, -0.57 to 0.62; all P<0.01) and the MOS (31 of 35 coefficients: range, -0.59 to 0.76; P<0.05), demonstrating convergent validity, and low correlations with the SDRS (range -0.22 to 0.06), demonstrating divergent validity. The SPSD had acceptable known-groups validity with RLS severity and SGI: worse SPSD scores were associated with greater symptom severity (all P<0.05) and worse impressions of sleep (P<0.0001, except sleep latency).
Conclusion: The 12-question, daily SPSD was developed to measure RLS-related sleep outcomes according to FDA guidelines on PRO development. The SPSD, completed via IVRS, was found to have acceptable psychometric properties of consistency and validity within an RLS population.

0933

APLINDORE, A PARTIAL DOPAMINE AGONIST, REDUCES PERIODIC LIMB MOVEMENTS IN PATIENTS WITH RESTLESS LEGS SYNDROME

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Introduction: Aplindore is a dopamine partial agonist evaluated for the treatment of RLS. Full agonists currently available have side effects such as daytime somnolence and nausea and require titration over several days or weeks. As a partial agonist, aplindore may be better tolerated with fewer side effects and greater dosing flexibility. This study was designed to evaluate the effect of aplindore on the periodic limb movements index (PLMI) during sleep.
Methods: This single-blind, multi-center study compared the mean change in PLMI from placebo (baseline) to the highest aplindore dose administered. RLS was confirmed by ICSD-2 criteria, an IRLS score of >15 at screening and PLMI >10 during an adaptation night in the sleep lab. Following adaptation, patients spent a placebo-dosed night in the lab and then single nights of sequentially increasing doses of aplindore from 0.05mg to 0.2mg. Additional doses to a maximum of 0.7mg were administered if >50% reduction in PLMI was not achieved. Other assessments included an RLS severity scale and IRLS.
Results: Twenty-seven patients were enrolled, 26 received at least 1 aplindore dose. A planned interim analysis (IA) of the primary endpoint was conducted on 19 per-protocol patients. IA indicated a significant reduction in mean PLMI, from baseline of 33.97 to 8.20 (p<0.0001). With initial dosing of 0.05mg, >60% of patients had a significant decrease in PLMI. Intention to treat analysis (n=26) showed a significant reduction in mean PLMI (p=0.0001). IRLS and RLS severity scales showed a reduction in symptoms. Headache and nausea were uncommon and the rate similar to placebo. There were no SAEs.
Conclusion: In this initial study in RLS patients, aplindore was efficacious at low doses and generally well tolerated. The absence of significant side effects with single low dose efficacy suggests the partial agonist properties of aplindore may be advantageous over current therapies.
Support (optional): This work was supported by Neurogen Corporation.

0934

A MAINTENANCE OF EFFICACY STUDY OF GABAPENTIN ENACARBIL VERSUS PLACEBO IN SUBJECTS WITH RESTLESS LEGS SYNDROME

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Introduction: Gabapentin enacarbil (GEn) is a non-dopaminergic treatment under investigation for Restless Legs Syndrome (RLS) that provides extended, dose-proportional gabapentin exposure. We evaluated the maintenance of efficacy and tolerability of GEn 1200 mg compared with placebo in the treatment of subjects with moderate-to-severe primary RLS.
Methods: Study XP060 comprised a 24-week, single-blind (SB) phase (GEn 1200 mg/day) followed by a 12-week, placebo-controlled, double-

blind (DB) phase. SB responders were randomized to GEn 1200mg/day or placebo once daily at 5 pm with food; placebo subjects received 600 mg/day for the first 2 weeks of the DB phase. Primary endpoint: proportion of subjects relapsing (an increase of ≥6 on the International Restless Legs Scale total score from Week 24 to a score ≥15, and a rating of 'much worse' or 'very much worse' on the investigator-rated Clinical Global Impression of Change scale, on two consecutive visits ≥1 week apart, or withdrawal due to lack of efficacy) during the DB phase. Tolerability assessments included all adverse events (AEs) during the SB phase and new/worsening AEs during the DB phase. Vital signs, electrocardiograms (ECGs), and laboratory tests were also used to assess tolerability.
Results: Of 327 subjects enrolled, 194 (GEn=96, placebo=98) were considered responders and randomized into the DB phase. Significantly more subjects receiving placebo relapsed during the DB phase compared with those receiving GEn (22.7% vs 9.4%; odds ratio: 0.353; 95% CI: 0.2, 0.8; p=0.0158). SB phase: the most commonly reported AEs were somnolence (29.8%), dizziness (22.1%), and headache (12.6%). DB phase: no AEs were reported by ≥5% of GEn-treated subjects; nasopharyngitis and viral gastroenteritis were each reported by 5.1% of subjects receiving placebo (GEn: 3.1% and 1.0%, respectively). No clinically relevant changes in laboratory values, vital signs or ECGs occurred in either phase or treatment group.
Conclusion: Improvement in RLS symptoms provided by GEn 1200 mg once daily is maintained compared with placebo, and treatment is generally well tolerated for up to 9 months.

0935

COMPARISON OF SYMPTOMATOLOGY AND ATTITUDES AND BELIEFS TOWARD RLS TREATMENT AMONG AFRICAN AMERICANS AND CAUCASIANS WITH UNTREATED RLS IN THE COMMUNITY

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Introduction: A recent community-based study reported that RLS is comparably prevalent among African-American (AA) and Caucasian (CA) adults. However, few AA patients with RLS are in treatment in the specialty clinic in the US. Barriers affecting access to care settings for AA RLS patients remain unclear. Objective: We compared RLS symptomatology, attitudes, and beliefs towards RLS between AAs and CAs.
Methods: Sample: Of 75, 33 subjects were AAs (mean age + SD: 66.1 + 8.1; female: 87%; with RLS: 45%) and 42 subjects (mean age + SD: 74.2 + 12.1; female: 71%; with RLS: 48%) were CAs. All subjects completed the RLS Attitude Scale, a 20-item measure of patients' attitudes and beliefs concerning: clinicians' need for specialized training in RLS; the seriousness of RLS as a disorder; the psychosocial impact of RLS; and the importance of patient autonomy. They also completed the Medical Skepticism Scale and the Trust in Physicians Scale. RLS symptomatology of those subjects with untreated RLS were assessed based on the Hopkins Telephone Diagnostic Interview for RLS, RLS Quality of Life Scale, International RLS Rating Scale, and patient's agreement/disagreement (on a Likert scale) with 21 RLS-related descriptors (e.g., "creepy-crawly" etc.) suggested by the RLS workshop sponsored by NIH/IRLSSG. Analysis: Attitudes and symptomatology were compared between AAs and CAs using independent samples t-tests and Fischer's exact tests as necessary.
Results: Severity and impact of RLS among CAs and AAs with untreated RLS did not differ, but CAs and AAs endorsed different words and phrases to describe their RLS symptoms. Attitudes and beliefs toward RLS did not differ between AAs and CAs.
Conclusion: No racial differences in attitudes and beliefs towards RLS explain the racial disparity in RLS treatment. Racial difference in description of RLS symptomatology may have implication in detection of RLS in the clinic. Further studies, with more diverse samples are needed to inform the valid assessment of RLS across racial and ethnic groups.

0936

FACTORS RELEVANT FOR PERSISTENCE OF RESTLESS LEGS SYNDROME AFTER KIDNEY TRANSPLANTATION

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Introduction: Restless Legs Syndrome (RLS) is prevalent in uremia and in dialysis patients. Symptomatic therapy is similar to that in non-uremic patients. Real cure is reported in most post-transplantation patients. Exceptions are possible, but rare. The aim of the study is delineation of factors prohibiting cure of RLS after transplantation.
Methods: Two male patients (53 and 60 y/o) still complained about severe RLS despite transplantation, requiring continuation of dopa therapy. Factors which might be of relevance for the unchanged situation were analysed
Results: The primary disorder was kidney cysts (patient A) and glomerulonephritis (patient B). They were treated with hemodialysis and peritoneal dialysis respectively. Co-morbidity was apnea syndrome (AHI: 35), morbus Bechterew, slight depression, psoriasis and atrial fibrillation in patient A and aortic stenosis, polyneuropathy and slight depression in patient B. Both patients had severe RLS before transplantation. Ferritine levels were normal. Patient A underwent a living donor procedure in 2007; patient B received a kidney from a brain-dead donor in 1991 and had a repeated, living donor transplantation in 2005. The transplant functions were estimated at 55% for patient A and 70% for patient B. Patient A had no improvement in his RLS symptoms (IRLS score: 21) at all and needed dopamine agonist therapy. Patient B was free from RLS between 1991 and the retransplantation procedure. After the second operation RLS recurred as severe as before 1991(IRLSS 34). RLS therapy was started. Both patients were on a triple immunosuppressant regime with cyclosporine, prednisolon and MMF. Patient A had CPAP as well; both patients needed a SSRI antidepressant.
Conclusion: Factors which may be important and are common for both patients, are a living donor transplantation and the use of similar immunodepressant regimes and SSRI's for depression. We postulate that all three factors are important with emphasis on the transplantation procedure that was chosen.

0937

RESTLESS LEGS SYNDROME IN FRIEDREICH ATAXIA: A POLYSOMNOGRAPHIC STUDY

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Introduction: Friedreich Ataxia (FA) is the most common autosomal recessive heredoataxia which affects one in 50.000 people. Clinically, FA is characterized by progressive spinocerebellar ataxia, peripheral neuropathy, diabetes mellitus and hypertrophic cardiomyopathy. Based on patients complaints about sleep disturbances and pathophysiological considerations, we systematically assessed sleep history and polysomnography in FA.
Methods: Sixteen consecutive FA patients (10 men, 6 women; mean age at time of investigation, 35.4 ± 11.1 years) with a mean disease duration of 16.5 ± 7.0 years were included in this study. All patients underwent a standardized protocol with a detailed sleep history, polysomnographic recordings, and a routine laboratory testing including iron parameters.
Results: All FA patients had an increased periodic limb movement (PLM) in wakefulness index > 15/h. Seven patients had an increased PLM in sleep index >15/h. Eight out of 16 patients had restless legs syn-

drome (RLS) according to standard criteria and after exclusion of RLS mimics. In 7 patients, RLS onset was after the onset of FA. FA patients with RLS had significant lower serum ferritin levels than FA patients without RLS (76.3 ± 56.0 µg/l vs. 176.3 ± 100.7 µg/l; P = 0.039).
Conclusion: We found that PLM and RLS are common findings in FA. Their increased frequency in this primarily spinal ataxia may strengthen the view of a substantial role of spinal sensorimotor integration in the pathophysiology of RLS and PLM. Moreover, low serum ferritin levels seem to be an additional trigger of RLS in FA.

0938

RESTLESS LEGS SYNDROME: A CIRCADIAN DISORDER?

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Introduction: In restless legs syndrome (RLS) symptom increase in the evening or at night is an essential diagnostic feature. Two previous studies suggested a circadian component in the pathophysiology of RLS. The objective of this study was to test the hypothesis of a circadian dysfunction in RLS patients based on temperature curves and melatonin secretion.
Methods: A baseline polysomnography was followed by a modified constant routine (20hr bedrest under 10 lux with sleep 23:00-7:00hr) in 10 drug-free, idiopathic RLS-patients (5 females, age 49.2±4.7 years, BMI 25.4±1.2) and 8 healthy age and gender-matched controls (BMI 24.1±1.0), in whom other sleep disorders had been ruled out by history and polysomnography. Salivary melatonin was assessed every 30min during waking. CBT, proximal and distal skin temperature was recorded continuously. The midrange crossing time of the evening decline of CBT was visually estimated and used as circadian phase marker along with the dim-light melatonin onset (DMLO). Subjective RLS symptom data, sleepiness and temperature sensation were assessed using visual analogue scales.
Results: Melatonin levels and DMLO did not differ between patients (21:09±0:41hr) and controls (21:15±0:28hr). In heart rate, controls had a prominent decline at lights off, whereas in patients heart rate was steadily declining from the early evening. CBT showed the typical time course with a peak in the late afternoon/early morning hours, whereas RLS patients had an earlier decline. The difference between the CBT maximum and minimum was significantly larger in controls (0.86°C vs. 0.66°C) and was mainly due to the lower minima of CBT in controls (36.34°C vs. 36.62°C; $p<0.1$).
Conclusion: In this study, similarity of DMLO and CBT in patients and controls does not support the hypothesis of a primary circadian dysfunction in RLS. Nevertheless slight differences between groups indicate a need for further studies, in particular under normal life conditions which could reveal larger significant differences.

0939

REMISSION RATES WITH ROTIGOTINE TRANSDERMAL SYSTEM IN IDIOPATHIC RLS: COMBINED RESULTS FROM TWO 6-MONTH, DOUBLE-BLIND, PLACEBO-CONTROLLED TRIALS

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Introduction: Rotigotine (Neupro®) is licensed in Europe and the US for the treatment of Parkinson's disease and is in development for treatment of restless legs syndrome (RLS). While all D_2-D_3 dopamine agonists tested appear to reduce RLS symptoms, they often fail to produce the desired nearly complete remission of symptoms. Therefore, a critical evaluation of any RLS treatment will be the rate of symptom remission, an outcome reported here from two well-controlled rotigotine studies.
Methods: Pooled data were analyzed from two 6-month, double-blind, placebo-controlled trials. Subjects were stratified by International RLS Study Group Rating Scale (IRLS) sum score at baseline (moderate [IRLS 11-20], severe [IRLS 21-30] or very severe [IRLS 31-40]). Remission rates were calculated as symptom-free remitters (IRLS sum score=0) and clinical remitters (IRLS≤10).
Results: A total of 843 patients were randomized to placebo or rotigotine (1-3mg/24h). In moderate RLS patients (n=187), the symptom-free remission rate with low-dose rotigotine (26%;1mg/24h) was similar to rates observed with 2mg/24h (33%) and 3mg/24h (27%) and higher than placebo (16%). As expected, higher rotigotine doses were required to achieve comparable symptom-free rates in more severe RLS patients (placebo, 1, 2, or 3mg/24h rotigotine: 9%, 18%, 24%, and 31% for severe patients[n=455] and 10%, 10%, 22%, and 31% for very severe patients[n=201]). Using less stringent clinical remission criteria (IRLS≤10), overall rates were higher in general. In all rotigotine groups, the remitter rates were ~50% (severe RLS) to ~60% (moderate RLS; placebo: 25% and 49%). In very severe RLS, only 2mg/24h (45%) and 3mg/24h (41%) showed markedly high remission rates (placebo and 1mg/24h rotigotine: 14%).
Conclusion: In this pooled analysis of RLS patients, rotigotine compared to placebo resulted in higher rates of both symptom-free and clinical remission following 6 months of treatment. Significant remission rates for severe to very severe patients required higher rotigotine doses (23mg/24h).
Support (optional): Supported by UCB, Inc.

0940

PERIODIC LIMB MOVEMENTS IN CHILDREN: PREVALENCE IN A NATURALISTIC SETTING - PENN STATE COHORT

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Introduction: Periodic limb movements in sleep is uncommon in the pediatric population. The purpose of this study was to evaluate the prevalence of periodic limb movements of sleep in a random sample of the local elementary school children.
Methods: The study was performed by evaluating local school children (kindergarten through grade 5) using a 2-phased strategy. During phase 1, a brief questionnaire was completed for all of the children (N=5740) with a response rate of 78.5%. During phase 2, 700 randomly selected children from phase 1 with a response rate of 70.0% were assessed with a full polysomnograph and a history/physical, including an ECG; ear, nose, and throat; and pulmonary evaluation.
Results: All Polysomnography records were reviewed, and the following data was extracted: periodic limb movement index (PLM Index), Periodic limb movements with arousal index (PLM w/arousal index), Leg movements in sleep (LM's) and Leg movements in sleep with arousal (Lm's w/arousal, Apnea- Hypopnea Index (AHI) and patient demographics (age, sex, comorbidities). A total of 700 PSG's were reviewed. Only a small fraction of the population fit the criteria of PLMS >5/hour.
Conclusion: Periodic Limb Movements in Sleep is an uncommon disorder in the pediatric population. In this naturalistic random population, PLMS were found to be a small percentage but significant when considering the subjective sleep complaint.

0941

NREM/REM CYCLIC FLUCTUATION OF SLEEP AROUSAL IS BLUNTED BY CLONIDINE

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Introduction: The distribution of sleep arousals is variable across NREM/REM ultradian cycles. We recently reported that clonidine (CLO) reduces sleep bruxism (SB) episodes by 60% in comparison to placebo (PLA). The aim of the present analysis is to determine the effect of CLO on the distribution of sleep arousal over NREM/REM cycles.
Methods: Polysomnographic data of 16 SB patients, who received PLA or CLO (0.3 mg/bedtime) in a cross-over design, were analyzed for sleep and SB activity. The following A phases of Cyclic Alternating Pattern (CAP) were identified: A2 (transition phase) and A3 (arousal window). Since CLO suppressed REM sleep, corresponding sections were identified in the CLO nights based on PLA night's REM timeline and SWA decrease in spectral power. Each NREM/REM cycle was divided in 4 NREM and 1 REM periods.
Results: A linear increase in the A2 and A3 phases was observed in PLA nights within consecutive NREM/REM cycles ($p \leq 0.0007$; ANOVA). This fluctuation disappeared with CLO for cycles 2 to 4 ($p > 0.2$). The A3 pressure with CLO remained high ($p = 0.07$) and relatively stable in comparison to PLA. A linear increase within NREM/REM cycles was also observed in PLA nights for SB index ($p = 0.045$), but was blunted under CLO ($p \geq 0.1$). Equipotent significant correlation between A3 phases and SB episodes ($r \geq 0.56$; $p < 0.001$) was found in both PLA and CLO nights.
Conclusion: CLO alters the dynamic of arousals (A2 and A3) and SB episodes within NREM/REM cycles. Although SB episodes were significantly reduced under CLO, the arousal pressure (A3) remained high. Our data confirms that SB activity and A3 phases are correlated. However they further suggest that the effect of CLO on SB is possibly linked to the reduction of sleep arousal oscillation/fluctuation.
Support (optional): Canadian Institutes of Health Research.

0942

EFFECTS OF ROTIGOTINE TRANSDERMAL SYSTEM ON QUALITY OF LIFE IN IDIOPATHIC RESTLESS LEGS SYNDROME

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Introduction: Restless Legs Syndrome (RLS), if clinically relevant, causes bothersome impairment of quality of life (QoL) and functioning in daily activities. The purpose of this study was to evaluate changes of QoL globally and in particular domains of QoL under treatment with rotigotine, a transdermally (patch) delivered dopamine agonist, in patients with moderate to very severe idiopathic RLS.
Methods: Multicenter, randomized, double-blind, placebo-controlled, 4-arm parallel-group trial with 3 fixed transdermal doses of rotigotine 1-3mg/24h over a 6-month period. QoL was assessed with the QoL-RLS quality of life questionnaire. The scale is analyzed by a total score of 12 items (range 0 - 60); in addition, four domains of QoL (impact of RLS symptoms, sleep disorders, other features like pain, coping behavior) as well as a global assessment of QoL "all in all" were evaluated.
Results: 549 subjects (58 ± 11 years, 73% female) were enrolled at 49 sites in 8 European countries and 458 subjects were randomized. The overall mean baseline IRLS score was 28.1±6.1 indicating on average severe RLS of the study population. QoL was moderately impaired at baseline (QoL-RLS total score: 32.2 + 11.8). Between baseline and the end of the trial, the QoL-RLS total score improved significantly more in the pooled rotigotine treatment groups than under placebo ($P < 0.001$, effect size ES=0.58). With the exception of the subscale covering pain and treatment side effects (ES=0.24), rotigotine showed markedly larger improvements than placebo with regard to the impact of RLS-specific symptoms (ES=0.56), sleep disorders (ES=0.49), and coping with RLS symptoms (ES=0.46) on QoL. QoL "all in all" was much better (ES=0.60).
Conclusion: Rotigotine in dosages of 1 to 3mg/24h improved overall quality of life and reduced the impact of RLS-specific symptoms, sleep disorders and coping behavior on the patients mood, efficiency and behavior in daily activities in this study.
Support (optional): Supported by UCB Inc.

0943

AUGMENTATION IN LONG-TERM THERAPY OF THE RESTLESS LEGS SYNDROME WITH TRANSDERMAL ROTIGOTINE - A RETROSPECTIVE SYSTEMATIC ANALYSIS OF TWO LARGE OPEN-LABEL 1-YEAR TRIALS

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Introduction: Augmentation of symptoms is the main long-term treatment complication with dopaminergic drugs in Restless Legs Syndrome (RLS). In previous double-blind RLS trials with rotigotine, a transdermally delivered dopamine agonist, no cases of augmentation were spontaneously reported. We performed a retrospective systematic evaluation of long-term data from two open-label trials by three experts applying the Max Planck Institute (MPI) criteria both for augmentation and clinically relevant augmentation.
Methods: Data from two (EU and US) 1-year prospective open-label extension trials of preceding double-blind studies to evaluate the safety, tolerability and efficacy of rotigotine in flexible dosages between 0.5 and 3 mg/24 hours were reanalyzed. Six-hundred and twenty patients were exposed to rotigotine for a total of 529 years. All study visits were systematically evaluated by means of the MPI criteria using the Augmentation Severity Rating Scale (ASRS), IRLS, RLS-6, and CGI as well as RLS Quality of Life scale (QoL-RLS) to assess clinically relevant augmentation.
Results: Sixty patients (9.7%) met MPI criteria for augmentation at least on one visit. The condition was clinically relevant in 18 patients (2.9%) for the 1 year treatment.. No relationship between rotigotine dose and augmentation could be detected. Clinically relevant cases of augmentation occurred at any time point of the study period.
Conclusion: This retrospective systematic analysis of a large dataset from two open-label 1-year trials with flexible dosages of the rotigotine patch shows that clinically relevant augmentation is an uncommon phenomenon. Nevertheless, as on any RLS treatment with dopaminergic agents, a long-term observation is recommended.
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0944

CARDIAC ACCELERATIONS ANTICIPATE THREE TYPES OF MICRO-AROUSAL

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Introduction: The work of Ferri (Ferri et al 2006) and others has established that PLMs are preceded by cardiac accelerations. We will present evidence that anticipatory cardiac accelerations are also a feature of non-PLM movements, even tiny twitches, and also of EEG micro-arousals.
Methods: Data were obtained from 97 participants in an ambulatory study of sleep in Posttraumatic Stress Disorder and Panic Disorder. PLM and EEG arousal data were derived from laboratory PSGs performed to exclude SDB and/or severe PLMD. Micro-twitches were obtained from 1000+ nights of home sleep recorded via mattress actigraphy. Instantaneous IBI time series were computed for the whole night either from lab ECG or mattress kinetocardiogram (Woodward et al 2007). PLM-locked IBI averages were calculated only for participants with substantial numbers of movements and comprised approximately ~4000+ events. EEG arousal-locked IBI averages were obtained from 85 subjects providing high-quality EEG and comprised ~19,000 events. Twitch-locked IBI averages were obtained from all 97 subjects and comprised ~80,000 events. PLMs, twitches, and EEG arousals were all detected automatically. Twitches were thresholded at >/= 1.5 times the local kinetocardiogram pulse and so included very small events. EEG arousals were detected with +/- 1 sec temporal precision.
Results: PLM-related cardiac accelerations (reductions in IBI) varied as a function of arousal type and sleep stage, averaged ~50 msec, and diverged from baseline ~2500 msec prior to the onset of the AT burst. Micro-twitch-related cardiac accelerations averaged ~15 msec and also commenced approximately 2500 msec prior to twitch onset. EEG-arousal-related cardiac accelerations averaged ~20 msec and also began ~2500 msec prior to EEG frequency increase.
Conclusion: All three types of micro-arousals were led by cardiac accelerations beginning about 2500 msec earlier. This lead time corresponds to prior observations re PLMs. If most or all sleep micro-arousal phenomena include anticipatory cardiac accelerations, this may indicate that stereotyped action programming - in which motor plans are preceded by autonomic support - is preserved in sleep.
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0945

RESTLESS LEGS SYNDROME (RLS) AND RLS MIMICS : CLINICAL CHARACTERISTICS AND NEUROLOGICAL COMORBIDITIES

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Introduction: RLS is a sensorimotor disorder characterized by an urge to move of the legs and most RLS patients experience uncomfortable sensation of the legs. Late-onset RLS symptoms may occur in association with lumber problems or neuropathy, thus, sensory discomfort could either be due to RLS or neurological comorbidities. The aim of our study was to identify clinical characteristics of patients with RLS like sensory symptom and its association with neurological comorbidities.
Methods: Forty patients (mean age: 65.2 SD 15.6) who complained of RLS like sensory symptom were included in the study. Diagnosis of RLS was confirmed based on the NIH/IRLSSG criteria. Comorbid neurological problems were assessed with neurological examination. Twelve patients underwent suggested immobilization test (SIT) and polysomnography (PSG).
Results: Twenty eight patients (70%) fulfilled the diagnostic criteria of definite RLS. Among the RLS patients, twelve patients (43%) had lumber problem and two patients (7%) had neuropathy. Among the twelve patients with RLS mimics, six patients (50%) had sensory symptom due to lumber problem and two patients (17%) had neuropathy. Among the patients who underwent SIT and PSG (n=9), all RLS patients showed worsening of leg discomfort during SIT, six patients (67%) showed SIT index>40, and six patients (67%) showed PLM index>15, while patients with RLS mimics did not show any of these positive findings. Medication for RLS was effective in all treated RLS patients, while RLS mimics did not show any effectiveness.
Conclusion: Neurological comorbidities were highly prevalent among elderly patients with RLS like sensory symptoms. Sensory discomfort associated with neurological problem may mimic RLS symptom. Objective testing in addition to detailed neurological assessment could be useful in refining the diagnosis of RLS especially in patients with comorbid neurological problems. Effectiveness of RLS medication was also helpful in discriminating patients with RLS.

0946

DOPAMINERGIC TREATMENT IN RESTLESS LEGS SYNDROME: EFFECTS ON EXCESSIVE DAYTIME SLEEPINESS

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Introduction: Whereas insomnia is a frequent complain in restless legs syndrome (RLS), there is little information on excessive daytime sleepiness (EDS). We analyzed data from the Swiss RLS study in order to assess frequency and characteristics of EDS and to evaluate the evolution of EDS under different RLS therapies.
Methods: The Swiss RLS study was conducted to compare treatment efficacy and safety of the dopamine agonist pramipexole (PPX) versus levodopa/benserazide (L/B) in de novo patients with idiopathic restless legs syndrome (RLS) and was performed as a randomized, double-dummy, comparative crossover trial. Primary outcome measure of the present study was the change in subjective sleepiness (Epworth sleepiness scale [ESS] score). We analyzed data from thirty- seven patients (21 women), mean age was 56.6 (range 25-85), mean body-mass-index was 24.6 (± 3.5 SD). Statistics: Significant differences were estimated by 2-way and 3-way rANOVA. Pearsons product correlations were performed to identify correlations. Significance was determined as $p \leq 0.05$.
Results: At baseline, EDS (as defined by ESS >10), was found in 32% of the patients. Sleepy RLS patients were younger ($p<0.001$) than non-sleepy, no other differences were found. PPX and L/B both were effective in the treatment of RLS symptoms (IRLS score, $p<0.001$ and $p=0.002$). Overall ESS was reduced (main effect for "time", $p=0.02$) independent from the dopaminergic substance. In sleepy patients (n=12), PPX improved ESS ($p=0.05$) from 14.3 (± 2.3 SD) to 10.5 (± 5.2), and L/B ($p=0.1$) from 12.3 (± 1.5) to 11 (± 2.8) respectively. In 5/37 patients ESS deteriorated under treatment (PPX=3 patients, L/B=2 patients), no sleep attacks occurred.
Conclusion: Excessive daytime sleepiness is present in 1/3 of RLS patients. Dopaminergic treatment usually promotes wakefulness, but infrequently leads to daytime sleepiness.

0947

OBJECTIVE MEASURES OF DAYTIME SLEEPINESS IN PATIENTS WITH PARKINSON'S DISEASE AND REM BEHAVIOR DISORDER

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Introduction: It is estimated that 15-47% of Parkinson's disease (PD) patients have REM Sleep Behavior Disorder (RBD). Patients with PD also frequently complain of excessive daytime sleepiness (EDS). The cause of the EDS is unknown and objective data regarding EDS in PD are limited. Furthermore, no data exist on the relationship between RBD and EDS in PD. As part of a larger ongoing study of sleep in PD, data are presented assessing objective EDS of PD patients with RBD.
Methods: 18 PD patients (Men=11; Mean Age=68.8 yrs, SD=7.8, Range=55-85 yrs) were evaluated. All had a PSG followed by a Multiple Sleep Latency Test (MSLT) and were assessed for sleep apnea, RLS and RBD. RBD was assessed with the RBD Screening Questionnaire (RBDSQ). Sleep onset latency (SOL) for all naps were averaged over the day. Pearson correlation analysis was used to examine the relationship between RBD (RBDSQ score) and EDS (SOL). The amount of EDS in patients with and without RBD was compared using independent samples t-tests.
Results: Eight patients (44%) met criteria for RBD (i.e., RBDSQ≥5). There was a significant negative correlation between mean SOL and RBDSQ score ($r = -0.51$; $p<0.05$) suggesting that those endorsing more symptoms of RBD were sleepier. Average SOL for RBD patients was 6.04 minutes (SD = 4.51) vs. 12.15 minutes (SD = 3.95) for patients with no RBD ($t = -3.06$; $p<0.01$).
Conclusion: Although preliminary, our results suggest that PD patients with RBD are significantly sleepier than those with no RBD. In this small sample we were not yet able to control for amount of sleep at night, medication use or other potentially confounding variables. As additional data are collected, we will be able to determine how much of the complaint of daytime sleepiness in PD ,is accounted for by RBD.
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0948

ASYMMETRICAL CEREBRAL FGD METABOLISM IN RESTLESS LEGS SYNDROME: A NOVEL STUDY DURING SYMPTOMOLOGY

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Introduction: The pathophysiology of restless legs syndrome (RLS) remains unclear although there is support for central dopaminergic hypoactivity. We aimed to evaluate and compare cerebral FDG metabolism in RLS patients and healthy controls.
Methods: Ten patients (5 female, mean age 46 years) with recently diagnosed and untreated RLS underwent a dedicated FDG PET/CT (Gemini, Philips). The scans were done in the evening with FDG injected at the onset of patient-reported symptomology. FDG PET images were analyzed for automated Z-scores, clusters and asymmetry indices (L/R%) using commercial software MIMneuro (MIMvista Corp.), which provides quantitative data of 83 brain regions on interest. Regions with abnormal Z-scores, clusters or L/R% were further compared with corresponding regions of 10 healthy controls (8 female, mean age 43 years) previously acquired in our institution. Independent t-tests and Mann-Whitney tests were used.
Results: All 10 RLS patients showed normal distribution in all 83 regions with mean ± standard deviation of Z-scores ranging between -2 and +2; average Z-score was 0.16 ± 1.24. Cluster analysis revealed no areas with consistent FDG abnormalities. In contrast, L/R% was not normally distributed because several regions showed high asymmetry in up to 20.5%. The following regions showed statistically significant higher L/R% ($p < 0.05$) in RLS patients compared to 10 healthy controls: Putamen, caudate nucleus, nucleus accumbens, olfactory cortex, fusiform gyrus, retrosplenial area, superior parietal lobule, and inferior cerebellar peduncle.
Conclusion: Cerebral FDG uptake in RLS patients may be normal as compared to normal data base (Z-score). However, RLS may manifest as asymmetric FDG uptake as seen in several brain regions; at least some of which belong to dopaminergic system (putamen, caudate nucleus, nucleus accumbens) that has been linked to RLS whereas other areas of asymmetry may represent secondary findings of RLS pathophysiology.

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REM SLEEP BEHAVIOR DISORDER IN PARKINSON'S DISEASE: A QUESTIONNAIRE BASED SURVEY

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Introduction: Rapid eye movement sleep behavior disorder (RBD), reported in up to 50% of patients with Parkinson's disease (PD), is characterized by loss of normal muscle atonia during REM sleep which leads to increased phasic motor activity and allows dream enactment behavior. There are three previous large questionnaire and interview based studies addressing RBD in PD including 289, 200 and 231 patients respectively. The aim of the present study was to assess the frequency and the characteristics of RBD in patients with PD.
Methods: A questionnaire including items on sleep quality, sleep disorders, PD characteristics and severity, was sent to the members of the national PD patients' organization in Switzerland. A 13-item validated questionnaire for RBD was included. A cut-off of five points is considered suggestive for RBD.
Results: 420 questionnaires were received. Three patients had to be excluded for diagnoses other than idiopathic PD. 210/417 patients (50%) had an RBD score>5. These patients reported concomitant sleep disorders like initial insomnia ($p=0.03$), night-time awakenings ($p=0.003$), apneas ($p=0.008$), shortness of breath ($p=0.005$), talking/crying in sleep ($p<0.001$), cursing/violent behavior in sleep ($p<0.001$), restless legs symptoms ($p<0.001$), nightmares ($p<0.001$) and hallucinations ($p<0.001$) significantly more often then the rest of the population studied. They also had longer disease duration ($p=0.04$) and higher Epworth sleepiness score ($p=0.019$). There was a trend for a lower score on activities of daily living ($p=0.08$).
Conclusion: RBD in PD patients is associated with various sleep disorders, including insomnia, sleep disordered breathing, restless legs, nightmares and hallucinations, leading to higher arousability and sleep fragmentation. Patients with RBD were also sleepier than patients without RBD.
Support (optional): The national PD patients' organization in Switzerland helped us to send the questionnaire together with its monthly magazine.

0950

DOES DECREASED CARDIAC UPTAKE IN ^{123}I-MIBG SCINTIGRAPHY CORRELATE THE PROGRESSION AND SEVERITY OF IDIOPATHIC REM SLEEP BEHAVIOR DISORDER?

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Introduction: Decrease in cardiac iodine-123 metaiodobenzylguanidine (^{123}I-MIBG) radioactivity has been reported in patients with idiopathic REM sleep behavior disorder (RBD) as well as in Lewy body diseases (LBD), namely Parkinson's disease (PD) and dementia with Lewy bodies (DLB). Pathological studies revealed that reduced cardiac ^{123}I-MIBG uptake represented degeneration of the cardiac sympathetic nervous system which might be one of the early signs of Lewy body pathology in the progression of LBD. From this viewpoint, iRBD could be pre-motor and/or pre-cognitive state of LBD, but the relationship between cardiac ^{123}I-MIBG uptake and progression and severity of iRBD has not been investigated.
Methods: Cardiac sympathetic denervation was examined using cardiac ^{123}I-MIBG scintigraphy in 22 patients with iRBD (20 men and 2 women, 68.4±5.8 years of age, disease) with disease duration of 7.6±5.5 (range: 1-21 years) from the consecutive 24 iRBD patients. One patient with diabetes mellitus and the other with cardiomyopathy were excluded. Diagnosis of RBD was based on clinical characteristics (dream-enacted behaviors and sleep talk) and PSG with video recording, which demonstrated at least jerky limb movements and/or sleep talk associated with REM sleep without atonia (RWA). As the quantification of abnormality in REM sleep mediated muscle atonia, %RWA (total time of RWA divided by total time of RWA and REM sleep with atonia) was calculated.
Results: The early heart-to-mediastinum uptake ratio (H/M ratio) of cardiac ^{123}I-MIBG uptake was 1.56±0.27, ranging from 1.2 to 2.3. There was no correlation between H/M ratio and the duration of RBD, the present clinical severity of RBD, nor %RWA.
Conclusion: The overall decreased cardiac ^{123}I-MIBG uptake indicates probable underlying Lewy body pathology of apparent 'idiopathic' RBD in most of the patients, but development of RBD symptoms and disruption of REM related muscle atonia could take diverse patterns.

0951

EARLY PATHOLOGY IN SLEEP STUDIES OF PATIENTS WITH FAMILIAL CREUTZFELDT-JAKOB DISEASE

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Introduction: JCD is a unique prion disease with a sporadic, genetic and infectious transmission. In the familial pattern there were a various mutation identifications, one of the known mutation is E200K. The largest cluster of fCJD is in Jews of Libyan origin and linked to the PRNP E200K mutation. The high index of suspicion in these patients often leads to early diagnosis with complaints of insomnia being a very common presenting symptom of disease.
Methods: The study included 10 fCJD patients diagnosed by clinical manifastations, MRI, elevated TAU protein in the CSF and positive PRNP E200K mutation. A standard polysomnography study (Embla® system by Flaga) was performed after a brief interview of sleep disturbances symptoms.
Results: All the patients presented a pathological sleep study in all scoring evaluation settings. The sleep stages were characterized by the disappearance of sleep spindels, outburst of three phasic waves, and shallowing of the sleep with increased stage 2 and increased wake periods during the night. The average hypnogram included- stage 1 2.3%, stage 2 68.8%, Slow wave sleep 2.2 % and REM 6%. The respiratory channels demonstrate an irregular breathing with central and obstructive apneas and hypopneas. The typical hypotonia during the night and the atonia during REM were replaced by hyperactive sleep in all the subjects with multiple jerks, movements and parasomnia (mainly talking) during the night.
Conclusion: Sleep studies are clearly pathological in early fCJD associated with the E200K mutation. Specific respiratory disturbances and lack of atonia may serve as new diagnostic tools in the disease.

0952

INSOMNIA IN MILD TRAUMATIC BRAIN INJURY (MTBI) PATIENTS

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Introduction: Insomnia symptoms are estimated to occur in at least 10% of the adult population and are thought to be due in part to imbalance in wake/sleep regulation. Mechanisms for sleep initiation and maintenance are distributed throughout the brain and brainstem, and require delicately balanced neuronal and glial interactions. Mild Traumatic Brain Injury (mTBI) is a diffuse process involving disruption of both neuronal synaptic circuitry and glial myelin maintenance. Because traumatic brain injury may disrupt components of the intricate wake/sleep regulatory network, we hypothesized the prevalence of insomnia symptoms in patients with mTBI would be higher than estimated for the general population.
Methods: A research psychologist reviewed the blinded records of 35 consecutive mTBI patients (M/F=31/4; ages = 20-76; mean = 31.2, median = 30.0) from a military neurology clinic for sleep-related complaints. No patients had insomnia complaints prior to the head injury. Chi Square was performed on combined and individual variables to determine prevalence of insomnia symptoms in the mTBI population.
Results: 31 of the 35 patients (88.6%) had complaints of insomnia ($\chi 2$ [1, N = 35] = 20.83, $p < .001$). 27 patients reported sleep onset insomnia, 37 patients reported difficulty staying asleep, and 10 patients reported terminal insomnia. 23 patients had more than one type of insomnia.
Conclusion: We conclude that insomnia is more prevalent in mTBI patients than reported in the general population. We suggest that screening for insomnia be considered in all patients suspected of having mTBI.
Support (optional): This research was performed in accordance with Army Regulation 40-38 (conduct of clinical investigations). The views expressed in this abstract are those of the authors and do not reflect the official policy or position of the Department of the Army, Department of Defense, or the U.S. Government.

0953

NOCTURNAL AWAKENING WITH HEADACHE AND OBSTRUCTIVE SLEEP APNEA SYNDROME IN A POPULATION BASED SAMPLE OF ADULT INHABITANTS OF SAO PAULO CITY, BRAZIL

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Introduction: It is generally agreed that patients presenting obstructive sleep apnea syndrome (OSAS) suffer more often from morning headache than healthy subjects. However, as far as we know, there are

no studies on the prevalence of headache-related nocturnal awakening complaint and/or its relationship with OSAS. Our aim was to investigate this prevalence and the relationship between this complaint and OSAS in the adult population of Sao Paulo city.
Methods: We used a population based survey and adopted a probabilistic three-stage cluster sample to represent the population of Sao Paulo city according to gender, age(20-80 years), and socioeconomic classes. "UNIFESP" Sleep Questionnaire, Pittsburgh Sleep Quality Index, Epworth Sleepiness Scale, Chalder Fatigue Scale, Beck Anxiety Inventory, Beck Depression Inventory, and WHOQOL-BREF quality of life assessment were applied face-to-face and in-lab full night polysomnography (PSG) was performed.
Results: Out of 1101 volunteers who answered questionnaires, 1042 underwent PSG (refusal rate=5.4%). Their mean age was 42±14ys, 55% were women and 60% presented BMI>25kg/m2.The complaint of nocturnal headache-related awakening at least once a week had a prevalence of 8.44% in the population studied, with predominance in women, aged 50-59 years. There was not a significant relationship between this complaint and the presence of OSAS (p=0.38), but we observed more somnolence, a worst quality of sleep, more fatigue, higher levels of anxiety and depression and worst quality of life in the group with complaint of nocturnal awakening with headache compared to the no complaint group (p<0.05). The PSG showed lower REM percentage in the former group (p=0.04).
Conclusion: We observed a high prevalence of frequent awakening during the night with headache in a probabilistic sample of the adult population of the largest South American city, which was related to poor sleep and quality of life, but there was no evidence of its relationship with OSAS.
Support (optional): AFIP, FAPESP, CNPq

0954

THE PREVALENCE OF SLEEP/WAKE DISTURBANCES IN MILD TRAUMATIC BRAIN INJURY PATIENTS

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Introduction: Mild Traumatic Brain Injury (mTBI) is a diffuse process involving disruption of both neuronal synaptic circuitry and glial myelin maintenance, and for this reason patients typically struggle to keep their former activities of daily living due to the development of many behavioral symptoms. Mechanisms for sleep initiation and maintenance are distributed throughout the brain and brainstem, and require delicately coordinated neuronal interactions. Because mTBI disrupts components of this intricate network, we hypothesized a high occurrence of sleep / wake disturbances in patients with mild traumatic brain injury.
Methods: Thirty-five consecutive medical records of patients who attended the Tripler Army Medical Center Neurology clinic were analyzed. All patients had a diagnosis of mTBI. Based on clinical interview notes patients were classified as either having or not having sleep and wake disturbances. Sleep / wake problems were defined as daytime dysfunction associated with not being able to fall sleep, feelings of restless at night, nightmares with arousals, awakenings at night, early morning awakenings, and having excessive daytime sleepiness. This data was then analyzed using the chi-square statistic to determine if sleep problems occurred at a greater than random rate.
Results: The sample was composed mostly of males (n = 30, 86%) between the ages of 20 and 76 years old (mean 31.7; median 30). Twenty of them (57%) were military service members. Results showed that 34 of the 35 patients reported sleep problems ($\chi 2$ [1, N = 35] = 31.11, p < .001).
Conclusion: We conclude that the prevalence of sleep/wake disturbances is highly associated with mTBI. We recommend that mTBI patients be carefully screened for sleep-related problems.
Support (optional): This research was performed in accordance with Army Regulation 40-38 (conduct of clinical investigations). The views expressed in this abstract are those of the authors and do not reflect the official policy or position of the Department of the Army, Department of Defense, or the U.S. Government.

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EXCESSIVE DAYTIME SLEEPINESS IN MILD TRAUMATIC BRAIN INJURY (MTBI) PATIENTS

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Introduction: A reported 20% of the population suffers from severe excessive daytime sleepiness, in part due to any combination of over 85 sleep disorders identified by the American Academy of Sleep Medicine. Mechanisms for wake maintenance are distributed throughout the brain and brainstem, and require a delicately coordinated balance of neuronal interactions. Mild Traumatic Brain Injury (mTBI) is a diffuse process involving disruption of neuronal synaptic circuitry and glial myelin maintenance. Because traumatic brain injury may disrupt the delicate wake maintenance network, we hypothesized the occurrence of excessive daytime sleepiness (EDS) in patients with mild traumatic brain injury would be significantly higher than that estimated in the general population.
Methods: Thirty-five consecutive medical records of mild traumatic brain injured patients who attended the Tripler Army Medical Center Neurology clinic were analyzed. Based on clinical interview notes patients were classified as either having or not having excessive daytime sleepiness. Criteria included direct complaints, naps, and decreased social and work performance due to sleepiness. No patients had excessive sleepiness prior to the head injury. This data was then analyzed using the chi-square statistic to determine if excessive sleepiness was more prevalent in this mTBI population.
Results: The sample was composed mostly of males (n = 30, 86%) between the ages of 20 and 76 years old (mean 31.7; median 30). Twenty of them (57%) were military service members. Results showed that 31 of the 35 patients (88.6%) had complaints of excessive daytime sleepiness ($\chi 2$ [1, N = 35] = 20.829, p < .001).
Conclusion: We conclude that excessive daytime sleepiness in mTBI patients is significantly more prevalent than in the general population. We recommend that screening for excessive daytime sleepiness be considered in every patient with a diagnosis of mTBI.
Support (optional): This research was performed in accordance with Army Regulation 40-38 (conduct of clinical investigations). The views expressed in this abstract are those of the authors and do not reflect the official policy or position of the Department of the Army, Department of Defense, or the U.S. Government.

0956

DAYTIME SLEEPINESS AFTER MODERATE/SEVERE TRAUMATIC BRAIN INJURY: PRELIMINARY FINDINGS

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Introduction: Excessive daytime sleepiness has been reported following traumatic brain injury (TBI). However, most studies have focused solely on the acute phase following TBI and/or have been conducted in

heterogeneous samples including both mild and moderate/severe TBI despite the well documented differences in expected outcomes between these injury severity levels. The aim of this study was to document long-term subjective and objective sleepiness symptoms after moderate/severe TBI.

Methods: Preliminary data are available for 15 participants having sustained a moderate or severe TBI (TBI group; mean age = 39.7 years old; 20% women; mean time elapsed since injury = 60.7 months, range: 14-141) and 8 age-, gender- and education-matched healthy controls (CTL group; mean age = 39.1 years old; 37.5% women). All participants underwent four 40-minute Maintenance of Wakefulness Tests (MWT) and completed the Epworth Sleepiness Scale (ESS), the Functional Outcome of Sleepiness Questionnaire (FOSQ) and nine hourly 100-mm visual analogue scales of sleepiness. T tests were computed to compare levels of sleepiness between TBI and CTL groups.

Results: Regarding physiological sleepiness, mean sleep onset latency on MWT was similar between TBI and CTL groups (33.1 vs. 34.5 minutes); 53.3% of TBI participants and 37.5% of CTL participants had at least one sleep onset episode among the four MWT. One TBI participant had 2 sleep onset REM periods. The two conditions were comparable on the ESS (TBI, mean total score = 7.3 vs. CTL, 6.8) but were significantly different on the FOSQ, with a higher mean total score for the TBI condition (7.3 vs. 5.7; p = .04). Although the difference was not statistically significant, TBI participants had higher mean ratings of sleepiness when averaging the nine VAS (20.1 vs. 13.6). This trend was even more pronounced in early to mid-afternoon (1:30 to 3:30 pm).

Conclusion: These results suggest that, as a group, individuals with moderate/severe TBI do not seem to be pathologically sleepy when assessed at least one year after the injury. On the other hand, according to these preliminary data, TBI patients could be more vulnerable to detrimental effects of sleepiness on activities of daily living as well as to circadian variations of alertness level. Additional participants are being recruited in order to confirm these results and to evaluate the association between sleepiness and other variables (i.e., fatigue, attention, driving performance).

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0957

AUTONOMIC ACTIVITY AND SLEEP ARCHITECTURE DURING SLEEP IN DOWN SYNDROME PATIENTS

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Introduction: Down syndrome (DS) has multiple organ and systemic functional abnormality; patients with DS were often known to have sleep apnea, and autonomic abnormality which can be multifactoral. Our goal is to see if this autonomic abnormality is related to fundamental disorder of DS or the associated sleep apnea syndrome since sleep apnea itself can also induce elevation of sympathetic tone.

Methods: Thirty six cases of DS and eight cases of normal controls were recruited for overnight polysomnography. The content of these polysomnography was analyzed for evaluation of sleep architecture and autonomic activities. The heart rate variability (HRV) was used to test the trend of autonomic activities in these cases; the statistical analysis of HRV was performed in 10 minutes segments of apnea or non-apnea periods between control cases, DS with and without CPAP treatment; the analysis was also performed between apnea period and non-apnea period within DS cases. The sleep architecture was compared between DS and normal cases.

Results: DS cases have higher respiratory disturbance index (RDI) and lower percentage of REM sleep. When compared the HRV between apnea and non-apnea segments within DS cases, it showed remarkable elevation of lower frequency (LF) power in apnea periods. As we concentrated in non-apnea periods, the CPAP treatment in DS cases did not alter individual autonomic activity with no statistical changes of LF and HF (high frequency) powers, either in NREM or REM sleep. As we compared the HRV between controls and DS cases (with or without CPAP treatment), it showed that the DS cases had lower power of LF and HF in NREM sleep, much lower in REM sleep.

Conclusion: The autonomic dysfunction of DS is a fundamental disorder with involvement of central nervous system; it is not secondary to associated sleep apnea. Its abnormality is particularly obvious in REM sleep as compared with normal controls.

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ASSOCIATIONS BETWEEN DAYTIME SLEEPINESS AND QUALITY OF LIFE IN PATIENTS WITH MYOTONIC DYSTROPHY TYPE 1

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Introduction: Daytime sleepiness is a frequent complaint of patients with myotonic dystrophy type 1 (DM1). Using a large patient sample, we sought to determine whether daytime sleepiness is associated with reduced quality of life in DM1.

Methods: A questionnaire-based cross-sectional study was carried out to investigate determinants of social participation and quality of life (QoL) in DM1. A total of 200 adult DM1 patients (79 men; mean (SD) age=47.0 (11.8) years) followed at the Clinique des maladies neuromusculaires completed the Epworth Sleepiness Scale (ESS) and the Short-form 36 (SF-36). ESS score (ES)≥11 and ES≥16 were respectively considered as indicative of moderate and severe daytime sleepiness. All patients received molecular confirmation of the DM1 diagnosis (mean (SD) number of CTG repeats=809 (529)). Also, muscular impairment was rated by a neurologist as mild (no or minimal signs of muscular impairment, n=40), moderate (distal weakness, n=36), and severe (mild to severe proximal weakness, n=124). T-tests for independent samples were used to assess the relationship between moderate and severe daytime sleepiness and SF-36 subscales.

Results: Moderate daytime sleepiness was present in 30.0% and severe daytime sleepiness in 8.5% of DM1 patients. DM1 patients with moderate daytime sleepiness reported lower scores than those without daytime sleepiness on all SF-36 subscales (physical functioning, $p<0.05$; role-physical, $p<0.05$; bodily pain, $p<0.05$; general health, $p<0.001$; vitality, $p<0.001$; social functioning, $p<0.01$; role-emotional, $p<0.01$; mental health, $p<0.01$). Also, DM1 patients with severe daytime sleepiness reported lower scores than those with ES<16 on all SF-36 subscales (all $p\leq0.05$) except bodily pain and role-emotional.

Conclusion: DM1 patients must be routinely assessed for daytime sleepiness since it is a treatable symptom that likely exacts a heavy toll on QoL in an otherwise progressive disease process.

0959

SLEEP QUALITY AND DISTURBANCES IN CHRONIC PROGRESSIVE EXTERNAL OPHTALMOPLEGIA

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Introduction: Chronic progressive external ophthalmoplegia (CPEO) is one of the most prevalent mitochondrial disorders in adulthood, with fatigue as a prominent clinical feature. The cause of fatigue in CPEO most likely is multifactorial, and may include sleep disturbances. We

performed a detailed study on sleep quality and sleep disturbances in 20 genetically confirmed CPEO patients.
Methods: Subjective sleep quality was assessed using the Pittsburgh Sleep Quality Index, and excessive daytime sleepiness with the Epworth Sleepiness Scale. We measured experienced fatigue (CIS fatigue), anxiety and depression (HADS) and dysphagia and pain (MPQ). Afterwards, all patients underwent nocturnal polysomnography in their home environment.
Results: Questionnaires revealed that 75% reported decreased nocturnal sleep quality (PSQI scores > 5). While 75% of all patients complained of severe fatigue, only 30% had severe daytime sleepiness (ESS score > 10). 35% met all four criteria of RLS. The amount of slow wave sleep was strikingly high (38.5±13.7% of total sleep time), at the cost of S2 sleep (28.5±8.1% of TST). The mean AHI in the whole group was 11,3±13,6/h, with an arousal index of 21,1±8/h. Five patients (25%) had an AHI over 15/h. Questionnaires were poor predictors of polysomnography results. Interestingly, patients with mutations in the nuclear polymerase-gamma gene (POLG, n= 6) had more sleep disturbances, compared to patients with mutations in the mitochondrial genome.
Conclusion: Quality of sleep is impaired in CPEO, especially in patients with POLG mutations. We found abnormalities in sleep architecture, with an increase in slow wave sleep, despite an increased arousal index. Furthermore, sleep related breathing disorders are common. Since questionnaires were poor predictors of sleep disturbances, polysomnography should be performed with a low threshold in the clinical setting.

0960

SLEEP QUALITY, DAYTIME SLEEPINESS AND FATIGUE IN PATIENTS WITH MYOTONIC DYSTROPHY TYPE 2 VERSUS TYPE 1

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Introduction: Excessive daytime sleepiness (EDS) is the most frequent non-muscular symptom of myotonic dystrophy type 1 (DM1), an autosomal dominant neuromuscular disease characterized by muscle weakness, myotonia, and multisystem involvement. Myotonic dystrophy type 2 (DM2) has similar clinical characteristics as DM1, but there have been no studies into the prevalence of EDS, nocturnal sleep disturbances, or fatigue. We performed a systematic analysis into these symptoms in a cohort of DM2 patients, and compared these to a matched group of DM1 patients.
Methods: Twenty-nine genetically proven DM2 patients completed the Epworth Sleepiness Scale (ESS), Pittsburgh Sleep Quality Index (PSQI) and the Checklist Individual Strength (CIS). The results were compared to those of 29 adult-onset DM1 patients.
Results: Almost half (46%) of DM1 patients had EDS (ESS>10) compared to only 4% of DM2 patients. The mean ESS score differed significantly as well (DM2: 3.7 ± 3.3; DM1: 9.6 ± 4.1, p <0.000). Comparable to the DM1 group, patients with DM2 experienced severe fatigue (CIS-fatigue DM2: 38.7 ± 13.1, DM1: 42.9 ± 8.5). Overall sleep quality in general (PSQI > 5) was poor in both the DM2 and DM1 group (PSQI DM2: 6.5 ± 3.0; DM1 6.2 ± 3.7). The PSQI subscore "sleep disturbances" was significantly higher in the DM2 group (DM2: 1.4 ± 0.8, DM1 1.0 ± 0.7, p=0.039). This difference was mainly due to sleep-disrupting pain in DM2 patients. There were no differences in sleep latency, sleep duration or the use of sleeping medication between the groups.
Conclusion: In contrast to DM1, EDS is not part of the clinical picture of DM2. However, DM2 patients show high levels of experienced fatigue and poor sleep quality, comparable to those of DM1 patients. Sleep in DM2 is more often disturbed compared to DM1, mainly because of nocturnal pain.

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SCN8A MUTANT MICE ARE A MODEL OF CHRONIC PARADOXICAL SLEEP REDUCTION

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Introduction: The voltage-gated sodium channel protein Nav1.6 encoded by the SCN8A gene is highly expressed in the CNS and at nodes of Ranvier in myelined axons. A mutation in the SCN8A gene in a human family was associated with cognitive impairment and neuropsychological abnormalities. Mice with a loss-of-function mutation in Scn8a display anxiety and depression-like behaviors. Since altered sleep patterns are observed in patients with emotional disorders, we characterized the sleep architecture in mice with two different heterozygous Scn8a mutations, Scn8amed, a loss-of-function allele, and Scn8amed-jo, an amino acid substitution.
Methods: Fourteen days after ECoG/EMG surgery, ECoG/EMG baseline data were collected over 48 hours from 10 Scn8amed/+ and 10 Scn8amed-jo/+ mutants and 10 respective wild-type littermates. Following the baseline recording, the animals were sleep deprived by gentle handling during the first 6 hours of the light phase. The sleep deprivation (SD) was followed by an additional 18 hours of ECoG/EMG recording of the recovery period.
Results: Scn8amed/+ and Scn8amed-jo/+ mutants showed a reduced amount of wakefulness and an increased amount of SWS during baseline recording when compared to wild-type littermates. Interestingly, Scn8amed-jo/+ mutants also showed decreased paradoxical sleep (PS) during the entire light phase. This alteration was not accompanied by an increase in sleep fragmentation or altered delta power homeostatic sleep drive. The analysis of sleep recovery following the 6 hours of SD showed that both mutants had an increased amount of SWS and PS, however Scn8amed-jo/+ mutants still did not achieve the basal amount of PS showed by the wild-type littermates.
Conclusion: These results suggest that sleep architecture is altered in Scn8a heterozygous mice. Interestingly, Scn8amed-jo/+ mutants also exhibit a robust decrease in amount of PS. This suggests that SCN8A may play a role in PS regulation. Additional behavioral studies are in progress.
Support (optional): Papale (FAPESP), Paul (NS060659), Tufik (AFIP, CEPID, CNPq), Escayg (NS046484).

0962

SLEEP-DISORDERED BREATHING IN AMYOTROPHIC LATERAL SCLEROSIS: WHO GETS DIAGNOSED, AND WHEN?

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Introduction: Non-invasive ventilation (NIV) has been reported to improve quality of life and prolong survival in amyotrophic lateral sclerosis (ALS) patients, but indications for treatment are based on pulmonary function testing (PFT) and do not include comprehensive sleep testing. Few studies examined ALS and sleep specifically. These study results are contradictory regarding the presence of sleep-disordered breathing (SDB) in ALS. Earlier identification of SDB in ALS may lead to earlier treatment with NIV. We hypothesize that many ALS patients have sleep-disordered breathing on polysomnography (PSG) prior to developing significant abnormalities on PFT.
Methods: Retrospective cohort study at the Vanderbilt MDA clinic, 2004-2008, of consecutive patients diagnosed with ALS. Charts of 144 patients with probable or definite ALS, not on NIV or invasive respiratory support, were reviewed for presence of a PSG evaluation. Data presented include demographics, presence or absence of significant abnormalities on 1st PFT, AHI, and time from 1st symptoms of ALS to PSG.

Results: 5 of 144 patients (4M, 1F) underwent PSG. 5/5 were positive for obstructive sleep apnea (OSA), AHI 38, SD=36.6; O2 Sat 81.2%, SD=8.6. All 5 patients were started on NIV at the time of diagnosis of OSA. For these 5 patients, mean age was 51.8 years, SD=10.5; BMI 23.9, SD=3.3. ALS was limb-predominant at presentation in 4/5 (1 had both limb and bulbar symptoms). Average time from the first symptom of ALS to PSG was 2.4 years (1-4 years). Only one patient had decreased PFT with FVC 46% and FEV1 51% of predicted. Mean FVC was 73.8% (20.9) and FEV1 71.4 % (16.2).
Conclusion: Sleep-disordered breathing can be a justification for early application of non-invasive ventilation and is severely under-recognized in amyotrophic lateral sclerosis. Sleep evaluation should be strongly considered early in the disease course of ALS.

0963

PREVALENCE OF SLEEP DISORDERS AMONG SOLDIERS WITH MILD TRAUMATIC BRAIN INJURY, RETURNING FROM OPERATION IRAQI FREEDOM / ENDURING FREEDOM

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Introduction: Recently published studies show that there is an increased incidence of sleep disorders among patients suffering from Traumatic Brain Injury (TBI). These studies were done on civilians and primarily among moderate and severe TBI patients. To date there is no study investigating sleep disorders in mild TBI (mTBI) patients alone. It is evident from Operation Enduring Freedom (OEF)/Operation Iraqi Freedom (OIF) data that there is increase in the incidence of mTBI among veterans returning from Iraq and Afghanistan. Through this present study we investigated the prevalence of sleep disorders among mTBI patients.
Methods: We conducted a cross sectional comparative study at North Chicago Veterans Affairs Medical Center (NCVAMC) from May 2008 to December 2008. The veterans diagnosed with mTBI were recruited from the TBI clinic and the controls from primary care clinics of NCVAMC. All participants were returning OEF/OIF veterans without any preexisting sleep disorders. Both groups were given the Sleep Disordered Questionnaire (SDQ) which contains 175 items. Each question is scored from 1 to 5 ((1=never, 2=rarely, 3=sometimes, 4=usually and 5= always have these symptoms). Four groups of sleep disorders, sleep apnea (SA); narcolepsy (NAR); psychiatric sleeps disorders (PSY); and periodic limb movement disorder (PLMD), were categorized based on the total cut-off scores obtained on the diagnostic specific questions in the SDQ.
Results: Preliminary analyses were conducted on 31 subjects with mean age 32.9, range between 20 to 59; 16 subjects were in the mTBI group and 15 in the control group. We found a significant difference in the prevalence of narcolepsy (p=0.047) and psychiatric related sleep disorders (p=0.026) within the mTBI group compared to control group.
Conclusion: This preliminary data from our study suggests that there is an increased prevalence of narcolepsy and psychiatric related sleep disorders such as insomnia in mTBI veterans returning from OEF/OIF. If these results are sustained in a larger cohort, screening veterans for sleep disorders among those with mTBI may have an impact on their management and rehabilitation.

0964

POLYSOMNOGRAPHIC EVALUATION OF SLEEP IN PATIENTS WITH MIGRAINE : A STUDY IN AN EGYPTIAN SAMPLE ASAAD T.,ABDEL-NASER A. DEPARTMENT OF NEURO-PSYCHIATRY,AIN SHAMS UNIVERSITY,CAIRO , EGYPT

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Introduction: The relationship between sleep and migraine is a complex one, with many facets. The aim of the present study is to highlight such a relation, identifying the pattern of sleep changes in patients with migraine, and whether "sleep related migraine" is a distinctive diagnostic subtype , or not.
Methods: The study included 26 patients with migraine according to HIS 2nd edition criteria, as well as 20 matched healthy controls. Participants were subjected to physical history and examination, psychiatric interview, standardized sleep assessment questionnaire, as well as all-night polysomnography.
Results: According to sleep questionnaire, patients were subdivided into two subgroups : "A" (patients with sleep related migraine)and "B" (patients with sleep unrelated migraine). Sleep complaints, especially interrupted sleep, were more frequent in patients with migraine, in general, and more significantly affected in the subgroup of " sleep related migraine ". PSG differences between patients and controls revealed significant decrease in sleep efficiency, increased arousal , as well as increased stage IV in the patients group. Patients with "sleep related migraine" differed significantly from patients with sleep unrelated migraine in having more arousals and more REM sleep percent. Awakening from sleep with headache was observed to be related to REM stage.
Conclusion: Migraine tends to be associated with decreased sleep efficiency and increased arousals. Association with NREM stage IV increase was noted in migraine patients in general, but for patients with "sleep related migraine", significant relation to REM sleep has been observed. Future large scale prospective and comparative studies are needed to evaluate such findings.

0965

OSAS WITH A HIGHER NON-RAPID EYE MOVEMENT APNEA-HYPOPNEA INDEX IS A POTENT RISK FACTOR FOR SILENT BRAIN INFARCTION

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Introduction: The aim of this study was to investigate consecutive patients with obstructive sleep apnea with a higher non-rapid eye movement (NREM) apnea-hypopnea index (AHI) than rapid eye movement (REM) AHI and to evaluate whether silent brain infarction (SBI) is increased in different subtypes of REM or NREM AHI cases.
Methods: The study population comprised four subgroup of patients. Group 1. Severe NREM OSAS N: 148 (NREM AHI more than 30/h) Group 2. Severe REM OSAS N:110 (REM AHI more than 30/h) Group 3. Sever NREM+REM OSAS N:162 (NREM and REM AHI both more than 30/h). Group 4. Control patients N: 80 without OSAS, hypoxia or sleep fragmentation (AHI and arousal index less than 5/h).Men /age 30-50 years/ with positive history of treated hypertension were recruited following diagnostic polysomnography. Patients with therapy resistant hypertension, or with other vascular comorbidities were excluded. Patients presenting with any type of hypoventilation syndrome were not eligible. Logistic regression analysis was carried out to confirm subgroup homogenity regarding BMI, drinking and smoking habit. After the polysomnography testing presence of SBI was assessed by head MRI. Appearance of one or more lacunar or terriotorial lesions, or clear cut deep white matter intensity changes, but not leukoaraiosis, were considered as positive finding.

Results: 45 NREM AHI patients (31%), 7 REM AHI patients (6%) and 54 NREM+REM AHI patients (33%) had positive MRI .In he control age, gender, and confounders matched group 8 patients (10%) had positive MRI findings.
Conclusion: OSAS cases characterized by NREM AHI were potent risk factor for SBI while OSAS cases with REM AHI did not represent elevated risk for SBI. This finding should be considered when recruiting OSAS patients for future studies investigating the relation between OSAS and cerebrovascular diseases.

0966

SLEEP DISORDERED BREATHING AND BEHAVIOR IN CHILDREN WITH CEREBRAL PALSY

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Introduction: Sleep disturbance in children is known to adversely affect behavior and quality of life. The majority of studies include only children with no other comorbid medical condition. Children with cerebral palsy (CP) may be at high risk of sleep disorders, particularly sleep-disordered breathing (SDB), which may exacerbate already compromised daytime functioning.
Methods: Children, ages 6-16 years, with CP were recruited from two Midwest regional rehabilitation centers and typically developing (TD) children were recruited from local community agencies and well-child clinics. Parents of all participants completed the Conners' Parent Rating Scale (CPRS) and the Pediatric Sleep Questionnaire (PSQ; Chervin 2000). The PSQ includes a sleep-related breathing disorder scale which was used (minus the behavioral items) to determine SDB risk. A score≥0.33 is considered risk for SDB.
Results: The samples included 52 children with CP and 80 TD children. There were no significant differences between groups for mean age (9.4±2.4 years vs. 9.1±1.9 years) or proportion of males (52% vs. 40%). Children with CP had higher T-scores on the CPRS, particularly the inattention/cognitive problem scale (61.3±14.1 vs. 48.7±7.4; $p<0.001$). Children with CP had greater SDB risk compared to TD children (12% vs. 1%; $p<0.02$). The SDB score was correlated with CPRS domain T-scores even after controlling for gestational age, socioeconomic status, and diagnosis of CP. In a linear regression controlling for group and demographics, SDB risk was independently predictive of CPRS T-scores, especially the inattention/cognitive and ADHD subscales (adjusted $R2=0.36$, $p<0.001$ in both cases). Similar results were obtained when analyses were repeated within the CP group.
Conclusion: Our findings suggest that children with CP are more likely to be at risk for SDB than typically developing children. Furthermore, SDB risk was predictive of worse performance on the CPRS. Clinicians should be aware of the potential adverse impact of sleep disturbance on the behavior of children with CP.

0967

THALAMIC HYPERPERFUSION DURING NOCTURNAL HYPERMOTOR SEIZURES

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Introduction: Previous studies using ictal single photon emission computed tomography (iSPECT) during nocturnal frontal seizures have demonstrated increased perfusion of the anterior cingulum. We report thalamic hyperperfusion as an iSPECT finding in two patients with nocturnal hypermotor seizures.
Methods: Two patients with nocturnal frontal lobe epilepsy (NFLE) since childhood underwent pre-surgical evaluation for surgical treatment of frequent pharmacoresistant sleep bound seizures. Technecium-99m was injected intravenously during a typical major seizure arising from slow wave sleep (SWS), and a brain scan was performed the next morning. Ictal images were compared to an interictal SPECT obtained after tracer injection during the same sleep stage on a subsequent night.
Results: Patient 1: Seizures in this 36-year old started with a feeling of chest tightness and palpitations, and progressed to dystonic posturing of the head and limbs, with hypermotor activity including pedaling. Consciousness was preserved. The tracer was injected 12 seconds after onset of a typical seizure which lasted 82 seconds in total. iSPECT showed increased striatal and thalamic perfusion bilaterally, and hypoperfusion in the left frontal area. The latter corresponded to the seizure onset zone determined previously by intracranial EEG recordings. Patient 2: Seizure in this 24-year old woman were characterized by prominent oral automatisms with tongue protrusion and dystonic posturing of the arms with superimposed stereotypic movements. The patient had no recollection of the seizures. The tracer was injected 4 seconds after onset of a typical seizure lasting 50 seconds in total. iSPECT documented increased thalamic perfusion bilaterally.
Conclusion: Our results suggest a major activation of the thalamus during sleep bound hypermotor seizures. They also show that nocturnal frontal seizures can be associated with local hypoperfusion of the epileptic focus, in contrast to the ictal hyperperfusion that is generally reported.

0968

SLEEP DISORDERS IN PARKINSON'S DISEASE (PD) IN SINGAPORE

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Introduction: Our objective is to describe the prevalence of sleep disorders in Singapore PD patients. Sleep problems are reported to occur frequently in PD, but are not well studied in Asian patients.
Methods: PD patients and healthy controls prospectively recruited from a tertiary hospital were evaluated by a Neurologist, including using questionnaires: Epworth Sleepiness Scale (ESS), Insomnia Severity Index (ISI), Pittsburg Sleep Quality Index (PSQI). All patients underwent polysomnography (PSG).
Results: 50 PD patients (30 male, 21 female; Mean age 65.0 years; 88.2% Chinese, 7.8% Indian, 2.0% Malay, 2% Other Race), and 64 Healthy Controls (35 male, 29 female; Mean age 58.7 years; 90.6% Chinese, 6.3% Indian, 1.6% Malay, 1.6% Other Race) were recruited over 1 year. Most PD patients had mild disease, 72.5% Stage 1 Hoehn & Yahr. PD patients had a mean ESS score of 8.98 + 5.81, not significantly different from controls ($p = 0.156$). Difference in PSQI scores for PD and controls was also not significant ($p = 0.63$). Obstructive sleep apnea (OSA) was found on PSG in 46.9% PD patients (mean AHI = 11.65 + 15.15)(14.3% mild, 20.4% moderate, 10.2% severe) vs 71.9% controls (mean AHI = 10.76 + 8.72) (40.6%, 17.2% moderate, 7.8% severe) ($p = 0.007$). Restless Legs Syndrome (RLS) was found in 7.8% PD patients and 3.1% controls ($p =0.24$).Insomnia was reported in 33.3% PD vs 3.1% controls ($p < 0.05$). However mean ISI score in PD patients was 8.78 + 7.382, not significantly different from controls ($p = 0.65$). Dream enactment behavior was reported in 23.5% PD patients suggestive of REM behavior disorder (RBD), but none of the controls. Sleep talking was reported in 47.1% PD patients, vs 4.7% controls ($p < 0.05$). Poorer sleep efficiency (mean sleep efficiency 59.70% + 21.93 in PD vs 76.79% + 18.68 in controls, $p = 0.027$) was found in PD. However percentages of light, deep and REM sleep, arousal indices, periodic limb movement (PLM) indices and mean AHI were not significantly different on PSG in PD vs controls.

Conclusion: PD patients report more insomnia and parasomnias than controls, and had poorer sleep efficiency on PSG. Of note however, hypersomnolence, RLS, PLMs and OSA were not found more frequently in our PD patients. An unusually high prevalence of OSA (majority mild to moderate) confirmed on PSG was found in our healthy control population. Besides reported insomnia and parasomnias, primary sleep disorders were not more common in our PD patients when compared to gender and age-matched controls.
Support (optional): National Medical Research Council (NMRC) Singapore

0969

COGNITION AND HIGH DENSITY EEG IN SLEEP AFTER PARAMEDIAN THALAMIC STROKE

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Introduction: Functional recovery after stroke depends on the adaptive plasticity of the human brain. Sleep contributes essentially to brain plasticity and learning. The exact link between sleep, EEG and cognition in stroke recovery remains unclear. The aim of the study is to investigate the relationship between sleep and stroke recovery by: 1) comparing EEG power in the slow wave (SWA) and spindle frequency ranges (SFR) in the acute phase after stroke and 3 months later, 2) correlating these EEG parameters to clinical and behavioral changes during the recovery process.
Methods: Seven patients, two with bilateral paramedian thalamic stroke (PMTS) and five with unilateral PMTS and five matched controls underwent detailed neuropsychological examination, actigraphy, 24h-polysomnography (PSG) and high density EEG (hd-EEG) during sleep. The patients were studied in the acute phase after stroke and 3 months later.
Results: Patients performed worse in verbal fluency test, had longer total sleep time in PSG and higher percentage of day rest in actigraphy (acute and chronic). The patients with bilateral PMTS had more profound hypersomnia and impairment in behavioral tests. In hd-EEG both SWA and sleep SFR were recorded in typical locations without gross asymmetry. In comparison to healthy controls patients had significantly lower power in SWA in frontal and occipital regions after 3 months; power in SFR was lower although not statistically significant. After 3 months hypersomnia and behavioral tests improved, especially in the patients with bilateral PMTS. A significant decrease in the SWA power was found while power in SFR did not change.
Conclusion: Behavioral and EEG changes were more profound after bilateral than after unilateral PMTS. Power in SWA after PMTS decreased after 3 months and was significantly lower than in controls while power in SFR was low initially and did not change. Improvement of cognition in bilateral PMTS was not accompanied by increase in SFR or SWA power.
Support (optional): The study is supported by the Zurich Center for Integrative Human Physiology (ZIHP).

0970

EXCESSIVE DAYTIME SLEEPINESS IN CERVICAL DYSTONIA

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Introduction: Few investigations have examined sleep-related symptoms in cervical dystonia (CD). Because CD patients may have sleep disturbances, we hypothesized that CD should be associated with greater likelihood of daytime sleepiness.
Methods: Forty-three CD patients (mean age 57, SD 10) were assessed for excessive daytime sleepiness using the Epworth Sleepiness Scale (ESS). Two control groups were also administered the ESS. The movement disorders control group (MD) consisted of 19 patients (mean age 59, SD = 13) with other focal movement disorders, including hemifacial spasm (n = 13), blepharospasm (n = 2), writer's cramp (n = 2), oromandibular dystonia (n = 1), and facial tics (n = 1). The healthy control group (HC) consisted of healthy subjects (mean age 55, SD 14) age- and gender-matched to the CD group. All CD and MD subjects were receiving botulinum toxin. Evaluations were all completed at the end of a treatment period. Excessive daytime sleepiness was defined as an ESS score > 10. Fisher's exact test was used to determine whether the proportion of CD subjects with abnormal scores was greater than other groups. In the CD group, patients were evaluated for severity, disability, and pain from CD using the Toronto Western Spasmodic Torticollis Rating Scale (TWSTRS) and for use of commonly prescribed medications with sedating properties (benzodiazepines, antidepressants, and anticholinergics). These features were tested for correlation with ESS scores.
Results: Twenty-one percent of CD patients had abnormal ESS scores, which was significantly higher than for the MD group (0%, $p = 0.028$) and the HC group (6%, $p = 0.036$). Age, TWSTRS scores, and medications were not associated with the presence of excessive daytime sleepiness in the CD group.
Conclusion: These preliminary results suggest that excessive daytime sleepiness is common in CD. Further investigation into disordered sleep in CD is warranted.

0971

DAYTIME FATIGUE / SLEEPINESS IN CHILDREN WITH DEMYELINATING DISORDERS

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Introduction: Fatigue is a common symptom in patients with central nervous system demyelinating disorders (DD). Existing research on this phenomenon has focused primarily on adult patients. The purpose of this study is to determine whether fatigue in pediatric patients with DD can be explained by nocturnal sleep disorders.
Methods: Patients with multiple sclerosis (MS), acute disseminated encephalomyelitis (ADEM) or clinically isolated syndromes (CIS) seen in the Pediatric MS and Related Disorders Program at Children's Hospital Boston were asked to complete the Pediatric Sleep Questionnaire and Pediatric Daytime Sleepiness Scale. Survey results were analyzed using the student's t-test and chi-square test.
Results: 11 patients aged 3-19y years were approached to enroll in this study over 5 months; all participated. The six patients with relapsing-remitting multiple sclerosis (RRMS) were significantly more likely to have daytime fatigue on PDSS compared to the five patients with monophasic disorders ($p = 0.025$; student t-test). None of the patients had sleep disordered breathing, insomnia, restless leg syndrome/periodic limb movements, symptoms of narcolepsy or parasomnia on the basis of the PSQ results. The presence of moderate/severe fatigue did not correlate with the presence of demyelinating lesions location in the brainstem, frontal cortex or thalamus on brain MRI ($p=0.8190$; chi-square).
Conclusion: This exploratory study showed that pediatric patients with RRMS have significantly more daytime fatigue than patients with monophasic disorders. Intrinsic sleep disturbances based on the PSQ did not account for this difference. Lesion location also did not correlate with daytime fatigue. Larger studies, which also explore other etiologic mechanisms and intervention strategies for fatigue, need to be conducted in this patient population.

0972

ARRAY COMPARATIVE GENOMIC HYBRIDIZATION (ACGH) TO IDENTIFY CANDIDATE REGIONS IN SLEEP DISORDERS

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Introduction: The purpose of this study is to identify candidate genes and novel genomic regions seen in children with various sleep disorders.
Methods: Genome-wide array-based comparative genomic hybridization on DNA microarrays with an average resolution of <0.5 Mb, ordered for diverse medical conditions, is routinely performed at our institutions. Medical records of the patients with copy number variants on oligonucleotide array comparative genomic hybridization (aCGH) results were then reviewed for sleep abnormalities.
Results: Out of 657 copy number variants (CNV) on aCGH detected in one year, 83 (12.6%) patients were identified with associated sleep abnormalities. The most relevant CNV were: 2q13 microdeletions in a region associated with juvenile nephronophthisis (n=4), 15q13.3 microdeletion associated with cognitive impairment, autism phenotype and epilepsy (n=6), 16p11.2 microduplication associated with autism and neurodevelopmental delay (n=3), 7p11.23 deletion associated with Williams syndrome (n=1), and 17q12 microduplication containing PER1, a gene previously associated with circadian dysfunction (n=2). The variety of sleep disorders in these cases included night terrors, sleep apnea, insomnia, rhythmic movement disorders of sleep, and hypersomnolence.
Conclusion: This exploratory study revealed interesting aCGH abnormalities in patients with diverse sleep problems. This may be of useful diagnostic value and may also help us better understand the mechanism underlying diverse sleep abnormalities. In the future, obtaining blood for aCGH may be considered in children with dysmorphic features, autism, and sleep problems. Characterizing sleep dysfunction with known aCGH abnormalities along with performing association and studies of these abnormal aCGH regions with known sleep related gene mutations may also be useful.

0973

SLEEP DISORDERED BREATHING IN THE PEDIATRIC PATIENTS WITH EPILEPSY

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Introduction: Previous studies show an increased prevalence of sleep disordered breathing (SDB) in adults with epilepsy and its detrimental impact on seizure frequency. However, information on SDB in children with epilepsy is limited. Factors predisposing the epileptic patients to SDB may include alteration of muscle tone, changes of neural control of breathing and the use of certain medications.
Methods: We conducted a prospective pilot study in the pediatric epileptic patients. Subjects were recruited from epilepsy clinics. All patients and/or their parents were asked to complete the Michigan Pediatric Sleep Questionnaire (PSQ, Chervin et al. 2000). Medical records were reviewed for the frequency and type of seizures and the number of antiepileptic medications (AEDs). The patients were classified based on the frequency of seizures: mild epilepsy (M, 0-1 seizure/month) and severe refractory epilepsy (S, >1 seizures/month). Patients with incomplete records were excluded.
Results: Eighty four patients met entry criteria: 32 were classified as S and 52 as M. Their average age was 9.4±3.6 (mean ± standard deviation) years. There were no significant differences in age (9.0±3.8 [S] vs. 9.9±3.3 [M]) or sex (22 m, 10 f [S]; 29 m, 23 f [M]) between the groups. The presence of SDB based on PSQ (cutoff 0.33) was significantly higher in the children with S (15.6%) than M (3.8%, $p<0.05$). There were no significant correlations between the PSQ scores and type of seizure or the number of AEDs.
Conclusion: Based on this data, using PSQ, SDB is more prevalent in the patients with epilepsy especially with refractory epilepsy. The prevalence of SDB is not related to the type of seizure or the number of AEDs. We are in the process of conducting a larger scale study to address this question. We speculate that SDB may have an adverse effect on clinical outcome in the children with epilepsy.
Support (optional): This study is supported by The Cincinnati Children's Hospital Research Fund.

0974

SLEEP SIGNING: A DISTINCT SYMPTOM OR A TYPE OF SLEEP TALKING?

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Introduction: Relatively little is known about the significance of sleep talking although it has been reported as having a strong genetic predisposition and is commonly reported among children and adults alone or in the setting of parasomnias or sleep disordered breathing. Evidence has shown localization of language in patients learning sign language as a primary language occurs in the dominant hemisphere similar to what is found in spoken language despite its visuospatial components. We report three cases of sleep signing in a family with a history of prelingual deafness. We propose this newly reported symptom as a clinical correlate to sleep talking in patients with sign language as a primary language in both normal hearing and prelingually deaf patients.
Methods: We analyzed clinical data including witnessed accounts from patients' bed partners and family members regarding age of onset, frequency, content and associated sleep disruptions. Overnight polysomnography and the Epworth sleepiness scales (ESS) was also used to characterize sleep signing as a clinical correlate to sleep talking.
Results: Patients included two women and one man with onset of sleep talking in childhood. All patients had witnessed accounts from a family member of hand movements during sleep recognized as language that was distinguishable from gestures or sleep related movement disorders. All three patients learned sign language as a primary language, but only two of the three patients were deaf. One patient had documented obstructive sleep apnea by overnight polysomnography while the other two had a high index of suspicion for obstructive sleep apnea by history of loud snoring and excessive daytime sleepiness.
Conclusion: To our knowledge, this group of patients represents the first report of a group of patients with a complaint of sleep signing. Sleep signing was seen in normal hearing and prelingually deaf patients but was associated with sign language as a primary language, sleep disordered breathing and a family history of sleep signing. Sleep signing may only be seen in patients who acquire sign language as a primary language suggesting the pathophysiology is specific to the localization in the dominant hemisphere and is a clinical correlate to sleep talking. Further studies with functional imaging to confirm language localization in these patients would help provide insight to the pathphysiology of sleep talking and sleep signing.

0975

DAYTIME SLEEPINESS AND SLEEP DISORDER SYMPTOMS IN CHILDREN WITH EPILEPSY AND MIGRAINES

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Introduction: Sleep complaints are common among children but extent of these complaints and the factors that underlie such complaints among children with epilepsy and migraines is not known. We evaluated the extent of daytime sleepiness and sleep complaints in a population of children with idiopathic generalized epilepsy (IGE) and migraines, and compared to that of healthy controls.
Methods: Children with IGE (n= 35) and migraine headaches (n=6) between ages 8-18 were recruited for the study. Two validated questionnaires Pediatric Sleep Questionnaire (PSQ) (completed by parents) and Pediatric Daytime Sleepiness Scale (PDSS) (completed by children) were obtained. Sleep disordered breathing and parasomnia subscales were extracted from the PSQ and daytime sleepiness score was obtained from PDSS. Both groups were compared to age-matched normal healthy controls taken from a prior study (n=24).
Results: Demographic characteristics were no different between the groups. Parents of children with IGE and Migraines more often reported significant symptoms of sleep disordered breathing (40% vs 33% vs 3.9% respectively; $p<0.001$) and parasomnias (42% VS 33% VS 8%; $p<0.001$) compared to controls. Parents of children with IGE also more often reported daytime sleepiness compared to those with migraines and healthy controls (65% vs 33% vs 24%, $p<0.01$). Children with IGE and Migraines had higher PDSS scores compared to that of normal controls (16.77±6.77 vs 17.67±3.88 vs 12.54±5.19 respectively; $p<0.011$). Symptoms of sleep apnea correlated well with PDSS score ($r= 0.64$) where as presence of symptoms of parasomnia weakly correlated with PDSS ($r=0.49$) in the IGE group but not in the migraine group. Demographic and epilepsy related factors did not correlate with PDSS.
Conclusion: Excessive daytime sleepiness is common among children with IGE as well as migraines. While further confirmatory studies are needed, daytime sleepiness in children with IGE may be due to underlying sleep disordered breathing or parasomnias.
Support (optional): Study supported by Barrow Womens Board

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SLEEP STUDY ABNORMALITIES IN ISODICENTRIC CHROMOSOME 15 DUPLICATION SYNDROME: A POSSIBLE EXPLANATION OF SUDDEN DEATH?

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Introduction: Isodicentric chromosome 15 syndrome is a neurogenetic syndrome characterized by the presence of an extra structurally abnormal chromosome formed by inverted duplication of chromosome 15q11-13. This leads to an extra isodicentric 15 chromosome. Clinically, this results in epilepsy, hypotonia, minor dysmorphisms, moderate-severe developmental delay, and autistic behaviors. Additionally, an increased risk of sudden and unexpected death has been reported in patients as young as seven years old, without clear cause. There is speculation that abnormalities of sleep, cardiorespiratory function, mitochondrial function, or epilepsy may be contributory, however there are few reports in the literature. We aim to determine the mechanism of sudden death in this patient population by reviewing patient data from our institution.
Methods: Children with a diagnosis of isodicentric chromosome 15 syndrome and epilepsy were identified from our Neurology and Genetics Programs at Children's Hospital Boston. Records were reviewed to identify subjects who also had sleep studies performed.
Results: Sixteen children with isodicentric chromosome 15 syndrome were identified. Two of these children had sleep studies performed. Patient 1 had 29 central apneas of 7-50 seconds duration, associated with desaturations to as low as 70%. Most of these apneas were associated with either right or left anterior parasagittal onset of electrographic seizure, with eye deviation and tonic body stiffening accompanying them. Patient 2 had 11 brief central apneas of 10-25 seconds duration, not associated with desaturations below 95%. Frequent brief generalized electrographic seizures without central apneas or clinical accompaniment were also seen.
Conclusion: The cause of sudden death in isodicentric chromosome 15 syndrome remains unclear. Our findings suggest that central sleep apnea associated with nocturnal seizures may be a potential explanation. Further understanding of nocturnal EEG and sleep patterns are required to explore this possibility.

0977

THE ASSESSMENT OF MIGRAINE SEVERITY, FREQUENCY AND DURATION IN PATIENTS WITH AIRFLOW LIMITATIONS AFTER THE NASAL CONTINUOUS POSITIVE AIRWAY PRESSURE (CPAP)

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Introduction: The association between migraine headaches and sleep disorders has been postulated since at least the 1970s. In a 2005 British study, respondents were asked about the nature of their headaches in the preceding three months, among all the variables, after adjusting for age and gender, sleep problems showed the strongest association with migraine headaches. It is also interesting to note that the association got stronger as the sleep quality decreased. In our study we are looking at the effect of correcting air flow limitations (i.e. obstructive sleep apnea or upper airway resistance syndrome) by using nasal CPAP on migraine headaches. We wanted to assess if better quality of sleep via the use of nasal CPAP improves migraine headaches. To our knowledge, this is the first time that anyone has studied the effects of CPAP therapy in migraine headaches.
Methods: This is a retrospective study. Patients, with a diagnosis of Migraine headaches were surveyed to determine if CPAP improved their MIDAS (Migraine disability assessment questionnaire) score. In this study, patients with a previous diagnosis of migraine headache, who were being evaluated for sleep study were identified. Their diagnosis of Migraine headache was confirmed using the International Headache Society's classification for Migraines. Patients who received at least one month of CPAP therapy for various sleep related breathing disorders were chosen. We then conducted a survey and asked patients to rate their migraine severity before and after the use of nasal CPAP using MIDAS questionnaire. This is an ongoing study which started in July 2008.
Results: Thus far, three out of our four patients who had CPAP therapy for at least one month noted a significant improvement in their Migraine disability scores. The one patient who did not have any change in her migraine disability after CPAP had a low MIDAS score of 3 at baseline. The average MIDAS score before the CPAP study was 22.25, reflecting a severe disability score. After the CPAP, the average score was 8.5, reflecting a mild disability score. Our results approached statistical significance using a paired t test with a two tailed t test with a two tailed p value of 0.08.
Conclusion: Correcting airflow limitations via nasal CPAP, increases the quality of sleep and likely contributes to a reduced disability from migraine headaches. Future, double blind, prospective studies are needed to assess this finding further.

0978

SLEEP DISORDERED BREATHING IN PATIENTS TAKING OPIOIDS FOR CHRONIC PAIN

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Introduction: This study was performed to examine the effects opioids have on sleep and sleep disordered breathing.
Methods: A prospective descriptive cross sectional study of patients referred to sleep disorders centers was conducted. There were two types of independent variables, (a) risk factors for sleep disordered breathing ,and (b) those that were directly related to the investigational hypothesis (pain incidence and intensity and/or opiate use and dose). Dependent Variables included: measures of sleep disordered breathing, sleep architecture, and sleep continuity. After orthogonally coding for group membership, regression models were used for statistical analysis.
Results: Data was collected on a total of 419 subjects (no pain [n = 171], pain -opiate Tx [n = 187], and pain +opiate Tx [n = 61]). Sample demographic (mean +/- SD) was as follows: age 50 yr + 12.; 51% male; BMI 33.8 + 7; Epworth Sleepiness Scale 10.3 + 5; pain intensity 3.8 + 2 (0-10 scale); morphine equivalent dose 152 + 195 mg; and 98% of subjects with pain had non-malignant chronic pain. Per study hypotheses (a) there was a positive dose response relationship between amount of opiate and frequency of central apneic events and percent of stage 3/4 sleep; (b) the [no pain vs. pain] group comparison revealed that subjects with pain had a lower percent of stage 1 sleep, and the [pain minus opiate vs. pain plus opiate]) group comparison revealed that subjects treated with opiates had significantly more central apneic events, more stage 2 sleep and less REM sleep; (c) the known risk factors for sleep disordered breathing differ in persons with and without chronic pain (chronic pain subjects were older, female and suffered from more comorbidity); (d) there was a relationship between pain intensity and frequency of central apneic events and obstructive apneic events. Greater pain intensity was associated with more frequent central apneic events and fewer obstructive apneic events.
Conclusion: These data suggest that the management of chronic pain with opiates is not likely to exacerbate obstructive sleep apnea at stable opiate doses; however; central sleep apnea may be worsened. The magnitude of the effect is modest, and the clinical relevance of the effect is unknown. Thus, the potential for marginal respiratory disturbance (an increase of 2.8 central events for every 100 mg. morphine equivalent opiate dose) must be weighed against the therapeutic value of pain management with opiates.

0979

INSOMNIA AND SLEEP DURATION AS MEDIATORS OF THE RELATIONSHIP BETWEEN DEPRESSION AND HYPERTENSION INCIDENCE IN MIDDLE-AGED SUBJECTS

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Introduction: Depression has been found to predict the incidence of hypertension and other adverse cardiovascular events in prospective studies. Insomnia and short sleep duration are typical symptoms of depression. Insomnia is associated with increased activation of the HPA axis and has been shown to increase the risk for hypertension incidence. Short sleep duration has also been shown to increase the risk for hypertension incidence and has been theorized to do so by raising average 24-hour blood pressure and elevating sympathetic nervous system activity, leading to structural adaptations that gradually reset the entire cardiovascular system to operate at an elevated pressure equilibrium. We are not aware of any published population studies that have examined whether insomnia and sleep duration mediate the relationship between depression and the incidence of hypertension.
Methods: Multivariate longitudinal (1982-1992) analyses stratified by age of the NHANES I (n=4,959) using Cox Proportional Hazards models to explore whether insomnia and sleep duration act as mediators of the relationship between depression and hypertension incidence.
Results: A total of 744 (15.0%) subjects suffered from depression at baseline and 670 (13.5%) subjects were diagnosed with hypertension over the follow-up period. Middle-aged subjects between the ages of 32 and 59 who suffered from depression at baseline were 46% more likely to be diagnosed with hypertension over the follow-up period after controlling for covariates (HR = 1.46, 95% CI 1.16-1.82). Both short sleep duration and insomnia were also significantly associated with hypertension incidence in multivariate models. Consistent with insomnia and sleep duration acting as mediators of the relationship between depression and the incidence of hypertension, the inclusion of these variables in the multivariate models appreciably attenuated the association (HR = 1.29, 95% CI 1.02-1.64). We found no significant relationships between the exposures of depression, insomnia, and sleep duration and the outcome of hypertension incidence in elderly subjects between the ages of 60 and 86.
Conclusion: We found depression to increase the risk for hypertension in middle-aged subjects and our results are consistent with insomnia and sleep duration acting as significant mediators of this relationship. Treatment of sleep problems in individuals suffering from depression could therefore reduce their risk for developing hypertension and its vascular and cardiac complications.
Support (optional): Financial support for this study was provided by R24 HL76857 from the NIH/National Heart Blood and Lung Institute to Columbia University's Behavioral Cardiovascular Health and Hypertension Program.

0980

CONTRIBUTION OF FATIGUE TO CHEMOBRAIN IN WOMEN UNDERGOING CHEMOTHERAPY FOR BREAST CANCER

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Introduction: Patients undergoing chemotherapy report decreased cognitive functioning, called chemobrain. Fatigue and problems sleeping are also commonly reported. Whether chemobrain reflects neurocognitive changes resulting from chemotherapy, or might be secondary to fatigue and/or sleep and circadian rhythm problems, has not yet been explored. We present interim data from an ongoing study examining the role of sleep disturbances and fatigue as potential proximal causes of cognitive impairment in women undergoing chemotherapy for breast cancer.
Methods: Participants in our study were women with breast cancer recruited before the start of chemotherapy, and tested pre-treatment and at the end of four cycles of chemotherapy. Non-cancer controls are also recruited and tested using one-to-one matching on age, demographic and socioeconomic factors. At both time points, data were collected on fatigue, sleep quality, depression, anxiety, menopausal symptoms and quality of life and a complete neuropsychological test battery administered.
Results: Interim analyses showed that patients (n=21), compared to controls (n=21), reported significantly more fatigue ($p<0.001$), anxiety ($p<0.001$), depressive symptoms ($p<0.001$) and worse sleep quality ($p=0.029$) even before starting chemotherapy. Patients also reported more deterioration from pre- to post-chemotherapy (approximately

12 weeks), compared to controls, in sleep quality (p=0.015), fatigue (p=0.028), depressive symptoms (p=0.0002), anxiety (p=0.004) and cognitive functioning (p=0.024). A linear regression analyses was computed to determine what factors, after controlling for baseline cognitive levels, predict a worsening of cognitive function over four weeks of chemotherapy, suggesting that only a worsening of fatigue was significantly related to a decrease in cognitive function (p=0.027) with the model explaining 19% of the variance.

Conclusion: Although based on interim analyses from an ongoing study, these preliminary data suggest that fatigue is related to decrements in cognition. If these results are supported with larger samples, intervention studies aimed at improving fatigue for patients undergoing chemotherapy should be considered.

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0981

DOES SLEEP DURATION INFLUENCE BODY MASS INDEX IN TWINS?

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Introduction: To investigate the association between sleep duration and body mass index (BMI) we used twins obtained from the University of Washington Twin Registry. Researching this genetically informative sample of twins allows assessment of the relative importance of genetic and environmental contributions to the relationship between sleep duration and BMI.

Methods: We surveyed 1,797 twins, including 634 twin pairs (437 monozygotic, 150 dizygotic, and 47 indeterminate pairs) and 529 individual twins. Habitual sleep duration was obtained by self-reported length of sleep per night and BMI was calculated by self-reported height and weight. We used a Generalized Estimating Equation linear regression model to analyze the overall, within, and between pair effects of sleep duration on BMI. Statistical significance was assessed based on the 2 degree of freedom chi-square test.

Results: The twin sample was 68.3% female, 88.2% Caucasian, with a mean age of 36.8 (SD=15.1) years. In an unadjusted analysis using all twins there was a significant relationship between sleep duration and BMI ($p<0.001$). Twins with 7-8.9 hours of sleep per night had a lower mean BMI (25.0 kg/m2) compared to those who regularly slept either more (25.2 kg/m2) or less (26.4 kg/m2) per night. These results persisted in a co-twin control analysis of within twin pair differences in sleep duration and BMI ($p<0.05$). The analysis of all twins ($p<0.01$) and the co-twin control within-pair analyses ($p<0.05$) remained significant after adjustment for age, gender, race, smoking status, alcohol use, cohabitation status, chronic disease, and number of children living in the household.

Conclusion: BMI varied as a function of habitual sleep duration. Even after careful adjustment for genetics and shared environment the relationship between sleep duration and BMI remains. These findings point toward an environmental cause of the relationship between habitual sleep duration and BMI.

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0982

ADVERSE CARDIOMETABOLIC RISK AND NAPPING: THE GUANGZHOU BIOBANK COHORT STUDY

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Introduction: Millions of people take an intentional nap, but data describing potential health effects of naps are limited. We report on possible associations between napping and cardiometabolic risk in a large well-characterized older Chinese cohort.

Methods: Data from 16,480 older participants (≥50 years) from Guangzhou Biobank Cohort Study were analysed. Sociodemographic parameters, including frequency of napping were collected by questionnaire. The relationship between frequency of napping and cardiometabolic risk factors (self-reported physician diagnosed vascular disease, metabolic syndrome, hypertension, diabetes, dyslipidaemia, central obesity) was investigated using analysis of covariance and logistic regression.

Results: 67.5% napped at least once per week. The prevalence of all cardiometabolic risk factors, except central obesity, increased with napping frequency. Napping remained independently associated with cardometabolic risk factors after adjustment for age, sex, education, occupation, smoking, physical activity, self-rated health, seasonality, and as appropriate, waist circumference, mean arterial pressure, glucose, HDL-cholesterol and triglycerides). The risk of having these conditions was increased by 14-30% in daily nappers vs. never nappers. Compared with never nappers, daily nappers had a 14% (95% CI 4, 25%) and a 25% (5, 48%) increase in the risk of having the metabolic syndrome and physician-diagnosed vascular disease, respectively. Removal of those with existing vascular disease did not alter the observed associations. Escalated risks of hypertension, diabetes and dyslipidaemia were also associated with increasing napping frequency. The corresponding adjusted ORs were 1.22 (95% CI 1.13, 1.32), 1.30 (1.16, 1.46), and 1.17 (1.08, 1.26), for those who napped daily. Snoring, a characteristic of sleep apnoea, was found to confound the relationship between napping and cardiometabolic risk

Conclusion: After adjustment for a range of confounding factors and examining the relationship for reverse causality, our data suggests napping is associated with cardiometabolic risk in older Chinese. This has important public health implications which should be confirmed in other populations.

0983

FREQUENT SNORING DURING PREGNANCY IS ASSOCIATED WITH AN INCREASED RISK OF GESTATIONAL DIABETES

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Introduction: The objective of this study was to determine the relationship between self reported snoring and adverse pregnancy outcomes in healthy nulliparous women.

Methods: This is a prospective, cohort study of healthy nulliparous women recruited between 6-20 weeks gestation who completed a sleep survey at the time of enrollment and in the third trimester. Frequent snoring was defined as snoring ≥ 3 nights/week. Subjects were followed prospectively and pregnancy outcomes were abstracted from the medical record by study personnel blinded to the sleep survey results. Uni-

variable comparisons were made evaluating the relationship of frequent snoring to adverse pregnancy outcomes. Factors that in univariable analysis were associated with snoring at a level of $p < 0.10$ were placed in a multivariable logistic regression to ascertain independent associations.
Results: Two hundred and one women were recruited of which 188 completed both surveys. The mean gestational age was 13.9 ± 3.8 weeks and 30.0 ± 2.2 at the first and second survey respectively. Eleven percent of women (21/188) reported frequent snoring in early pregnancy, 16.5% (31/188) reported frequent snoring in the third trimester, and 9% (17/188) reported frequent snoring in both early and late pregnancy. Women who reported any frequent snoring in pregnancy (early and/or third trimester) were more likely to develop gestational diabetes (14.3% vs. 3.3%; OR 4.9, 95% CI 1.3, 18.1). For women who reported frequent snoring in both early and late pregnancy the odds ratio for developing gestational diabetes was 8.5 (95% CI 2.1, 33.8). Even after controlling for BMI, frequent snoring continued to be significantly associated with gestational diabetes: adjusted OR 4.9 (95% CI 1.3, 19.3) for women with any frequent snoring, adjusted OR 6.5 (95% CI 1.6, 27.3) for those with frequent snoring both in early and late pregnancy.
Conclusion: Frequent snoring during pregnancy is associated with an increased risk of gestational diabetes.

0984

SODIUM OXYBATE IMPROVES PAIN, FATIGUE, AND SLEEP IN FIBROMYALGIA: RESULTS FROM A 14-WEEK RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL

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Introduction: Fibromyalgia is characterized by widespread pain, often with chronic fatigue, disturbed unrefreshing sleep, and psychophysiologic distress. This study is the largest clinical trial to date examining the treatment effects of sodium oxybate (SXB) in fibromyalgia.
Methods: 548 subjects meeting American College of Rheumatology criteria for fibromyalgia were randomly assigned to sodium oxybate 4.5g/night (SXB4.5g), 6g/night (SXB6g), or placebo (PBO) in a 1:1:1 ratio. Treatments were administered as two equally divided doses at bedtime and 2.5-4 hours later. The primary outcome measure was the percentage of subjects who reported a >=30% reduction on the Pain Visual Analog Scale (VAS) from baseline to week 14. Other measures included Fatigue VAS, Jenkins Sleep Scale (JSS; a validated, 4-item, self-report questionnaire for sleep disturbance), and patient global impression of change (PGIc). Safety was assessed via treatment-emergent adverse events, vital signs, laboratory, and ECG measures.
Results: SXB4.5g and SXB6g resulted in significantly more patients reporting >=30% improvement in Pain VAS compared with PBO (54.2% and 58.5%, respectively, vs 35.2%, $p<0.001$). Compared with PBO, treatment with SXB4.5g and SXB6g resulted in significantly greater reductions in mean JSS scores (-6.1 and -6.2, respectively, vs -2.9, both $p<0.001$) and significantly greater reductions in mean Fatigue VAS scores (-27.94 and -30.02, respectively, vs -17.57, both $p<0.001$). In addition, a significantly greater percentage of subjects treated with SXB4.5g and SXB6g perceived meaningful improvement in symptoms, evidenced by PGIc scores of "much better" or "very much better" compared with PBO (48.3% and 45.4%, respectively, vs 27.2%, both $p<0.001$). Adverse events occurring with SXB treatment with incidence >=5% and >=2X the incidence of PBO were: headache, nausea, dizziness, vomiting, diarrhea, anxiety, and sinusitis.
Conclusion: SXB 4.5g/night and 6g/night in two divided doses appear to be safe and efficacious for the treatment of pain, fatigue, and sleep disturbance in patients with fibromyalgia.
Support (optional): Study funded by Jazz Pharmaceuticals, Inc.

0985

SLEEP-DISORDERED BREATHING (SDB) SYMPTOMS AND ASTHMA CONTROL IN THE ELDERLY

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Introduction: Asthma is an important cause of morbidity and mortality in older individuals, who also are at increased risk for SDB. Associations with potential clinical significance have been identified between asthma and SDB, but the relationship has not been studied specifically among the aged. We therefore used data from an ongoing sizeable survey (Sleep Med 7[8], 2006:607-613) to explore associations between SDB and asthma in this age group.
Methods: Patients >60 years old seen at tertiary Pulmonary/Allergy Clinics completed the Sleep Apnea scale of Sleep Disorders Questionnaire (SA-SDQ, Douglass et al, 1994) and questions about asthma symptom frequency (1997 NAEPP). Medical records were reviewed to assess comorbidities and asthma severity step.
Results: Among n=131 subjects (58% females, mean age [±s.d.]=65±4, BMI=29±6) not on treatment for SDB, 51 (39%) were in asthma severity step 1, 12 (9%) step 2, 38 (29% step 3), and 30 (23%) step 4; mean SA-SDQ was 31±7. In univariate ordinal logistic regression models, asthma severity step was associated with SA-SDQ ($p<0.0001$), BMI ($p=0.002$), and GERD ($p=0.02$), and almost inversely with chronic sinusitis ($p=0.05$). In the multivariate model, only the SA-SDQ predicted an increased asthma step, after controlling for BMI, GERD, gender, rhinitis, chronic sinusitis, and a psychiatric history: a one standard deviation increase in the SA-SDQ nearly doubled the likelihood of a higher asthma step (OR=1.8, 95% C.I. [1.1, 2.8]). Chronic sinusitis acted as a protective factor (OR=0.4, [0.2, 0.9]), perhaps because of highly specialized medical care.
Conclusion: Among older persons, asthma severity step is predicted by SDB symptoms even after adjustment for multiple recognized aggravators of asthma. These findings raise the possibility that identification and treatment of SDB could offer an opportunity to improve asthma control for older patients.
Support (optional): NCRR GCRC M01-RR00042 (to University of Michigan) and CTSA 1UL1RR025011 (to University of Wisconsin); University of Wisconsin SMPH, Department of Medicine, and Medical Education and Research Committee-New Investigator Award (MT)

0986

SLEEP PATTERN IN AN EXPERIMENTAL MODEL OF OSTEOARTHRITIS

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Introduction: Osteoarthritis (OA) is a major healthcare burden of increasing prevalence. It has been demonstrated that the relationship between pain and sleep produces changes in sleep patterns and pain perception. However, electrophysiological studies in animal models of pain are limited. The current study examined the effect of chronic articular pain on sleep patterns in an experimental model of OA.
Methods: Rats were implanted with electrodes for electrocorticography and electromyography. OA was induced in these rats by the intra-articular administration of monosodium iodoacetate into the left knee joint. Sleep recordings were monitored during light and dark periods lasting

12 h each and were evaluated at baseline as well as on days 1, 10, 15, 20 and 28 after iodoacetate injection or assignment to sham or control groups. The pain threshold was also assessed by hot plate testing in other groups of rats at the same time points.
Results: The results demonstrated that OA significantly reduced the thermal pain threshold from day 10 until the end of experiment. OA rats exhibited reduced sleep efficiency, slow wave sleep, paradoxical sleep and an increased number of microarousals during the light periods compared with the baseline as well as control and sham groups. These changes in sleep pattern occurred mostly between days 10 and 28. In the dark period, sleep disturbances were also characterized by decreased sleep efficiency, slow wave sleep, and paradoxical sleep, although sleep was only initially fragmented.
Conclusion: Pain associated with the rat OA model causes alterations in sleep architecture by disrupting the sleep pattern.
Support (optional): Research supported by AFIP and FAPESP (CEPID #98/14303-3 to S.T. and #07/56620-6 to A.S.). Sergio Tufik and Monica Andersen are recipients of fellowships from CNPq.

0987

PREVALENCE AND RISK FACTORS FOR ERECTILE DYSFUNCTION IN SAO PAULO, BRAZIL: A POPULATION BASED SURVEY

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Introduction: The aim of this study was to estimate the prevalence of erectile dysfunction (ED) complaint and to determine its associations with sleep disturbances, testosterone levels, age, body mass index (BMI), socioeconomic factors, family history of selected medical conditions (diabetes, obesity and hypertension), and lifestyle factors (smoking habits and alcohol consumption) in based sample from Sao Paulo city.
Methods: The survey was based on 1101 participants (467 men), aged 20 to 80 years at enrollment in the Epidemiologic Sleep Study (EPISONO), population-based study of sleep and related risk factors for sleep disturbances in the largest Brazilian city using up-to-date clinical and epidemiologic techniques and procedures. This study adopted a probabilistic three-stage cluster sample of the Sao Paulo city to represent the population according to gender, age and socioeconomic classes. Questionnaire concerning sexual and erection complaints, polysomnography (1042 volunteers, refusal rate=5.4%), and fasting blood samples were collected.
Results: The prevalence of ED complaint was 17.08%. The prevalence of ED complaint increased from 7.3 to 40.1% in older individuals (>50y) compared with younger men (20-29y) (OR=8.09; p<0.0001). The age-adjusted prevalence of ED complaint (<50y) was 14.8% in individuals with reduced REM sleep and 11.3% in those with fragmented sleep. Obesity (OR=1.8; p<0.056), low testosterone concentrations (OR=4.28; p<0.01), low quality of life (OR=4.4; p<0.001), apnea-hypopnea index over 15 (OR=2.75; p<0.0001) and obstructive sleep apnea syndrome (OR=2.13; p<0.001) were associated with higher risks of ED complaint.
Conclusion: Present data indicate that ED complaint is relatively common, especially in older men. Adequate sleep pattern and normal or high levels of testosterone, a marker for sexual motivation, represent a protective factor against the ED. Sleep apnea has a strong effect on erectile function, especially by impacting negatively sexual life.
Support (optional): AFIP, CNPq and FAPESP (CEPID #98/14303-3).

0988

SLEEP ARCHITECTURE IN A MEDICAL INTENSIVE CARE UNIT PATIENT POPULATION NOT REQUIRING VENTILATORY SUPPORT

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Introduction: The few studies that have examined sleep architecture in critically ill adults have generally addressed individuals admitted for surgical procedures, or those requiring ventilatory support. Presently there are no published studies concerning sleep architecture that specifically address the general medical-intensive care unit (MICU) patient population not requiring ventilatory support. This study specifically examines the sleep architecture of this patient population.
Methods: Prospective Observational Study Data was compiled over a 47 day period. Forty-four of 131 consecutively encountered MICU patients (33.6%) were entered into this study. Eighty-seven individuals were excluded; 44 required ventilatory support, 3 were less than 18 years of age, 2 died during screening, 20 were discharged or unavailable for intended polysomnography (PSG) and permission could not be obtained in 18 cases. Attended, overnight, portable PSG studies, utilizing standard methodologies were performed on every patient. All studies were scored by an individual board certified in sleep medicine.
Results: The patient population consisted of 21 males (48%) and 23 females (52%), with a mean (+/-SD) age in years of 57.2 +/- 21.1 (with a range of 19 to 91). Sleep was characterized by median values: total sleep time = 298 minutes, sleep efficiency = 67.4%, sleep latency = 4.5 minutes, and sleep stage percentages, 35.6% for N (non-rapid eye movement)-1 sleep, 10.3% for N-2, 26.1% for N-3, and 1.2% for REM sleep. The mean APACHE II score was 17.6 (SD 7.0), and the mean SOFA score was 4.7 (SD 2.9). Higher APACHE II scores correlated with shorter sleep latencies ($P < 0.05$); no other significant correlations between severity of illness and sleep architecture were found.
Conclusion: This study shows that subjects in the general MICU population have a relative elevation of N-1 and N-3 sleep, a relative reduction of N-2 and REM sleep, short sleep latencies, and decreased sleep efficiencies. The only strong correlation between sleep architecture and severity of illness was short sleep latency.

0989

ASSESSMENT OF IMPACT OF SLEEP DISORDERS/ SYMPTOMS ON THE HEALTH STATUS OF HEART FAILURE (HF) PATIENTS USING KANSAS CITY CARDIOMYOPATHY QUESTIONNAIRE (KCCQ)

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Introduction: As major advances in HF management have significantly improved life expectancy, greater attention has turned to optimize health related quality of life (HRQL) by identifying and modifying contributing factors. Mounting evidence indicates that sleep disorders are a significant contributing factor to poor HRQL in HF patients; yet most of the published data is limited to sleep disordered breathing. Several HF-specific instruments were developed to assess HRQL in HF population. No prior studies have assessed impact of subjective and objective sleep variables on HRQL using KCCQ. This study intended to determine the impact of sleep disturbances on HRQL in HF patients as determined by KCCQ, a HF-specific HRQL questionnaire.
Methods: Prospective analysis of stable HF patients recruited from the Cleveland Clinic HF Center. Patients were subjected to comprehensive

history and physical exam, a series of questionnaires (Epworth Sleepiness Scale [ESS], Insomnia Severity Index [ISI]), Fatigue Severity Scale [FSS], Functional Outcome of Sleep Questionnaire [FOSQ] and KCCQ), PSG, MSLT, and echocardiogram. Univariate analyses and linear regression were performed to identify predictors of the KCCQ overall score.
Results: The study included 26 subjects (22 male) with mean (±sd) age 52±13.57 years; New York Heart Association functional class (NYHA FC) I-III; EF 33.88%±12.2; BMI 33.36±7.3; and AHI 33.52±22.67. KCCQ overall score (69.97±19.26) negatively correlated with BMI, FSS, ISS and NYHA FC (significant with BMI [p=0.049] and NYHA FC [p=0.006]). Linear regression revealed that BMI (p=0.002), AHI (p=0.017), ISI (p=0.009) and FSS (p< 0.001) were significant predictors of KCCQ overall score.
Conclusion: Preliminary findings suggest that three sleep related variables (AHI, ISI, FSS) are significant predictors of HRQL in HF patients. Although this study is limited due to sample size and potential selection bias, these findings underscore the importance of routine sleep assessment in the HF population.

0990

ASSOCIATION OF SELF-REPORTED SLEEP MEDICATION USE TO SLEEP, DEPRESSION, FATIGUE AND MENOPAUSAL SYMPTOMS IN WOMEN UNDERGOING CHEMOTHERAPY FOR BREAST CANCER

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Introduction: Sleeping pills are frequently prescribed for the sleep disturbance and anxiety during chemotherapy. However, there is little research on the impact of these medications during cancer therapy.
Methods: 33 women (mean age=49.72 yrs, SD=8.9, range:29-76) diagnosed with stage I-III breast cancer were divided into three groups based on sleep medication use immediately before (baseline, BL) and after 4 cycles of chemotherapy (cycle 4, C4): No medication at either phase, "No Meds", N=13; No medication at BL but medication(s) added by C4, "Add Meds", N=13; Medication(s) at both phases ,"Both Meds", N=7. Actigraphy (Ambulatory Monitoring, Inc. and Respironics) was used to record sleep/wake activity for 72-hours and sleep quality (PQSI), depression (CES-D), fatigue (MFSI) and menopausal symptoms (Greene Climacteric Scale) were evaluated at both time points. Preliminary examination of data included looking at changes from BL to C4 of %-sleep and number and length of sleep bouts.
Results: Preliminary results suggest that women who added medications during treatment showed increased %-sleep with fewer and longer sleep bouts while those with no medications at either time point had no change in %-sleep but had shorter and more frequent sleep bouts. Women who used sleeping medications at both time points showed increased %-sleep but had no change in the number or length of sleep bouts. All groups increased in self-reported sleep difficulty, depression, fatigue and menopausal symptoms, but the "Add Meds" group had the largest increases.
Conclusion: Preliminary results suggest that women who added sleep medications during treatment showed more of an improvement in sleep than those who had already been on sleep medications or those never taking sleep medications. All three groups however, reported more symptoms of depression, fatigue and menopausal symptoms at the end of chemotherapy. Larger sample sizes will help determine if these changes are clinical and statistically significant.

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0991

ACTIGRAPHY-BASED PRE-TREATMENT NAP TIME PREDICTS QUALITY OF LIFE DURING CHEMOTHERAPY IN BREAST CANCER PATIENTS

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Introduction: Quality of life (QOL) of cancer patients is associated with multiple factors including the quality of their sleep. In this study we explored the relationship between actigraphy-based pre-treatment total nap time (TNT) and QOL during chemotherapy in breast cancer patients.
Methods: Eighty-six women (age=51.0±9.9 years, range=34-79) with newly diagnosed stages I-III breast cancer and scheduled to receive anthracycline-based adjuvant/neoadjuvant chemotherapy participated. Data were collected at seven time points: before and during weeks 1-3 of cycles 1&4 treatment. At each time point, patients wore an Actillume recorder (Ambulatory Monitoring Inc.) for three days, and completed a sleep log together with other questionnaires. A nap was defined as any actigraphic sleep ≥10minutes during out-of-bed time (based on sleep logs) during the day; TNT was the sum of all naps prior to chemotherapy and a daily mean was reported. Four groups were formed according to TNT quartiles: Q1 (TNT<18 minutes, n=22), Q2 (18≤TNT<47 minutes, n=21), Q3 (47≤TNT<99 minutes, n=21), and Q4 (TNT≥99 minutes, n=22). QOL was assessed with the Medical Outcomes Study Short-Form (SF-36); the Physical Component Summary (PCS) and Mental Component Summary (MCS) scores were calculated. The PCS and MCS both have a mean of 50, with a score <50 indicating poorer QOL. Generalized estimating equation approaches with a logit link were used; odds ratio (OR) for poor QOL for TNT groups Q2-Q4 versus Q1 were calculated.
Results: Compared to Q1, women napping more than 99 minutes (Q4) before the start of chemotherapy had an OR of 3.06 (95%CI=1.14-8.22, p=0.027) of poor mental QOL during chemotherapy. There were no significant differences between the other quartiles and Q1 and no significant results for PCS.
Conclusion: Patients with longer pre-treatment nap time (≥99minutes) reported poorer mental QOL during chemotherapy compared to patients with no/short naps (<18minutes). Further studies need to determine the cause of napping and whether treatment of sleep disturbances at night will improve both the daytime sleepiness and QOL.
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0992

DOES APNEA-HYPOPNEA INDEX INCREASE DURING THE NATURAL COURSE OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE?

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Introduction: Apnea-hypopnea index (AHI) is much higher in chronic obstructive pulmonary disease (COPD) patients than in general population. This study was conducted to compare the AHI in two groups of COPD patients: COPD with cor pulmonale vs. COPD without cor pulmonale.

Methods: A case control study was conducted at the referral sleep laboratory of a tertiary care teaching hospital in India. 21 patients of COPD with cor pulmonale (mean pulmonary artery pressure > 25 mm Hg) and 29 patients of COPD without cor pulmonale were taken. Whole night polysomnography (Medcare polygraph, Medcare Flaga, Reykjavik, Iceland) was done in all the patients of both groups. AHI was then compared in both the groups.
Results: The average apnea-hypopnea index (per hour) was 14.78 ± 25.81 and 7.88 ± 6.87 in cor pulmonale and COPD groups respectively (p=0.174).
Conclusion: There is no significant increase in apnea-hypopnea index in COPD patients who develop cor pulmonale in the natural course of disease.

0993

DO SLEEP-WAKE CYCLES GET IMPAIRED DURING CHEMOTHERAPY FOR BREAST CANCER?

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Introduction: Prior cross-sectional studies have shown that cancer patients have sleep-wake activity cycles that show little distinction between daytime and nighttime, a pattern indicative of circadian disruption. This pattern is seen both before and during cancer treatment. Long term data are needed, however, to assess to what extent circadian rhythm impairments evolve over the course of chemotherapy. The goal of this study was to assess the longitudinal course of sleep-wake activity rhythms before and during chemotherapy for breast cancer.
Methods: Ninety-five women scheduled to receive neoadjuvant or adjuvant chemotherapy for a stage I-III breast cancer participated. The participants wore a wrist actigraph for 72 consecutive hours at baseline (pre-chemotherapy), as well as during the weeks 1, 2 and 3 (W1, W2, W3) of cycle 1 and cycle 4 of chemotherapy. Circadian activity variables were computed based on actigraphic data.
Results: Mixed-effects models were used to investigate variations in circadian rhythm variables over time. Compared to baseline, with the exception of acrophase, all circadian rhythm variables examined, including amplitude, mesor, up-mesor, down-mesor, and rhythmicity were significantly impaired on the first week of both chemotherapy cycles (C1: ps from .05 to .0001; C4: ps from .01 to .0001). Although the circadian variables approached baseline values during W2 (ps from .10 to .93) and W3 (ps from .05 to .92) of cycle 1, most remained significantly more impaired during W2 (ps from .13 to .0001) and W3 of cycle 4 (ps from .60 to .0001).
Conclusion: These data suggest that the first administration of chemotherapy is associated with transient circadian disruption, while repeated administration of chemotherapy results in progressively worse and more enduring impairments in sleep-wake cycles.
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0994

ELEVATED ECONOMIC BURDEN IN OBSTRUCTIVE LUNG DISEASE PATIENTS WITH CONCOMITANT SLEEP APNEA SYNDROME

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Introduction: Sleep Apnea Syndrome (SAS) and obstructive lung disease (OLD) carry with them a substantial burden in terms of health care utilization and costs. In this study we examined the incremental economic burden of SAS among individuals with concomitant OLD. We hypothesized that SAS would incrementally add to the health care burden in these individuals.
Methods: This was a retrospective cohort study utilizing data from the Maryland Medicaid database for 2001 through 2003. Beneficiaries aged 40 to 64 years were identified for asthma (n=3,072), COPD (n=3,455), or both (n=2,604) based on diagnosis codes in medical claims for physician visits, inpatient care, and outpatient care. Chi-square tests and t-tests were performed to compare demographic characteristics, obesity, comorbidities (Charlson comorbidity index), and follow-up time by SAS. We stratified the analyses and examined the effect of SAS on medical utilization and cost by disease cohort using a generalized linear model.
Results: SAS was most prevalent among beneficiaries with asthma/COPD (6.72%), followed by COPD (2.87%) and asthma (2.15%). After adjustment for comorbidity, age, gender and obesity, asthma/COPD and COPD beneficiaries who had SAS incurred a significantly higher number of medical service claims (p<0.001) and higher annualized medical cost than beneficiaries without SAS: $20,239 vs. $14,466 in asthma/COPD (p<0.037), and $8,903 vs. $4,748 in COPD (p=0.035). Medical utilization and cost did not differ by SAS in the asthma cohort.
Conclusion: SAS adds significant additional economic burden on beneficiaries who already have COPD or asthma/COPD. Future research is warranted to evaluate the cost effectiveness of early interventions and disease management programs for beneficiaries at high risk of developing SAS along with other chronic respiratory conditions.

0995

PREECLAMPSIA AND SLEEP DISORDERED BREATHING: POSTPARTUM FOLLOW UP STUDY

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Introduction: Women with preeclampsia have a high prevalence of sleep disordered breathing, and much higher than women with uncomplicated pregnancies. Furthermore, preeclampsia has recently been recognized as a risk factor for cardiovascular disease later in life. The persistence of sleep disordered breathing after delivery is a possible explanation for increased cardiovascular morbidity and warrants evaluation.
Methods: Previously, we studied 60 pregnant women (34 with preeclampsia and 26 with healthy uncomplicated pregnancies) with a series of sleep questionnaires and full night polysomnography. Between one and two years post partum, these women were invited to complete follow up sleep surveys and polysomnography. We compared the postpartum survey scores and polysomnography results of women with a preeclampsia history versus the healthy cohort, as well as compared against their own values while pregnant.
Results: This study is ongoing and we are reporting interim results here. So far, twenty six women have completed the sleep surveys and all women have reported improved sleep compared to during their pregnancy. Eleven women (seven preeclamptic and four healthy) have so far agreed to return to the sleep lab for polysomnography. From the pregnant state to postpartum, the mean body mass index (BMI) of the preeclamptic women decreased from 39.4 to 33.4 and the mean respi-

ratory disturbance index (RDI) improved 13.9 to 3.4. For the healthy cohort, the BMI decreased from 38.3 to 22.6. The mean RDI for the healthy women was below one at both testing times. The mean age of both groups was 32 years.
Conclusion: Sleep disordered breathing in women with preeclampsia improves dramatically in the first two years post partum. Although the RDI improved to within the normal range, it remained elevated compared to healthy post partum women of the same age.
Support (optional): This research was supported by the Saskatchewan Health Research Foundation, the Lung Association of Saskatchewan and the University of Saskatchewan.

0996

CIRCADIAN RHYTHM SLEEP-WAKE CYCLES, FATIGUE, AND ANXIETY/DEPRESSION IN WOMEN TREATED WITH BREAST CANCER ADJUVANT CHEMOTHERAPY

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Introduction: This study examined the patterns of circadian rhythm sleep-wake cycles and their relationships with fatigue, anxiety/depression, and demographic/medical variables in women receiving breast cancer adjuvant chemotherapy treatments (Tx).
Methods: Secondary analysis from a randomized clinical trial testing a behavioral therapy sleep intervention group to a healthy eating control group. Subjects (n=175 of the larger sample of 219) with actigraphy data were post-operative for Stage I -IIIA breast cancer, receiving anthracycline-based adjuvant chemotherapy treatments; mean age 52.2 yrs. Measurements were collected at 3 times at Tx 1, Tx 3, and 30 days after the last Tx including: circadian rhythm sleep-wake cycles (wrist actigraphy for 7 days), fatigue (Piper Fatigue Scale, PFS & daily fatigue item, DFI), anxiety/depression (Hospital Anxiety and Depression Scale, HADS); and demographic/medical variables.
Results: Circadian rhythm sleep-wake cycle values for mesor, amplitude, peak activity, acrophase, circadian quotient, and 24-hr autocorrelation at all times in both groups reflected disrupted rhythms compared to healthy adults, but were similar to values reported in cancer patients. Significant differences were found over time in both groups for mesor, amplitude, peak activity, acrophase, and 24-hour auto-correlation. Significantly stronger rhythms were found over time in the intervention group for amplitude and circadian quotient. More robust circadian rhythms were associated with lower fatigue (PFS & DFI), lower depressive symptoms (HADS), higher performance status (KPS), and lower body mass index (BMI) in both groups.
Conclusion: Disrupted circadian rhythms are prevalent and associated with distressing fatigue and depressive symptoms during and after chemotherapy. Women who begin chemotherapy with lower KPS and higher BMI experience less robust circadian rhythms during and after chemotherapy. The sleep intervention resulted in higher magnitude and more robust rhythms that were related to lower fatigue.
Support (optional): Funded by NIH, 5R01NR007762-05

0997

ONE-YEAR OUTCOMES OF A BEHAVIORAL THERAPY INTERVENTION TRIAL ON SLEEP QUALITY AND CANCER-RELATED FATIGUE

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Introduction: Sleep-wake disturbances and fatigue are the two most frequent and distressing symptoms among breast cancer survivors. We initiated a sleep intervention before the first chemotherapy treatment, reinforced and revised it during and after treatment, to improve long-term outcomes. This study determined the effects of a four-component behavioral therapy intervention (Individualized Sleep Promotion Plan [ISPP©] on sleep quality and cancer-related fatigue in women 1-year after the first breast cancer adjuvant chemotherapy treatment.
Methods: This randomized clinical trial recruited participants (N=219) from 12 oncology clinics. Research nurses coached intervention group participants to develop a BT plan before their first treatment that was regularly reinforced and revised during treatments, and 30, 60, and 90 days after the last treatment. BT components were stimulus control, modified sleep restriction, relaxation therapy, and sleep hygiene. Healthy eating control group participants received nutritional information and equal attention. Measures included: Pittsburgh Sleep Quality Index (PSQI), Daily Diary, Wrist Actigraph, and Piper Fatigue Scale. Repeated Linear Mixed Model and Intent to Treat Analysis were used.
Results: Before the first treatment, global PSQI scores for both groups reflected poor sleep compared to the general population (>5), but not compared to breast cancer patients (>8). Sleep quality (PSQI) changed over 1-year's time ($p=0.01$), was better in the intervention group ($p<0.029$), and resulted in better sleep over time in the intervention group ($p<.001$). Diary data revealed the BT group had fewer WASO minutes and higher sleep efficiency after sleep onset. Fatigue increased during treatments and returned to mild levels over time ($p<0.001$), but no group effects were found.
Conclusion: This RCT delivered a sleep intervention before, during, and after breast cancer adjuvant chemotherapy. One-year following the first treatment, we found positive effects on sleep quality, but no group differences on fatigue. Future interventions need to include other factors associated with fatigue.
Support (optional): Funded by NIH, 5R01NR007762-05

0998

CAN THE CANNABINOID NABILONE HELP WITH PAIN AND SLEEP IN FIBROMYALGIA PATIENTS?

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Introduction: Cannabinoids can alleviate pain and improve sleep. In a group of fibromyalgia patients, the aim of this study was to: (1) to evaluate the short-term effect of nabilone (1mg) on pain, sleep and fatigue; and (2) to review patient charts one year after receiving 1 mg nabilone treatment.
Methods: Six female fibromyalgia patients (median 52 years) were investigated. There was an initial 4-week double-blinded, placebo-controlled, randomized, crossover clinical pilot trial with overnight sleep assessment, tests of daytime sleepiness and questionnaires administered at the start and end of the study. Following the research study, patients' charts were reviewed one year later.
Results: All fibromyalgia patients had a significant ($p<0.05$) reduction in pain with nabilone treatment. 5 of the 6 had improvements in sleep efficiency (72% to 82%) and total sleep time (5.8 to 6.8 hrs). There were no changes in sleep onset latency, percentage slow wave sleep or fatigue levels. Nabilone treatment did not result in daytime sleepiness. Five of the six fibromyalgia patients received prescriptions for nabilone (1mg) and took nabilone (without concomitant pain medications) for one year. Based on clinical interview, all five patients reported that their sleep quality remained improved while taking nabilone. There were also reports of continued pain relief, improved quality of life, deeper sleep and reduction in fatigue symptoms. There were no serious adverse events or side-effects requiring withdrawal of nabilone treatment.
Conclusion: Nabilone (1mg) was effective in decreasing pain symptoms and improving sleep in most of the fibromyalgia patients. The short-term effects of nabilone were sustained during a year of treatment and which included reports of improved quality of life and reduced fatigue levels. Further investigations on the use of synthetic cannabinoids for the treatment of pain and insomnia are needed in a larger fibromyalgia patient

population to quantify the long-term improvements with nabilone treatment.
Support (optional): Funding for this work provided by Valeant Pharmaceuticals (Canada).

0999

EXERCISE INDUCED VENTRICULAR ARRHYTHMIAS: ANALYSES IN A SLEEP COMPLAINED POPULATION

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Introduction: The physiological alterations during exercise could trigger exercise induced ventricular arrhythmias (EIVA). Increase in catecholamine plasma level, sympathetic activation, and low left ventricle ejection fraction are the main factors related to this arrhythmias in a coronary artery disease population. However it unknown if polysomnographic parameters could be related to EIVA. The aim of this study is to analyze cardiopulmonary, polysomnographic and echocardiography parameters related to EIVA in a sleep complained population.
Methods: Patients were selected from Sleep Clinic database, between October 2007 and April 2008. All participants had performed a full overnight polysomnography to investigate sleep breathing disorder and were submitted to a clinical evaluation, 2D- echocardiogram (IE 33®) and symptom-limited cardiopulmonary exercise test (CPET) (VISTA®). Exclusion criteria were: BMI>40 kg/m2, heart disease, pulmonary disease, and osteomuscular conditions.
Results: Three hundred twelve patients, 139 male gender, mean age: 50.74 ± 7.51. EIVA were observed in 18 patients (6%), who were matched for age and gender with patients without EIVA (case-control study). The polysomnography and laboratorial parameters shows no difference between groups. Oxygen saturation in the peak of exercise was lower in EIVA group when compared to controls (92.75 ± 3.05; 95.50 ± 1.73; p=0.01), respectively. The baseline saturation was similar between groups. The echocardiography results shows a larger aortic diameter in EIVA group when compared to controls (3.44 ± 0.30, 3.16 ± 0.36; p=0.04), respectively.
Conclusion: The aortic diameter and the oxygen saturation in the peak of exercise were related to EIVA in this population.
Support (optional): AFIP/FAPESP

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SLEEP DISTURBANCES AND CYTOKINES IN EARLY GESTATION

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Introduction: Sleep disturbances (SD) are risk factors for adverse health outcomes. SD is also associated with increased circulating concentrations of proinflammatory cytokines. Excessive inflammation is associated with the adverse pregnancy outcomes. As an initial step in assessing the implications of disturbed sleep in pregnancy, we evaluated the relationship between SD and circulating cytokines in early gestation.
Methods: Sleep duration and sleep quality were determined by self-report. The inflammatory cytokines IL-2, -6, -8, IFNα, TNFα and anti-inflammatory cytokines IL-4, -5, and -10 were measured by Luminex technology. Data were analyzed using nonparametric correlations. The pro:anti-inflammatory ratio was calculated as the mean multiple of the median (MOM) for each relevant cytokine type to normalize the data for comparison
Results: Data were collected as part of a trial of exercise to reduce the frequency of recurrent preeclampsia. (Exercise did not have an effect on sleep in early pregnancy therefore, all women were combined). Participants (N = 85) were at 15 ± 2.8 weeks gestation and were 30 ± 4.9 years. Short sleep duration (< 7h/night) was reported in13%. Sleep quality was deemed poor in 35 (41%) women. Total sleep duration was correlated with both pro- and anti-inflammatory cytokine concentrations (ρ = .32, p = .003; ρ = .30, p = .006). Sleep quality was not related to cytokine concentrations. The ratio of pro- to anti-inflammatory cytokines was not related to sleep duration or sleep quality.
Conclusion: Almost half of women report poor sleep quality in early pregnancy. Nonetheless, sleep quality was not associated with cytokine concentrations. Sleep duration was quite variable and was positively correlated with circulating cytokines. The ratio of these inflammatory markers did not relate to either sleep variable, thus the implications for net inflammatory effect is indeterminate. Longitudinal examination of sleep and cytokine across pregnancy may provide additional insight.

1001

RESTLESS LEGS SYNDROME SYMPTOMS IN PATIENTS WITH LIVER TRANSPLANT AND QUALITY OF LIFE: PRELIMINARY RESULTS

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Introduction: Restless legs syndrome (RLS) may occur in 5%- 20% of the general population. Recent studies have shown a higher prevalence of RLS in patients with chronic liver disease and in lung transplant recipients leading to diminished quality of life. No data exists on the prevalence of RLS in liver transplant recipients and its impact on quality of life.
Methods: Liver transplant recipients presenting to an outpatient university-based hepatology clinic for routine follow up were invited to complete a one page survey without prior knowledge of the survey content. The survey queried for the core clinical features associated with RLS. Participants found to have at least three of five core symptoms were considered positive and then contacted via telephone to confirm the survey. For those with core RLS symptoms, the Johns Hopkins RLS Quality of Life (QoL) Questionnaire and International RLS Rating Scale (IRLSRS) were administered.
Results: Seventeen of forty-one subjects (41.5%: 95% confidence 26.3-57.9) reported core symptoms of RLS by survey. Three of forty-one (7.3%) with positive core symptoms at the time of the initial survey reported symptoms had resolved at the time of the phone contact. Additionally, 3 of 41 (7.3%) were not available to complete the follow up phone survey. For the eleven subjects who completed the IRLSRS, the mean score was 17 with a range of 8-31, falling in the moderate severity category when compared to other studies using this tool. The average calculated score of Quality of Life was 79.55 [0 (poor) - 100 (good)].
Conclusion: Liver transplant recipients may have a higher prevalence of RLS with moderate symptoms leading to a diminished quality of life when compared to the general population. The cause for increased prevalence of RLS in transplant patients is unknown and warrants further investigation.

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INFERTILITY AND OBSTRUCTIVE SLEEP APNEA: THE EFFECT OF CONTINUOUS POSITIVE AIRWAY PRESSURE THERAPY ON SERUM PROLACTIN LEVELS IN PATIENTS WITH OBSTRUCTIVE SLEEP APNEA

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Introduction: Male factor infertility is the sole cause, or a contributing cause, of infertility in about 40 percent of infertile couples. More so, about 20 percent of couples have no identifiable cause for their infertility after medical investigation. Prolactin levels are known to be increased in infertile male and after various stressors. We believe that obstructive

sleep apnea (OSA) is a stressor that may silently contribute to infertility by means of increased prolactin; therefore we hypothesize that continuous positive airway pressure (CPAP) therapy may lower prolactin levels in patients with OSA with subsequent improved fertility.

Methods: Ten patients who were diagnosed with OSA at the Salem Veterans Affairs Medical Center had fasting serum cortisol (Cor), estradiol (E2), follicle stimulant-hormone (FSH), testosterone (Test), sex-hormone binding globulin (SHBG) and prolactin (PRL) levels measured at 7 a.m., the morning after polysomnogram and after 30 days of effective CPAP therapy. Patients with diabetes, chronic lung or thyroid disease, cardiac failure, eating disorders, continuous oxygen or chronic glucocorticoid therapy were excluded. Data was expressed as mean and standard deviation (SD); correlations were described using Spearman correlations. Differences between PRL before and after CPAP therapy were evaluated using the Wilcoxon test for paired samples.

Results: All patients were male. Before CPAP therapy fasting Cor, E2, FSH, Test, SHBG and PRL levels were 15.9mcg/dl/ml±5.6, 35.9mIU/mL±19.4, 6.2mIU/ml±3.51, 339ng/dL±117, 31.8nmol/L±16.7 and 10.7ng/ml±5.31, respectively; after CPAP therapy serum levels were as follows: 15.1mcg/dl/ml±4.2, 40.8mIU/mL±16.4, 6.9mIU/ml±3.6, 340ng/dL±126, 33.2nmol/L±20.4 and 6.7ng/ml±1.77, respectively. As expected, before CPAP therapy there was a strong correlation between serum PRL and Cor (p=0.16, r =0.733) and PRL and FSH (p=0.04, r=0.648). CPAP therapy was associated with a significant decrease in the serum PRL levels (p=0.037, Z=-2.09).

Conclusion: Infertile couples should be screened for OSA.

1003

EVALUATION OF THE FUNCTIONAL OUTCOMES OF SLEEP QUESTIONNAIRE (FOSQ) IN BARIATRIC PATIENTS REFERRED FOR SLEEP STUDIES

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Introduction: Bariatric surgery is a treatment for obesity for which evaluation of obstructive sleep apnea (OSA) is often required. We evaluated the FOSQ for assessing consequences of OSA in patients planning bariatric surgery.

Methods: Data were examined from 110 bariatric-surgery seeking patients (100 females; age=42.7±9.0 years; BMI=49.9±7.4) who had overnight polysomnography and completed the FOSQ between 2003-2005. Obstructive apneas were defined as absence of airflow ≥10 seconds with persistent effort; hypopneas were defined as 50% decrease in airflow for ≥10 seconds accompanied by oxygen desaturation ≥3% or EEG arousal. Apnea-hypopnea index (AHI) was calculated to classify patients as none/mild (AHI<15), moderate (AHI≥15<30), or severe (AHI≥30). We calculated proportion of unique variance (PUV) for the FOSQ subscales. ANOVA was used to determine if total FOSQ score and/or subscales contributing meaningful PUV were associated with OSA severity. Single sample t-tests compared FOSQ scores in our sample with previously published data (Weaver et al., 1997).

Results: Average AHI was 31.0±33.0 (range=0.3-175.8). Mean total FOSQ score was 100.0±18.1. PUVs for FOSQ subscales were: Intimacy=0.38, Social=0.30, Vigilance=0.25, Activity=0.12, and Productivity=0.09, indicating small/medium contributions to variance. Total FOSQ score did not differ based on AHI. Only vigilance differed between OSA severity groups (F=3.097; df=2,109; p=.049), with the severe group (n=36) demonstrating lower vigilance scores (mean=3.41) than the none/mild group (n=46; mean=3.69; p=.012). Average total FOSQ scores were higher than published means of sleep clinic patients (mean=68.1±21.2; t=18.5; df=109; p<.001) and controls (mean=89.6±8.6; df=109; p<.001).

Conclusion: Total FOSQ score did not predict severity of sleep apnea in our bariatric-surgery seeking sample; FOSQ vigilance subscale was lower only in patients with severe OSA. These data raise the question of whether vigilance tasks might better reflect consequences of OSA than questionnaires in this population. Furthermore, our participants had higher FOSQ scores than were observed previously in a clinical population. Obese patients planning bariatric surgery may underreport symptoms for various reasons: belief that surgery will be denied if they endorse symptoms, inability to recognize impairment, or absence of sleepiness.

Support (optional): Department of Psychiatry and Division of Pulmonary, Critical Care, and Sleep Medicine, Rhode Island Hospital

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CONTENT VALIDITY OF THE SLEEP QUALITY NUMERIC RATING SCALE (NRS) AND THE MEDICAL OUTCOMES STUDY SLEEP SCALE (MOS-SLEEP) IN PATIENTS WITH FIBROMYALGIA (FM)

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Introduction: Disturbed sleep is a commonly reported symptom in FM. Both the Sleep Quality NRS and the MOS-Sleep have demonstrated positive psychometric properties in patients with FM; however, as generic sleep assessments, neither included FM patient input at concept elicitation nor item generation phases. This study evaluated the content validity of both measures in FM patients.

Methods: Qualitative interviews were conducted in Raleigh, North Carolina and Detroit, Michigan with 20 adults who reported a physician-diagnosis of FM. Sixteen participants were female, 13 were white, and the average age was 50 years. For consistency, the same two researchers conducted all interviews using a structured guide. Participants shared their general experiences with sleep in regard to FM and evaluated the measures in detail.

Results: Participants responded positively to the Sleep Quality NRS as an overall assessment of their sleep. The majority of the participants (n = 14) stated they would not change the response numbering or anchor wording of the item. Participants also responded positively to the 24-hour recall of the Sleep Quality NRS. Similarly, participants found the MOS-Sleep appropriate and relevant, with 19 participants stating the measure captured all of their sleep-related symptoms. However, areas for potential modification were identified for the MOS-Sleep: one item combines the issues of awakening short of breath and awakening with a headache; most participants thought these should be split into two items. Participants also questioned the relevance of the snoring item, and half of the participants expressed a preference for a daily rather than a weekly recall.

Conclusion: While patients with FM were not part of the development of these generic sleep assessments, this study provides evidence of content validity for both measures, supporting their use in FM studies. Modifications to the MOS-Sleep may further improve the relevance of the measure to patients with FM.

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PSYCHOMETRIC PROPERTIES OF A SINGLE-ITEM SCALE TO ASSESS SLEEP QUALITY AMONG INDIVIDUALS WITH FIBROMYALGIA

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Introduction: Sleep disturbances are common in patients with fibromyalgia (FM). This study reports psychometric properties of a single-item scale to assess sleep quality in FM.
Methods: Analyses were based on data from two randomized, double-blind, placebo-controlled trials of pregabalin (studies 1056 and 1077). In a daily diary, patients reported the quality of their sleep on a numeric rating scale ranging from 0 ("best possible sleep") to 10 ("worst possible sleep"). Test re-test reliability of the Sleep Quality Scale was evaluated by an intraclass correlation coefficient. Validity of the Sleep Quality Scale was assessed by 1) Pearson correlation coefficients of its scores with daily pain scores and with Medical Outcomes Study (MOS) Sleep scores at baseline and 2) standardized effect sizes to gauge its responsiveness to beneficial treatment.
Results: Studies 1056 and 1077 included 748 and 745 patients, respectively. Most patients were female (study 1056: 94.4%; study 1077: 94.5%) and white (study 1056: 90.2%; study 1077: 91.0%). Mean ages were 48.8 years (study 1056) and 50.1 years (study 1077). Test re-test reliability coefficients of the Sleep Quality Scale were 0.91 (study 1056) and 0.90 (study 1077). Correlations between Sleep Quality and pain were 0.64 ($p<0.001$) and 0.58 ($p<0.001$) for studies 1056 and 1077, respectively. Correlations between the Sleep Quality Scale and the MOS Sleep subscales were statistically significant ($p<0.01$), except for the MOS Snoring subscale. Standardized effect sizes were generally moderate (0.46-0.52) for the pregabalin 300mg group and moderate (0.59) or moderate-to-large (0.70) for the 450mg group. The effect size for the 600mg group was moderate-to-large (0.73) for study 1056 and large (0.82) for study 1077.
Conclusion: These results provide evidence of the reproducibility, convergent validity, and responsiveness to treatment of the Sleep Quality Scale and provide a foundation for its further use and evaluation in FM patients.
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A COMPARISON OF SLEEP INSTRUMENT SCORES ACROSS DIAGNOSTIC CATEGORIES IN A RHEUMATOLOGY CLINIC PATIENT POPULATION

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Introduction: Rheumatology clinic patients often report poor sleep quality and fatigue. It is not clear what differences exist in sleep quality amongst different diagnostic categories of rheumatologic diseases. The objective of this study was to compare sleep instrument scores in different diagnostic patient groups seen in a Rheumatology Clinic population.
Methods: Consecutive Rheumatology Clinic patients were invited to participate in a self-administered questionnaire study which included visual analogue scale (VAS) measures for pain, fatigue and global functioning, modified Health Assessment Questionnaire (mHAQ), Depression scores, Stress scores, SF-36 quality of life score, Epworth Sleepiness Score (ESS), Berlin sleep scores, and the Pittsburgh global sleep quality index (PSQI). Patients were grouped into five diagnostic categories: rheumatoid arthritis (RA), sero-negative arthropathies (SNA), crystalline arthritis and osteoarthritis (OA), connective tissue disorders (CTD), and soft-tissue disorders (STD).
Results: Of 341 consecutive Rheumatology Clinic patients invited to participate in this questionnaire study, 280 agreed. The population consisted of 34.9% RA, 28.5% SNA, 16.7% OA, 11.7% CTD, and 8.2% STD. For the total study population, mean ESS was 7.72 (SD 5.0, range 22). 34% of patients had an ESS ≥ 10. Mean PSQI score was 7.98 (SD 4.12), and was abnormal (> 5) in 66.3% of study patients. The mean Berlin 1 was 1.48 (SD 1.45), and Berlin 2 was 1.10 (SD 1.04). The Pittsburgh score and ESS both correlated ($p < .001$) with the Berlin 1, Berlin 2, VAS global function, VAS fatigue, VAS pain, mHAQ, Depression and Stress scores. Comparison between patient groups revealed higher pain, fatigue, depression, stress scores as well as poorer global function, mHAQ scores and SF-36 scores in those with the abnormal Pittsburgh or ESS results ($p < .001$ for each). No significant differences in age or body mass index (BMI) were observed between patients with normal or abnormal sleep scores. Between group comparisons revealed statistically significant differences in mHAQ scores ($p = 0.006$) and SF-36 bodily pain domain ($p = .002$), but not in ESS, Pittsburgh, Berlin, VAS pain, fatigue, global function, Depression or Stress scores.
Conclusion: Abnormal sleep scores are common in Rheumatology clinic patients, with abnormal ESS in one-third, and abnormal PSQI in two-thirds. These findings were seen across the spectrum of musculoskeletal diagnoses and were not specific to one form of arthropathy.
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SLEEP QUALITY IN WOMEN WITH RHEUMATOID ARTHRITIS

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Introduction: Patients with rheumatoid arthritis (RA) have symptoms of pain and stiffness that affects their daytime function. RA is common among women and the incidence of women with RA is increasing given the aging population. However, there is little research examining the association of pain, depression, and adherence to RA medications to sleep quality in women with RA.
Methods: This study was a secondary analysis of cross-sectional data of 133 women with RA (mean age = 56.21 ± 11.82 years, range: 21-82). The sample was predominately Caucasian, married, had at least a high school education, not depressed (86% with Beck II total score < 14), and had RA for 14.76 ± 11.20 years. Sleep quality was assessed using the Pittsburgh Sleep Quality Index (PSQI). Self-reports of pain and depression were measured by the Jette Functional Status Index and the Beck Depression Inventory-II, respectively. Medication adherence to RA drugs was measured by an electronic medication monitor on medication bottle-caps. A series of hierarchical multiple regression analyses controlling for demographic variables were performed with SPSS 15.0, the level of significance was set at $p<.05$.
Results: 71% of the subjects had poor sleep quality (global PSQI score ≥ 6). Disease-related variables (RA duration, pain, and disease activity) accounted for 20% of the variance in sleep quality ($p <.001$). Increased pain was associated with poorer sleep quality ($r = .60$, $p <.001$). Symptoms of depression accounted for 14% of the variance of sleep quality ($p <.001$). Poor medication adherence was associated with poorer sleep quality ($p <.05$). When all variables were entered simultaneously, the full model accounted for 47% of the variance in sleep quality ($p <.001$).
Conclusion: Women with RA report poor sleep quality. Pain, depression, and poor adherence to RA medications contribute to impaired sleep. These findings emphasize the importance of assessing sleep in women with RA.
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IS SLEEP DURATION ASSOCIATED WITH PAIN IN TWINS?

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Introduction: To investigate the relative importance of genetic and environmental contributions to the association between sleep duration and pain we researched twins in the genetically informative University of Washington Twin Registry.
Methods: We surveyed 1,797 twins, including 634 twin pairs (437 monozygotic, 150 dizygotic, and 47 indeterminate pairs) and 529 individual twins. Habitual sleep duration was obtained by self-reported nightly sleep length. Pain over the past 4 weeks was assessed on a scale of 0 (no pain) to 10 (severe pain). We modeled the best linear spline function relating pain to 3 nightly sleep duration categories (<7, 7-8.9, and ≥9 hours). Category-specific slopes, within-pair effects, and between-pair effects were assessed using Wald-type tests of regression coefficients. Age, gender, body mass index, and depression were covariates. Overall effects were assessed with a 2 degree of freedom chi-square test.
Results: Twins were 68% female, 88% Caucasian, with a mean age of 36.8 (SD=15.1) years. Sleep duration was associated with pain in the overall unadjusted ($p<0.0001$) and adjusted ($p<0.001$) analyses driven predominantly by between twin pair effects. Twins sleeping <7 hours/night had a 0.76 (95% CI: -0.54, -0.98) point reduction in pain for each additional hour of sleep ($p<0.001$). This reduction was attenuated after covariate adjustment to 0.54 (95% CI: -0.35, -0.73), but remained significant ($p<0.001$). This finding was also observed both between and within twin pairs. Sleep duration was not significantly associated with pain in the 7-8.9 and ≥9 hour groups in the overall, between, or within twin pair analyses.
Conclusion: Pain varied as a function of habitual sleep duration with the strongest association observed in short sleepers. The overall association was driven mostly by between twin pair effects suggesting residual familial confounding or shared genetic effects between sleep duration and pain.
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ACROMEGALY AND SLEEP APNEA SYNDROME (SAS)

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Introduction: Acromegaly has been associated with sleep disordered breathing (SDB). Previous reports have described a high rate of central sleep apnea (CSA) in acromegalic patients. Our goal was to describe the SDB characteristics and response to positive airway pressure therapy in patients with acromegaly seen at our institution.
Methods: Retrospective study of patients with confirmed diagnosis of acromegaly seen at the Mayo Clinic Center for Sleep Medicine from 1998 to 2008, with polysomnographic (PSG) evaluation.
Results: Eighteen patients were identified (33% females, age 54 +/- 12 SD, BMI 34 +/- 8 SD). Twelve (67%) patients had been treated for acromegaly at the time of their initial sleep evaluation, 11 by surgical adenomectomy. Obstructive sleep apnea (OSA) was present in 17 patients (94%). The mean apnea hypopnea index (AHI) was 50 (+/- 41SD) and 10 (56%) patients had an AHI of >30. The mean central AHI for the whole group was 0.83 (+/- 2 SD). Pre- and post-adenomectomy PSG in 2 patients revealed persistent severe OSA with AHI of 38 and 79 respectively. Three patients developed a complex sleep apnea response to CPAP which resolved by the end of CPAP trial in one patient, and with adaptive servo ventilation in another subject. Fourteen patients (78%) had abnormalities on the EKG during PSG, predominantly atrial and ventricular premature complexes. Seven out of 10 patients prescribed CPAP and seen in follow-up were using CPAP less than 4 hours per night and/or less than 70% of the nights.
Conclusion: Most patients had severe OSA despite treatment for acromegaly. We did not find a high prevalence of CSA. Cardiac ectopy was common in the absence of known coronary disease. Lack of CPAP adherence deserves further study. Our data suggests that because SDB persists after primary treatment of acromegaly, close clinical follow up is necessary.

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PATTERNS OF SLEEP DISTURBANCE IN HEALTHY NULLIPAROUS WOMEN

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Introduction: The objective of this study was to determine the prevalence of sleep disturbances among healthy nulliparous women, and to quantify changes in sleep during pregnancy
Methods: Prospective, cohort study of healthy nulliparous women recruited between 6-20 weeks gestation who completed a sleep survey at the time of enrollment and in the third trimester. The survey was comprised of the following validated sleep questionnaires: Berlin Questionnaire for sleep apnea syndrome, Epworth Sleepiness Scale (ESS), Pittsburgh Sleep Quality Index (PSQI), NIH/International Restless Legs Syndrome (RLS) Question Set, and the Women's Health Initiative Insomnia Rating Scale (WHI-IRS). Survey results from the initial and third trimester survey were compared using the paired t-test and McNemar's test as appropriate.
Results: One hundred and eighty-eight women completed both sleep surveys. The mean gestational age was 13.9 ± 3.8 weeks and 30.0 ± 2.2 at the first and second survey respectively. The frequency of poor sleep (PSQI > 5) increased significantly during pregnancy (39.2% vs. 53.2%, $p = 0.001$). Insomnia (WHI-IRS ≥ 9) was more prevalent in the third trimester (37.3% vs. 54.1%, $p < 0.001$). Compared to the initial assessment, mean sleep duration was significantly shorter in the third trimester (7.4 ± 1.2 vs. 7.0 ± 1.3, $p < 0.001$), and the percentage of patients who slept less than 7 hours per night increased (26.4% vs. 39.6% $p = 0.001$). The percentage of patients who met diagnostic criteria for RLS increased from 17.6% at recruitment to 30.9% in the third trimester ($p = 0.001$). The proportion of patients who screened positive for sleep apnea on the Berlin Questionnaire also increased from 10.6% to 19.7% ($p =0.002$).
Conclusion: Sleep disturbances are prevalent among healthy nulliparous women, and increase significantly during pregnancy.

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EFFECT OF SLEEPING POSITION ON IOP IN PROGRESSIVE GLAUCOMA

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Introduction: To determine if a 30 degree sleeping position improves nocturnal IOP control in patients with progressive glaucoma.
Methods: Patients with progressive NTG or POAG as evidenced by disc hemorrhage despite well-controlled IOP were evaluated in a sleep laboratory on two separate nights one week apart. During the first night patients were evaluated lying flat and during the second night they were elevated to 30 degree head up. IOP and blood pressure (BP) were mea-

sured at 10 PM as the baseline measurement and at 12 PM, 2 AM, 4 AM and 6 AM. IOP was measured as the average of two reading with less than 5% error using a Tonopen. Ocular perfusion pressure was calculated using mean arterial BP - IOP. Data were analyzed with profile analysis to take into account the correlation of repeated IOP readings from the same individuals.
Results: Seventeen eyes of 17 patients were included. There were no significant differences between the IOP levels at baseline and the two sleeping positions (flat versus elevated) (p=0.6131). Between 2400 and 0600 IOP was a mean of 3.2 mmHg lower in the 30 degree elevated position (p=0.03). 16 of 17 patients (94.1%) had lower IOP in the 30 degrees position and this reduction was 20% or more in 35% of patients. There was no statistically significant difference comparing the two sleeping positions in mean ocular perfusion pressure over time.
Conclusion: A 30-degree sleeping position lowers nocturnal IOP in patients with progressive glaucoma. Although this benefit varies between individual patients, mean IOP was 20% lower in a third of patients in this series.

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THE IMPACT OF SEVERITY OF SLEEP APNEA AND BODY FAT DISTRIBUTION ON THE TESTOSTERONE SECRETION

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Introduction: We investigated the impact of obstructive sleep apnea syndrome (OSAS) on testosterone levels in abdominally obese men. The objective of this study was to explore the relationship between the quantity and distribution of body fat, the severity of sleep apnea and total and free testosterone levels.
Methods: The quantity of total and regional body fat was determined using DEXA (dual energy x-ray absorptiometry). The severity of obstructive sleep apnea was appraised with a polysomnograph. The end of the sleep study we collected blood samples and measured testosterone level.
Results: The study population comprised 40 male with a mean age of 48.54±6,25 years. The severity of apnea was rated according to the apnea-hypopnea index (AHI). Mild apnea was diagnosed in patients with AHI 0-10, whereas moderate and severe apnea was denoted by AHI 10-30 and >30, respectively. The ratio of android/gynoid obesity was determined as the quotient of percentage body fat in the abdominal and hip regions. A quotient of >1 indicated severe android obesity. Analysis using the khi square test revealed non-independence of android obesity and severe OSAS (df: 2, p=0,031). The same was demonstrated for obesity (BMI >30 kg/m2) and the severity of apnea (df: 4, p=0,035). Both total and free testosterone levels were lower in cases with advanced OSAS in contrast to the mild-to-moderate OSAS patients. Two-tailed t-testing demonstrated a statistically significant (p=0,026) difference between the means of these two groups. A negative correlation between polysomnographic parameters (ODI, minSaO2 and arousal index) and testosterone levels was found.
Conclusion: Severe OSAS and android obesity may depress testosterone secretion in men with OSAS.

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IMPAIRED SLEEP AND DAYTIME FUNCTIONING AT BASELINE IN SUBJECTS WITH FIBROMYALGIA FROM A 14-WEEK RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL OF SODIUM OXYBATE

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Introduction: Disturbed and unrefreshing sleep are frequent complaints in patients with fibromyalgia syndrome and can lead to impairment in daytime functioning. In order to better describe the nature of these symptoms prior to treatment, data on subjective measures of sleep quality and daytime functioning were collected during the baseline period of a 14-week, double-blind, placebo-controlled trial of sodium oxybate 4.5g/night (SXB4.5g), sodium oxybate 6g/night (SXB 6g), and placebo (PBO) in the treatment of fibromyalgia.
Methods: A total of 548 subjects meeting American College of Rheumatology criteria for fibromyalgia were randomized to one of three treatment groups: SXB4.5g (n=182), SXB6g (n=183), or PBO (n=183). Subjects were administered the Jenkins Sleep Scale (JSS; a validated, 4-item, self-report questionnaire for sleep disturbance, range 0-20), Fatigue Visual Analog Scale (VAS; range 0-100), Functional Outcomes of Sleep Questionnaire (FOSQ), Short Form-36 Questionnaire (Version 2) (SF-36), Fibromyalgia Impact Questionnaire (FIQ) and Pain VAS (range 0-100).
Results: The mean age (SD) was 47.0 years (11.3), mean body mass index (SD) was 28.5 (4.8), 91% were female, and 91% were Caucasian. Mean time since first fibromyalgia symptoms (SD) was 9.7 years (8.5) and 5% were >=65 years. The baseline mean (SE) JSS at baseline for the PBO, SXB4.5g, and SXB6g groups were 14.3 (0.34), 15.3 (0.33), and 15.2 (0.32), respectively. The mean (SE) Fatigue VAS scores were 73.00 (1.05), 72.77 (1.03), and 74.26 (1.03), and the mean (SE) Pain VAS scores were 71.23 (1.02), 71.63 (1.00), and 72.14 (1.00), respectively. The combined dataset indicated that study subjects scored high in sleep and function scales, with higher scores indicating greater impairment.
Conclusion: These results demonstrate that patients with fibromyalgia syndrome manifest high levels of impaired sleep quality and daytime functioning in this study. Improving these symptoms of disturbed and unrefreshing sleep in fibromyalgia represents an important goal of therapy.
Support (optional): Study funded by Jazz Pharmaceuticals, Inc.

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SLEEP CHARACTERISTICS OF MORBIDLY OBESE PATIENTS AND ITS COMPARISON TO OBESE PATIENTS

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Introduction: Morbid obesity does not simply represent excess adiposity than in subjects with less massive obesity. In this study we tested the hypothesis that significant differences in sleep disturbances exist between obese and morbidly obese patients.
Methods: Fifty obese patients attending an Obesity Program in a referral Institution in Mexico City (INCMNSZ) were stratified according to obesity severity: Obese (O) BMI 30 < 40 Kg/m2 and Morbidly Obese (MO) BMI ≥ 40 kg/m2. Patients were studied during two subsequent

nights by polysomnography (PSG) and the day after by MSLT. They answered a sleep habits and symptoms questionnaire previous PSG study. Exclusion criteria were alcohol or drug addiction, fever o infection, cancer, chronic inflammatory illness, and hypothyroidism. Patients were not taking any medication that may affect sleep or respiration.
Results: A total of 26 Women and 24 Men were studied, with mean age (O) 43±11.6 yrs, and MO 38.2±10.9 years old. BMI for O=34.8±2.7 Kg/m2, and MO BMI=53.3±9.9 Kg/m2. Statistically significant differences were noted in sleep efficiency % (O=86.9±9.6 vs. MO=79.5±13.2, p<0.04), Wake % (O=10.8±8.7, MO=19.4±7.3, p<0.007), REM sleep % (O=15.5±5.5, MO=7.6±4.9, p<0.008), and # Awakenings >1 min (O=8.1±5.3, MO=13.5±8.5, p<0.004). MO had a tendency to a higher AHI (O=29.7±33.7, MO=50.1±40.9, p=ns). The reported level of sleepiness was similar in both groups (Epworth Score O=9.5±4.9, MO=7.6±5.3, p=ns). The mean MSLT (O=4.2±2.5, MO=5.4±4.2, p=ns). Interestingly the reported duration of the sleepiness symptom (O=7.9±6.4, MO=12.3±10.1 years, p<0.04) was longer than the snoring (O=4.9±7.6, MO=2.4±4.3 years) in both groups.
Conclusion: MO patients had more fragmented sleep, less REM sleep % and higher wakefulness percentage, with a tendency to duplicate the severity of AHI. However, sleepiness did not change as the BMI increase. Data suggest that sleepiness predates the obstruction respiratory symptom in both O and MO with more chonicity in MO.
Support (optional): CONACYT- 462547-H

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COMPARISON OF THE SYMPTOM OF NOCTURIA AND SLEEP APNEA SYNDROME IN THE PATIENTS OF UROLOGICAL CLINIC AND SLEEP APNEA CLINIC
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Introduction: Nocturia is known as one of major conditions related to insomnia and worsens the sleep quality of the patients. Recently, sleep apnea syndrome (SAS) has been recognized as one of major causes of nocturia. We performed this study to elucidate the prevalence and severity of SAS in the patients who visited urological clinic complaining nocturia, as well as the prevalence and urological complaint in the patients who visited sleep apnea clinic in same hospital setting.
Methods: We conducted quantitative questionnaire study about nocturia using international prostatic symptom score (IPSS) and about sleepiness using modified Epworth sleepiness scale (ESS) on all the patients who visited urological clinic (U, n=10, mean age=71±9) or SAS clinic (S, n=10, mean age=64±12). We also examined the degree and the frequency of nocturnal desaturation using the pulse oxymetory device.
Results: Questionnaire study using IPSS revealed that the values were not different in the two groups (11±7 vs 9±8 in U and S respectively, P=ns). Number of those whose IPSS exceed 6 (significantly uncomfortable urinary habit) was 80% in U and 60% in S (P=ns). Epworth sleepiness scale (Japanese modification) was higher in S (8±5) than in U (4±3). Oxygen desaturation index (ODI) >3% was 14±17/hr in U and 22±24/hr in S (P=ns). The proportion of the patients whose ODI>3% was 5/hr (significant desaturation) was 50% in U and 80% in S.
Conclusion: More than half of patients who complain nocturia have significant sleep disordered breathing though they do not recognize themselves. On the other hand, many of the patients who visit SAS clinic have nocturia problem though most of them do not know the relationship between two disorders.

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DAYTIME PAIN AND NIGHTTIME SLEEP IN PATIENTS WITH FIBROMYALGIA: AN UPDATE
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Introduction: Fibromyalgia (FM) has been conceptualized as a disorder in which symptom presence/severity is modulated by the reciprocal interaction of nocturnal sleep disturbance and cardinal daytime symptoms. This analysis was conducted in subjects enrolled to date in an ongoing insomnia research study. We examined the relationship between objective and subjective sleep measures and daytime pain in these FM patients.
Methods: Participants were 47 FM patients meeting Research Diagnostic Criteria for insomnia who completed sleep logs and actigraphy throughout a two-week assessment, from which subjective and objective estimates of time in bed (TIB), total sleep time (TST), total wake time (TWT), and sleep efficiency (SE%) were derived. Pain was rated on a 0-10 scale in response to an alarm on the actigraph, with ratings collected at 10AM, 3PM, and 7PM averaged together. Linear mixed models with random intercepts were used to determine if pain ratings predict subsequent night's objective or subjective sleep and if objective or subjective sleep parameters predict next day's pain.
Results: Results showed that subjective TIB and objective TIB and TST were statistically significant predictors of next day's pain, with increased TIB/TST predicting increased pain ($p < .05$). Similarly, increased pain predicted increased objective TIB/TST on the subsequent night ($p < .05$). At this point, no significant relationships were detected between pain and any other objective or subjective sleep parameter.
Conclusion: In these analyses, objective actigraphic data indicate a positive relationship between daytime pain and nighttime sleep, with elevated pain predicting increased TIB and TST, and increased TIB and TST predicting elevated pain the subsequent day. These results suggest that FM patients respond to pain with excessive time in bed, which in turn may disrupt the homeostatic and circadian mechanisms that control the normal sleep/wake rhythm.
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IMPROVING SLEEP QUANTITY DECREASES BLOOD PRESSURE IN HYPERTENSIVE PATIENTS
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Introduction: Short sleep duration of <6 hours has been shown to be associated with increased risk of cardiovascular disease, including hypertension. We hypothesize that restoring sleep homeostasis, i.e. improving sleep duration and quality, is an effective behavioral intervention in the treatment of elevated blood pressure (BP).
Methods: Fifteen pre-hypertensive and hypertensive patients (25-65yrs, 9 females) with a habitual sleep duration of <7hrs, as verified by a 2-week sleep log and actigraphy recording period. Patients had no sleep disorders (verified by polysomnography during first overnight stay), and were either untreated or on stable anti-hypertensive medication (no change in medication/dose 6 weeks prior to study start until study end). Patients were randomized to either a bedtime extension group (1hr of additional bedtime, N=9) or maintained their usual bedtime (N=6) for a 6-week period. In addition, both groups were provided with sleep hygiene instructional set (i.e. regularity of bedtimes, timing of eating/drinking habits,

napping etc.) and asked to follow recommendations as close as possible. 24h-BP recordings (Portapres system) and sleep recordings were carried out in the CRC before and after the intervention period.
Results: The sleep intervention protocol led to an average increase of daily self-estimated sleep duration of 33min in the bedtime extension group and a decrease of 7min in the active control bedtime maintenance group ($p<0.05$). 24h systolic BP sig. decreased in the sleep extension group ($p<0.01$), and trended towards a decrease in the sleep maintenance group ($p<0.10$). Diastolic BP and MAP trended towards a decrease in the sleep extension group during the nighttime (bedtime) period in the sleep extension group ($p<0.10$), but did not change in the sleep maintenance group (n.s.).
Conclusion: These preliminary data suggest that sleep extension may serve as an effective intervention in the treatment and prevention of hypertension. Though preliminary, data further suggest that sleep hygiene itself, i.e. keeping regular bedtimes and rising times, may have a BP lowering effect.
Support (optional): AHA #0535241N

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PAIN COMPLAINTS, SLEEP, AND DAYTIME FUNCTIONING: ASSESSMENT IN A CLINICAL SLEEP POPULATION

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Introduction: The relationship between sleep and pain is common sense, but not thoroughly studied until recently. Many chronic pain and inflammatory conditions have shown sleep quality impairments. However, there is minimal focus on the relationship of pain complaints in a clinical sleep population.
Methods: As part of diagnostic evaluation during polysomnography (PSG), patients completed several subjective measures including the Owestrey Pain Scale (OPS), Pittsburgh Sleep Quality Index (PSQI), and various daytime functioning scales including the Clayton Daytime Functioning Scale (CDFS). Inclusion criteria were patients undergoing diagnostic PSG only, ages 18-76, and no shift work.
Results: A total of 295 patients completed all measures and were included in the correlation analysis. Pain scores were significantly correlated with the PSQI ($r= .371$, $p< .001$), CDFS ($r= .374$, $p< .001$), as well as Stage 1% ($r= .14$, $p< .05$), and negatively correlated with Stage 3% ($r= -.18$, $p< .01$) and REM% ($r= -.19$, $p< .01$). Comparing patients with no pain complaint vs. those with a pain complaint (OPS >20), and controlling for those with a diagnosed pain condition, patients with a pain complaint reported significantly more daytime functioning impairments (CDFS, $F= 24,7$, $p< .001$) and higher PSQI scores ($F= 16.5$, $p< .001$). In addition, the pain group had significantly less Stage 3% ($F= 4.3$, $p< .05$) and Stage REM% ($F= 6.6$, $p< .05$) on their diagnostic PSG than the no pain group.
Conclusion: Although further study in a larger sample clinical sleep patient population is needed assessing pain and sleep relationships, our data indicate that patients with a pain complaint report significantly more daytime functioning and sleep quality impairments than those without a pain complaint. Although with cautious interpretation, differences were also apparent in sleep stage distribution on the PSG between the groups. Routine assessment for pain complaints in a clinical sleep patient population may be a beneficial measurement tool.

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PAIN COMPLAINTS, SLEEP, AND DAYTIME FUNCTIONING: ARE THERE DIFFERENCES IN THOSE WITH A DIAGNOSED PAIN CONDITION?

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Introduction: There is an ever growing body of literature documenting the relationship of various pain and inflammatory conditions, such as chronic back pain, neuropathy, arthritis, and fibromyalgia, with impaired sleep and daytime functioning. However, there is a paucity of data looking at those who report pain but have no history of a pain condition in comparison to those with a diagnosed pain condition.
Methods: A total of 109 patients with a significant pain complaint according to the Owestrey Pain Scale (OPS) presented to a Midwestern metropolitan sleep center for diagnostic PSG. In addition, patients completed subjective sleep measures including the Epworth Sleepiness Scale (ESS), Fatigue Severity Scale (FSS), Clayton Daytime Functioning Scale (CDFS), and the Pittsburgh Sleep Quality Index (PSQI). Inclusion criteria were ages 18-79, no shift work, no prior sleep disorder diagnosis, and no split-night studies. Patients were divided into two groups: those with a history of a diagnosed pain condition (Diagnosed) and those with no history of a pain condition (Non-diagnosed).
Results: Patients in the Diagnosed group were slightly older than the Non-diagnosed group (51.9 vs. 47.4), but were comparable according to gender and BMI. The non-diagnosed group had a higher incidence of diabetes than the diagnosed group ($F= 4.83$, $p<. 05$). No significant differences were observed between the groups according to subjective sleep quality (PSQI), daytime functioning (FSS, ESS, CDFS), nor relevant PSG variables (arousal index, Stage 1%, Stage 3%, REM%). However, both groups scored in abnormal or clinically significant ranges of all study variables suggestive of impaired sleep.
Conclusion: Although the potential cause for pain complaints in the non-diagnosed group is unknown, the degree of impact to sleep quality and daytime functioning are comparable to a diagnosed pain population. Further work is needed to understand these findings, but routine assessment of pain in clinical sleep patients is recommended.

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SELF-REPORTED SLEEP QUALITY AND DAYTIME FUNCTIONING RELATIONSHIP TO ACTIGRAPHY IN MENOPAUSAL WOMEN

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Introduction: During the menopausal transition the incidence of insomnia and other sleep disturbances significantly increases. However, there is limited data investigating the relationships of self-reported sleep quality and daytime functioning with actigraphy in this population.
Methods: Twenty-two menopausal status women (Ages 41-59 years) with sleep onset insomnia complaints, completed self-report sleep quality, insomnia, and daytime functioning measures. These included the Pittsburgh Sleep Quality Index (PSQI), Clayton Daytime Functioning Scale (CDFS), Sleep Self-Efficacy Scale (SSES), Pre-Sleep Arousal Scale (PSAS), and the SF36. All data were baseline descriptive data as part of a larger study investigating treatment efficacy for menopausal related insomnia. Actigraphy was worn for two weeks on the non-dominant wrist with sleep diary and hot flash reporting documented during the same time period.
Results: Actigraphy sleep latency (SL) was significantly correlated with the SSES ($r= -.582$, $p<.01$), the PSAS somatic scale ($r= .554$, $p< .05$), and the diary SL ($r= .472$, $p< .05$). Diary sleep time also correlated with actigraphy WASO ($r= .601$, $p< .01$) and sleep efficiency ($r= -.534$, $p< .05$). Actigraphy time in bed (TIB) and sleep time both were significantly correlated with the CDFS ($p <.05$). Interestingly, increased TIB and lower daytime activity counts were significantly correlated with fatigue severity ($p< .05$). The frequency of daytime and sleep-related hot flashes (HF) was significantly correlated to impaired SSES ($p< .05$) and daytime functioning impairments ($p< .05$). However, only daytime HF intensity correlated with the PSQI ($r= .478$, $p<.05$), but sleep-related HF intensity was related to actigraphy fragmentation index ($r= .475$, $p< .05$).
Conclusion: As expected menopausal women report abnormal scores on self-report measures of sleep quality and daytime functioning. Even

in a small sample, actigraphy data demonstrated a strong relationship to various self-report measures and HF intensity. This suggests actigraphy is a useful tool in assessing sleep impairments in menopausal women.
Support (optional): Study funded by Takeda Pharmaceuticals North America, Inc.

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NON-INVASIVE AIRWAY ASSESSMENT AND ADVERSE PREGNANCY OUTCOME

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Introduction: An important predictor of the presence and severity of sleep-disordered breathing (SDB) is the anatomical patency of the upper airway. An increased Mallampati grade (MP; a simple airway classification used to determine risk for difficult intubation) has been reported during pregnancy. Increased MP (i.e., grades III/IV) is also associated with SDB. However, no study has investigated whether MP III/IV may identify women at risk for adverse pregnancy outcomes.
Methods: A medical record review was undertaken of women admitted to the labor and delivery unit between September 2005 - September 2008. Results of routine airway assessments by anesthesiologists were obtained, as were diagnoses of chronic hypertension, gestational hypertension, and pre-eclampsia. Route of delivery was also obtained.
Results: A total of 7251 records were analyzed. Mean age was 29.3±5.9 years and mean BMI was 31.3±6.6Kg/m2. Ten percent of women had gestational hypertension (including 5.6% with pre-eclampsia). Thirty percent of women were delivered by caesarean section. Women with MP III/IV were more likely to have gestational hypertension (16% vs. 9%; $p<0.001$) as well as pre-eclampsia (10% vs. 5%; $p<0.001$) compared to women with MP I/II. MP III/IV was also associated with caesarean section (43% vs.29%; $p<0.001$). In a logistic regression, MP III/IV was independently associated with pre-eclampsia (odds ratio of 1.7, 95%CI 1.2-2.3; $p=0.002$) after adjusting for age, parity, gestational age, and BMI. Also, MP III/IV was associated with having a caesarean section (adjusted odds ratio of 1.6, 95%CI 1.0-2.4; $p<0.05$) including birth weight and previous caesarean section in the model. Results were similar in the sub-group of primiparous women.
Conclusion: Mallampati grade may be useful in identifying women at risk for adverse pregnancy outcomes such as pre-eclampsia and caesarean section. The association between Mallampati grade and SDB also raises the possibility that SDB may play a role in adverse pregnancy outcomes.

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SLEEP DURING MECHANICAL VENTILATION: ASSIST-CONTROL VS. BIPHASIC POSITIVE AIRWAY PRESSURE VENTILATION

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Introduction: In critically ill ventilated patients sleep disturbances are common and partially attributed to mechanical ventilation. We are evaluating the effect of ventilation mode on sleep parameters by comparing assist-control ventilation (ACV) with biphasic positive airway pressure ventilation (BiPAP) - a ventilation mode that allows unrestricted spontaneous breathing and improves synchronization.
Methods: We conducted an interim mid-study analysis of a prospective randomized cross-over study on 25 intubated and mechanically ventilated critically ill patients. Patients were sequentially ventilated four hours each with ACV and BiPAP for two consecutive nights, the order of ventilation being random. Nocturnal sleep was monitored by standard attended polysomnography. Paired t test was used to detect differences in sleep quantity and quality, expressed in the sleep efficiency index, percentage of REM and non-REM sleep and arousals index.
Results: 21 patient-nights were analyzed with a mean monitored time of 224.5 minutes for ACV and 240.5 minutes for BiPAP. Mean sleep efficiencies were 55.4% for ACV and 53.2% for BiPAP (difference 2.18, 95% CI -19.95 to 15.59, $p=0.80$) with a mean difference in total sleep time of 5.8 minutes. Sleep architecture was severely disturbed with decreased REM (8.7% for ACV and 6.3% for BiPAP, $p = 0.40$) and N3 sleep (4.2% for ACV and 3.8% for BiPAP, $p = 0.87$) and increased arousal index (16.0 for ACV and 12.0 for BiPAP, $p=0.36$).
Conclusion: The preliminary results suggest that ACV and BiPAP are equivalent in terms of sleep efficacy, but BiPAP is associated with decreased levels of sleep fragmentation while ACV was associated with minimal increase in percent of REM and N3 sleep. If these results are confirmed in the final analysis, they will support the use of BiPAP in critically ill patients with the intent of improving their sleep and possibly even decreasing morbidity and/or mortality.

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THE RELATIONSHIP BETWEEN SLEEP, FUNCTIONAL ABILITY, AND DISEASE COMPLICATIONS IN PEDIATRIC SICKLE CELL DISEASE

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Introduction: Children with sickle cell disease (SCD) have rated their functional ability in the moderate to high range of disability and sleep disturbances have been shown to negatively affect functional ability. However, to date, the relationship between health, functional ability, and sleep has not been studied in pediatric SCD. The purpose of the current study was to understand how sleep quality and quantity interact with disease complications to affect functional ability. It was hypothesized that poorer sleep would enhance the association between complications and disability.
Methods: As part of a 28-day diary study of pain and quality of life, 30 children, ages 8-18, and their parents reported the child's sleep quality and quantity for the night before completing a measure of functional ability, the Child Activities Limitations Questionnaire. Medical charts were reviewed for the year prior to completing measures to collect information SCD related complications as a proxy for disease severity.
Results: The current study is on-going and sample size will increase. Preliminary analyses of baseline data suggest that parent-reported sleep quality moderates the relationship between complications and functional ability (R^2= .530, model p = .003, interaction term p = .020). Parent and child reports of total sleep time did not moderate the relationship between complications and functional ability.
Conclusion: These preliminary results suggest that for children with better sleep quality, higher complications were associated with higher functional disability. Also, sleep time alone is not sufficient to predict functional ability and other factors, such as pain frequency and intensity, may be more important to functional outcomes. Furthermore, the importance of sleep quality in children with high disease complications suggests that sleep may serve as an escape from complications or that parents may perceive their child's sleep as better in children with more complications and more disability. This relationship is counter to hypotheses and requires further study. Analyses of prospective data for this study are planned.

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DEPRESSION, SUBJECTIVE SLEEP AND SLEEP ARCHITECTURE IN WOMEN DURING PREGNANCY

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Introduction: Sleeping problem and mood disorder are often related in the general population. Over 50% women during pregnancy have depressive symptom and sleep disturbance. We evaluated subjective and objective sleeping amount and quality in the pregnant women with (WDS) and with no (NDS) depressive symptoms.
Methods: We collected the data of Pittsburgh Sleep Quality Index (PSQI) and examined overnight polysomonographic sleep in the women with WDS (depression score of self-rating depression scale was 50 or greater, n=45) and NDS (depression score was fewer than 50, n=45) during the pregnancy of week 16-24.
Results: PSQI data revealed that WDS group showed significantly greater score in the factors of problems in sleep latency, sleep duration, sleep efficiency, sleep continuity and daytime functioning, compared to NDS. Overnight polysomonographic examination revealed that WDS women had reduced total sleep time and sleep efficiency, increased sleep latency and number of wakefulness episode relative to NDS. WDS women also exhibited significantly increased time spent in stage 1, decreased time spent in stages 3 and 4, shortened latency to rapid eye movement and increased time spent in rapid eye movement sleep than those did NDS.
Conclusion: The results demonstrated that WDS women have similar characteristics as those seen in the patients with major depression in the general population, including poor sleep quality and decreased amount of sleep with the tool of subjective sleep evaluation. For sleep architecture, WDS women have worsened sleep in non-rapid eye movement sleep and exhibit typical changes in rapid eye movement sleep as those have been reported in major depression in general population.

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HABITUAL SNORING DURING PREGNANCY IS NOT ASSOCIATED WITH LOWER INFANT BIRTH WEIGHT

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Introduction: Emerging data suggests that maternal habitual snoring may be a risk factor for adverse fetal outcome such as lower birth-weight and reduced Apgar scores. However, the small available literature is conflicting. Given the potential impact of habitual snoring on fetal outcome, data are urgently required to address this significant public health issue. Therefore, we aimed to determine whether habitual snoring in the last trimester of pregnancy is associated with adverse infant outcome.
Methods: Women carrying a single fetus were recruited during their last trimester of pregnancy and invited to complete several sleep questionnaires. Habitual snoring was defined as snoring ≥3 nights/week. Following delivery, medical records were reviewed to determine infant outcomes.
Results: In total, 429 women (mean age 30.1±5.8 years) have been studied as part of an ongoing investigation. Thirty-five percent reported habitual snoring and 25% were obese (BMI≥30kg/m^2). No differences were found in birth-weight between infants born to women with and without habitual snoring (3.29±0.7kg vs. 3.28±0.6kg respectively). Similarly, no differences were found in 1 or 5 minute Apgar scores (7.3±1.9 vs. 7.7±1.8kg and 8.6±1.1 vs. 8.7±1.1 respectively). There was a tendency for the habitual snorers to have 1 and 5 minute Apgar scores ≤7 (34% vs. 25% and 11% vs. 6%) although this did not reach statistical significance (p≤0.16). In a regression model including habitual snoring, presence of diabetes, maternal age, and race, only gestational age at delivery, and pre-pregnancy BMI were independent predictors of birth-weight (adjusted R^2 0.31 p<0.001) and 1-minute Apgar (adjusted R^2 0.42, p=0.001). Only gestational age at delivery was predictive of 5-minute Apgar score (adjusted R^2 0.31, p=0.002).
Conclusion: Contrary to several reports, our findings do not support the hypothesis that habitual snoring in pregnancy is a predictor of adverse infant outcomes such as lower birth-weight or poor Apgar scores.
Support (optional): University of Michigan Institute for Research on Women and Gender; University of Michigan Institute for Clinical and Health Research Seed Pilot Grant F021024; Gilmore Fund donation

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INTRA-INDIVIDUAL VARIABILITY IN DAILY SLEEP AND PAIN RATINGS AMONG CHRONIC PAIN PATIENTS

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Introduction: Sleep disturbances are reported by 50-70% of chronic pain patients, and experimental and cross-sectional studies support the relationship between sleep disturbance and pain. However, limited research has prospectively examined the reciprocal relationship among sleep and pain among chronic pain patients. The present study prospectively investigated the relationship among sleep and pain over a 2-week period within a sample of chronic pain patients.
Methods: Twenty-two chronic pain patients completed 2-weeks of daily sleep diaries and actigraphy monitoring, providing information about sleep and pain. Hierarchical linear modeling (HLM) was used to examine prospective relationships among daily ratings of pain and sleep across the study period. Initial levels of negative mood were also assessed, and were included in the prospective models.
Results: Both objective and subjective sleep measures revealed longer SOL, increased WASO, shorter TST, and lower SE among self-reported poorer sleepers (p<.01 to p<.001). HLM examined intra-individual variability in sleep and pain across the study period and found that a day of higher pain ratings was followed by a night of poorer sleep quality (p<.001). This finding was even more pronounced among participants who reported higher initial depression ratings (p<.05). Also, a night of poor sleep quality was followed by a day of higher average pain ratings (p<.001). This relationship was again found to be stronger among participants reporting higher initial levels of depression (p<.05).
Conclusion: These data provide preliminary evidence for a significant bi-directional relationship between daily pain ratings and sleep, within a sample of chronic pain patients. These relationships appear to be further impacted by baseline measures of negative mood, particularly depression. Future research should examine how these daily interactions between sleep and pain may be affected by interventions designed to treat sleep disturbance or chronic pain.
Support (optional): Equipment for this research was provided by MiniMitter/Respironics, Inc.

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THE SUBJECTIVE SLEEP QUALITY AND HEART RATE VARIABILITY IN HEMODIALYSIS PATIENTS

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Introduction: Sleep disturbances have a major influence on life quality in hemodialysis patients. Cardiovascular autonomic dysfunction is

another complication of chronic renal failure. The goal of this study was to identify clinical, heart rate variability (HRV) or laboratory parameters that were independently associated with subjective sleep quality.
Methods: From January 1, 2008, to November 30, 2008, adult stable hemodialysis patients (female=24, male=22) filled out a sleep questionnaires including Pittsburgh sleep quality index (PSQI), Athens insomnia scale (AIS) and Epworth sleepiness scale (ESS). In addition, they received twice analyses of five minutes HRV in lying posture before and after hemodialysis. We also recruited 50 healthy subjects received five minutes HRV as controls.
Results: The duration of hemodialysis was 2.57± 2.20. The mean PSQI was 12.71± 4.23; the mean AIS was 11.56 ± 4.38 and the ESS was 5.54± 4.22. The activities of total power (TP, 0-0.5 Hz), very-low-frequency (VLF, 0.003-0.04Hz), low-frequency power (LF, 0.04-0.15Hz) and high-frequency power (HF, 0.15-0.40Hz) in hemodialysis patients were obviously lower then the health. The relationship between parameters of HRV and sleep quality scales did not showed obvious significances except only the high-frequency power (HF, 0.15-0.40Hz) of pre-hemodialysis was showed positive significance with PSQI in linear regression models (P= 0.048, R2=0.086). The hemoglobin (Hb) levels were associated with PSQI (P= 0.032, R2=0.08) and sleep latencies (P= 0.023, R2=0.092).
Conclusion: Hemodialysis patients had a high rate of poor sleep quality and cardiovascular autonomic dysfunction. The relationship between sleep quality and HRV did not be clarified in this study. The Hb levels should be one of important roles to sleep quality in hemodialysis patients.

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NOVEL APPROACH TO INTERPRETING TREATMENT RESPONDERS WHEN ASSESSING SLEEP IN PATIENTS WITH FIBROMYALGIA (FM)

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Introduction: There are several approaches to assess the relevance and strength of treatment effects for patient-reported outcomes including effect size (strength), comparison of treatment effect with clinical important difference (relevance), and responder analysis (strength and relevance). Using a novel methodology, we evaluated the responder profiles for two sleep measures included in clinical trials of pregabalin in patients with FM. The objective was to provide a simple and clear way of interpreting responder profiles.
Methods: Analyses were based on data from three randomized, double-blind, placebo-controlled trials of pregabalin (studies 1056, 1077, 1100). Pregabalin doses of 300, 450, or 600mg per day were compared against placebo. Sleep measures included the Medical Outcomes Study (MOS) Sleep Disturbance domain and the single-item Sleep Quality Scale. Response profiles and differences between pregabalin and placebo were assessed using area under the curve (AUC) with the entire information from the responder curve (vertical axis: percentage of subjects; horizontal axis: minimum percentage improvement in sleep measure). We show that AUC can be interpreted as if all responders were improved by the same percentage equal to the AUC.
Results: For MOS Sleep Disturbance, responder profiles can be interpreted as if all responders on pregabalin improved by 28-45%, depending on study and dose; whereas responders on placebo improved by 20-31%, depending on study. Overall, responder profiles here can be interpreted as if all responders on pregabalin improved 8-22% more than responders on placebo. Similarly, for Sleep Quality, responder profiles can be interpreted as if all responders on pregabalin improved by 29-43%, whereas responders on placebo improved by 22-24%, and, overall, all responders on pregabalin improved 7-19% more than responders on placebo.
Conclusion: Using AUC, we provide a simple and clear approach of interpreting treatment responder profiles when assessing sleep in patients with FM.
Support (optional): Supported by Pfizer Inc.

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SLEEP DISRUPTION AND MODE OF DELIVERY IN PREGNANT WOMEN

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Introduction: Sleep disturbances are known to impact physical and psychological wellbeing. Limited available data from women with a moderate-to-high socioeconomic background suggest that poor sleep in late pregnancy is associated with an increased risk for cesarean section. Such an association has important clinical implications. However, the impact of sleep disruption on mode of delivery has not been investigated in a heterogeneous sample of pregnant women attending a large academic medical center.
Methods: Pregnant women ≥18 years, carrying a single fetus, were recruited from the labor and delivery unit and invited to complete several sleep questionnaires including the General Sleep Disturbance Scale (GSDS). Total score ranges from 0-147 and a mean score ≥3 is considered a threshold for poor sleep. Women with snoring ≥3 nights/week were considered to have habitual snoring. Non-pregnant women of child bearing age (18-45 years) were recruited as controls. Medical records were accessed to obtain delivery information.
Results: In total, 141 pregnant women and 83 controls have been studied. Mean ages were 29.8±5.7 years vs. 32.7±8.0 years respectively. There were no differences in pre-pregnancy BMI between groups (26.5±7.2 vs. 26.7±7.1kg/m2). Total GSDS score was higher for pregnant women than controls (61.6±17.6 vs. 47.8±15.7; $p<0.001$). In addition, pregnant women were more likely than controls to have a mean GSDS score ≥3 (55% vs.19%; $p<0.001$) and report habitual snoring (34% vs. 17%; $p=0.006$). Overall, 38% of pregnancies resulted in a cesarean section. In a logistic regression with mode of delivery as the dependent variable, and controlling for previous cesarean section, parity, maternal age, BMI, gestational age, and birth weight, no sleep-related parameters were found to be significant predictors of mode of delivery.
Conclusion: Contrary to previous findings, our data do not support the hypotheses that sleep disruption in pregnancy is associated with an increased risk for cesarean section.
Support (optional): University of Michigan Institute for Research on Women and Gender; University of Michigan Institute for Clinical and Health Research Seed Pilot Grant F021024; Gilmore Fund donation.

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THE EFFECT OF BACLOFEN ON SLEEP AND NIGHTTIME REFLUX IN PATIENTS WITH GASTROESOPHAGEAL REFLUX DISEASE (GERD)

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Introduction: Baclofen (B) is a GABAb agonist which acts as an inhibitory neurotransmitter which decreases gastroesophageal reflux (GER) events and has hypnotic properties. GERD patients often have sleep complaints as well as sleep related GER. It was hypothesized that B would decrease sleep related GER as well as improve sleep quality in GERD patients with sleep complaints.
Methods: Thirteen individuals with nighttime heartburn at least 2 times/wk and an elevated Carlesson GERD questionnaire score were studied. Patients were studied via polysomnography (PSG) for two nights to

include simultaneous esophageal pH monitoring. Patients were given 40mg of B or placebo (P) in random order prior to sleep. In order to provoke reflux events during sleep, a provocative meal was given 1 hr prior to lights out. Sleep quality was assessed via objective and subjective measures.
Results: Number of reflux events was significantly decreased on B (P = 3.4, B =1.2, P<.05) Acid contact time was reduced, but not significantly (P=7.5%, B= 4.0%);. The mean PSQI was 7.1. PSG measures on B showed a marked increase in total sleep time (P=385, B=438min, P<.001); sleep efficiency (P=80%, B= 91%, P<.001) and a very substantial decrease in WASO (P=76, B=29min, P<.001). Sleep onset latency was reduced but not significantly on B (P=26, B=16min). Subjective sleep was significantly improved on B in terms of reports of total sleep time, sleep quality and number of awakenings (all P<.05).
Conclusion: 1. Baclofen could be a useful adjunct in the treatment of GERD patients with sleep complaints; 2. The highly significant improvement in objective and subjective sleep parameters would warrant further investigation of the efficacy of this drug in a population of insomniac patients.

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THE RELATIONSHIP BETWEEN UNCERTAINTY OF ILLNESS, CANCER SPECIFIC STRESS AND INSOMNIA SEVERITY AMONG CANCER PATIENTS

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Introduction: Sleep is a vital, yet vulnerable, component of well-being that can be significantly affected by worry or increased cognitive arousal associated with insomnia (Harvey, 2003). Uncertainty of illness (worry over one's health outcomes) may be a possible contributor to insomnia symptoms among cancer patients. Given that significant relationships have emerged between one's social and emotional functioning and uncertainty of illness among cancer patients (Paterson, 2001), we aimed to examine the relationship between insomnia symptom severity and one's uncertainty of illness, and their relation to cancer specific stress.
Methods: As part of a larger study, data from a heterogeneous sample of cancer patients (N=120) at the Cancer Institute of New Jersey at Cooper Hospital was evaluated. Cancer patients completed questionnaires at their outpatient appointment on social and emotional functioning, cancer specific stress, and sleep quality, including the Insomnia Severity Index (ISI) and a measure of uncertainty of illness (the Mishel Uncertainty of Illness Scale; MUIS). Data on the ISI, MUIS, and Questionnaire on Stress in Cancer Patients (QSC) were extracted for this investigation.
Results: Preliminary analysis indicated that 51.6% of the sample endorsed mild to severe symptoms of insomnia. Insomnia symptom severity and uncertainty of illness were positively correlated (r =.21, p < .05). Insomnia severity and uncertainty of illness were also correlated with cancer specific stress (r=.59, p<.01; r=.45, p<.01 respectively).
Conclusion: While the bidirectional nature of this correlational data is appreciated, the significant association between uncertainty of illness and insomnia severity calls our attention to further investigate this potential precipitant of insomnia among cancer patients. Development and testing of interventions specifically about uncertainty of illness may be indicated given its relationship with insomnia symptoms. In addition, the relationship between uncertainty of illness, sleep quality and the implications for cancer specific stress warrant further discussion.

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SLEEPINESS AND FATIGUE IN FIBROMYALGIA AND RHEUMATOID ARTHRITIS PATIENTS

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Introduction: High levels of daytime sleepiness and fatigue are reported by patients with chronic pain. This study is the first to compare physiological sleepiness to self-reported sleepiness and fatigue in patients with fibromyalgia (FM) and rheumatoid arthritis (RA).
Methods: Volunteers were women with FM (N=20; age M= 49), RA (N=18; age M=49) and age-matched pain free normal controls (NC) (N=20; age M=46) all without co-morbid depression, or primary sleep disorders based on a screening 8-hour NPSG. After screening and an adaptation night of laboratory sleep, volunteers underwent a baseline 8-hour NPSG. Self-reported sleepiness was assessed using the Epworth Sleepiness Scale (ESS) and fatigue with the Fatigue Assessment Inventory (FAI) completed the day before the MSLT. Physiological sleepiness was assessed after the baseline night using a standard MSLT (1000, 1200, 1400, 1600, and 1800 hrs).
Results: MSLT scores were higher in FM patients (14.06±4.16) than in RA patients (11.18±4.60) and NC (10.17±4.71) (p<.05). Self-reported ratings of sleepiness (ESS) showed a trend towards higher scores in patients with FM (8.83±4.52) as compared to RA patients (6.00±3.71) and NC (6.67±3.01) (p<.08). FAI severity scores in FM patients (5.05±1.24) were higher than NC (1.83±0.69) (p<.001) and were intermediate in RA patients (3.56±1.29) differing from both FM and NC (p<.001). ESS scores were correlated with FAI severity scores in FM and RA patients (r=.485; p<.02) while MSLT scores did not correlate with ESS and FAI scores. In contrast there was no relation between ESS and FAI scores in NC, while MSLT scores correlated with ESS (r=-.61; p<.02) and FAI scores (r=-.56; p<.02).
Conclusion: These data show that, although FM patients report higher levels of sleepiness and fatigue, they are physiologically less sleepy than controls. MSLT does not correlate with self-reported sleepiness and fatigue in pain patients, while it does in controls.
Support (optional): The Arthritis Foundation awarded to Dr. Gillis.

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DIFFERENCES BETWEEN PRIMARY AND PAIN-RELATED INSOMNIA: INSPIRATIONS FOR CBT-I ADAPTATION?

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Introduction: The application of cognitive behavior therapy for primary insomnia (CBT-I) to sleep disturbance co-occurring with other physical/psychological disorders is based on the assumption that the factors perpetuating the sleep problems are largely the same. Although this strategy works, findings of a few randomized controlled trials testing the utility of CBT-I in treating pain-related insomnia have suggested that further adaptations may be required to optimize treatment outcomes in chronic pain patients. This study aimed to take a step back and examine the possible differences between primary and pain-related insomnia in terms of their clinical presentations, general psychological attributes and sleep-specific psychological processes.
Methods: Participants were 103 chronic pain patients with clinical insomnia (CPI) and 31 patients with primary insomnia (PI). They were asked to complete a set of questionnaires that comprise measures of sleep patterns, general psychological characteristics and sleep-specific psychological processes that have been linked to the persistence of insomnia.
Results: Comparisons between the 31 PIs and 31 CPIs matched in insomnia severity indicated no significant differences in their sleep disturbance patterns and most of their general psychological characteristics

(e.g., anxiety and depression). However, the PIs did exhibit a higher tendency to worry and report a greater degree of sleep-related anxiety and preoccupation and pre-sleep cognitive arousal than the CPIs. Regression analyses performed with the data of all 103 CPIs revealed that insomnia severity was predicted by the levels of health anxiety, pain intensity and pain-related mental defeat, which together with age and body mass index accounted for 35% of the total variance.
Conclusion: These findings suggest that CPI may differ from PI in several sleep-specific psychological processes. They also highlight the areas where more attention is required in the process of adapting CBT-I for use with pain-related insomnia, including health anxiety, pain intensity and pain-related mental defeat.
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EFFECTS OF NOISE ON SLEEP QUALITY IN A HOSPITAL

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Introduction: Effects of noise on sleep and life quality or life expectancy have high medical importance. In order to treat sleep disorders evidence based, a solid differential diagnosis has to be performed first. Part of this is to distinguish internal and external reasons for sleep disorders. External noise can trigger and maintain sleep disorders.
Methods: In the main ward building at the University Hospital Charité in Berlin, Germany, we initiated a study to investigate effects of subjective noise exposition on subjective sleep quality. In total 757 patients were recruited, and out of them 313 (41.35%) agreed to complete our questionnaire.
Results: The subjective sleep quality in the hospital environment is poor: 34.3% (n = 91) of 265 patients complained about non-restorative sleep. In addition, 20.8% (n = 55) reported at least temporarily a non-restorative sleep. Every second patient complains about difficulties maintaining sleep, and every third patient complains about difficulties initiating sleep. Patients complain about noise from outside the building, noise from other patients sharing the same room, and noise from the nurses on the ward.
Conclusion: To achieve an at least partially restorative sleep in the hospital, it is of great importance to recognize and minimize external noise sources as far as possible.

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INSOMNIA AND HIV INFECTION AMONG PARTICIPANTS IN THE WOMEN'S INTERAGENCY HIV STUDY

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Introduction: Insomnia is common among women, but those infected with HIV may be particularly vulnerable. In this study, we assessed the prevalence of insomnia in HIV-infected women enrolled in the Women's Interagency HIV Study and examined factors associated with insomnia.
Methods: Participants (n=1804) were enrolled in the Women's Interagency HIV Study, a multisite prospective cohort study of HIV-infected women in the United States; 71% were HIV+ and 29%, HIV-; 12% were white; 57%, black; 27%, Hispanic; and 4%, other ethnicities. This was a cross-sectional analysis of data obtained during a study visit (#26) using standardized interviewer-administered instruments and physical exams. Our analysis focused on sociodemographics, sleep measures, depressive symptoms, quality of life, drug use, alcohol consumption, medication (HAART and others), and HIV-related clinical variables. Insomnia was defined as a report of either difficulty initiating sleep, difficulty maintaining sleep, or early morning awakening, at least once a week in the past two weeks.
Results: Prevalence of insomnia varied based on HIV status and age groups. Among women ages 20-40 years, prevalence was 59% (HIV+) and 49% (HIV-) [OR=1.48, 95% CI:1.06-2.06, p=0.02]; among women ages 51-80 years, prevalence was 71% (HIV+) and 76% (HIV-) [OR=0.79, 95% CI:0.46-1.38, NS]; and among women 41-50 years, prevalence was equivalent [66%]. Prevalence of insomnia differed by ethnicity [white=69%, Hispanic=67%, and black=61% ($\chi 2$=19.48, p<0.001)], but no significant interaction was noted between HIV status and ethnicity. Adjusting effects of ethnicity, household income, depressive symptoms, medication, and menopausal status did not attenuate the magnitude of the association between HIV and the prevalence of insomnia symptoms, whereas adjusting age effects did. Quality of life of women reporting insomnia symptoms was lower than those who did not, independently of their HIV status or other covariates [F(7,1492)=56, p<0.001].
Conclusion: Insomnia is more prevalent among younger HIV-infected women, relative to uninfected women. Insomnia treatment targeting younger HIV infected women is encouraged.
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SLEEP DISORDERED BREATHING AND SICKLE CELL ANAEMIA IN A LONDON COHORT

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Introduction: Sleep Disordered Breathing (SDB) and Obstructive Sleep Apnoea (OSA) are common in the general paediatric population and can have consequences such as failure to thrive and learning difficulties. Sickle Cell Anemia (SCA) is the most prevalent inherited disorder in inner cities in the UK. In addition to painful crises and stroke, difficulties with attention, executive function and reduced IQ are common in SCA and may be related to SDB. Hypoxemia related to OSA may lead to increased nocturnal sickling and crises with resultant exacerbation of the disease. However there are few data SDB in SCA. The aim of this study was to document our experience of SDB in SCA.
Methods: Retrospective study of SCA children referred to Great Ormond Street Hospital for Children NHS Trust for overnight cardiorespiratory sleep studies between 1999 and 2007. Continuous and simultaneous recordings were made during natural sleep. Sleep studies were analyzed using Alice4® sleepware. Artefact and poor signal quality were excluded by visual inspection of the raw data.
Results: 92 (50 boys) children with HbSS aged 2.1 to 18.2 (median 8.0) years were studied. Duration of sleep 108.5 to 625.5 (median 449.3) mins. The median (range) Apnoea-hyponoea (AHI) and Respiratory disturbance indices (RDI) were 3.2 (0-42.9) and 3.7 (0-52.7) respectively. AHI >5 in 37 (40%) children (22 boys). AHI and RDI were higher in younger children (R^2=.6, p=.02 for both) and in boys (p=.04 for both).

AHI >5 was 2.8 times more common (95% confidence intervals 1.1, 7.2) in ages >10 years. Median BMI was 16 (range 12.9 to 25.7). No correlation of AHI and RDI to body mass index, birth weight, gestational age or haemoglobin was shown. AHI and RDI were lower after CNS event (p=.04 for both).

Conclusion: Sleep disordered breathing appears to be more common than previously recognized in SCA. However, these children were referred for overnight cardio-respiratory sleep studies and therefore population-based studies, focusing on the younger age group, are required to establish prevalence. The SCA population may be susceptible to SDB due to repeated infections, allergies and airway narrowing related to anatomic effects of bone marrow hyperplasia, rather than obesity or neurological complications. Hypoxemia related to obstructive sleep apnoea may lead to increased sickling of red blood cells overnight and potentially to pain and other complications. Evidence-based treatment options should be investigated in children with sickle cell anemia.

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ONE MONTH CHANGES IN DAILY PAIN AND INSOMNIA SEVERITY IN THE CONTEXT OF TEMPOROMANDIBULAR JOINT DISORDER (TMD): CROSS-LAGGED PANEL ANALYSES

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Introduction: Pain is the cardinal symptom of TMD, presenting with a waxing and waning course. Cross-sectional work by our group suggests that primary insomnia is also common in TMD, perhaps threefold more so than insomnia due to pain or psychiatric disorders. The temporal sequencing of pain and insomnia symptoms has yet to be studied in TMD and the degree to which insomnia predicts clinical pain, or vice-versa, has not been systematically examined. We hypothesized that insomnia is a risk factor for emergence and/or aggravation of TMD pain, at least to a greater extent than pain is a risk factor for exacerbations in insomnia.

Methods: Fifty-one RDC-diagnosed TMD patients (M age = 33; 60% Female; 77% Caucasian; 10% African American) provided measures of insomnia severity (ISI) and usual daily pain at baseline and 2, 4, 6, 8, 10, and 12 week follow-ups. Participants also completed Beck Depression and Brief Pain Inventories at baseline. To examine the extent to which insomnia predicted pain, and vice-versa, we conducted cross-lagged analyses using linear mixed effects models for 1-month lags. Residualized change scores were computed for each 1-month lag for ISI and usual daily pain ratings. BDI and BPI scores were modeled as covariates.

Results: Initial increases in ISI (e.g., from initial-to-4 week) correlated with subsequent (e.g., 4-to-8 week) increases in usual daily pain ratings ($t = 2.48$, $p = .017$). Conversely, initial increases in pain ratings were not related to subsequent increases in ISI ($t = 1.06$, $p = .30$).

Conclusion: These findings suggest temporal precedence for insomnia in relationships between sleep and clinical pain in TMD. Specifically, exacerbations in insomnia predicted increased daily pain over the subsequent month, but changes in daily pain were not related to subsequent increases in insomnia. Pharmacologic and/or cognitive-behavioral treatments for insomnia may attenuate pain and suffering for those with TMD.

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SLEEP ARCHITECTURE IN STROKE AT THE VA CARIBBEAN HEALTHCARE SYSTEM

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Introduction: The relationship between stroke and sleep disordered breathing (SDB) have been revised in the past few years. We sought to document differences in clinical comorbidities and sleep architecture in patients with evidence of SDB who where treated with nasal C-PAP (C-PAP +) or not treated with C-PAP (C-PAP -) before the stroke.

Methods: Retrospective review of 79 records from January 2007 up to the present. Data included age, BMI, co-morbidities, AHI, O2 saturation < 90%, total sleep time, sleep efficiency, sleep latency, REM sleep, REM latency, sleep stages, and date of both diagnosis. A comparison of two groups was done using paired t-test, and Chi2.

Results: The records of 79 subjects were reviewed. The average age was 66.2 years, the mean BMI was 31.3, being the more prevalent co-morbidities: diabetes mellitus, hypertension, and dyslipidemia in both group. There was statistical difference between groups based on sleep architecture in the following: total sleep time and stage 1 were increased in C-PAP - group 362.1 vs 285.2 [p 0.006] and 12.8 vs 18.7% [p 0.03], respectively. Stage 3, 4, and mixed apneas were increased in C-PAP - group 7.7 vs 4.4 % [p 0.01], 4 vs 0.2% [p < 0.005] respectively. The AHI and RDI were increased in C-PAP + group 27.7 vs 18.0 [p 0.017]; 25.7 vs 36.9 [p 0.008] respectively.

Conclusion: There were statistically significant differences among the sleep architecture in both groups. Subjects with SDB who developed a stroke have more comorbidities and increasing age. The absence of C-PAP therapy correlated with increased sleep fragmentation as expected.

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USE OF THE EPWORTH SLEEPINESS SCALE IN A GENERAL MEDICINE POPULATION

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Introduction: Up to 24% people in the general population have excessive daytime sleepiness (EDS), measured by the Epworth Sleepiness Scale (ESS). The purpose of this study was to determine predictors of elevated ESS scores in a General Medicine clinic.

Methods: The ESS was administered to consecutive adults in a General Medicine Clinic over 4 weeks. Medical records were reviewed for a variety of demographic, medical and sleep variables. ESS scores were categorized as normal (<9) or abnormal (≥10). Chi-Square and Student's t-tests were performed as appropriate.

Results: 212 subjects [age 58.3 + 16.1 (mean +standard deviation); 34.9% male; BMI 30.4 ± 8.4] were included. Abnormal ESS scores were found in 45 (21.2%) subjects. Mean ESS was 6.4 ± 4.5. Only 19 (9.0 %) and 24 (11.3 %) subjects had a prior sleep referral or were diagnosed with sleep disorders, respectively. There was a positive correlation between ESS and BMI (p=0.01). Abnormal ESS was associated with prior sleep referral (p< 0.001), previous sleep diagnosis (p=0.01), and use of CPAP (p=0.04). No correlation was found between abnormal ESS and cardiovascular disease, COPD, arrythmia or smoking status. Abnormal ESS was more likely in subjects taking wake-promoting (p=0.04) and antiepileptic (p=0.04) medications.

Conclusion: EDS as measured by the ESS is highly prevalent in General Medicine populations, often not assessed in routine visits. Subjects with elevated ESS scores are more likely to have a higher BMI, previous sleep referral/diagnosis and to be using CPAP. However, no particular medical co-morbidity predicted ESS. These findings will be used to educate clinicians about the importance of sleep screening and measure its impact on referrals to the sleep center.

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SLEEP DISORDERED BREATHING IS ASSOCIATED WITH A TRAJECTORY OF INCREASED PAIN IN TEMPOROMANDIBULAR JOINT DISORDER (TMD): A THREE MONTH PROSPECTIVE STUDY

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Introduction: TMD is a chronic pain syndrome marked by frequent, intermittent exacerbations in pain. Prior work by our group identified insomnia, sleep bruxism, and sleep apnea as prevalent disorders in TMD. It is unknown whether objective indices of these sleep disturbances are prospectively associated with exacerbations in TMD pain.
Methods: Fifty-one RDC-diagnosed TMD patients (M age = 33; 60% Female; 77% Caucasian and 10% African American) completed overnight polysomnography (PSG), Beck Depression (BDI) and Brief Pain Inventories (BPI) at baseline. Participants provided usual daily pain ratings at baseline and 2, 4, 6, 8, 10, and 12 week follow-ups. Linear mixed effects analyses were conducted on usual daily pain ratings. PSG indices of sleep apnea [respiratory disturbance index (RDI)], insomnia (sleep efficiency and latency), and sleep bruxism (masseter EMG bursts/hour sleep) were modeled as between-person predictors. Of primary interest were interaction effects between sleep indices and time on pain ratings. BDI and baseline BPI scores were modeled as covariates.
Results: Baseline pain ratings ($t = 5.13$, $p < .0001$), but not BDI scores ($p > .05$) predicted subsequent pain ratings. Sleep efficiency, latency, and bruxism were not significantly associated with prospective pain ratings ($p \geq .10$). There was, however, a significant interaction between RDI and time, such that increased sleep disordered breathing, predicted a trajectory of increased usual daily pain ratings ($t = 2.73$, $p = .03$).
Conclusion: Results suggest that sleep disordered breathing predicts a pattern of pain flare over three months in TMD, above and beyond baseline depressed mood and pain. These findings are critical in light of recent evidence indicating a high prevalence of sleep apnea in TMD. Although insomnia and sleep bruxism are also common in TMD, corresponding PSG indices did not predict pain in the present analyses. Treating sleep apnea may minimize exacerbations in pain and suffering for those with TMD.
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SLEEP DISTURBANCE IN PATIENTS WITH HEAD AND NECK CANCER RECEIVING RADIATION THERAPY

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Introduction: Sleep disturbance in head and neck cancer patients (HNC) undergoing radiation therapy has been understudied. It is not known whether HNC patients experience sleep disturbance during and/or after RT and whether there is a correlation with other prevalent symptoms such as fatigue and depression in cancer patients. The purpose of this study were to measure sleep disturbance in head and neck cancer (HNC) patients during radiation therapy (RT) and follow up (i.e., 1st week, 3rd week, end of RT week, and one-month follow up), and its association with depression, fatigue, and daytime sleepiness.
Methods: A longitudinal repeated measure design was used to recruit 38 HNC patients in an outpatient radiation oncology clinic. Subjects were asked to fill out the self-report General Sleep Disturbance Scale, Epworth Sleepiness Scale, CES-Depression, and Lee Fatigue Scale, at four time points. Internal consistency of all instruments ranged from 0.79 to .86. Descriptive statistics, Pearson correlation, and mixed effects for overall differences over time were used.
Results: HNC patients experienced sleep disturbance at the beginning of RT, and the rate changes of sleep disturbance, depression, daytime sleepiness, and fatigue were not significantly different over time. Patients experienced the worst sleep disturbance, depression, and fatigue at the end of RT with less sleep disturbance, depression, and fatigue at one month after radiation therapy. The magnitude of associations between sleep and depression ($.42 < r < .64$, $p < .01$), fatigue ($.61 < r < .75$, $p < .01$), and daytime sleepiness ($.42 < r < .64$, $p < .05$) were moderate and positive at all time points except for daytime sleepiness at the end of RT ($r = .23$).
Conclusion: These findings suggest anticipating the prevalence of these symptoms in HNC patients at the beginning of the RT and its increase in the severity of symptom at the end of RT. Potential supportive care intervention may suggest providing HNC patients with ongoing care to RT.
Support (optional): Oncology Nursing Foundation

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IMPROVEMENT OF SEVERE PRECAPILLARY PULMONARY HYPERTENSION AFTER OSA TREATMENT

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Introduction: There are references about improvement of pulmonary hypertension (PH) after CPAP treatment in literature. Clear amelioration of severe PH after CPAP treatment was described in only one patient. We compared the effect of CPAP treatment on severe precapillary PH after 12 months to verify if the improvement is present in all patients with severe precapillary PH and OSA.
Methods: Six patients (3 men, 3 women, average age 57 years, average BMI 36.5 kg.m -2) with severe precapillary PH (average pulmonary artery systolic pressure - PASP 72 mm Hg) and OSA (average RDI 53 +/- 36) were treated using CPAP (5 patients); one patient underwent maxilomandibular advancement by reason of intolerance of CPAP treatment. Compliance of OSA treatment using CPAP or after surgery was evaluated after 3 and then after 12 months. Echocardiographic examination was performed before CPAP treatment and at the end of the study. Precapillary PH was judged according to echocardiographic criteria: size of right ventricle (RV), size of right atrium (RA) and PASP.
Results: OSA was satisfactorily treated in all patients (RDI > 5). Considerable improvement of all measured echocardiographic parameters was noted in 3 patients. The clinical status improved also at these subjects. Adjustment of OSA didn't conduct to improvement of measured echocardiographic parameters at the other 3 patients at all.
Conclusion: PH parameters improved at a half of patients after successful OSA treatment (responders to OSA treatment), the second half (non-responders) didn't show the improvement. We assume that the pathophysiological role of OSA on PH is confirmed by the response to CPAP treatment and not only by the apneas finding during PSG examination.
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PERFORMANCE OF ACTIGRAPHY IN TEMPOROMANDIBULAR JOINT DISORDER

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Introduction: Subjective complaints of sleep disturbance are common among patients with Temporomandibular Joint Disorder (TMD), but little is known about objective measurements of sleep in this population. Actigraphy has been validated as a measure of sleep in chronic insomniacs and may represent an important tool for the assessment of sleep in TMD.

Methods: Thirty-nine patients with TMD (84.6% female, mean age=26.2±3.8 years, BMI=23.2±3.5) and thirty-nine matched healthy controls underwent diagnostic interviews and one night standard in-lab polysomnography. All participants wore a MiniMitter wrist actigraph during their PSG.

Results: Relative to PSG, among TMD patients actigraphy underestimated total sleep time (TST; 426.0±37.0m versus 442.6±23.2m; t=2.5, p=.02) and sleep efficiency (SE; 88.7±5.0% versus 92.3±4.5%; t=3.9, p=.001), and overestimated sleep onset latency (SOL; 10.9±11.4m versus 10.7±9.3m; t=0.1, p=.90) and wake after sleep onset (WASO; 35.5±20.0m versus 25.7±19.3m; t=2.7, p=.01). Among TMD patients, correlations between actigraphy and PSG measures ranged from r=.30 to r=.51. Among healthy controls, no significant differences between PSG and actigraphy-based measures of TST, SE, SOL, or WASO were detected. Measures of sleep continuity did not differ between patients with TMD and healthy controls, whether measured by actigraphy or PSG. However, patients with TMD had more S1 (7.0% versus 5.0%; t=2.0, p=.05) and less S2 (t=2.9, p=.005) than controls. Finally, no significant differences in PSG-actigraphy discrepancy scores for each of the 4 sleep continuity variables were detected between TMD patients and healthy control subjects.

Conclusion: Among patients with TMD, actigraphy appears to overestimate sleep continuity disturbance. However, the magnitudes of PSG-actigraph differences were relatively small, and PSG-actigraphy discrepancy scores did not differ between TMD patients and healthy matched controls. These results suggest that actigraphy may be a reasonable estimate of sleep continuity when compared to PSG, and further evaluation of actigraphy as an objective assessment tool in this population is warranted.

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SLEEP DISORDERED BREATHING IN PATIENTS WITH NON-SMALL CELL LUNG CANCER

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Introduction: Although disturbed sleep is common in patients with lung cancer, little is known of the underlying etiology. We hypothesized that disease/treatment effects on lung function superimposed on normal sleep-wake state-dependent alterations in respiratory control would place these patients at risk for sleep disordered breathing (SDB).

Methods: Subjects with non-small cell lung cancer (NSCLC) underwent overnight polysomnography. Records were scored by a single scorer using standard criteria. Measures included: sleep parameters, apnea/hypopnea index [AHI], oxygen desaturation index (ODI), and hypoxic burden (percentage of TST with an SaO2 <90). Statistical analyses included descriptive and nonparametric procedures.

Results: We report on the first 13 subjects (8 males, mean age 60.92±7.88 and BMI 24±7.06). Mean sleep parameters showed expected distribution of sleep stages for age and gender. However, mean SE was low (82.31±11.14%) and sleep was characterized by frequent awakenings (mean AWI = 5.58±4.37) and arousals (mean AI = 46.41±11.72). The mean AHI was 24.59±15.86 (range 6.40-54.90): 4/13 had AHI >5<15; 5/13 had an AHI of 15-30; and 4/13 had an AHI of >30 indicating mild to severe SDB in all subjects. The preponderance of the breathing events were hypopneas (mean/hour 17.699±10.53) with other events including obstructive, central, and mixed apneas occurring with much less frequency. Subjects experienced frequent oxygen desaturations (mean ODI 16.54±10.95) and mean percent TST with SaO2<90% was 7.31±14.23 (range 0 - 53.10). The AHI was associated with more time in NREM stage 1 sleep (r=.555, p=.049), lower sleep efficiency (r=-.649,p=.016), and more frequent awakenings (r=.802,p=.001) and arousals (r=.703,p=.007). Likewise, the ODI was positively associated with both awakenings (r=.813,p=.001) and arousals (r=.577,p=.039).

Conclusion: These preliminary data indicate that SDB may be prevalent in NSCLC and may contribute to disturbing sleep in this population. As we enroll additional subjects we will be able to analyze the factors associated with SDB in order to formulate appropriate treatments to improve sleep and patient outcomes.

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EXCESSIVE DAYTIME SLEEPINESS IN OVERLAP SYNDROME

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Introduction: Excessive daytime sleepiness (EDS) is one of the most prominent symptoms in obstructive sleep apnea (OSA). There are some suggesting factors determining EDS like sleep fragmentation, hypoxia, etc. As a similar symptom but different clinical findings to OSA, this study has investigated the difference in EDS in patients with OSA as well as chronic obstructive pulmonary disease (COPD) (overlap syndrome).

Methods: Forty one patients diagnosed with overlap syndrome who had more than 5.5 h total sleep time (TST) during 8 h of nocturnal polygraphic recordings, were included in the study. Patients were divided into two groups according to partial arterial carbon dioxide (PaCO2) level. Patients who had PaCO2 above 45mmHg consisted the hypercapnic group while the patients of whose PaCO2 below 45mmHg consisted the normocapnic group. Demographical data, pulmonary function tests, body mass index, polysomnographical data, and data about daytime sleepiness, including Epworth sleepiness scale (ESS) were evaluated. For the statistical analysis, student t- test and Fisher's exact test were used and $p< 0.05$ was taken as a statistical significant value.

Results: There were 41 patients diagnosed as overlap syndrome (age: 35-77 years; 80 % male, BMI mean: 36±7). There were 16 patients in hypercapnic group (39%) while remaining 25 patients were normocapnic (61%). ESS was found to be above 10 in all hypercapnic patients (100%) but only in 9 of 25 normocapnic patients (36%), ($p<0.001$). The mean REM % was significantly shorter in hypercapnic group (10.15±6.25) than in normocapnic group (15.80± 7.78), $p<0.01$. Nocturnal desaturation level did not show any statistical differences between two groups. All the other parameters were similar in both groups.

Conclusion: Excessive daytime sleepiness is more prominent in hypercapnic group in overlap syndrome. In overlap syndrome, hypercapnia is more prominent factor determining daytime sleepiness than other nocturnal parameters.

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TUMOR NECROSIS FACTOR-ALPHA IN ACUTE LYMPHOCYTIC LEUKEMIA (ALL) PATIENTS WITH DISTURBED SLEEP AND FATIGUE

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Introduction: Pediatric oncology patients have rated disrupted sleep and fatigue as two of the most distressing symptoms related to their illness and treatment. Sleep efficiency in pediatric oncology patients is poor during treatment with an average of 84% in ALL patients in home environment and 72% in hospitalized patients. Clinical researchers have proposed that a shared biological mechanism such as a cytokine-neuroimmunologic model involving pro-inflammatory cytokine, TNFα, may explain these debilitating symptoms of cancer/cancer-related treatment. We report here the relationship between TNFα and sleep/fatigue in 88 pediatric oncology patients.
Methods: A multi-institutional prospective study by Hinds et al. measured sleep and fatigue of 100 children and adolescents. Patients wore an actigraph during two consecutive 5-day periods with fatigue and sleep measurements on Days 2 and 5 of each period (Fatigue Scale-Child/Adolescent/Parent and sleep diaries). In a secondary analysis, genotyping for TNFα(-308G/A) polymorphism was completed on 88 patients who had with total actigraphy data. Multiple regression models were used to study the associations between sleep/fatigue variables and TNFα after controlling for patient characteristics which were significantly correlated with sleep/fatigue.
Results: 88 children analyzed with mean age 9.24 ± 3.23 years (range, 5.03-18.14). At significance level 0.05, the TNFα gene is significantly associated with the number of nocturnal awakenings in week 2. Patients with TNFα genotype AA had significantly more awakenings than patients with other TNFα genotypes (17.84 awakenings in A/A vs 13.11 in A/G or G/G p=0.0074). Patients with TNFα genotype A/A had significantly longer WASO than patients with TNFα genotype G/A (102.79 minutes in A/A versus 64.85 in G/A p=0.0205). No relationship with fatigue was observed.
Conclusion: Patients with pro-inflammatory polymorphism TNFα demonstrate disturbed sleep by increased WASO and nocturnal awakenings. This indicates a role of TNFα(-308A>G) in cancer treatment- related disturbances in sleep. This is the first study to find a relationship between cytokine polymorphisms and sleep disturbance in pediatric oncology patients.
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VALIDATION OF OBSTRUCTIVE SLEEP APNEA SCREENING OF PATIENTS IN AN ACADEMIC WOUND CENTER

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Introduction: Obstructive Sleep Apnea (OSA) is associated with cardiovascular consequences that may impede wound healing. We evaluated the prevalence and impact of OSA in patients with chronic non-healing wounds.
Methods: Consecutive unscreened patients of the OSU Comprehensive Wound Center completed a surveillance questionnaire consisting of two validated tools (Berlin Questionnaire and Epworth Sleepiness Scale-ESS). Also, ambulatory sleep studies (Stardust®Respironics, Murrysville, PA) were performed on consecutive wound clinic patients on one day of the week at the Wound Center (a period of two months is reported).
Results: Two hundred and one consecutive patients of the wound center completed the survey. Patients were 52% female, age 54±15, and BMI 33±9 kg/cm2. Of the 201 patients, 26 patients (13%) were already diagnosed with OSA. Ninety nine patients (99/201) 49% had positive Berlin questionnaire consistent with high risk for OSA, and 41 (46%) had pathological sleepiness (ESS >10). Twelve patients had successful recordings from the portable devices. AHI was 11 +/-7 events/hour. Five patients (42%) had an apnea hypopnea index > 15. The correlation coefficient between wound age at enrollment and number of individuals with high risk status for OSA was 0.96. The prevalence of OSA risk was higher in patients with older (>6 months) wounds at 56% than patients with newer wounds (<1 month) at 42%.
Conclusion: Patients with chronic non-healing wounds are at high risk for having OSA compared to the general population. The prevalence of high risk status for OSA was 49%. Only thirty percent of potential patients with OSA were already diagnosed. Similar prevalence (42%) is validated so far with ambulatory sleep studies. There was a correlation between risk status for OSA and the duration of non-healing wound.

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NEURAL INJURY IN DIABETIC VERSUS NON-DIABETIC OBSTRUCTIVE SLEEP APNEA PATIENTS: A PILOT STUDY

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Introduction: Both obstructive sleep apnea (OSA) and Type II diabetic patients show a range of tissue injury in multiple brain areas, and a high proportion of diabetic patients show OSA. We therefore assessed whether the presence of diabetes in OSA exacerbated neural injury relative to the sleep disorder alone.
Methods: We examined OSA patients with and without Type II diabetes by T2 relaxation time, an MRI-derived measure sensitive to neural injury. Four OSA patients with Type II diabetes and 12 age/gender/severity matched OSA subjects were evaluated with a Siemens 3 Tesla MRI scanner. We performed whole-brain voxel-based analyses with SPM5 software, and assessed group differences with ANCOVA ($p < 0.001$, age and AHI as covariates). Areas of significant difference were further assessed by region-of-interest comparisons.
Results: The four diabetic OSA subjects showed neural injury, i.e., increased T2 relaxation time, relative to non-diabetic OSA patients. Region-of-interest measurements showed minimal overlap in the distribution of T2 relaxation time values between the two groups, with three of the diabetic subjects showing T2 levels higher than all controls in most affected areas. Affected regions included the bilateral anterior insula (important for sympathetic regulation), anterior cingulate, left posterior cingulum, and bilateral hippocampus, as well as white matter adjacent to those structures. No regions showed lesser injury (i.e., lower T2 relation time) in the diabetic group.
Conclusion: The previously-demonstrated neural injury in OSA patients is exacerbated in the presence of diabetes. While the present sample of diabetics is small, the findings are strengthened by 1) matching of non-diabetic OSA subjects by age and severity, 2) use of a relatively conservative statistical threshold, and 3) the minimal overlap of the two groups' distributions of the measure of injury (T2 relaxation time). The additional injury in diabetic OSA patients likely impairs central nervous system control of autonomic regulation, and may contribute to mood and cognitive deficits additional to those already seen in the sleep disorder.
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SNORING, OBESITY, AND GESTATIONAL HYPERTENSION IN THE LAST TRIMESTER OF PREGNANCY

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Introduction: Obesity during pregnancy increases the risk of maternal complications. Emerging data suggest that habitual snoring, a cardinal symptom of sleep-disordered breathing (SDB), during pregnancy is also associated with adverse outcomes. The goal of this study is to determine the relationship between habitual snoring, obesity, and gestational hypertension.
Methods: Women with singleton pregnancies were invited in their last trimester to answer several sleep-related questionnaires. Risk for SDB was defined as the presence of habitual snoring (≥3-4 nights/week). Pre-pregnancy BMI was used to classify subjects as underweight (BMI<20); normal weight (BMI 20-24.9); overweight (BMI 25-29.9) and obese (BMI >30). Subjects were further grouped according to whether their absolute weight gain exceeded Institute of Medicine (IOM) recommendations, which are 28-40lbs for underweight women, 25-35lbs for normal weight women, 15-25lbs for overweight women, and ≤15lbs for obese women. Medical records were reviewed after delivery to obtain information on gestational hypertension.
Results: Of 363 subjects, 90 (25%) were obese. Weight gain in excess of IOM recommendations was an independent predictor of SDB risk (OR: 1.9 [1.2-3.1]) after adjusting for pre-pregnancy BMI, maternal age, and race. Compared to non-obese women, obese women were more likely to be at risk for SDB (61% vs. 27%, $p<0.002$) and gestational hypertension (30% vs. 14%, $p<0.001$). In a logistic regression, after adjusting for confounders including pre-pregnancy BMI and excess pounds gained, SDB risk remained an independent predictor of gestational hypertension(OR:2.0[95% CI 1.11-3.6]). A significant interaction was observed between obesity and SDB risk for gestational hypertension (OR:4.1 [2.1-7.8]; $p<0.001$).
Conclusion: Weight gain greater than IOM recommendations during pregnancy independently increases risk for SDB, as reflected by habitual snoring. These data suggest that SDB may help explain why obesity and excess weight gain promote gestational hypertension.
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HOT FLASHES IN WOMEN WITH RHEUMATOID ARTHRITIS AND EFFECTS ON SLEEP DISTURBANCES

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Introduction: Much has been written about the influence of hot flashes (HF) on sleep in healthy postmenopausal women; however, little has been reported about the effects of HF on sleep disturbances in women with rheumatoid arthritis (RA). Therefore, the purpose of this study was to examine the effects of self-reported hot flashes and other factors on sleep disturbances (measured by wrist actigraphy) in postmenopausal women with RA.
Methods: Measures included: experience of HF; Arthritis Helplessness Index (AHI); Positive Affect-Negative Affect Scale (NA); Stress Numeric Rating Scale (0-10); Short Form McGill Pain Questionnaire; wrist actigraphy: sleep efficiency, sleep onset latency, and number of awakenings.
Results: The 60 women on average were 59.4 (SD 7.7) years, with 13.5 (2.8) years of education, 10.7 (11.3) years RA duration, and 13.6 (10.9) years since menopause. Hot flashes (HF) were present in 50. HF currently last 3.3 minutes and lasted 10.1 minutes in the past. The bothersome impact of current HF (0-10 scale) was 4.4, with a higher level of bother in the past, 6.7. About 65% rated HF as better than in the past, however 12% rated HF as worse. Using multiple regression, sleep efficiency (sleep time / time-in-bed) was significantly predicted by arthritis helplessness, stress, pain, and negative affect (trend), with HF not a significant predictor. Sleep onset latency was significantly predicted by arthritis helplessness, stress, and pain, with HF and negative affect not significant predictors. The only significant predictor of number of awakenings was HF.
Conclusion: Women with RA experienced HF that were greater and more bothersome in the past compared to the present. Sleep disturbances were present. HF only significantly predicted number of awakenings, but AHI, stress, and pain predicted other sleep disturbances.
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ASSESSMENT OF SLEEP COMPLAINTS IN PEDIATRIC ONCOLOGY PATIENTS

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Introduction: Adult oncology patients have been found to have significant sleep disturbance. Only recently have sleep and fatigue in pediatric oncology patients begun to receive attention. The majority of these studies, however, have focused on children with acute lymphoblastic leukemia.
Methods: The goal of this pilot study was to determine the prevalence of sleep problems in 3 groups of pediatric oncology patients--solid tumor, hematologic malignancies, and brain tumors, ages 2 to 18, by parent report within 14 days of diagnosis. Parents were administered the Children's Sleep Hygiene Scale (CSHS) and the Childhood Cancer Fatigue Scale. Children ages 8 - 18 completed the Children's Report of Sleep Patterns.
Results: Thus far, 14 children (50% male; mean age = 10.1) have been recruited. Diagnoses include leukemia (n = 9), solid tumors (n = 5), and brain tumor (n = 1). The children self-reported a mean bedtime the previous night of 10:30 pm with a mean rise time of 8:45 am. Children reported an average of a 1.8 hour delay in bedtime and a 4 hour delay in rise time from weekdays to weekends. Parental report on the CSHS indicated a total sleep hygiene score of 4.39, indicating generally good sleep hygiene in this small sample. Parents reported a relatively high degree of fatigue with 50% reporting their children were very tired at some point in the day over the previous week.
Conclusion: These preliminary data have revealed parentally reported high level of fatigue with adequate sleep hygiene in newly diagnosed pediatric oncology patients. The children self-reported significant delay in weekday to weekend bedtime and rise time, particularly with sleeping late on the weekends, which may be related to the parent-reported fatigue in this primarily pre-adolescent sample. These preliminary data present potential for intervening to improve pediatric oncology patients' sleep and fatigue early in their treatment.

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UNIQUE CONTRIBUTION OF CHRONIC PAIN TO FATIGUE

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Introduction: Fatigue is a common complaint in chronic pain patients, in addition to other physical illnesses, depressed mood, and sleep disturbance. However, previous research has rarely examined the relative contribution of pain to fatigue when controlling for these confounding variables.

Methods: Random-digit dialing was used to recruit a stratified sample from Shelby County, Tennessee. Participants completed self-report measures of health, mood, daytime functioning, and two-weeks of sleep diaries. The present study performed a hierarchical regression analysis predicting Fatigue Severity Scale scores on data from 771 participants (381 men and 390 women; mean age= 53.8 years). Step one entered total number of health problems other than pain, step two entered Beck Depression Inventory (BDI) scores, and step three entered all seven sleep diary variables using forward stepwise regression procedures. The last step entered the presence/absence of chronic pain.

Results: Health problems in step one accounted for a significant amount of variance (R^2=.07, p< .001) and BDI scores in step two significantly increased the variance explained (ΔR^2=.17, p< .001). The forward stepwise selection procedure in step three entered nap time (ΔR^2=.008, p< .01), followed by sleep quality (ΔR^2=.006, p= .01), and total sleep time (ΔR^2=.01, p< .01). Importantly, adding chronic pain on the last step significantly increased variance explained by the model (ΔR^2=.007, p< .01). The presence of chronic pain was related to more severe fatigue, β =.09, t(764)= 2.75, p< .01. Cumulatively, the final model accounted for 26.9% variance in fatigue severity (F [6,764] = 46.84, p< .001).

Conclusion: Chronic pain appears to make a unique contribution to fatigue, above and beyond the effects of other health problems, depression, and sleep. Future studies should employ prospective designs to investigate this possible etiological relationship.

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SLEEP QUALITY AND INTERSTITIAL CYSTITIS SYMPTOMS IN WOMEN

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Introduction: Interstitial cystitis (IC) is a chronic painful condition of the bladder lining with no known etiology or cure, affecting 1.2 million women in the US. In clinical practice, sleep complaints are common however; no studies have documented this relationship. We present the first data describing the relationship between subjective sleep quality and IC symptoms in women.

Methods: Female subjects with IC (N=261) were recruited through the Interstitial Cystitis Association website. Subjects completed a web-based questionnaire which included demographic variables, the number of years with IC diagnosis, and menopause status. Depressive symptoms were measured using a single question. The O'Leary Sant IC Symptom and Problem Index and the Pittsburgh Sleep Quality Index were completed.

Results: Respondents were female, 94% Caucasian median age 46-50, 44% were menstruating and 56% post menopausal. Mean global PSQI was 13.4 with 100% scoring above 5. The 3 predictors depression, symptom severity, and symptom impact, moderately and significantly correlated with PSQI global score (r =0.37, 0.21, 0.84 respectively, all p < 0.001) The linear multiple regression analysis revealed that the overall model with the set of independent variables (symptom severity, symptom impact, and depression) were significant predictors of sleep quality when controlling for age and menopausal status (F (5, 243) = 32.93, p<0.001). Together, the predictors accounted for 39% of the variance in sleep quality scores (p<0.001). When examined separately, symptom impact and depression made significant contribution to the estimation of sleep quality (p<0.001). The specific factor with the largest relationship to sleep quality is symptom impact (β=0.39, p<0.001) and depression (β =0.21, p<0.001). Symptom severity was not a significant predictor (p=0.15) of sleep quality.

Conclusion: Women with IC have demonstrated poor sleep quality related to depression and their symptoms. Clinical interventions to improve depression and symptoms may help improve sleep quality. Further research is needed.

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SLEEP MISPERCEPTION AMONG OLDER ADULTS WITH PAIN, DEPRESSION, OR SLEEP COMPLAINTS

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Introduction: Insomnia patients commonly misperceive sleep as wakefulness. Compared to objective measures, they report protracted sleep onset latency (SOL) and wake after sleep onset (WASO). Sleep misperceptions (SM) may result from simultaneously high activation of sleep and arousal systems of the brain allowing self-awareness to occur during sleep. It is hypothesized health conditions associated with physiological and cognitive hyperarousal, expressly pain and depression complaints, will relate to greater SM, even in the absence of sleep complaint.
Methods: 103 community dwelling older adults (M_{age}=72.81, SD=7.12) wore Actiwatch-L® (24hrs/day/2 weeks) and concurrently completed sleep diaries. Daily actigraphically-measured SOL and WASO were subtracted from respective diary measures to calculate average SM that occurred at SOL (SOL_{sm}) and at WASO ($WASO_{sm}$). A 2 (sleep complaint/no sleep complaint) x 2 (pain complaint/no pain complain) MANCOVA was employed. Number of chronic health conditions, number of medications, and BDI-II scores were co-varied. SOL_{sm} and $WASO_{sm}$ were the dependent variables.
Results: The omnibus test was significant for depression [Wilks'Λ=.85,F(2,96)=8.75,p<.001,η^2=.15], pain [Wilks'Λ=.94,F(2,96)=3.27, p<.01,η^2=.06], and sleep [Wilks'Λ=.90,F(2.96)=5.22,p<.05,η^2=.10] complaint. Follow-up ANOVAs investigating SOLsm revealed a significant main effect for depression [F(1,97)=10.13,p<.01,η^2=.10] and sleep complaint [F(1,97)=6.00,p=.02,η^2=.06]; Follow-ANOVAs investigating $WASO_{sm}$ revealed a significant main effect for depression [F(1,8.17,p<.01,η^2=.08], sleep [F(1,97)=4.91,p<.05,η^2=.05], and pain [F(1,97)=5.55,p<.05,η^2=.05] complaint. For SOL and WASO, the presence of depression, sleep, or pain complaint was related to greater SM. There were no significant interactions or effects for number of health complaints or medications.
Conclusion: Results suggest that regardless of sleep complaint, pain and depression relate to SM. Hyperarousal during sleep that results in SM may induce a form of localized sleep deprivation in affective/executive areas of the brain leading to localized daytime dysfunctions. SM research may help explain the underlying mechanisms to a variety of health conditions that predispose to and emerge from insomnia. Potential treatment implications are considered. Additional research with greater control and diagnostic categories is warranted.
Support (optional): Intramural grants from the College of Liberal Arts and Sciences and the College of Nursing, University of Florida.

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COMPARISON OF PRE-SLEEP WAKING QEEG IN VETERANS WITH PTSD, ADULTS WITH PRIMARY INSOMNIA, AND GOOD SLEEPERS

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Introduction: Increased central nervous system arousal prior to sleep may contribute to sleep difficulties in patients with Posttraumatic Stress Disorder (PTSD) or Primary Insomnia (PI). Fast-frequency quantitative EEG (qEEG) activity (sigma: 12-16 Hz; beta: 16-32Hz) during waking EEG, a potential indicator of this arousal, was compared in patients with PTSD, PI, and Good Sleeper (GS). We hypothesized that both patients groups would show increased fast-frequency activity during evening wakefulness compared to GS. The relationships between qEEG measures, PSG sleep measures, and symptoms of PTSD, depression, and anxiety in the PTSD group were also explored.
Methods: Ten military veterans with PTSD (mean 37.6 ± 11.7 years old), 10 PI subjects (mean 35.3 ± 9. 7 years old) and 8 GSC (mean 40.1±22.8 years old) were included in this study. PI and GSC were free of medications, medical conditions, psychiatric disorders and other sleep disorders. Six of the 10 PTSD subjects were medication free. Automated and visual artifact rejection were conducted on 5-minute waking EEG samples recorded within 2 hours of participants' habitual bedtime using FFT. Non-parametric Kruskal-Wallis tests and Spearman's rho correlations were conducted.
Results: There was no significant group difference in absolute or relative power for sigma or beta activity bands. In PTSD subjects, absolute beta power during waking EEG was significantly and positively correlated with the severity of PTSD, depression, and anxiety symptoms were (all $p < 0.05$), but not with PSG sleep measures.
Conclusion: In this sample, PTSD and PI subjects did not show greater indices of EEG arousal during evening wakefulness compared to GS. Increased fast-frequency activity during pre-sleep wakefulness was positively associated clinical symptom severity in subjects with PTSD. Previously-described changes in qEEG during sleep in PTSD and PI may suggest a state-dependent form of electrophysiological arousal.
Support (optional): US Department of Defense (W81XWH-06-1-0257) and National Institutes of Health (RR 00052, RR 024153, MH24652).

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STABILIZING SLEEP AND DAILY ROUTINE IN VETERANS WITH COMORBID PTSD AND DEPRESSION: FOLLOW-UP OUTCOMES FOR COGNITIVE BEHAVIORAL SOCIAL RHYTHM THERAPY

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Introduction: Cognitive Behavioral Social Rhythm Therapy (CBSRT) is a 12-week skills-based group therapy designed to improve sleep and increase the frequency and regularity of daily habitual behaviors in veterans with Posttraumatic Stress Disorder (PTSD) and Major Depressive Disorder (MDD). CBSRT is designed to facilitate readjustment after a traumatic event by stabilizing social rhythms and improving sleep. We report outcomes for a two-year open CBSRT trial to improve sleep and social rhythms.
Methods: Twenty three veterans (*M* age = 55.25 years, *SD* = 9.84) with PTSD and MDD assessed by the Structured Clinical Interview for the DSM-IV have completed this pilot program. Pre- to post-treatment symptom scores were measured via actigraphy, Pittsburgh Sleep Quality Index (PSQI), Hamilton Depression Rating Scale (HDRS), and the Clinician Assessment of PTSD (CAPS).
Results: Mixed linear modeling analyses indicated improvements in (a) sleep (global PSQI scores, γ_{10} = -.18, *SE* = .06, *p* = .005; PSQI-Addendum scores γ_{10} = -.13, *SE* = .07, *p* < .05; PSQI sleep onset latency (SOL), γ_{10} = -2.95, *SE* = .64, *p* < .001; actiwatch SOL, γ_{10} = -1.55, *SE* = .77, *p* < .05), (b) depression (HDRS γ_{10} = -.59, *SE* = .13, *p* < .001), and (c) PTSD (CAPS γ_{10} = -2.65, *SE* = .29, *p* < .001). There was rebound in all symptom scores at 3-month follow-up, although not to pre-treatment levels. Attrition rate was 17%, which is lower than seen in exposure therapies for PTSD (~30%).
Conclusion: These data demonstrate that CBSRT is both feasible to administer and an effective treatment for sleep, depression, and PTSD symptoms. Regularization of daily routine may be particularly important for this population, as patients with PTSD/MDD have a tendency to avoid activities and isolate from others on a daily basis. A randomized controlled trial should be performed to confirm these findings.
Support (optional): American Sleep Medicine Foundation

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ALPHA-DELTA SLEEP IN MAJOR DEPRESSIVE DISORDER

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Introduction: Major depressive disorder (MDD) is often associated with difficulty falling/staying asleep and early morning awakenings. Polysomnogram (PSG) findings in MDD include short rapid eye movement (REM) latency, increase in REM sleep time, REM density, decreased slow wave sleep and sleep disruption. An EEG pattern of alpha intrusion in delta sleep (alpha-delta sleep) is noted in some subjects with MDD, similar to patients with rheumatologic/chronic pain patients. However, the exact prevalence of alpha-delta sleep in MDD is unknown.
Methods: Retrospective review of 150 PSGs of subjects ≥ 18 y.o. without a history of chronic pain or rheumatologic conditions were identified and divided into depressed (n=75) and non-depressed (n=75) based on clinical history. Subjects with co-morbid sleep disorders (sleep apnea, restless legs syndrome, Periodic limb movements disorder), significant medical disorders affecting sleep architecture were excluded. The polysomnographic data of interest, particularly the percent of slow wave sleep with alpha intrusion was collected.
Results: MDD compared to subjects with no depression had greater sleep efficiency (83.0±9.6; 78.1±8.2%), shorter REM latency (85.0±44.5; 189.9±25.6 min), lower stage N3 sleep (8.3±3.0; 13.5±6.2%), and greater REM density (24.7±7.0; 19.2±8.2%) and all of these were statistically significant ($p<0.01$). Most importantly, the prevalence of alpha-delta sleep was much higher in MDD compared to non-depressed subjects (23.4±24.2 %; 2.33±6.7%, $p<0.01$). Within MDD group, logistic regression analysis showed that only age and selective serotonin reuptake inhibitors (SSRIs) use, inversely correlated with the prevalence of alpha-delta sleep ($p<0.01$); Interestingly, history of co-morbid insomnia or other co-morbid psychiatric disorders did not significantly effect on the prevalence of alpha-delta sleep.
Conclusion: Patients with MDD have a higher prevalence of alpha-delta sleep. Within MDD patients, it appears that SSRIs and increasing age decrease alpha-delta sleep. The higher prevalence of alpha-delta sleep in MDD may account for the non-restorative sleep, so often seen in these patients.

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ACUTE SLEEP DEPRIVATION AND PANIC VULNERABILITY: EXAMINING THE ROLE OF ANXIETY SENSITIVITY

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Introduction: The effects of sleep deprivation on panic vulnerability were examined. Relative elevations in Anxiety Sensitivity - Mental Incapacitation Concerns (AS-MI), defined as the fear of the mental consequences of anxiety (e.g., difficulty concentrating), was expected to increase panic-relevant reactivity potentiated by sleep deprivation because persons higher in AS-MI would be more anxious in the presence of psychological consequences of sleep deprivation.
Methods: 102 participants were randomly assigned to an experimental (24-hour sleep deprivation) or control (full sleep) group. The day before and after the experimental manipulation, participants completed a well-established 5-minute administration of 10% carbon dioxide-enriched air. Anxiety and panic symptoms elicited by the challenge, which predict panic onset, were measured throughout.
Results: No group differences in day 1 responding emerged. In terms of day 2, the experimental group reported greater pre-challenge anxiety than controls ($F = 4.06$, $p < .01$). The experimental group also reported more intense cognitive panic symptoms ($F = 2.85$, $p < .01$). An interaction ($F = 2.22$, $p < .05$) suggested group was related to cognitive panic symptoms among participants lower in AS-MI ($t = 2.82$, $p < .05$) but not among participants endorsing higher AS-MI ($t = .54$, ns). The experimental group also reported more intense physical panic symptoms ($t = 2.15$, $p < .05$). An interaction ($F = 2.23$, $p < .05$) suggested group was related to physical panic symptoms among participants lower in AS-MI ($t = 2.43$, $p < .05$) but not among those higher in AS-MI ($t = .02$, ns).
Conclusion: Sleep deprivation increased panic-relevant responding to a challenge that marks panic vulnerability and AS-MI moderated this relation. Sleep deprivation increased panic vulnerability among panic resilient people to a level comparable to people with elevated AS-MI, which is a well-established risk factor for panic onset.

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PHASE RELATIONSHIPS BETWEEN CORE BODY TEMPERATURE, MELATONIN, AND SLEEP ARE ASSOCIATED WITH DEPRESSION SEVERITY: PRELIMINARY EVIDENCE FOR CIRCADIAN MISALIGNMENT IN NON-SEASONAL DEPRESSION

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Introduction: Both theory (e.g., the internal coincidence model) and empirical evidence link misalignment between the timing of sleep and the endogenous circadian pacemaker to depressive symptomatology in mood disorders. However, less attention has been paid to the respective phase angles between circadian processes other than sleep. We sought to determine if the respective phase angles between dim light melatonin onset (DLMO), core body temperature (CBT) minimum, and mid-sleep differed between healthy controls and individuals with major depressive disorder (MDD), and if these phase angles correlated with depression severity.
Methods: 13 unmedicated adults with MDD, and 13 healthy controls completed two weeks of sleep diaries. Overnight studies were conducted between 1900 and one hour after wake-up time under dim light conditions, and included polysomnography, CBT measurement (every 30 sec via rectal thermistor) and blood sampling for melatonin measurement (every 15 min). CBT minimum was visually-determined. Plasma melatonin concentrations were measured via RIA; DLMOs were assessed using a 10 pg/ml threshold. Three phase angles were calculated between DLMO, the CBT minimum, and PSG-based mid-sleep. Finally, severity of depression was assessed using the 17-item Hamilton Depression Rating Scale (HAM-D).
Results: Only the interval between midsleep and CBTmin was longer in the depressed group relative to the control group ($t(24)=1.69$, $p=.10$). However, the two groups showed at least trend-level differences in the within-group variability of all three phase angles ($F=7.63$, $p=.01$; $F=3.60$, $p=.07$; $F=3.10$, $p=.09$), with greater variability among the depressed individuals. Finally, the depressed group's CBTmin-midsleep and DLMO-CBTmin phase angles were positively correlated with HAM-D scores ($r=.65$, $p<.05$; $r=.58$, $p=.10$).
Conclusion: Misalignment between sleep, CBT, and/or melatonin may be linked to depressive symptomatology in non-seasonal depression. Although the findings are preliminary, phase-angle heterogeneity may indicate the presence of multiple depressive phenotypes.
Support (optional): This research was supported by grant RO1 MH24652 from the National Institutes of Health.

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ACTIGRAPHIC COMPARISON OF SLEEP IN COMORBID POSTTRAUMATIC STRESS DISORDER AND DEPRESSION VERSUS DEPRESSION ALONE

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Introduction: Individuals with both Posttraumatic Stress Disorder (PTSD) and Major Depressive Disorder (MDD) have more severe depression and worse treatment outcomes. Few studies have examined sleep in individuals with comorbid PTSD/MDD versus MDD alone and none to our knowledge have employed actigraphy. We hypothesized that patients with PTSD/MDD would have more severe sleep disturbances than patients with MDD alone or normal controls (NC) as determined by actigraphy.
Methods: Actigraphic data from a total of 102 participants were examined (M age = 46.5 years, SD = 12.7 years). Data were separated into 3 groups: (a) 31 patients with PTSD/MDD, (b) 32 patients with MDD alone, and (c) 39 normal controls. Movement data were examined over an average of 5.2 nights (SD = 1.6 nights) using two different actigraphic systems. One-way ANOVAs were conducted to assess differences in sleep between groups. Significant differences in the omnibus analyses were followed-up by Bonferroni contrast comparisons.
Results: On measures of sleep continuity, significant differences were seen on the following variables: wake after sleep onset (WASO, $F = 11.17$, $p < .05$, MDD > NC, no differences with PTSD/MDD), mean duration of awakenings ($F = 0.45$, $p < .05$, MDD > NC > PTSD/MDD), and number of awakenings ($F = 20.02$, $p < .05$, PTSD/MDD > MDD, PTSD/MDD > NC). On measures of sleep quantity, there were no differences between the PTSD/MDD group and the MDD group on sleep percent ($F = 43.71$, $p < .05$, NC > PTSD/MDD, NC > MDD) or wake percent ($F = 9.74$, $p < .05$, MDD > NC, PTSD/MDD > NC), although the PTSD/MDD group the lowest total sleep time (TST, $F = 9.67$, $p < .05$, MDD > PTSD/MDD, NC > PTSD/MDD). The PTSD/MDD group had the lowest sleep efficiency (SE, $F = 24.00$, $p < .05$, NC > MDD > PTSD/MDD).
Conclusion: Both subjects with comorbid PTSD/MDD and MDD alone experienced more sleep disturbances than controls. The PTSD/MDD group had lower TST and SE than the MDD group. Additionally, the PTSD/MDD group had more frequent but shorter awakenings than the MDD group, although there were no differences in WASO between the two groups. This finding is consistent with previous research indicating that patients with PTSD may overestimate WASO.
Support (optional): American Sleep Medicine Foundation and NIMH NRSA 1F31MH064255

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THE IMPACT OF ALCOHOLISM IN MEN AND WOMEN ON POLYSOMNOGRAPHY AND SLEEP EEG

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Introduction: Sleep is known to be subjectively poor in detoxified alcoholics, however few polysomnography studies have been conducted and these have largely involved men. Results have typically shown some evidence of an exacerbation of the normal age-related changes in sleep such as increased wakefulness, decreased REM sleep and decreased slow wave sleep (SWS). We have recently reported decreased evoked delta activity in alcoholic men and women that is significant only over frontal scalp regions. Few studies have evaluated the effect of alcoholism on the spectral properties of sleep EEG in humans. We tested the hypothesis that SWS would be lower in alcoholics and that quantitative delta EEG would be diminished selectively at frontal sites.
Methods: Eighty four subjects completed the study, 27 abstinent long-term alcoholic (A) men (aged 49.3 ±7.6 y), 15 A women (aged 47.7 ± 9.6 y), 19 control (C) men (aged 50.5 ± 9.9 y) and 23 C women (aged 51.0 ± 9.8 y). Estimated lifetime alcohol consumption was 54.4 ± 84.7 kg for C and 1294.7 ± 784.8 Kg for A. All night recordings using 6 midline electrodes (Fz, FCz, Cz, CPz, Pz, and O2) were conducted. Sleep stage determination was made using standard criteria. EEG data from non REM sleep were subjected to power spectral analysis using PASS PLUS EEG software.
Results: Alcoholics had significantly less SWS ($p = 0.002$), more REM sleep ($p = 0.012$) and more stage 1 sleep ($p=0.04$) than controls, with no significant diagnosis by sex interactions. Women had better sleep efficiency ($p = 0.033$) and fewer in-bed wake periods ($p < 0.001$) than men and tended to have a higher percentage of SWS ($p = 0.066$). WASO increased ($p = 0.02$) and total sleep time ($p = 0.035$), SWS% ($p = 0.002$) and REM sleep% ($p = 0.01$) decreased with age. Delta power was lower in alcoholics ($p=0.048$) with a significant diagnosis by site interaction ($p = 0.001$) with the group difference appearing largest at frontal sites. Women had higher delta power than men ($p = 0.012$) with no diagnosis by sex interaction. Delta power decreased significantly with age($p = 0.002$).
Conclusion: The data support previous results of a decrease in SWS in alcoholics and indicate that it is equally prevalent in alcoholic men and women. Delta power was significantly impacted by alcoholism at frontal sites in both men and women, despite women having overall higher delta levels.
Support (optional): AA14211 from the National Institute on Alcoholism and Alcohol Abuse

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THE PREVALENCE OF OBSTRUCTIVE SLEEP APNEA IN HOSPITALIZED PSYCHIATRIC PATIENTS RECEIVING ELECTROCONVULSIVE THERAPY

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Introduction: Recent studies suggest the importance of recognizing obstructive sleep apnea (OSA) in patients requiring anesthesia. OSA patients also have a high prevalence of major depressive disorder (MDD). Electroconvulsive therapy (ECT) is a treatment for MDD, uses anesthesia, and may therefore increase the risk of morbidity and mortality in OSA patients. Hospitalized patients receiving ECT were evaluated to determine OSA prevalence. Additionally anesthesia records of all ECT patients between 8/1/2002 and 7/31/2007 were examined for OSA prevalence.
Methods: Following IRB approval, hospitalized patients receiving ECT were asked to complete the Berlin questionnaire (BQ) and undergo one night of continuous nocturnal oximetry. An abnormal oxygen desaturation index (ODI) was > 5/hour. ECT anesthesia records were reviewed for OSA diagnoses.
Results: Data from 27 patients was analyzed (9 males and 18 females; median age=51). Thirty percent (N=8) were "high risk" on the BQ and had an average ODI of 25.5±18.1. Forty-four percent (N=12) had an average ODI of 16.1±10.4 but were "low risk" on the BQ. Three patients reported a previous diagnosis of OSA, but were all untreated. The prevalence of OSA in the ECT anesthesia records was 18% for men and 9.7% for women (N=559 patients, mean age=49.8).
Conclusion: Sixty-three percent (N=17) had findings suggestive for OSA without a prior diagnosis, indicating that there may be a substantial number of undiagnosed OSA in this population, especially when compared to the prevalence of OSA in the general population (2-9%).

The cause for the higher prevalence is uncertain, but implicates the relationship between mood and OSA. For instance, do patients with MDD receiving ECT have more refractory forms of MDD due to untreated OSA? Furthermore, do ECT patients with OSA have increased morbidity and mortality due to OSA? This strong association may be helpful when evaluating patients prior to ECT.

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POSTPARTUM SLEEP AND MOOD IN MULTIPAROUS AND NULLIPAROUS WOMEN

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Introduction: Previous findings have suggested an association between women's poor subjective sleep during and immediately after pregnancy, and postpartum blues (PPB) symptoms. This study further explored the roles of objectively and subjectively measured sleep in PPB as a function of parity.
Methods: During the third trimester (Time-1), 24 multiparous (MP) and 20 nulliparous (NP) completed questionnaires on mood and sleep; among them, 23 MP and 18 NP wore actigraphs for 7 days. In the second part of the study, 16MP and 12 NP wore actigraphs during the first postpartum week (Time-2), and 21 MP and 16 NP completed the same mood and sleep questionnaires.
Results: For MP mood improved significantly after delivery across all scales, whereas for NP mood significantly worsened on some scales and showed no improvement on others. After delivery, both MP and NP had significantly poorer objective and subjective nighttime sleep and they increased their daytime naps. The deterioration in objective nighttime sleep and the increase in daytime nap numbers were significantly greater in NP than in MP. When regression analyses were applied to MP and NP combined, or to NP alone, poorer subjective but not objective sleep measures were associated with poorer mood at Time-2. However, regression analyses in MP revealed three significant predicting models for postpartum mood: Time-1 objective nighttime sleep, Time-2 subjective nighttime sleep, and sleep-related daytime dysfunction at both times.
Conclusion: Subjective perception of poor sleep as a reflection of women's coping and adjustment is a critical factor in postpartum mental health for both MP and NP. Objectively disrupted sleep throughout late pregnancy may predispose healthy MP to postpartum mood disturbances. However, the role of objective sleep disruption among NP is less clear and needs to be examined in a larger sample as non-sleep related factors might be particularly relevant in this sub-group.
Support (optional): Funded by the School of Behavioural Science, University of Melbourne, Australia. Participants recruited through the Antenatal Clinic, Northern Hospital, Australia.

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EARLIER PARENTAL MANDATED BEDTIMES FOR ADOLESCENTS AS A PROTECTIVE FACTOR AGAINST DEPRESSION AND SUICIDAL IDEATION AS MEDIATED BY SLEEP DURATION

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Introduction: The relationship between short sleep duration and depression has been theorized to be bidirectional. Experimental partial sleep restriction has been shown to negatively affect mood. Short sleep duration has been shown to precede depression in epidemiological studies, but this finding could be explained by short sleep duration being a prodromal symptom of depression. An examination of the relationship between parental mandated bedtimes and depression represents a natural experiment to address the question of bidirectionality between short sleep duration and depression. The presence of depression in an adolescent can affect their choice of bedtime, but it is unlikely to affect their parent's choice of a mandated bedtime. Parental mandated bedtimes establish a stable upper limit on bedtimes that can directly affect sleep duration.
Methods: Multivariate hierarchical logistic regression analyses of National Longitudinal Study of Adolescent Health (ADD Health) data (n= 15,659) to explore whether later parental mandated bedtimes are associated with depression and suicidal ideation and whether sleep duration mediates these relationships.
Results: A total of 1,143 (7.3%) adolescent subjects suffered from depression and 2,038 (13.0%) had suicidal ideation. Adolescents with parental mandated bedtimes of 12:00/Midnight or after were 25% more likely to suffer from depression (OR = 1.25, 95% CI 1.05-1.50) and 20% more likely to have suicidal ideation (OR = 1.20, 95% CI 1.02-1.41) in comparison to adolescents with parental mandated bedtimes of 10:00 PM or earlier after controlling for covariates. Consistent with sleep duration acting as a mediator, the inclusion of sleep duration in the multivariate models appreciably attenuated the associations for depression (OR = 1.07, 95% CI 0.88-1.30) and suicidal ideation (OR = 1.09, 95% CI 0.91-1.29).
Conclusion: We found an association between later parental mandated bedtimes and increased risk for adolescent depression and suicidal ideation. Our results are consistent with short sleep duration acting as a mediator in this relationship and functioning as a risk factor for depression and suicidal ideation. Earlier parental mandated bedtimes could therefore be protective against adolescent depression and suicidal ideation by lengthening sleep duration.
Support (optional): Financial support for this study was provided by a grant from the Robert Wood Johnson Health and Society Scholars Program at Columbia University.

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RESTLESS SYMPTOMS AT NIGHT ARE ASSOCIATED WITH ATTENTION DEFICIT SYMPTOMS DURING THE DAY IN CHILDREN OF ALCOHOLICS

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Introduction: Sleep disturbance in children can be associated with behavioral, psychological, and health consequences in adulthood. Parental ratings of sleep problems in children have predicted behavioral and emotional problems and early onset of substance use during adolescence. The purpose of this study was to measure subjective and objective sleep and their behavioral consequences in children of alcoholics (COAs) and non-alcoholics (non-COAs).
Methods: 36 children recruited from the community (9 females; 26 COAs), ages 8-12 (mean=10.4 +/-1) were studied. Children wore an actigraph for one week to measure nocturnal activity and total sleep time (TST). The Pediatric Sleep Questionnaire (PSQ) was completed by a parent to measure nocturnal restlessness and the Child Behavior Checklist (CBCL) was completed by child's parents and teacher to measure daytime behaviors.
Results: Chi-square analysis revealed more COAs were described as restless sleepers (35% vs. 8%, p=.09). For COAs, regression analyses showed nocturnal activity predicted thought, listening, and fidgeting problems (all $p<.05$). TST in COAs predicted teacher-rated thought problems and impulsivity ($p<.05$). Restlessness (PSQ) predicted externalizing behavior, aggressive behavior, thought and teacher-rated attention problems (all $p<.05$). For non-COAs, nocturnal activity predicted daytime problems with attention, thought, and fidgeting (all $p<.05$). TST predicted thought problems, impulsivity, teacher-reported thought problems, somatic complaints, and "other" problems. Restlessness predicted aggressiveness, distractibility, fidgeting, and "on the go", teacher-reported externalizing, aggression, and thought problems.
Conclusion: Children with motor restlessness at night and decreased sleep time appear to be at more risk for behavioral, mood, and cognitive

problems as reported by both parents and teachers. COAs were more likely than non-COAs to be described by parents as restless sleepers.
Support (optional): Grant to RA Zucker from the National Institute on Alcohol Abuse and Alcoholism R37 AA07065.

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RANDOMIZED CONTROLLED TRIAL OF IMAGERY REHEARSAL FOR POSTTRAUMATIC NIGHTMARES IN VIETNAM VETERANS

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Introduction: There is evidence that posttraumatic nightmares respond to an empirically promising cognitive-behavioral therapy called Imagery Rehearsal (IR). In IR, patients choose a repetitive nightmare, create a changed version that is less distressing, and then mentally rehearse the changed script. Several studies support the efficacy of IR, but to date no randomized controlled trial (RCT) has been conducted to compare IR against a credible psychotherapy comparison condition. This report describes the outcome of a RCT in Vietnam War veterans with PTSD.
Methods: Male Vietnam War veterans with combat-related PTSD were randomized to receive 6 group sessions of IR (n=61) or Sleep and Nightmare Management (SN), a psychoeducational intervention (n=63). Mean (SD) age was 59.4 (3.6). Veterans were assessed pretreatment and 1-month post treatment with the Clinician Administered PTSD Scale (CAPS), Nightmare Frequency Questionnaire (NFQ), Nightmare Effects Survey (NES), and Pittsburgh Sleep Quality Index (PSQI). Intent-to-treat analyses were conducted using mixed effects models.
Results: Neither treatment had a statistically significant effect on CAPS total or subscale scores, or on the PSQI. Similarly, there was no change in either the NFQ or the NES, although there was a reduction in nightmare intensity on the CAPS item for the IR group only (IR: 5.7 to 4.9; SN 5.8 to 5.5; $p<0.01$). Treatment dropout was significantly greater in the IR group (n=16) compared to the SN group (n=7).
Conclusion: This RCT did not find a significant effect of IR, except for a reduction in nightmare intensity. Veteran populations with chronic, severe PTSD may be less responsive to treatments that are effective for other groups, as has been observed in previous RCTs. Positive results that we have found with Operation Iraqi Freedom and Operation Enduring Freedom veterans support this possibility. Additional RCTs in samples including younger veterans with PTSD are needed before conclusions about treatment efficacy can be made.
Support (optional): Veterans Health Administration Research and Development Service

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SLEEP APNEA AND DEPRESSION IN A VA MENTAL HEALTH POPULATION

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Introduction: Obstructive sleep apnea (OSA) has been associated with depression in the clinical literature but the nature of the relationship is not well defined. Neurovegetative symptoms of depression may resemble daytime symptoms of OSA. Untreated OSA may contribute to development of depression. The presence of OSA may interfere with successful treatment of and recovery from depression. Mental health professionals, and referring primary care providers, may not be recognizing this potentially confounding condition while caring for depressed Veterans Administration (VA) patients. The purpose of this study is to estimate the prevalence of sleep apnea in new VA mental health patients.
Methods: Prior to initial psychiatric assessment, new patients referred for VA mental health evaluations were screened for evidence of OSA and assessed by chart review for other medical conditions associated with OSA. Participants completed the SA-SDQ, a validated and published instrument screening for obstructive sleep apnea, as well as an Epworth scale to assess for sleepiness. Mental health evaluators were blinded to the presence of the study, and their diagnostic impressions were recorded.
Results: 55 patients consented to participate and completed psychiatric evaluations. 52 (95%) were male and all were Caucasian. Average age was 46 and average BMI 29.8. 31 of the 55 participants (56%) were considered to be depressed by their psychiatric evaluator. 14 of these 31 "depressed" patients (45%) scored positive for OSA based on their SA-SDQ responses, compared to 3 of the 24 (12.5%) of those not given a diagnosis of depression ($P=0.005$). In this mental health population overall, 31% screened positive for OSA on the SA-SDQ and 44% had Epworth scores greater than or equal to 10, indicating excessive sleepiness. Based on 1997 guidelines for polysomnography indications by the American Sleep Disorders Association, 56% warranted further sleep evaluation. Of the participants in the study, only 2 had clinically documented consideration of sleep apnea, 1 from the assessing psychiatrist and 1 from the referring primary care provider.
Conclusion: A large proportion of VA patients undergoing initial psychiatric evaluation may have comorbid sleep apnea, particularly those subsequently diagnosed with depression. Despite its potentially negative impact on psychiatric and general physical health, sleep apnea is not being considered in the majority of cases by either mental health or primary care providers.

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ESZOPICLONE AT BEDTIME IMPROVES THE QUALITY OF LIFE IN DEPRESSED INSOMNIACS RECEIVING FLUOXETINE

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Introduction: A recent large study demonstrated that the addition of eszopiclone (ESZ) at bedtime improved the reported sleep and depression scores of depressed insomniacs receiving fluoxetine (FLX). However, that study did not report effects on quality of life (QOL). Our prior work indicates that insomnia adds an additional QOL burden in depressed patients, as reflected in the Daily Living and Role Functioning (DLRF) subscale of the Basis 32. In this new study, we again examine the addition of ESZ to FLX in depressed insomniacs; however, our primary endpoint is the QOL effects of ESZ, compared with placebo.
Methods: The project was approved by the local IRB, and participants provided written, informed consent. Participants were psychotropic medication-free adults with major depression (diagnosis via SCID; HRSD score > 20) who had either (a) sleep latency > 30 minutes and sleep efficiency < 85% at least 4 nights per week, or (b) met Research Diagnostic Criteria for insomnia at least 4 nights per week. After one week of prospective baseline measurements, participants received one week of open label FLX 20 mg in the morning, followed by 8 more weeks of FLX with either ESZ 3 mg or placebo at bedtime. The DLRF subscale was administered at baseline and at the end of randomized treatment. The DLRF subscale is scored 0-4, with 0 indicating no difficulty in daily living and role functioning, and 4 indicating extreme difficulty.

Results: Sixty patients were randomized, and 51 completed the protocol. ANCOVA, adjusted for age and baseline DLRF, identified a significant effect of drug assignment on DLRF (p=0.01). Patients on ESZ finished with significantly better DLRF adjusted means + s.e. (0.8 + 0.14) compared with those receiving placebo (1.3 + 0.14).
Conclusion: This study is unique among hypnotic clinical trials in specifying a QOL measurement as the a priori primary endpoint. Compared with placebo, treatment of insomnia with ESZ led to greater improvement in QOL scores in depressed insomniacs treated with FLX.
Support (optional): NIH MH70821 and M01-RR07122; Sepracor; Mini Mitter

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CHILDREN WITH SUBSTANCE ABUSING PARENTS SHOW A MISMATCH BETWEEN SLEEP IN THE LABORATORY AND SUBJECTIVE SLEEP IN AN AGE AND SEX MATCHED SAMPLE

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Introduction: Children with family histories of substance use disorders (SUDs) or depression may be at risk for substance use and major depressive disorder (MDD) in the future. Sleep electroencephalogram differences have been found in these populations. We compared objective and subjective differences in sleep of children with a positive family history of substance abuse or dependence (FHP) to children without a family history of substance use (FHN).
Methods: Eighteen children, mean age 12.8 (SD=3.6), 14 females, were matched according to FHP (n=9) or FHN (n=9) of SUD in the past six months. Of the 9 FHP children, SUD was present in 6 fathers, one mother, and in 2, both parents. Twelve children had MDD, 1 had oppositional defiant disorder, and 5 had no psychiatric disorder. Children slept two nights in the sleep laboratory (adaptation and study night). Subjective sleep information was from parent and child Schedule for Affective Disorders and Schizophrenia for School-Aged Children scale (KSADS).
Results: Chi-square analyses revealed that FHP (father) children reported more sleep disturbance (75% vs. 25% p=.02), initial insomnia (75% vs. 25%, p=.09) and terminal insomnia (100%, p=.08) than FHN on the KSADS. Subjective sleep disturbance and non-restorative sleep correlated with increased total sleep time (r=.88, p=.01), time in bed (r=.75, p=.05), %REM sleep (r=.74, p=.05), and less stage 1 sleep (r=-.99, p=.00) in the lab. Duration of objective wakefulness was inversely correlated with cognitive disturbances (r=-.97, p=.00), inattention (r=-.97, p=.00), and death wishes (r=-78, p=.04). REM density in the first REM period in FHP was inversely correlated with thoughts of death (r=-84, p=.02).
Conclusion: Children with FHP for SUDs report more sleep disturbance than FHN, but show consolidated sleep in the sleep laboratory. Cognitive and emotional disturbances during the day were inversely related to less wake time in the night. This mismatch may reflect prior partial sleep deprivation.
Support (optional): NIH/NIMH Grant R01 MH-56953 awarded to Dr. Armitage.

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AMBIENT DAYLIGHT INFLUENCES POLYSOMNOGRAPHIC SLEEP IN HEALTHY AND DEPRESSED MENOPAUSAL WOMEN

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Introduction: Previous work showed increased 24-hour illumination measured by wrist actigraphy was associated with shorter sleep latency and reduced wake after sleep onset in postmenopausal women. The aim of the present study was to replicate these findings using polysomnography (PSG). We hypothesized that increased ambient daylight would be associated with enhanced PSG sleep quality variables in both healthy and depressed menopausal women.
Methods: In 29 menopausal women, 11 normal controls (NC; mean age=56.7+7.3 years) and 18 depressed patients (DP; mean age=51.9+5.0 years) who met DSM-IV criteria for a major depressive episode, sleep was recorded by PSG. Hours of ambient daylight were determined from U.S. Naval Observatory sunrise/sunset tables [http://aa.usno.navy.mil/data/docs/RS_OneYear.php]. Pearson correlations were calculated to examine the relationship between hours of ambient daylight and PSG variables.
Results: Pearson correlations revealed a similar pattern of results for both NC and DP women. Consequently, NC and DP women were combined for subsequent analysis. For combined NC and DP, hours of ambient daylight was positively associated with total sleep time (TST; r=.56, p=.002); sleep efficiency (SE; r=.45, p=.013); stage 3 minutes (r=.44, p=.018); stage 3 percent (r=.48, p=.009); REM minutes (r=.41, p=.029); and negatively associated with sleep latency (SL; r=-.41, p=.028); wake after sleep onset (WASO; r=-.59, p=.001); and REM latency (r=-.45, p=.015).
Conclusion: These results confirm previous findings and support the hypothesis that increased day length is associated with improved sleep in menopausal women (i.e., increased TST and SE and decreased SL and WASO) and increased measures of deeper, restorative sleep (i.e., stage 3 and REM sleep) as measured by PSG. These findings are also consistent with results from a sample of pregnant and postpartum healthy and depressed women presented by our group.

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AMBIENT DAYLIGHT INFLUENCES POLYSOMNOGRAPHIC SLEEP IN HEALTHY AND DEPRESSED PREGNANT AND POSTPARTUM WOMEN

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Introduction: The aim of the present study was to examine the relationship between amount of ambient daylight and polysomnographic (PSG) sleep in healthy and depressed pregnant and postpartum women. We hypothesized that a greater amount of ambient daylight would be associated with enhanced PSG sleep quality in healthy and depressed women.
Methods: In 25 pregnant women, 15 normal controls (NC; mean age=24.9+4.8 years) and 10 depressed patients (DP; mean age=27.4+5.4 years) and 24 postpartum women, 11 NC (mean age=28.5+6.9 years) and 13 DP (mean age=28.9+6.7 years) who met DSM-IV criteria for a major depressive episode, sleep was recorded by PSG. Hours of ambient daylight were determined via U.S. Naval Observatory sunrise/sunset tables [http://aa.usno.navy.mil/data/docs/RS_OneYear.php]. Pearson correlations were calculated to examine the relationship between hours of ambient daylight and PSG variables.
Results: For combined pregnant NC and DP, hours of ambient daylight was positively associated with stage 2 percent (r=.57, p=.003); and negatively associated with sleep latency (r=-.48, p=.015); delta minutes (r=-.42, p=.035); delta percent (r=-.46, p=.022); and sleep onset time (r=-.40, p=.045). For combined postpartum NC and DP, hours of ambient light was negatively associated with sleep latency (SL; r=-.47, p=.025) and sleep onset time (r=-.53, p=.010).
Conclusion: These findings support the hypothesis that increased day length is associated with improved sleep continuity in pregnant and postpartum women (i.e., earlier sleep onset and shortened sleep latency). Our group has also reported increased day length was associated with improved sleep quality measured by PSG in healthy and depressed menopausal women. The amount of ambient daylight, however, also was associated with a greater percentage of stage 2 sleep and a decreased

amount of delta sleep, which was contrary to findings in menopausal women.

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AN ANALYSIS OF DISORDERS OF SLEEP ASSOCIATED WITH DEPRESSION: A PROSPECTIVE CLINICAL AND POLYSOMNOGRAPHIC STUDY

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Introduction: There is limited data in the literature on polysomnographically (PSG) proven co-morbid factors associated with depression. We set out to answer this question in a prospective study of patients evaluated at two sleep centers.
Methods: 738 consecutive patients (393 male, 345 female; mean age 49.12 + 15.35) evaluated at two AASM-accredited sleep centers over one and two years respectively were included in the analysis. Sleep questionnaire captured variables which included questions regarding sleep hygiene, restless leg syndrome (RLS), pain, Epworth Sleepiness Score (ESS), and Beck Depression Inventory (BDI). Depression was defined as BDI score > 9 or current use of antidepressant medication. ESS score >=11 was used to define Excessive Daytime Sleepiness (EDS), RLS was measured with the 4-question clinical survey, and Body Mass Index (BMI) was used to define obesity. Data obtained from PSG included periodic leg movement index (PLMI), and respiratory disturbance index (RDI). Data were analyzed using univariate analysis and factors with p-value <0.1 were included in multivariate analysis with stepwise logistic regression to determine factors associated with depression.
Results: 513 patients (69.5%) were depressed. Factors associated with depression were gender (p= 0.006, females more likely to have depression), BMI (p= 0.010), EDS (p <0.001), PLMI (p <0.001), and RLS (p <0.001). There was a high correlation (r= 0.412, p <0.001) between RLS and PLMI. Multivariate analysis yielded EDS (p <0.001) and PLMI (p <0.001) as factors associated with depression. RDI severity was not correlated with depression.
Conclusion: This large PSG supported study showed that patients with depression were more likely to have EDS and a strong association with periodic leg movements of sleep. The effects of antidepressant medications such as selective serotonin receptor inhibitors (SSRI) may be one of the contributors. Sleep related breathing disorder was however not found to be associated with depression.

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PREDICTORS OF SLEEP DISTURBANCES IN OEF/OIF VETERANS REPORTING A TRAUMA

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Introduction: Few studies have assessed the predictors of insomnia and nightmares in those recovering from trauma, and it is currently unclear whether factors other than PTSD severity play a role in the sleep disturbances in this population. This study focuses on assessing the potential predictors of nightmares and difficulties initiating and maintaining sleep among OEF/OIF veterans reporting an emotional trauma.
Methods: OEF/OIF veterans {N = 201, including 177 (88.1%) males, mean age = 34.2 (SD = 10.1), 119 (59.2%) with PTSD} were referred to behavioral health from primary care upon evidence of psychiatric problems and responded to standardized questionnaires assessing psychiatric and other health problems. Those reporting a previous trauma were evaluated for 'trouble falling or staying asleep' and 'repeated disturbing dreams of a stressful experience' during the past month using two questions from the PTSD Symptom Checklist. Three categories of sleep problems were derived from this measure (None or little, Moderate, or Severe).
Results: Stepwise multivariate multinomial logistic regression was used to identify significant psychiatric and physical health predictors of sleep disturbance. The 'none or little' group was used as the reference. Non-sleep PTSD severity explained the most variance in predicting severe trouble falling or staying asleep (OR = 1.09, CI = 1.04-1.14, p < .001) and disturbed dreaming (OR = 1.15, CI = 1.09-1.22, p < .001). Severe trouble falling or staying asleep was also predicted by non-sleep depression severity (OR = 1.16, CI = 1.01-1.33, p =.03). Severe disturbed dreaming was also predicted by losing consciousness from a previous head injury (OR = 5.9, CI = 1.61-21.46, p = .007).
Conclusion: Not surprisingly, trouble falling or staying asleep and disturbed dreaming are strongly associated with non-sleep PTSD symptoms. However, other factors may be contributing to sleep disturbances in this population including traumatic brain injury and non-sleep depression severity.

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EEG COHERENCE AND DREAM CONTENT IN AUTISTIC AND TYPICAL ADULTS

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Introduction: Dreaming constitutes a cognitive aspect of sleep that requires the optimal functioning of neural substrates. We have shown that the number of dream elements in reports collected from REM sleep awakenings correlate with REM sleep EEG activity in autistic and typical adults (Daoust & al., Psychophysiology 2008). In the present study we investigated the link between the ability to generate a dream report following REM sleep awakenings and EEG coherence, a marker of cortical connectivity that has been shown to be high in the visual areas of autistics compared to typical persons (Léveillé & al., ESRS 2006).
Methods: Nine participants (three autistics (20.7 ± 1.4 years), 6 typically-developed controls (20.7 ± 1.7 years) were recorded with a 22-electrode montage for 3 consecutive nights in a sleep laboratory. EEG coherence between inter- and intrahemispheric pairs of electrodes was calculated on samples of REM sleep taken from the second night. On the third night, dream narratives were obtained following REM sleep awakenings. The correlation between coherence values and number of words in dream reports was obtained by calculating Pearson's r coefficients.
Results: We found a significant negative correlations between dream report length and interhemispheric EEG coherence in the primary visual areas (O1-O2: theta and total spectrum activity) and for the right frontal-occipital axis (O2-F4: total spectrum activity).
Conclusion: These results show that the ability to generate a dream report is associated with low connectivity within the primary visual area and between the later and associative cortex. These results also support the notion that short dream reports in autistics may be related to atypical patterns of inter-regional transfer of information.
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REM AND NON-REM SLEEP EEG ACTIVITY IN ADOLESCENTS WITH ANXIETY DISORDERS

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Introduction: EEG recordings performed during wake in adolescents with anxiety disorders but not complaining of sleep disorders show no differences in the evening compared to a control group while morning results are characterized by increased EEG spectral activity over central and occipital electrodes (Gauthier et al., J. Anxiety Disord. 2008). These results are possibly related to some sleep disturbance that does not translate into complaints from the patients. The purpose of the present study was to investigate nonREM and REM sleep EEG in the same sample of anxious adolescents.
Methods: Fifteen adolescents (9 boys, 6 girls, 14.15±1.25 years old) diagnosed with anxiety disorders and without sleep complaints and 15 healthy controls (8 boys, 7 girls, 15 ±1.25 years old) were recorded for two nights. NonREM sleep (stages 2, 3, 4) and REM sleep (15 four-seconds epochs) EEG spectral amplitude was computed for the first seven hours of the second night for C3, C4, O1 and O2 electrodes, referenced to linked earlobes. Delta (0.05-3,75Hz), Theta (4-7.75Hz), Alpha (8-12,75Hz), and Beta (13-30Hz) activity was extracted. Groups were compared using ANOVAs and Bonferroni corrected post-hoc t-tests.
Results: During NonREM sleep (S2+S3+S4) and during slow-wave sleep (SWS: S3+S4), anxious patients showed more EEG activity than controls for the four frequency bands studied, on the central electrodes. During stage 2, differences were restricted to Theta, Alpha and Beta, not for Delta activity. During REM sleep, differences were restricted to Alpha and Beta activity, not for Theta or Delta. No differences were found on the occipital electrodes whatsoever.
Conclusion: These results show that quantified EEG analysis can disclose sleep abnormalities in anxious adolescents not complaining of sleep disorders. The fact that EEG differences increase together with hyperpolarization of the thalamo-cortical loop suggests the existence of CNS malfunctioning in pediatric anxiety disorders.
Support (optional): Canadian Institutes of Health Research and FRSQ.

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RANDOMIZED PLACEBO-CONTROLLED TRIAL OF RAMELTEON FOR INSOMNIA AND DEPRESSIVE SYMPTOMS IN PATIENTS WITH SEASONAL AFFECTIVE DISORDER

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Introduction: One theory regarding seasonal affective disorder (SAD) suggests that lack of natural light accompanying the winter season causes misalignment of the circadian rhythm. This study assessed if ramelteon, a novel sleep-promoting, could resynchronize the circadian rhythm, improve sleep, and decrease depressive symptoms associated with SAD.
Methods: In this single-site, single-blind, parallel-group study, participants with a DSM-IV diagnosis of SAD were randomly assigned to receive either ramelteon 8 mg or placebo in addition to their usual care by a psychiatrist and assessed monthly for four months. The mean change from baseline in Pittsburgh Sleep Quality Index (PSQI) scores was used to measure sleep. In addition, the mean change from baseline in the Zung depression scale and the Structured Interview Guide for the Hamilton Depression Rating Scale, SAD version (SIGH-SAD) were used to measure depressive symptoms.
Results: Fifty participants were enrolled, 49 were randomized to receive ramelteon or placebo with a mean age of 46.6 years and predominantly female (74%). The efficacy sample included 45 participants who had at least 1 follow-up (ramelteon, n=24; placebo, n=21). The ramelteon group reported marginally better sleep at months 2 ($p=.06$), 3 ($p=.08$), and significantly improved month 4 ($p<.05$). As a secondary measure of sleep, the average score of 3 insomnia items from the SIGH-SAD (HDRS insomnia), was marginally improved at month 2 ($p=.02$) and significantly improved at months 3 and 4 ($p<.01$) for the ramelteon group. In addition, the ramelteon group had significantly lower Zung scores and SIGH-SAD scores at months 2, 3, and 4 ($p<.05$).
Conclusion: This study shows that over time, ramelteon was effective at improving sleep quality and reducing depressive symptoms of SAD. This study suggests that ramelteon is another option for those who suffer from SAD.
Support (optional): This investigator initiated clinical trial was sponsored by Takeda Pharmaceuticals North America, Inc.

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SLEEP DIFFICULTIES IN INFANTS OF WOMAN WITH CHILDHOOD TRAUMA ARE MEDIATED BY POSTPARTUM PTSD BUT NOT DEPRESSIVE SYMPTOMS

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Introduction: A third of women who experienced childhood abuse develop post-traumatic stress disorder (PTSD) as adults. Both a history of trauma and PTSD are associated with hypothalamic-pituitary-adrenal (HPA) dysregulation, depression and poor health, which in turn may affect maternal care. Animal studies demonstrate that prenatal stress impacts the offspring's cognitive and emotional function. Additionally, studies report that prenatal stress alters offspring's sleep. As sleep difficulties are a core symptom for several Axis I disorders and behavioral problems in children, they may be a mediating factor for inter-generational transfer of trauma-related symptoms. This study assessed the relationship between antenatal trauma-related symptoms and sleep difficulties in infants.
Methods: Women (age 27.2±5.7) with a history of childhood trauma with PTSD (n=59) or without (n=71), were recruited when initiating prenatal care for their first child. Infant sleep was assessed with a questionnaire administered at four and six months postpartum. Prenatal maternal measures included trauma exposure, PTSD symptoms, substance use, and cortisol. Postnatal maternal measures included depression and PTSD symptoms.
Results: Overall, infant sleep improved between four and six months. Postnatal PTSD but not depressive symptoms were associated with more wake after sleep onset (WASO) and less total sleep time (TST). WASO was also associated with severity of childhood trauma and diurnal cortisol change during gestation, while TST only with the former. The highest WASO and lowest TST were observed in infants of mothers with PTSD symptoms both during pregnancy and postpartum. Factor analysis of the sleep questionnaire suggested that WASO was associated with separation anxiety at bedtime, and difficulty initiating sleep, while TST was associated with the latter.
Conclusion: Pre and postnatal maternal PTSD symptom severity work additively to exacerbate sleep difficulties in infants. Potentially, in addition to the deleterious effects of prenatal stress, PTSD impacts mother-infant interactions around bedtime that are associated with sleep initiation.
Support (optional): NIH/NCRR K12 RR017607-01 (MM); NIH/NIAAA T32 AA07477 (ISH); Fogarty Int'l Center/NIDA Int'l Substance Abuse Research Program Grant D43-TW05818 (JW)

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IMPROVEMENT IN SUBJECTIVE SLEEP QUALITY AND MOOD AFTER INSOMNIA TREATMENT IS ASSOCIATED WITH PRE-TREATMENT OBJECTIVE SLEEP CHARACTERISTICS IN RECOVERING ALCOHOLICS

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Introduction: Sleep difficulties during recovery from alcohol dependence are prevalent in up to 90% of alcoholics, potentially contributing to relapse. There has been growing attention to the importance of targeting sleep disturbances during alcohol recovery. We previously reported that cognitive behavioral therapy for insomnia, adapted for recovering alcoholics (CBTI-A), improved subjective sleep quality and daytime functioning more than a behavioral placebo treatment (BPT). As chronic alcohol consumption can affect sleep physiology, this study assessed whether objective measures of sleep were predictive of treatment outcome for insomnia.
Methods: Thirteen participants meeting DSMIV-TR criteria for lifetime alcohol dependence and chronic insomnia, but who were otherwise healthy, completed treatment. Nine received CBTI-A, and the remainder received BPT. One night of polysomnography was used to rule out occult sleep disorders. Subjective measures included two weeks of daily sleep logs before and after treatment. Objective measures included parameters from pre-treatment polysomnography. Additionally, the Beck Depression inventory (BDI) was administered before and after treatment.
Results: A composite value for change in subjective sleep quality (post/pre-treatment) was derived from sleep logs by summing magnitude positive change (sleep efficiency, sleep onset latency, wake after sleep onset, number awakenings, feeling rested). Both groups showed improvement in subjective sleep quality ($t=3.0$, $p=0.01$), with a trend towards a better outcome for CBTI-A ($t=2.2$, $p=0.059$). Controlling for alcoholism severity, regression analysis using percent time in sleep stages 1-4, sleep efficiency, sleep latency, REM latency, and REM density as predictors showed that improvement in subjective sleep quality was predicted by lower pre-treatment REM density across groups (beta=-0.75, $p=0.005$). Both groups showed significantly reduced depressive symptoms at the end of treatment ($F=21.35$, $p=0.001$). Change in BDI-II scores was predicted by shorter sleep onset latency before treatment (beta=-0.63, $p=0.039$).
Conclusion: Post-treatment subjective sleep quality and depressive symptoms in alcoholics were associated with pre-treatment objective sleep characteristics.
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POLYSOMNOGRAPHIC ABNORMALITIES AND PARENT REPORT IN YOUNG CHILDREN WITH AUTISM

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Introduction: Questionnaire studies consistently show high rates of reported sleep problems in children with autism. These disorders can be characterized as either disorders of sleep continuity or circadian rhythm. Few studies have explored the relationship between report and physiologic sleep parameters. We present PSG data from 60 children with autism (aged 2 - 13 yrs). Sleep architecture aberrancies were most significant for a prolonged latency to REM sleep and significantly less time spent in REM sleep when compared to normative age matched data. We sought to evaluate whether any particular category of sleep complaint was associated with REM sleep abnormalities.
Methods: 60 children (ages 2 - 13) who met research criteria for autism underwent an overnight EEG at the NIH Clinical Center. Sleep habit histories were collected via parent report on the Children's Sleep Habits Questionnaire (CSHQ) and NIH Morning Sleep Questionnaire. Sleep architecture was analyzed.
Results: Our cohort showed significantly longer latencies to REM sleep and significantly less time spent in REM sleep than age-matched controls from normative data. Of those reported to have sleep difficulties, complaints of fragmented sleep and early morning awakening were common. Higher scores, either on the total sleep score or by subdomain of the CSHQ, were not predictive of REM sleep abnormalities.
Conclusion: Polysomnography is a non-invasive technique that provides important insight into the possible aberrant neurobiology of developmental and psychiatric disorders. Sleep disturbances are hypothesized to play a role in behavioral difficulties. Our study will add to the understanding of the relationship between behavioral sleep reports and sleep architecture abnormalities with emphasis on sleep/wake cycles, sleep stage transitions and daytime behavior.

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COULD DEPRESSION BE OVER-DIAGNOSED IN A SLEEP DISORDERED POPULATION? DIFFERENTIAL DIAGNOSIS AND TREATMENT CONSIDERATIONS

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Introduction: Previous studies have suggested high rates of depression in insomnia patients and other sleep-disordered individuals. Many symptoms considered in the diagnosis of depression may instead reflect the impact of sleep disturbance and contribute to complicated differential diagnosis. The current investigation sought to further evaluate the relationship between sleep disturbance and depression through analysis of depression subscales as measured by the Personality Assessment Inventory, an objective and validated inventory.
Methods: PAI profiles of 138 consecutive patients referred for evaluation and treatment at a behavioral sleep medicine clinic were analyzed to explore reports of depression by the group. Preliminary results suggested elevated rates of depression in the group (mean = 62.64). Further review of depression subscales (cognitive, affective and physiological) was conducted to investigate the relative contribution of each "type" of depression experienced.
Results: Review of depression subscales suggests differential expression of cognitive (mean = 54.83), affective (mean = 57.80), and physiological (mean = 69.94) depression. Frequency analysis suggests physiological symptoms of depression were predominant and experienced at severe levels ($t \geq 70$) by 44% of those in the group, whereas far fewer reported experience of severe affective and cognitive depression (20% and 12%, respectively). Paired-samples t-tests showed that the physiological subscale was significantly higher than the cognitive, $t(137)= -15.005$, $p<.0005$, and affective, $t(137)= -12.133$, $p<.0005$.
Conclusion: Results suggest a high prevalence of physiologic features of depression (changes in physical function, activity level, and energy) relative to cognitive and affective features. Hence, depression may be over-diagnosed in a sleep disordered population if steps are not taken to review the relative contribution of sleep disturbance to the clinical picture. Clinical evaluation may benefit from including use of psychometrics and diagnostic procedures capable of differentiating the particular subtypes of symptoms experienced to increase the specificity of diagnosis and treatment planning.

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A PRELIMINARY ATTEMPT AT DEFINING 'SLEEP MARKERS OF DEPRESSION' CATEGORICALLY AND EXAMINING THEIR ASSOCIATION WITH SUBJECTIVE LOW MOOD

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Introduction: Sleep is the most commonly observed physical complaint in depressed patients and polysomnographic sleep disturbances have been extensively studied as possible etiological and specific markers of depressive state. However, no previous attempt has been made to operationalize the observed macroarchitectural sleep changes observed in Major Depressive Disorder (Slow wave sleep abnormalities, REM sleep abnormalities, and decreased sleep continuity) into a categorical model which could be applied in the clinical setting.
Methods: In a sample of 2467 patients with no prior sleep complaint screened for possible sleep apnea prior to surgery, 74 patients who underwent polysomnographic sleep studies and completed a battery of questionnaires relating to their sleep and mood were studied. Using predetermined cutpoints for the Epworth Sleepiness Scale (ESS), Fatigue Severity Scale (FSS), Athens Insomnia Scale (AIS) and Center for Epidemiologic Studies Depression Scale (CES-D), we retrospectively compared categorical results of these scales to presence or absence of sleep markers of depression, which were defined in the context of previous depression literature and normative polysomnographic data.
Results: No significant associations were found between the CES-D and total sleep markers of depression. However, there was a significant trend toward subjective insomnia in those with sleep markers of depression.
Conclusion: This study does not indicate a high specificity of sleep markers of depression for low mood. However, controlled, cross-sectional prospective studies are required to clearly determine whether a more specific model can be constructed for either subjective or objective depression.

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THE RELATIONSHIP BETWEEN EARLY CHILDHOOD TRAUMA AND SLEEP IN YOUNG ADULTS

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Introduction: Sleep loss has been linked to impairments in daytime function as well as the risk of medical and psychiatric morbidity. Exposure to severe trauma in childhood and PTSD have also been associated with deleterious outcomes, including disturbances of sleep. Exposure to trauma could interfere with the feeling of safety that is necessary for initiating and maintaining sleep. In fact, insomnia is the most frequent complaint in the aftermath of trauma. Given these relationships it is likely that severe trauma in childhood could lead to long lasting effects on sleep in adulthood. This study seeks to examine the relationship between severe childhood trauma and sleep disturbances in early adulthood as indexed by the presence of insomnia, and the role of sleep vigilance.
Methods: We administered questionnaires to 112 healthy, adult volunteers of African descent that were between the ages of 18 and 34. The measures assessed trauma, severity of Posttraumatic Stress Disorder (PTSD), insomnia severity, and sleep-related vigilance (defined as feeling on guard when falling to sleep).
Results: Sexual assault, but no other form of trauma, was significantly related to insomnia (p=.016; Fisher's Exact). Of the 11 sexually abused participants all but one were exposed during childhood. A significant relationship was also revealed between sexual assault and "feeling on guard" (p = .039; Fisher's Exact). A logistic regression model indicated that the risk for insomnia was almost 5 times greater in sexual assault survivors after adjusting for PTSD diagnosis [OR = 4.6, CI = (1.11, 19.37)] and this effect appears to be moderated by nighttime vigilance (B = .90, p <.05).
Conclusion: Our sample revealed that sexual trauma during childhood is predictive of adult insomnia independent of PTSD diagnosis and a role for nighttime vigilance is suggested.

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PERSONALITY CHARACTERISTICS OF PATIENTS SEEKING TREATMENT AT A BEHAVIORAL SLEEP MEDICINE CLINIC

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Introduction: The following investigation sought to evaluate the prevalence of psychopathology in a sleep-disordered population using the Personality Assessment Inventory (PAI). The PAI is a self-administered, objective inventory of adult personality designed to provide critical clinical information with 4 validity scales, 11 clinical scales, 5 treatment scales, and 2 interpersonal scales. It was designed to facilitate interpretation and coverage of the full breadth of complex clinical constructs. Previous investigations of personality features of those with sleep disorders revealed elevated rates of psychopathology, including depression, anxiety and somatization. Personality features of those referred for treatment at a behavioral sleep medicine clinic were examined.
Methods: Participants completed the PAI as part of their initial evaluation at a behavioral sleep medicine clinic. Clinical profiles were analyzed with mean t-scores reported for each clinical scale.
Results: The population exhibited a clinically relevant elevation on the Depression scale (mean = 62.64), suggesting a greater depressive experience within the group as a whole. Frequency analysis indicated 53% of the group experienced at least mild-moderate depressive symptoms (t≥60), with 28% reporting severe symptoms (t≥70). The Somatic Complaints and the Anxiety clinical scales were elevated as well, although to a lesser degree (mean = 59.68 and mean = 58.85, respectively). Frequency analyses indicated elevated rates of mild to moderate somatic complaints (44%) and anxiety (42%), with 22% and 18% respectively showing severe levels.
Conclusion: As with previous studies, depression, anxiety, and somatic complaints were common within this sleep-disordered population. The prevalence of such symptoms suggests a need for comprehensive and sensitive evaluation of potential co-morbid psychiatric symptoms/disorders in sleep center populations. Those involved in the treatment of sleep disorders, and particularly insomnia, may benefit from experience and training in the management of anxiety, depression, and somatization disorders.

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A MICE MODEL OF PTSD: PSYCHOLOGICAL STRESS BUT NOT PHYSICAL STRESS ENHANCES REM SLEEP

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Introduction: PTSD is an anxiety disorder that can develop after exposure to one or more terrifying events that threaten the patient. Sleep disturbances such as difficulty falling sleep and nightmares are common symptoms of PTSD. Although altered brain functions by psychological stress is likely a major mechanism of PTSD, the neurobiology underlying PTSD is largely unknown. This is likely due to the lack of validated

animal models of PTSD. In the current study, we evaluated the sleep changes after physical and psychological stress, and we propose a new mice model of PTSD.
Methods: Mice (male, C57/BL6, 8 month old) with sleep headstage implantation were divided into three groups: electrical foot shock (FS), observation (OB), and cage control (CC) groups (n=4 for each group). Physical and psychological stress was induced using a communication box (60x60x30cm), equipped with a metal floor grid. The box consisted of 8 compartments (30x15cm) divided by non-transparent or transparent acrylic walls (with holes). A foot shock (2mA) was applied through the floor grid lasting for 10sec at 60sec intervals for 30 minutes for the FS mice. The OB mice could see the mice receiving the foot shock via transparent acrylic panels and could perceive the sounds and smells. After the baseline sleep recording session (day 0), electric shock was applied to FS group (day 1, day 8 to 10, and day 15) and sleep was monitored for 6 hours from 10:00 am each experimental day.
Results: We found that both NR and REM sleep were significantly reduced in FS mice, sleep changes typically observed with acute physical stress, while no change in sleep parameters were found in the CC group. Interestingly, sleep changes in OB mice were different from those in FS mice, and REM sleep enhancement associated with reduction in NR was observed. These sleep changes in OB and FS mice lasted for 2 days, and sleep patterns returned to the baseline values on day 3. After 3 consecutive foot shock sessions, the sleep changes lasted longer. Furthermore, a single foot shock session on day 16 produced a much longer period (compared to the 1st session) of sleep changes.
Conclusion: Sleep changes in the OB mice resemble those observed in human PTSD. The number of stress exposure affects the duration of sleep changes, and repeated exposures to psychological stress enhance the vulnerability to these sleep changes (sensitization). We propose our OB mouse as a new PTSD animal model, and experiments using this model are in progress.

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HYPOCRETIN NEUROTRANSMISSION DIFFERENTIATES REM SLEEP CHANGES BY PHYSICAL AND PSYCHOLOGICAL STRESSES

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Introduction: In the accompanying presentation, we had demonstrated that sleep changes by physical (electric foot shock stress) and psychological stress are different, and the latter, with REM sleep enhancement and reduction in NR sleep, is more similar to the sleep changes seen in human PTSD (post-traumatic stress disorder). Since a series of experiential evidence demonstrated that hypocretin is important for sleep regulation and since hypocretin mediates the stress response, sleep changes with exposures to two types of stress were also evaluated in hypocretin deficient narcoleptic and wild type (WT) mice.
Methods: Orexin/ataxin-3 TG narcoleptic mice (N9, backcrossed to C57BL/6) and their littermate WT mice were divided in two groups (n=4 each group). One group (FS) of each genotype received one electric foot shock session (2mA, 10sec, 60 sec interval for 30 min), and the other group (OB) observed the mice receiving foot shock through the window of communication box. The mice were surgically prepared for EEG and EMG recordings, and sleep changes (from respective 6 hr baseline recordings) after these manipulations were evaluated between genotypes.
Results: As we have shown in the companion study, REM sleep enhancement and NR sleep reduction was observed in WT mice after the exposures to psychological stress. Similar changes were also observed in TG mice. Similarly, in the FS group, REM and NR sleep reductions were observed in WT mice. However, REM suppression (but not NR reduction) was completely abolished in TG mice. The differential effects on REM between TG and WT mice lasted for 3 days after the exposure to the stress.
Conclusion: Our results suggest that sleep changes after psychological and physical stress are mediated by different neuroral mechanisms and an intact hypocretin neurotransmission is essential for REM sleep suppression after the physical stress exposure. The differential effects on REM between TG and WT mice lasted for 3 days, suggesting that hypocretin tonus is also involved in long-term sleep changes in sleep after exposure to physical stress.

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PREVALENCE AND RISK FACTORS OF SLEEP DISORDERED BREATHING AMONG PATIENTS WITH SCHIZOPHRENIA AND MOOD DISORDER

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Introduction: Change in mental function are common symptoms in sleep disordered breathing (SDB) and psychiatric disorders. Therefore, screening comorbid SDB in patients with psychiatric disorders is considered essential to treat both SDB and psychiatric disorders adequately. The aim of the study is to investigate the prevalence and risk factors of SDB among patients with schizophrenia and mood disorder.
Methods: Patients with schizophrenia (n=507, 279 men and 228 women, mean age of 57.9±15.2) and patients with mood disorder (n=124, 59 men and 65 women, mean age of 57.3±14.8) participated in screening SDB protocol using the pulse-oximetry. Probable SDB group and probable non-SDB group were defined as patients whose 3% oxygen desaturation index (3%ODI) was more than 15 and less than 5, respectively.
Results: Mean score of 3%ODI among schizophrenia group and mood disorder group was 11.6±13.0 and 9.8±12.0, respectively. The prevalence of a 3%ODI more than 15 was 25.8% among schizophrenia group and 17.7% among mood disorder group. Among schizophrenia group, sex, age and Body Mass Index (BMI) were closely associated with an increased risk of SDB in the univariate model. After adjustment for age and significant variables in the univariate model, sex (men vs. women, odds ratio (OR):3.98, 95%CI: 2.74-8.36, $p<0.001$), BMI (>25.0 vs. <18.5, OR:3.98, 95%CI: 3.38-19.23, $p<0.001$) were identified as factors independently associated with SDB in schizophrenia group. Among mood disorder group, dose of hypnotics use were closely associated with an increased risk of SDB in the univariate model. After adjustment for age and significant variables in the univariate model, dose of hypnotic use (diazepam equivalence, >15mg vs. <5mg, OR:4.73, 95%CI:1.18-19.00, $p<0.05$) was identified as factors independently associated with SDB in mood disorder group.
Conclusion: There is the possibility that excess body weight is the predisposing factor of SDB in patients with schizophrenia, and high dose hypnotics use is the predisposing factor of SDB in patients with mood disorder.

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A SLEEP SCREENING TOOL FOR MILITARY PERSONNEL: THE POST TRAUMATIC STRESS DISORDER CHECKLIST

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Introduction: Warfighters supporting the Global War on Terror are experiencing both mild Traumatic Brain Injury concurrent with combat-related stress. Both of these medical conditions can result in sleep deprivation and hyper-alertness, which affect daily battlefield performance. The Epworth Sleepiness Scale subjectively assesses sleepiness, while the Post Traumatic Stress Disorder (PTSD) Checklist for Military

personnel (PCL-M) assesses combat stress (The PCL-M is a screening tool of 17 items used to assist in the diagnosis of PTSD). The purpose of this report is to remind clinicians already administering the PCL-M that they can learn more about their patients' sleep quality by looking into this tool's sleep symptom items ("Trouble falling or staying asleep"?) and alertness ("Being 'superalert' or watchful or on guard?").
Methods: 283 soldiers serving in Iraq responded to an in-theater survey. This survey contained both the Epworth and the PCL-M. Statistical analysis was done on the Epworth, the two PCL-M sleep items, and a question to see if they were waking up rested. For the purpose of this study, only those reporting head injury were analyzed.
Results: 22 of the 283 (8%) soldiers self-reported head injury (21 (96%) male, ages 18-44 years). Furthermore, 18 (82%) scored higher than eight points on the Epworth scale. 14 (67%) of the participants indicated that they have some trouble falling or staying asleep, per the PCL-M item. Responses to the alertness PCL-M item indicated that 11 (50%) usually felt superalert. Finally, 14 (70%) of the participants responded with "No" when asked if they were waking up feeling "rested." A correlational analysis between both of the PCL-M items and the Epworth showed significance between "trouble falling asleep" and the Epworth scale (-.45, $\alpha < .05$).
Conclusion: A large number of individuals who self-reported head trauma also self-reported sleep problems. This suggests that evaluation of sleep should be an important component of the evaluation of TBI patients. In addition, one of the items found in the heavily used PCL-M was significantly correlated with the Epworth. This finding also suggests that researchers could/should use the PCL-M to gain a better understanding of sleep problems in deploying and returning warfighters.
Support (optional): This research was performed in accordance with Army Regulation 40-38 (conduct of clinical investigations). The views expressed in this abstract are those of the authors and do not reflect the official policy or position of the Department of the Army, Department of Defense, or the U.S. Government.

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SLEEP IN SCHIZOPHRENIA: A NIGHT- AND DAYTIME ACTIGRAPHY STUDY IN PATIENTS WITH TREATED WITH ORAL RISPERIDONE, OLANZAPINE OR PALIPERIDONE

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Introduction: Schizophrenia is a chronic and severely debilitating mental disorder. Patients with schizophrenia have overt "positive," symptoms such as psychosis, auditory hallucinations, and delusions, and "negative" symptoms, such as affective flattening. Sleep disturbances are common in schizophrenia and are characterized by prolonged sleep latency and increased wake after sleep onset duration. Severity of sleep disturbances is correlated with intensity of clinical symptoms in patients with schizophrenia.
Methods: This analysis evaluated the actigraphy (Actiwatch) data collected at the baseline visit of a 4-week, double-blind, placebo-controlled, proof-of-concept study that evaluated adjunctive armodafinil therapy in adults with stable schizophrenia managed with oral risperidone, paliperidone, or olanzapine. Patients with sleep disorders were excluded based on history. Spontaneous motor activity of the patients was continuously evaluated using an actigraphy device, worn from screening through the duration of the study. The actigraphy device was used to assess night- and daytime sleep in all patients. Data from the actigraphy device were downloaded at each visit.
Results: Sixty patients (18 - 60 years of age) were randomized to participate in the study. Average (SD) median sleep latency was 21.1 (15.3) minutes; sleep efficiency was 78.3% (10.3), total sleep time was 422.9 (105.9) minutes. Wake after sleep onset was 74.2 (45.4) minutes. Patients experienced an average median number of 39.0 (15.8) sleep bouts with an average median duration of 12.9 (6.9) minutes. Patients experienced an average median number of 39.0 (15.7) wake bouts with an average duration of 1.9 (0.8) minutes. Average median daytime total sleep time was 95.1 (53.9) minutes.
Conclusion: Patients with stable schizophrenia who are being treated with oral risperidone, paliperidone, or olanzapine exhibit abnormal patterns of sleep and wakefulness. Disturbances in sleep continuity and daytime sleepiness were evident.
Support (optional): Study sponsored by Cephalon, Inc.

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PERSISTENT SLEEP DISTURBANCE DURING PREGNANCY PREDICTS REEMERGENCE OF A CORE SYMPTOM OF DEPRESSION IN THE POSTPARTUM

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Introduction: Persistent disturbed sleep after successful treatment of a major depressive disorder (MDD) is a risk factor for future relapse. Within the context of pregnancy sleep disturbance during the 3rd trimester predicts depressed mood during the postpartum period. The present study sought to determine whether the level of disturbed sleep during the 3rd trimester in 65 pregnant women who recently remitted from MDD would predict a reemergence of a core symptom of MDD (reemergence) at 10 weeks postpartum.
Methods: The sample consisted of 65 pregnant women who entered a randomized controlled study of acupuncture for the treatment of MDD but no longer met criteria for either of the two core MDD symptoms in the third trimester. Measures included the Hamilton Rating Scale for Depression (HRSD) and the depression section of the Structured Clinical Interview for the DSM-IV (SCID), administered during the last trimester and at 10 weeks postpartum.
Results: The following predictors were entered into a binary logistic regression to predict reemergence of the core symptoms of depression at 10 weeks postpartum: the third trimester HRSD sleep subscale, the HRSD score without the sleep items, randomization group (3 levels), and a dichotomous variable indicating continued treatment in the postpartum. Disturbed sleep was the only significant predictor ($\chi 2 = 12.01$, $p < 0.05$; Nagelkerke r-square = 0.29.). Exploratory analyses revealed sleep disturbance at the beginning of the night, but not in the middle or at the end of the night, was predictive of reemergence of a core symptom (OR = 3.33 95% CI[1.14 - 9.71]).
Conclusion: Pregnant women with persistent sleep difficulties following successful treatment of depression are at greater risk for a reemergence of a core symptom of depression during the postpartum period. Implications of this study in the prevention of depressed symptoms in the postpartum period are discussed.
Support (optional): This research was supported by the Agency for Health Research and Quality (AHRQ) grant number HS09988.

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SUB-CLINICAL DYSPHORIA CORRELATES WITH PHASE-DELAYED CIRCADIAN MISALIGNMENT IN HEALTHY INDIVIDUALS

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Introduction: We previously demonstrated that the time interval (phase angle difference or PAD) between the dim light melatonin onset (DLMO) and the mid-point of sleep correlates with symptom severity in both seasonal and non-seasonal unipolar depression: in most subjects, the greater the phase delay in the DLMO relative to sleep (the shorter the PAD),

the greater depression severity. We sought to determine whether a correlation between circadian misalignment and mood existed in healthy, euthymic individuals as well.
Methods: Subjects (12 F, 7 M; 21-34 y.o.) were first-year medical students at Oregon Health & Science University (OHSU). In two subjects DLMOs were not obtained. One other subject was excluded because she was taking an antidepressant medication and another was excluded because he routinely exposed himself to light during the middle of night. The remaining 17 subjects were in generally good health as documented by a Health and Screening Questionnaire. Subjects kept a sleep/wake schedule of their choosing for seven weeks and kept a sleep/wake diary. Hourly saliva samples were collected every 2 weeks for six hours in dim light (< 10 lux) at OHSU. Melatonin concentrations were measured by radioimmunoassay (ALPCO) and the salivary DLMO was calculated (3 pg/ml threshold). Mood was assessed using the Profile of Mood States, brief form (POMS-B). Circadian misalignment was measured using the time interval between the DLMO and the average mid-sleep of the prior week (PAD).
Results: The mean (± SD) total mood disturbance (TMD) score was 22.1 ± 14.3 (below that characteristic of psychiatric disorders). Average bedtimes and waketimes were 23:31 ± 0:31 and 07:44 ± 0:28, respectively. The average DLMO and PAD for the remaining subjects was 21:20 ± 01:20 and 6:01 ± 01:00 h, respectively. There was a negative correlation between the POMS-B score and the PAD: shorter (more phase delayed) PADs were associated with worse mood (rs = -0.617, p = 0.014). The POMS-B score decreased by ~20% for each hour advance in the PAD.
Conclusion: Although subjects' mood fell within the normal range and both the average DLMO and PAD were consistent with historical controls, we found that a delay of the circadian pacemaker relative to the timing of sleep was associated with worse mood. These data suggest that circadian misalignment may play a role in every day variations in mood and that circadian misalignment may be a significant and treatable component in a number of clinical disorders, including non-restorative sleep.
Support (optional): PHS Grants K23RR017636 (JSE); R01 EY018312, R01 HD42125, and R01 AG21826 (AJL); and MO1 RR000334 and UL1 RR024120 (OHSU and the Oregon Clinical and Translational Research Institute, respectively). NARSAD Young Investigator Award and the Sleep Research Society Foundation Gillin Award (JSE) and the NARSAD Distinguished Investigator Award (AJL).

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SLEEP DISTURBANCES IN 1603 CHINESE EARTHQUAKE VICTIMS AND THEIR RELATIONSHIPS WITH POSTTRAUMATIC STRESS DISORDER AND DEPRESSION

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Introduction: The objective of this study was to investigate sleep problems in Chinese earthquake survivors and their relationships with posttraumatic stress disorder (PTSD) and depression.
Methods: An investigator-administered questionnaire was used to explore subjects' sleep latency (SL), number of wake (WN), wake duration (WD), wake-up time (WUT), and total sleep time (TST) and sleep efficiency (SE). Each measurement included two time frames: "last week" and "the week before the earthquake". A 17-item subscale and a 4-item subscale of the Los Angeles Symptom Checklist were used to measure the severity of PTSD and depression, respectively. Based on the mean values, subjects were divided into groups of high PTSD and low PTSD, and groups of high depression and low depression. Data collection was performed 3 months (90.3±2.8 days) after the grade-8 earthquake, which was on May 12, 2008.
Results: A total of 1603 subjects (55.8% female) completed the study and met the inclusion criteria. Age distribution was 41.5±16.9 for males and 40.4±16.0 for females. Compared with results from the week before the earthquake, during the past week of the study the subjects' SL (58.1±51.3 vs. 29.4±32.9 min), WN (1.8±1.5 vs. 0.8±1.0) and WD (43.1±52.3 vs. 19.0±36.0 min) were increased (all P<0.001), WUT (6:12 vs. 6:30) was earlier (P<0.001), and TST (6.6±2.3 vs. 7.8±1.8 hrs) and SE (%78±22 vs. %91±12) were decreased (both P<0.001). Compared with those in the low PTSD group, subjects in high PTSD group had an increased SL, WN and WD (all P<0.001), earlier WUT (P<0.001) and decreased TST and SE (both P<0.001). Results of the comparison between the groups of low depression and high depression are similar to those between the groups of low PTSD and high PTSD.
Conclusion: Sleep disturbances in Chinese earthquake victims are significant. The sleep disturbances are affected by the severity of PTSD and depression.

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INVESTIGATION OF SLEEP IN CHRONIC TREATMENT-RESISTANT DEPRESSED PATIENTS

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Introduction: The existing literature supports a bi-directional relationship between sleep disorders and depression. Sleep disorders are often undiagnosed in the general population and in the psychiatric population. However, once detected treatment of sleep disorders among depressed patients has been shown to improve mood and alleviate depression. Among depressed patients, about 12-15% will remain chronically depressed and will not respond to treatment. The aim of this study was to investigate the sleep architecture and prevalence of sleep disorders among a group of chronic treatment-resistant depressed patients.
Methods: Nine patients who met diagnostic criteria for chronic treatment-resistant depression were recruited from local mood disorder clinics. Depression severity was assessed using the 21-item Hamilton Depression Scale (HAM-D). The patients underwent an overnight polysomnographic (PSG) study followed by Multiple Sleep Latency Test (MSLT).
Results: Seven of the participants were females and the average age for the whole group was 50±7 years. The average HAM-D score (± SD) was 24± 4. The average sleep onset latency and the average REM latency after sleep onset were 22±14 min and 253±119 min respectively (all patients were on antidepressants). The average sleep efficiency was 81±4%. The average slow wave was sleep percentage was 8±9% and the average REM sleep percentage was 13±8%. The average arousal index was 27±15/hr. Three of the nine patients had an undiagnosed moderate to severe sleep apnea. Three of the patients had a moderate to severe periodic leg movement disorder and five of the patients had "fragmented" sleep. The average mean MSLT was 10±4 min and two of the patients had severe daytime sleepiness.
Conclusion: The results suggest that chronic treatment-resistant depressed patients often have disturbed sleep architecture. A significant proportion of patients in this pilot study had an undiagnosed sleep disorder that might have been the underlying cause or contributor to their chronic treatment-resistant depression.

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AN INVESTIGATION INTO THE INTERACTION OF PSYCHOPATHOLOGY, PERSONALITY, AND SLEEP DISTURBANCES IN CLIENTS FROM A COMMUNITY MENTAL HEALTH CENTER

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Introduction: Studies have found a relationship between psychopathology and sleep disturbances, as well as between psychopathology and personality traits. What has not received attention to date, however, is the interplay amongst all three factors: psychopathology, sleep disturbances, and personality characteristics. This study begins to explore the interaction amongst the three areas.
Methods: Nine clients were recruited from a community mental health center. Participants were receiving outpatient psychological services, were over 18, and did not have a diagnosis of active psychosis. Participants completed 9 questionnaires covering items about demographic information, psychological concerns (Brief Symptom Inventory), sleep (Pittsburgh Sleep Quality Index, Insomnia Symptom Questionnaire, Epworth Sleepiness Scale, Insomnia Severity Index, and Dysfunctional Beliefs and Attitudes about Sleep), personality style (Eysenck Personality Questionnaire), and social desirability (Marlowe-Crowne Social Desirability Scale). Participants received a $10 gift card.
Results: Participants had a mean age of 42 (77% female, 67% Caucasian). A significant relationship between psychological symptoms and poor overall sleep quality was found ($r = .686$, $p < .05$). Dysfunctional beliefs about sleep were significantly related to an increased likelihood of insomnia symptoms on the ISQ and ISI ($r = .701$, $p < .05$; $r = .713$, $p < .05$, respectively). The personality characteristic of Neuroticism was significantly related to elevated symptoms of Depression ($r = .682$, $p < .05$) and Anxiety ($r = .683$, $p < .05$). Neuroticism was also related to difficulty sleeping due to feeling too hot ($r = .727$, $p < .05$), and Psychoticism was related to an increase in night sweats ($r = .854$, $p < .01$).
Conclusion: Preliminary findings suggest that relationships exist among psychopathology, personality, and sleep disturbances. Psychological symptoms and certain personality traits can contribute to unhealthy sleep behaviors and thoughts. It is hoped that continued investigation into this topic will enhance the understanding of how these 3 constructs are interrelated.

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INFLUENCE OF ANXIETY ON INSOMNIA IN OLDER ADULTS WHEN CONTROLLING FOR DEPRESSION

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Introduction: Sleep problems are common in older adults and are often associated with anxiety as well as depression. Distinguishing anxiety from depression is difficult in the general adult population and becomes more difficult in older adults. Examining the relationship between anxiety, depression, and insomnia more rigorously in older adults may help providers become better equipped to recognize and treat insomnia in this population.
Methods: Three self-report measures [Beck Anxiety Inventory (BAI), Geriatric Depression Scale - Short Form (GDS-Short Form), and Insomnia Severity Index (ISI)] were administered in a structured interview format to 71 older adults in assisted living communities. A Pearson bivariate correlation was computed between BAI total scores and ISI total scores. A partial correlation between BAI total scores and ISI total scores while controlling for GDS-Short Form total scores was also computed.
Results: The Pearson bivariate correlation between BAI total score and the ISI total score indicated a significant positive relationship ($r = .47$, $p < .01$), with 22% of the variance in ISI being accounted for by anxiety. The results of the partial correlation also revealed a significant positive relationship ($r = .38$, $p < .01$) between BAI total scores and ISI total scores even when controlling for GDS total scores. The partial correlation revealed that 14% of the variance in ISI was attributable to anxiety when controlling for depression.
Conclusion: The results indicate that anxiety is an independent predictor of insomnia severity even when controlling for depression. Further, the results imply a functional distinction between anxiety and depression. This adds credibility to the importance of differentiating between anxiety and depression when diagnosing and/or determining an optimal treatment approach for insomnia in older adults living in assisted living communities.

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THE ASSOCIATION BETWEEN SLEEP AND SUBSEQUENT SYMPTOMS IN INTER-EPISODE BIPOLAR DISORDER

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Introduction: Despite advances in the treatment of bipolar disorder (BD), the risk of relapse remains high, even among individuals who adhere to treatment. Disturbed sleep appears to have a critical role in BD. Insomnia and hypersomnia are not only core symptoms of episodes of illness but also features of inter-episode periods. Moreover, disturbed sleep has been found to be the most common prodrome of mania, suggesting that it may be a trigger of relapse. The present study examines the relationship between naturally occurring sleep and subsequent symptom severity in a sample of inter-episode BD adults.
Methods: Twelve adults (9F, 3M; mean age = 40 ±12.25 years) with inter-episode BD wore wrist actigraphy devices and filled out a sleep diary for 28 consecutive days. All participants were under the care of a psychiatrists. Actigraphy data was computed using 1-minute epochs. One month later, participants were interviewed using the Young Mania Rating Scale (YMRS) and the Inventory of Depressive Symptomatology - Clinician Rated (IDS-C) to assess for severity of manic and depressive symptoms.
Results: Sleep diary results indicated that longer and more variable total wake time (TWT) were correlated with higher YMRS scores at one month follow-up ($r=.66$, $p<.05$ and $r=.73$, $p<.01$, respectively). Similarly, longer sleep onset latency (SOL) as measured using sleep diary was correlated with higher YMRS scores at one-month follow-up ($r=.70$, $p<.05$). Actigraphy results indicated that shorter TWT was correlated with higher IDS-C scores at one month follow-up ($r=.58$, $p=.05$).
Conclusion: Our findings illustrate significant associations between disturbed sleep and subsequent symptoms among adults with inter-episode BD. Interestingly, subjective and objective measures of sleep are differentially associated with future symptoms, suggesting that the perception of less sleep may precede manic symptoms while a tendency towards more sleep (assessed with actigraphy) may precede depressive symptoms.

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A RELATIONSHIP BETWEEN SLEEP DISORDERED BREATHING AND ANGER SYMPTOMS FOR PATIENTS IN ANGER MANAGEMENT

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Introduction: Obstructive Sleep Apnea Hypopnea Syndrome (OSAHS) is characterized by repeated pharyngeal obstructions causing airflow cessation (apnea) or reduction (hypopnea) during sleep. Little attention has been given to the relationship between OSAHS and anger. The State Trait Anger Expression Inventory - 2 (STAXI-2), a 57-item measure of the state, trait, control and expression of anger, is a well researched instrument designed to measure anger. To investigate this relationship, we retrospectively reviewed 26 patients referred from the Anger Disorders

Clinic to the Sleep Disorders Clinic at the Royal Ottawa Mental Health Center. We hypothesized patients with more severe sleep-disordered breathing measured by Apnea Hypopnea Index (AHI) and Respiratory Disturbance Index (RDI) would have a positive correlation with higher Anger scores on STAXI subscales. Because REM sleep may have a mood regulatory function, we also speculated that patients with elevated REM related sleep-disordered breathing (REM SDB) will have a positive correlation with higher anger scores on STAXI subscales.
Methods: 26 patients were evaluated using the STAXI-2 in their anger evaluation, and subsequently had a polysomnogram conducted in accordance with the American Academy of Sleep Medicine Task Force guidelines.
Results: All patients had some sleep disordered breathing, but only 16 patients had REM sleep during their polysomnogram. Using Pearson correlation coefficients, there was a strong correlation between STAXI subscale "Anger Expression -- In" and AHI (r = 0.56) and RDI (r=0.64). A stronger correlation was found between "Anger Expression -- In" and REM SDB (r = 0.78) in 16 patients.
Conclusion: These findings suggest AHI and RDI are significantly associated with anger, and REM SDB may be more significant for patients with high scores on the "Anger Expression -In" subscale of the STAXI-2. Evaluation for OSAHS in patients with anger disorders may offer a novel mechanism of evaluation and management of anger.

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DOES SLEEP MEDIATE THE RELATIONSHIP BETWEEN NIGHTMARES AND SYMPTOM SEVERITY IN PATIENTS WITH PTSD AND DEPRESSION?

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Introduction: Nightmares are often considered to be a hallmark feature of Posttraumatic Stress Disorder (PTSD). Difficulty falling and staying asleep is frequently associated with PTSD and Major Depressive Disorder (MDD). This is the first study to ask whether sleep mediates the relationship between nightmares and severity of PTSD and MDD in participants with both disorders.
Methods: Data were obtained from 20 male veterans between the ages of 18 and 66 over two separate visits. At the first visit, MDD and PTSD were diagnosed using the Structured Clinical Interview for the DSM-IV. Nightmare frequency and intensity over the prior month were assessed by the Pittsburgh Sleep Quality Index Addendum for PTSD (PSQI-A). For the next week, sleep was measured prospectively with actigraphy. One week later, participants completed the Beck Depression Inventory II (BDI) and the PTSD Checklist (PCL) to measure MDD and PTSD symptom severity over the prior week.
Results: Regression analyses indicated that actigraphic sleep indices did not significantly mediate the relationship between nightmares and psychiatric symptom severity scores. Sleep did not correlate with BDI or PCL scores. However, nightmare frequency and intensity were negatively correlated with sleep efficiency (r = -.51, p = .03) and total sleep time (r = -.62, p = .006) and positively correlated with BDI (r = .51, p = .03) and PCL scores (r = .74, p = .001).
Conclusion: These analyses provide preliminary data that nightmares, rather than insomnia, play a particularly important role in psychiatric disturbance in patients with comorbid PTSD/MDD. Findings suggest that nightmares are influencing both sleep disturbance and psychiatric symptom severity. Consistent with previous literature, sleep disturbance was not correlated with MDD/ PTSD symptom severity, even though all participants reported sleep complaints. However, given the correlational nature of the data and the fact that prior sleep disturbance was not controlled for, no causal conclusions about the relationship can be drawn.
Support (optional): American Sleep Medicine Foundation

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EXAMINING SLEEP-WAKE PATTERNS IN PATIENTS WITH BIPOLAR DISORDER

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Introduction: Bipolar disorder, as with many psychiatric disorders, is symptomatically associated with changes in sleep-wake behavior, including sleep-wake timing, sleep architecture and sleep quality. Despite these observations, few studies have quantified the changes in sleep-wake behavior across time in patients with bipolar disorder.
Methods: o date, n=11 patients (6M; 5F; mean age ± sd = 37 ± 12 years) with a clinical diagnosis of bipolar disorder have been studied. All patients were recruited from a large, specialist psychiatric practice. Patients wore a wrist actigraph (AW64, MiniMitter, OR) on their non-dominant wrist and completed a sleep-wake diary for approximately 14 days. Data from the first 7 days was then analyzed.
Results: The majority of participants in this study had minimal positive symptom expression during the assessment period. Mean (± sd) clock time of sleep onset across 7 days was 23:05±125mins, with a mean wake time of 08:25±135mins. The range of sleep onset times was 21:15-00:34; and the range of sleep offset times was 05:45-11:00. The mean sleep duration was 573.8±71.7mins. The majority of participants (10/11) had relatively normal sleep-wake timing, while one participant had a delayed sleep phase relative to normal. Median sleep onset time was 22:45 and median sleep offset time was 08:00.
Conclusion: The average timing of sleep onset was similar to what is seen with many 'healthy' individuals. The mean sleep duration of >9 hours, along with slightly later sleep offsets may be due to bipolar-related changes in sleep-wake behavior, but also may reflect many participants not having regular employment requiring them to rise early each day.

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THE CO-OCCURRENCE OF INSOMNIA AND DEPRESSION SYMPTOMS IN AN ADOLESCENT MEDICAL CLINIC: A PILOT STUDY

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Introduction: Amongst community samples of adolescents, approximately 30% have insomnia symptom(s), 4 -11% insomnia symptoms meeting severity criteria or accompanied by daytime impairment, and 5-8% Major Depressive Disorder. Amongst those with clinically significant insomnia symptoms 30-50% have a psychiatric co-morbidity, predominantly anxiety or depressive. There are scant data on rates of co-occurrence of insomnia and depression for adolescents seeking medical care.
Methods: We reviewed health questionnaires completed during routine care by 103 consecutive patients (mean age 15.3, ± 1.7, range 12-18) presenting to an adolescent medicine clinic from 1/1/2008-6/30/2008. We determined rates of insomnia symptoms ("Trouble falling asleep", "Awakening during the night", "Being very tired during the day") and depressive symptoms ("Feel as though I am sad or anxious a lot of the time", "Sometimes I'm so sad that I think about dying"). We defined insomnia syndrome as at least one nocturnal symptom, plus daytime tiredness.
Results: Ninety-three charts had complete data. Of these 52.7% were female, 37.6% White, 8.6% African-American, 7.5% Asian/Pacific Islander, 8.6% Latino/a, 14.0 % "Other", with 23.7% missing race/ethnicity data. Forty-seven (50.5%) reported one or more insomnia symptom (23% sleep onset, 29% sleep maintenance, 40% daytime tiredness);

11 (12%) nocturnal symptoms plus tiredness; 35 (38%) depressive symptom(s); 15 (16%) both insomnia and depressive symptom(s). Rates of insomnia symptoms did not differ by gender, age or insurance status. However, co-occurring symptoms of insomnia and depression were more frequent in females (22% vs. 9%; Chi Sq = 3.06; p=.08) and in older adolescents (23% vs. 3%; Chi Sq= 6.49; p =.011). Four female adolescents met our criteria for insomnia syndrome and had co-occurring depressive symptom(s).
Conclusion: Insomnia symptoms are common in adolescents seeking medical care and often co-occur with depressive symptoms, particularly in older girls. Our pilot data suggest that this may be an important group to target for sleep intervention.

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SELECTIVE SEROTONIN REUPTAKE INHIBITORS: THE RELATIONSHIP WITH RESTLESS LEG SYNDROME

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Introduction: Limited and conflicting data has been found regarding the effects of Selective Serotonin Reuptake Inhibitors (SSRIs) on Restless Leg Syndrome (RLS). Our goal is to explore the rate of RLS in the depressed population and to evaluate the effects that SSRIs have on this rate.
Methods: Depressed and matched non-depressed subjects with available PSGs were included. The database was reviewed for demographics, medical, medications and PSG variables. Descriptive procedures, independent sample t-tests, Unifactorial ANOVA, partial correlations and cross tabulation using Chi-Square tests were conducted on four groups of patients; A): depressed subjects not taking SSRIs, B) depressed patients taking SSRIs, C) non-depressed patients not taking SSRIs (controls) and D) non-depressed patients taking SSRIs for other reasons. Subjects on other antidepressants were excluded.
Results: 440 consecutive patients were included, 186 females and 255 males. Mean (SD) age was 46.97(14.29) and mean BMI was 36.85 (10.14). Subjects' distribution in groups A, B, C and D were:152, 53, 194 and 39 subjects. 55 subjects (12.5%) had the diagnosis of RLS. RLS diagnosis correlated significantly with depressed status (groups A+B) (t=2.55, p=0.011) however it became non-significant when controlling for age, AHI and SSRI use (p=0.148). We found that group B had a significantly higher rate of RLS when compared to that of group C (19.69% vs. 8.38%, LR=11.04, p= 0.026). This finding continued to be significant when controlling for age and AHI (t= 0.124, p=0.031). In the depressed populations, 19.6% of group A and 17.8% group B had the diagnosis of RLS (LR=0.054, p= 0.82).
Conclusion: RLS diagnosis is prevalent in the depressed population. Depressed patients taking SSRIs have significantly higher rate of RLS when compared to non-depressed controls. When we evaluated the effects of SSRI on RLS rate in the depressed subgroup population we found a small, but non-significant effect. This suggests a baseline RLS-tendency in depressed population even before being treated with SSRIs.
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REM SLEEP IN PATIENTS WITH OBSTRUCTIVE SLEEP APNEA SYNDROME AND DEPRESSION: ASSESSMENT OF "REM PRESSURE"

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Introduction: Patients with Obstructive Sleep Apnea Syndrome (OSAS) are often REM-deprived with associated increase of "REM pressure". Elevated REM pressure, achieved via "arousal-type" of REM-deprivation, has been postulated to ameliorate depression. (Vogel et al. 1990). CPAP treatment usually increases REM percentage (REM%); the resulting decreased REM pressure might thus be predicted to aggravate depression. However, in practice, untreated OSAS is strongly associated with depression and successful CPAP therapy may ameliorate depressive symptoms. We surmised that initiation of CPAP therapy in patients with severe OSAS might represent a way to explore the complex relationship of REM pressure to depression and OSAS.
Methods: Data were obtained via database review of 3000 outpatients evaluated by attended overnight polysomnography for OSAS. Patients were divided into groups based on severity of OSAS, REM% before and after CPAP titration, severity of depressive symptoms (Goldberg Depression Scale - GDS) and self-reported nocturnal pain (l −10 scale). Comparison was controlled for BMI, gender and medications.
Results: Patients with high GDS scores (>30, depressed) and severe OSAS (AHI >30/hr) displayed higher REM% (7.8 ± 0.4 vs.5.3 ± 0.6) than those with low GDS scores (<12, non-depressed) with similarly severe OSAS. This finding was most evident in patients with the most severe OSAS (AHI >54/hr), in whom REM% was much higher (14.7 ± 4.2 vs.3.9 ± 0.8, P <0.01) in severely depressed patients (GDS >35) compared with non-depressed patients (GDS 5.6 ± 0.8). "REM-rebound" after CPAP titration was equally prominent (27% − 38%) in both depressed and non-depressed groups and proportional to severity of OSAS rather than depression.
Conclusion: OSAS may represent a clinical model of "arousal-type" REM sleep deprivation. Vigorous REM-rebound in non-depressed OSAS patients with profound REM suppression was not surprising. However, equally vigorous REM-rebound in depressed patients with less REM-suppression was unexpected and implies higher intrinsic REM pressure and possible REM dysregulation in the latter group.

1102

DEVELOPMENT OF POSTTRAUMATIC STRESS DISORDER AND SLEEP PROBLEMS IN INDIVIDUALS ESCAPED FROM SHIDA KARTLI, GEORGIA

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Introduction: Sleep problems have been often documented in individuals who develop posttraumatic stress disorder (PTSD).This study aimed at investigating the prevalence of PTSD and sleep disturbances in Georgian refugees recently escaped from war zone of Shida Kartli because of Russia-Georgia conflict.
Methods: 45 individuals (28 females, 19 males), aged 18-63 years (mean age 35.4) were asked to complete a comprehensive self-report questionnaire with 22 items assessing sleep-wake habits, sleep symptoms and demographic status. Each subject filled out Hand-Scoring option for Posttraumatic stress Diagnostic Scale (PDS). Questionnaires with too many missing answers were rejected.
Results: 43 questionnaires were correctly completed. Overall, 64.4% of the subjects reported having non-restorative sleep. Sleep complaints were prevalent in women than in men (67.8% vs. 52.9%). Nightmares were reported by 35.5% of total sample individuals with no gender differences. Mean sleep latency was 39.6(4.8) min; Mean sleep duration was 7.46(0.21) hr; 55% of individuals slept less than 7 hrs. 19 subjects (44.18%), more females (57.7%) than males (23.5%), endorsed items in a manner that is consistent with a DSM-IV diagnosis of PTSD (all of the six criteria were met). 41 subjects (95.3%) marked traumatic event "Military combat or war zone" that bothered them most. This occurred one to three months ago. The Symptom Severity rating was as follow: Mild in 39.5%, Moderate in 23.3%, Moderate to severe in 20.9% and Severe in 16.3 of subjects. Level of Impairment in Functioning of 16

individuals (37.2%) was Severe, of 18 (41.9%) was Moderate and of 9 (20.9%) was Mild.
Conclusion: The findings indicate that poor sleep is a common problem in refugees with PTSD. These findings highlight the importance of assessing sleep disturbance in individuals with PTSD symptoms. Further research is necessary to observe and evaluate sleep quality and PTSD developing process in people who escaped from war zone of Shida Kartli.
Support (optional): GNSF/ST07/6-237

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ASSOCIATIONS BETWEEN SLEEP QUALITY AND ANXIETY AND DEPRESSION SYMPTOMS IN A SAMPLE OF YOUNG ADULT TWINS AND SIBLINGS

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Introduction: Associations between sleep quality, anxiety and depression are well-established. Multiple theories have been provided to explain these associations, but limited genetic research has been conducted to address this issue. The purpose of this study was to examine the associations between sleep quality, anxiety and depression symptoms in a sample of young adult twins.
Methods: 1586 twins and siblings aged 18-27 years (62% female) completed the Pittsburgh Sleep Quality Index; an age-adjusted version of the Revised Child Depression and Anxiety Scale; and the Mood and Feelings Questionnaire. Genetic, shared environmental (those making twins alike) and non-shared environmental (those making twins dissimilar) influences were estimated on traits and their associations. This was achieved by comparing the magnitude of associations between monozygotic twins (who are genetically identical) and dizygotic twins/ siblings (who share on average half of their segregating genes).
Results: Variance in sleep quality was mainly explained by genetic (36%) and non-shared environmental factors (58%) with smaller shared environmental influence (6%). Sleep quality was associated with anxiety (r = .39, 95% confidence interval [CI], .34 - .43) and depression (r = .50, 95% CI, .46 - .54). Results from a trivariate correlated factors model suggest substantial overlap between genes influencing sleep quality and anxiety (rA = .65, 95% CI, .40 - 1); and those influencing sleep quality and depression (rA = .81, 95% CI, .53 - 1). Genes accounted for much of the overlap between sleep and anxiety (74%) and sleep and depression (61%).
Conclusion: Results from this twin study suggest that sleep quality is genetically influenced and that the main environmental influence is non-shared. There was substantial overlap between genes influencing sleep quality, anxiety and depression which suggests that specific genes known to be associated with anxiety and depression symptoms may be worthwhile investigating with regards to sleep quality and vice versa.
Support (optional): Wave 4 of the G1219 study was supported by the Economic and Social Research Council (RES-000-22-2206) and the Institute of Social Psychiatry to Alice M. Gregory who is currently supported by a Leverhulme Research Fellowship.

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SLEEP MACROARCHITECTURE AND SLOW-WAVE ACTIVITY IN DEPRESSED PATIENTS

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Introduction: It has been shown that there are sex differences in the distribution of sleep delta activity throughout the night in depressed patients. This is a prospective and multicentric study in depressed patient which explores polysomnographic sleep characteristics in depressed patients
Methods: Depressed patients with a Hamilton depression score(HD-17 items) over 22 were recruited after an adaptation night during which other sleep pathologies were excluded (more than 10 PLMs with arousal or more than 10 apnoeas and hypopnoea per hour of sleep). Patient were free of all psychotropic treatment for at least 15 days. A 4 channel EEG, two EOG, a CHIN EMG and the two tibialis EMG were recorded. Manual sleep scoring was performed by 30 seconds epochs seldom following Rechtschafen and Kales rules. Spectral analysis by Fast Fourier transformation (FFT) was performed by the MEDATEC software. Patients were divided in two groups: young patients (20- 40 years) and older patients (41-60 years). Statistical analysis was performed with the SAS statistical package. Comparisons between groups were performed by the Chi2 for qualitative variables and with an ANOVA for quantitative analysis. Descriptive analysis is given by mean ± standard deviation.
Results: 138 patients were included men and women. Mean age of 41 ± 12, mean Hamilton score of 26 ± 3. There were 89 women and 49 men. Comparisons of sleep analysis, whole night delta and delta ratio (delta 1st sleep cycle /delta 2nd sleep cycle) were similar for both sexes. Then comparison of ages groups showed a sex difference in delta distribution for the young population with a lower delta ratio in males (1.04 ± 0.04) than in females (1.14 ± 0.03).
Conclusion: This multicentric study with a large sample of depressed patients replicates the results of other smaller studies (1) and showed that depression impairs slow wave activity regulation in younger men from 20 to 40 years old but not in women.
Support (optional): (1) Armitage R et al Psychiatry Res 2000

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PERSISTENCE OF SLEEP DISTURBANCES FOLLOWING COGNITIVE-BEHAVIOR THERAPY AMONG REMITTED INDIVIDUALS WITH POST-TRAUMATIC STRESS DISORDER

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Introduction: Individuals with Post-Traumatic Stress Disorder (PTSD) report a wide array of sleep disturbances, including insomnia, restless sleep, nightmares, anxious dreams, and nocturnal panic attacks. Although cognitive-behavior therapy (CBT) has been shown efficient to decrease symptomatology and increase functioning among individuals with PTSD, its impact on associated sleep disturbances is unclear. This study was designed to assess the impact of CBT for PTSD on concomitant sleep disturbances.
Methods: Fifty-five individuals with PTSD (38 women; mean age = 41, SD = 13) received a mean of 19 individual CBT sessions (SD = 3) focusing on psychoeducation, anxiety management, imaginal and in vivo exposition, and cognitive restructuring. Traumas preceding current PTSD included physical aggression (40%), motor vehicle accident (26%), or witnessing a traumatic event (18%). PTSD diagnosis, sleep, anxiety, de-

pression, and health-related quality of life were assessed before and after treatment, and again six months later.
Results: All participants reported sleep disturbances (Pittsburgh Sleep Quality Index > 5) at baseline. Improvement of sleep was moderately correlated with improvement of PTSD symptomatology (r = 0.61). Further analyses were executed on a restricted sample of individuals who no longer met the diagnostic criteria for PTSD at post-treatment (n = 40). Persistence of sleep disturbances in remitted individuals with PTSD was observed in 55% of the sample (22/40), and was associated with greater severity of anxious and depressive symptoms, poorer self-perception of mental and physical health, and a greater number of residual symptoms of arousal immediately and six months after treatment.
Conclusion: While PTSD symptomatology has been demonstrated to remit following CBT, sleep disturbances do not necessarily follow the same course. For many individuals, sleep problems persist after successful treatment for PTSD. Furthermore, persistence of sleep disturbances is associated with poorer physical and mental health. These results suggest a need to include interventions focusing on sleep to PTSD treatment.

1106
AN EMPIRICAL EXAMINATION OF DIFFERENTIAL RELATIONS WITH SLEEP PROBLEMS AND SPECIFIC PTSD SYMPTOM CLUSTERS

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Introduction: Research has identified a relation between posttraumatic stress disorder (PTSD) and self-reported sleep problems. The current study sought to uniquely extend this literature by investigating the relation between PTSD symptom clusters (i.e., reexperiencing, hyperarousal, avoidance) and self-reported sleep problems. It was expected, based on previous laboratory and naturalistic research linking hyperarousal to sleep problems, that the hyperarousal symptoms of PTSD would be most strongly linked to sleep problems.
Methods: Participants included a community sample of 44 adults (M age = 34.39 years) with PTSD who were recruited from a semi-rural southern city. The Clinician Administered PTSD Scale was used to index PTSD diagnoses. Participants were asked to complete a battery of self-report questionnaires including the PSQI and smoking measures. Participants were debriefed and compensated with a $130 gift card.
Results: After controlling for gender and smoking status, subjective sleep quality was positively associated with hyperarousal symptoms [F (1, 40) = 4.99, p < .05]. Covariates in level 1 of the model did not account for significant variance in subjective sleep quality (R2 = .01, ns). Hyperarousal symptoms at level 2 significantly contributed to the overall model (R2 = .10, p < .05). Steps 1 and 2 combined to account for 12.5% of the total variance. Further analyses supported the specificity of this relation, such that alternatively entering main effects of reexperiencing and avoidance symptoms into level 2 produced non-significant regression models [F (1, 40) = 2.19, p > .05], and [F (1, 40) =.16, p > .05], respectively.
Conclusion: Results suggest sleep problems among individuals with PTSD may be associated with hyperarousal symptoms to a greater degree than other aspects of the posttraumatic stress syndrome. Experimental and longitudinal tests of this relation are now needed in order to better understand this relation.

1107
EFFECTIVENESS OF IMAGERY REHEARSAL THERAPY FOR THE TREATMENT OF COMBAT-RELATED NIGHTMARES IN VETERANS

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Introduction: Chronic nightmares are commonly reported by veterans with Posttraumatic Stress Disorder (PTSD). Imagery Rehearsal Therapy (IRT) has been shown efficacious in reducing chronic, trauma-related nightmares, but is not well-studied in veterans. We aimed to determine feasibility, acceptability, and effectiveness of IRT among veterans. We hypothesized IRT would be associated with reductions in nightmare frequency/intensity, insomnia, and daytime PTSD symptoms.
Methods: Data were extracted retrospectively from medical records of 91 consecutive veterans who were referred for IRT treatment. We compared demographic, medical, and psychiatric variables between: a) referred veterans who did and did not participate in treatment and b) participants who did and did not complete treatment. Groups were also compared on baseline treatment-related variables. For treatment completers, we used paired samples t-tests to assess changes in treatment-related variables extracted from daily nightmare logs, Insomnia Severity Index, Pittsburgh Sleep Quality Index, and PTSD Checklist.
Results: Fifty-eight veterans initiated treatment. Those completing a full course of treatment for PTSD in the past year were more likely to initiate IRT treatment. However, completion of IRT was not related to previous treatment, demographic variables, or baseline nightmare severity. Treatment completers (n=35) reported significant reductions in nightmare frequency (33%) and intensity (36%), severity of insomnia (27%), and subjective daytime PTSD symptoms (28%). Insomnia and PTSD symptoms, on average, were below clinical cut-offs following treatment, and 23% of patients showed a complete treatment response (< 2 nightmares/week). Veterans completing individual IRT demonstrated greater reductions in insomnia than those completing group IRT.
Conclusion: Findings suggest IRT is an effective, short-term treatment for nighttime and daytime PTSD symptoms in a clinic-based sample of trauma-exposed veterans. Furthermore, data indicate veterans who report persisting sleep difficulties following treatment for PTSD may be more likely to engage in a nightmare treatment. Thus, IRT may be a suitable adjunct to treatment as usual for PTSD.

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ASSOCIATION OF MATERNAL SLEEP CHANGES DURING THE PERINATAL PERIOD TO DEPRESSIVE AND HYPOMANIC SYMPTOMS: PRELIMINARY RESULTS

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Introduction: Sleep changes in women during pregnancy and the postpartum period. No studies have elucidated clear associations between alterations in sleep duration, timing, or quality and postpartum depressive symptoms, and hypomanic symptoms have not been examined with regard to sleep. This ongoing study begins to address this gap.
Methods: Six women (ages 31.1±4.6 yrs) enrolled from May-August 2008. Participants wore wrist actigraphs and kept daily sleep diaries for 1 week during the 3rd trimester (3rdT) and postpartum weeks 1, 2, 6, and 12. Sleep onset (SleepOn), sleep offset (SleepOff), total sleep time (TST), sleep efficiency (SLEF), and sleep period time (SPT) were estimated from actigraphy data using the Sadeh algorithm (1994) in Action-W software (AMI, Ardsley, NY). We gave the Center for Epidemiologic Studies Depression Scale (CES-D) for depressive symptoms and the Altman Self-Rating Mania Scale (Altman) for hypomanic symp-

toms at the end of each week. Data are presented from 3rdT and postpartum week 2 (Wk2).
Results: Mean SPT was significantly shorter during 3rdT (488±34 min) than Wk2 (590±26 min, t=-6.15, p<.01), yet average TST did not differ (3rdT=427±28 min, Wk2=402±47, t=1.07, p=.33). Average SLEF reflects this phenomenon: 3rdT=88.2±4.9%, Wk2=69.3±8.6% (t=5.04, p<.01). Mean SleepOn was 23:17±74 min for 3rdT and 22:39±53 min for Wk2 (t=1.70, p=.15) and mean SleepOff was 7:22±55 min for 3rdT and 8:28±49 min for Wk2 (t=-3.40, p=.02). All women were euthymic during 3rdT (means: CES-D=5.2±2.5; Altman=1.0±1.1) with individual differences emerging in Wk2 (means: CES-D=9.3±7.1; Altman=1.5±1.2). Correlation coefficients computed for postpartum TST vs. postpartum mood showed no significant associations in this small sample: CES-D vs. TST: r=-.20 (p=.71); Altman vs. TST: r=-.05 (p=.93). Correlation coefficients associating postpartum mood to changes in sleep timing were more promising, particularly for hypomanic symptoms: Altman vs. SleepOn Change: r=.82 (p<.05); Altman vs. SleepOff Change: r=.68 (p=.14); CES-D vs. SleepOn Change: r=.19 (p=.72); CES-D vs. SleepOff Change: r=.48 (p=.34).
Conclusion: These data confirm that substantial changes in sleep behavior occur during the early postpartum period. Concomitant mood changes may be related more to altered sleep timing rather than to sleep amount. These data from a small sample and a period associated with mood lability will be expanded with future analyses that include more women and data from postpartum weeks 6 and 12.
Support (optional): Division of Pulmonary, Critical Care, and Sleep Medicine, Rhode Island Hospital.

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REM AND NREM-RELATED MOOD REGULATION IN UNMEDICATED ANXIOUS DEPRESSION

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Introduction: Depression and anxiety often present together as a single disorder. Anxious-depression co-segregates in families and is resistant to traditional anti-depressants. Sleep disturbance is prominent in anxious depression. The aims of this study were to characterize sleep architecture as well as REM and NREM mood processing disturbances in unmedicated anxious depressives.
Methods: After one habituation night, 35 healthy young adults (mean age=20) and 20 anxious depressives (mean age=21; n.s.) (as determined by responses on DASS and POMS mood scales) were assessed with overnight polysomnography and then awakened from REM and NREM sleep states. Awakenings were counterbalanced across subjects. After each awakening, subjects completed self versus 'significant other' positive and negative trait rankings. Participants were also given tests of daytime mood function in the morning.
Results: The anxious depressed group evidenced significantly lower sleep efficiency (mean=0.78(sd=.02)) scores than healthy controls (mean=0.83(sd=.01), p=.014), significantly higher Pittsburgh Sleep Quality Index scores (mean= 6.3 (.43)) than healthy controls (mean=4.2 (sd=.32), p=.0001); and significantly higher 'Difficulties in Emotion Regulation Scale' scores (mean=87.7(sd=3.5) than controls (mean=69.1(sd=2.6), p=.0001). Endorsements of positive trait ratings for self versus a significant other were significantly decreased (mean= -5.7 (sd=1.5) as compared to the control group self ratings (mean= -1.1 (sd=1.0), p=.01 after awakenings from REM but not NREM (control group mean=-1.6(sd=.79) versus anxious depressed mean=-1.3 (sd=1.1), p=.88).
Conclusion: Anxious depression is characterized by sleep disturbance and REM-related mood and Self-regulation dysfunction.
Support (optional): This work was support by NIMH Grant no. 1R21 MH076916-01A2 to the first author.

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AGE- AND SEX-RELATED DIFFERENCES IN SLOW-WAVE ACTIVITY IN HEALTHY AND DEPRESSED CHILDREN AND ADOLESCENTS

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Introduction: Early-onset major depressive disorder (MDD) is a severe and chronic condition associated with longer duration of illness, more episodes, and higher mortality than late-onset MDD. Sleep disturbance is one of the main characteristics of patients with MDD. Previous studies have shown a developmental decrease in delta power in healthy children and adolescents. However, it is not certain whether MDD in the same population is associated with changes in the developmental course of delta power. In the present study, we investigated age and sex related changes in slow wave activity (SWA) in healthy and depressed children and adolescents.
Methods: Data were obtained from 170 MDD (85 M, 85 F) and 98 healthy controls (HC) (44 M, 54 F) children (age 8-12) and adolescents (age 13-17). Participants maintained a regularized sleep/wake cycle for one week followed by 2 consecutive nights in the sleep lab. Night 1 served as adaptation and as a screening for independent sleep disorders. Data are expressed as SWA, which is defined as the average delta power in stage 2-4 in the first 4 NREM periods.
Results: Age-related changes in SWA differed between depressed and healthy, and by sex. SWA power was lower among young healthy boys than MDD boys, an effect that was reversed in adolescence. In fact, the age-related changes in SWA were steeper among MDD males. In the case of female children, HCs showed more SWA than those with MDD, but among adolescents, the two groups were identical.
Conclusion: The present observations in a large sample of children and adolescents suggest that developmental changes in SWA differ between those with early-onset MDD and healthy controls. However, the group differences in SWA are strongly modulated by sex. These results highlight the need to assess age and sex effects on sleep EEG in early-onset depression.
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REM SLEEP BOUT DURATION AND FREQUENCY IN THOSE WITH PTSD

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Introduction: A number of prior studies indicate alterations in REM sleep in those with PTSD, including more fragmented REM sleep following trauma in those who ultimately develop PTSD relative to those who do not. In the current study, we sought to further examine this relationship by comparing polysomnographic (PSG) sleep in a group of PTSD patients compared to insomnia patients and normal sleepers. We hypothesized shorter duration and increased frequency of REM bouts in PTSD patients.
Methods: PSG data were derived from: 17 PTSD patients following civilian trauma; 11 normal controls; and 15 patients with primary insomnia. We assessed average REM bout duration and number of REM episodes, with REM bout defined as a period of REM interrupted by a non-REM stage lasting between 30 seconds and 2 minutes. We also compared groups on the number of short REM episodes, defined as a REM episode lasting between 30 seconds and 2 minutes.

Results: There was a trend ($p<0.10$) for PTSD patients to have longer REM bout durations terminated by at least 30 seconds of non-REM activity relative to comparison groups. There was also a trend ($p<0.10$) for PTSD patients to have a greater number of REM periods terminated by 2 minutes or more of non-REM activity.
Conclusion: In this exploratory analysis, we found no evidence that those with PTSD have shorter REM bout lengths than normal sleepers or insomnia patients. We found preliminary evidence that PTSD patients may have longer REM periods disturbed by very brief awakenings and more frequent REM periods ending in awakenings lasting longer than 2 minutes. Further studies will be needed to better establish the nature of the alteration of REM sleep in PTSD patients.

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SLEEP DISORDERS AMONG PATIENTS WITH MAJOR DEPRESSIVE DISORDER IN A LARGE MANAGED-CARE POPULATION

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Introduction: Sleep disturbances are very common in patients with major depressive disorder (MDD). However, little is known about the comorbidity of specific sleep disorders in depressed patients. This study examined the prevalence and age and gender differences of specific sleep disorders among MDD patients.
Methods: A total of 153,913 patients in a private payer insurance claims database, who had at least 1 diagnosis of MDD during 2006, were included in the analysis. The sample consisted of 106,804 (69.4%) females and 47,109 (30.6%) males, with a mean age of 43.6 years. In accordance with the ICD-9-CM, sleep disorders were grouped into 5 categories: nonorganic disorders, organic disorders, restless legs syndrome, narcolepsy, and sleep disturbances.
Results: Overall, 15.3% of MDD patients had any sleep disorder. Prevalence rates for specific sleep disorders were distributed as follows: 1.1% for nonorganic sleep disorders, 3.1% for obstructive sleep apnea (OSA), 7.2% for insomnia, 4.6% for hypersomnia, and less than 1% for any other sleep disorder. The prevalence rates of sleep disorders significantly increased with age, ranging from 7.7% for patients aged 18-24 years to 18.8% for those aged 55 and above. OSA was more prevalent in males than in females (4.4% vs. 2.5%, $p < .0001$), as was hypersomnia (6.5% vs. 3.8%, $p < .0001$). Most sleep disorders were more prevalent in patients with recurrent depression than in those with a single episode of depression (OR = 1.2 - 2.0, $p < .001$).
Conclusion: This study found lower prevalence rates of sleep disorders in MDD patients than previous studies, possibly due to different diagnostic criteria or under-diagnosis in the managed-care settings. This study also found that sleep disorders increased with age, and OSA was more common in males than in females. Further research is needed to examine the impact of sleep disorders in the treatment of depression.
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CHRONIC PAIN ASSOCIATED WITH SLEEP DISORDERS AMONG PATIENTS WITH MAJOR DEPRESSIVE DISORDER

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Introduction: Chronic pain, sleep disturbances, and depression are common in the general population and primary care patients. The relationships between these conditions are complex. This study examined the association between chronic pain and sleep disorders in patients with major depressive disorder (MDD) and also examined if chronic pain is associated with a specific sleep disorder.
Methods: A total of 153,913 patients in a private payer insurance claims database, who had at least 1 diagnosis of MDD during 2006, were included in the analysis. The sample consisted of 106,804 (69.4%) females and 47,109 (30.6%) males, with a mean age of 43.6 (SD = 12.7) years. Chronic pain was defined as any pain in the following 5 categories: headache, rheumatoid arthritis (RA)/osteoarthritis (OA), low back pain (LBP), fibromyalgia, and neuropathic pain. In accordance with the ICD-9-CM, sleep disorders were grouped into 5 categories: nonorganic origin, organic sleep disorders, restless legs syndrome, narcolepsy, and sleep disturbances. Logistic regression was used to examine the association between chronic pain and sleep disorders.
Results: The overall prevalence rates of chronic pain and sleep disorders in patients with MDD were 42.7% and 15.3%, respectively. The rate of overall sleep disorders in MDD patients with chronic pain was approximately twice that of patients without chronic pain (20.6% vs. 11.4%, $p < .0001$). Chronic pain was significantly associated with increased odds of all types of sleep disorders (OR = 1.8 - 3.2, $p < .0001$), independent of age, gender, and recurrent depression.
Conclusion: Our findings suggest that chronic pain is associated with elevated risks for all types of sleep disorders in MDD patients. Further research is needed to examine the neuropathological mechanisms of chronic pain, sleep, and depression. Clinical pharmacological studies are also warranted to examine the interplay of pain medications, sleep medications, and antidepressants in the treatment of depression.
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DISSOCIATION BETWEEN STAGE 2 SIGMA EEG ACTIVITY AND SLEEP SPINDLE DENSITY IN HIGH-FUNCTIONING AUTISM

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Introduction: Adults with high functioning autism (HFA) display fewer stage 2 sleep spindles than controls (Limoges et al., 2005). Since EEG sigma activity is in the same frequency range as sleep spindles, we verified whether sigma activity is also diminished in HFA.
Methods: Sixteen adults with HFA (14 men, 2 women, 22.1±3.6 years) and 16 comparison participants(COM: 20.6±3.9 years) were recorded for two consecutive nights. Stage 2 sleep spindles of night 2 were visually identified on the C3 and Fp1 electrodes as bursts of EEG activity at 12-15 Hz, lasting 0.5-2.0 sec, with no amplitude criteria applied. Spectral amplitude of stage 2 sigma EEG activity (11.75-14.75 Hz) was computed for the first seven hours of sleep of night 2 in a subgroup of

nine HFA and six comparison participants. Data is expressed as mean ± sem. Groups were compared using t-tests.
Results: Minutes of stage 2 was the same in the two groups (HFA: 275.6±2.1, COM: 283.6±2.1, n.s.). Number of spindles per hour of stage 2 at Fp1 was the same in the two groups (HFA= 46.9±11.9, COM: 62.1±9.9, n.s.) but C3 spindle density was lower in the HFA group (146.2±15.3 vs. 215.4±16.6; p<.004). The whole first 7 hours of sleep did not show group differences on stage 2 sigma activity for the Fp1 (HFA=6.±5.7, COM=3.9±2.1) nor the C3 electrode (10.4 ±4.8, COM=11.1±4.1), neither did an hour by hour breakdown of the data.
Conclusion: These results show that, contrary to sleep spindles, the quantity of sigma activity during stage 2 is typical in HFA. This supports the hypothesis that visually identified sleep spindle waveforms and quantified EEG sigma spectral activity reflect two distinct processes (see also Gais et al., 2002). Since persons with Asperger syndrome are known to display fewer sleep spindles than those with HFA, further analyses will compare these two subgroups.
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THE EFFECT OF COMORBID DEPRESSIVE DISORDER ON SLEEP IN ATTENTION-DEFICIT HYPERACTIVITY DISORDER PATIENTS

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Introduction: ADHD patients (pts) have extensive sleep disturbances including increased nighttime activity, reduced rapid eye movement, and significant daytime somnolence. This activity concerned mostly upper and lower limb movements. ADHD co-occurs with depressive disorders in high prevalence. Our goal was to explore retrospectively the effect of comorbid depressive disorder on sleep architecture, respiratory findings and Periodic Limb Movements Indices in ADHD pts undergoing polysomnographic evaluations (PSG). We compared two groups: Group A: pts with ADHD and depressive disorder and Group B: pts with ADHD without comorbid depressive disorder.
Methods: ADHD pts who had PSG in our sleep center were included. The database was reviewed for demographic data, medical and mental history, medications used at the time of the PSG, and other PSG findings. Descriptive procedures for each variable were conducted to determine measures of central tendency, variability and shape of score distributions. The presence of outliers and the violations of parametrical tests were determined using exploratory analyses. Sleep architectures, respiratory data and PLM indices were compared between group A and group B using independent sample t tests, Chi- Square test and Partial correlations test.
Results: 95 ADHD pts were included in the final analysis, 34 females(35.8%) and 61 males(64.2%), mean age 20.5(15.00)years. In this group other comorbidities included depression 30(31.6%); asthma 19(20%); and HTN 6(6.3%). Of the 95 patients, 63(66.3%) were taking stimulants at the time of the PSG evaluation. Only 8(8.4%) pts were diagnosed with Restless Leg Syndrome(RLS).Of the 30 depressed pts (15 females, 15 males) 14 pts were on SSRI medications and 16 were on no antidepressant medications. Three other pts were taking SSRI for anxiety diagnoses. Pts in Group A were significantly older and had higher BMIs than group B. Pts in Group A had significantly less time spent in stage 3, higher arousal index and stage shifts, lower minimum oxygen saturation, and higher AHI, REM index and PLMAI. When controlling for age, the only significant finding left was higher arousal index in Group A when compared to group B(22.297/13.3167 vs. 12.718/7.2371) (r=0.274,p=0.012).
Conclusion: ADHD pts have higher arousal index during sleep when comorbid with depressive disorders. Other differences in sleep architecture, respiratory findings and limb movements indices may be explained by the age differences between the two groups.

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THE IMPACT OF SMOKING CESSATION AND PHARMACOTHERAPY ON SLEEP ASSESSED ACROSS THE FIRST 10 DAYS AFTER QUITTING

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Introduction: Subjective sleep disruption is a prominent symptom of smoking cessation. Polysomnography (PSG) studies tracking the period following smoking cessation are rare. We report data from a randomized, double-blind placebo controlled trial of nicotine replacement therapy (NRT) and bupropion (BP) treatment for smoking cessation with repeated assessments over the first 10 days following quitting.
Methods: 27 smokers (15 men, 40.9 ± 13.9 years) underwent full night PSG on a baseline night (B) (still smoking) and the first night following quitting (Q1). 25 smokers had an additional night 3-5 days post quit (Q5) and 16 a fourth night 7-10 (Q10) days post quit. BP and NRT were administered as per current clinical practice guidelines. Data at Q1, Q5 and Q10 were analyzed using a regression model with a constant assuming no difference from B and terms for, NRT and BP, controlling for age, sex, smoking intensity and baseline Epworth Sleepiness Scale score
Results: Independent of treatment, sleep efficiency (SE%) was reduced at Q1 (-4.2 ±1.6 %, p =0.016) but not at Q5 or Q10. Similarly, wakefulness after sleep onset and percentage of stage 1 sleep (S1%) showed significant deterioration at Q1 but not at Q5 or Q10. Number of wake periods was increased at Q1 (5.3 ± 1.6, p= 0.004) and at Q5 (3.2 ± 1.1, p= 0.007) but was no longer significantly elevated at Q10. SE% showed additional effects of BP at Q5 and NRT at Q10 with continued deterioration with active medications. S1% showed continued deterioration with active NRT at Q10.
Conclusion: Smoking cessation leads to a negative impact on sleep continuity on the first night of quitting smoking with rapid recovery in the direction of baseline within 5 to 10 days post-quit. There is some evidence that active NRT and BP may prolong the sleep disturbance.
Support (optional): Supported by DA16427 from the National Institute on Drug Abuse.

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DECREASED MOVEMENT AT NIGHT PREDICTS HIGHER DEPRESSION SCORES IN A NONDEPRESSED ADULT POPULATION

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Introduction: Across the spectrum of depression severity, there are likely various degrees of impact on ones physical movement, with less activity in those most depressed.
Methods: 30 healthy adult subjects aged 45-67, without a history of depression and not on antidepressants were assessed by means including surveys and 24 hour actigraphy worn on the waist. Surveys included BDI-II (Beck Depression Inventory-II), PSQI (Pittsburg Sleep Quality Index), QOL (quality of life scale), and POMS (profiles of mood state).
Results: Subjects with less absolute movement in their sleep period were more likely to have higher scores on the BDI-II than subjects with more absolute movement at night, as measured by actigraphy. Activity measures in sleep ranged from 458 to 88469 (units). Ranking by activity in sleep, the bottom 15 averaged 2051 on movement and had a BDI-II average of 3.57, compared to 13747 in the 14 with most movement, who had a BDI-II average of 1.60 (difference between means=1.97, sd=5.3). Two of the 3 highest BDI scores were in the 3 subjects with the least movement in their sleep period. Subjects with less movement at night as reflected in their night movement versus 24 hour movement ratio were more likely to have higher depression scores on the BDI-II. Ranking the

movement ratios in order (0.0037 to 0.27), the first 14 had an average BDI-II of 3.14, versus an average of 2.00 for the last 15 (one data not readable). The top 3 high scores of the 29 subjects' BDI-II were in the lowest 4 ranked by ratio of night/24 hour movement. 3 of the 4 highest movement at night ratios had a BDI-II score of 0. Subjects with a higher PSQI score, indicating more sleep subjective sleep problems, were more likely to have lower quality of life scores, though not statistically significant. PSQI scores ranged from 0 to 27. Ranking these in order, the 15 lowest scores had an average QOL score of 71.46, versus the 15 highest scores where the average was 68.13.

Conclusion: Decreased movement at night in absolute value, and in comparison with 24 hour activity is correlated with higher depression scores in a non-depressed healthy adult population. Higher scores on the PSQI are correlated with a slightly lower subjective quality of life score, though not significantly.

Support (optional): This study is funded by the Wisconsin Comprehensive Memory Program.

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A PRELIMINARY EXAMINATION OF CO-SLEEPING AND RELATIONSHIP QUALITY IN VETERANS WITH PTSD AND DEPRESSION

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Introduction: Sleep disruptions such as insomnia, arousals and nightmares are common in people with Post-Traumatic Stress Disorder (PTSD) and Major Depressive Disorder (MDD). To our knowledge, no research has examined how these disruptions might impact their bed partners' (BP) sleep. We examined whether patients with PTSD/MDD report receiving more complaints from their BPs about their sleep than normal controls. Next, we qualitatively examined BP sleep and relationship quality in a subset of patients with PTSD/MDD.

Methods: Using a cross-sectional design, we compared BP item scores from the Pittsburgh Sleep Quality Index (PSQI) in 27 patients with PTSD and MDD (PTSD/MDD group) and 32 normal controls (NC). In a subset of the PTSD/MDD group (n = 5), we examined (a) BP sleep via the PSQI and (b) marital satisfaction via subscales on the Dyadic Adjustment Scale (DyAS). Data were analyzed using chi-square and ANOVA techniques.

Results: Compared to NCs, individuals in the PTSD/MDD group stated that their BPs were more likely to frequently report long pauses in breathing (χ^2 = 18.21,p<.01), legs twitching during sleep (χ^2= 33.75,p<.001), and episodes of confusion (χ^2=35.66, p<.001). There were no differences between the PTSD and NC groups on the frequency with which partners were sharing beds. Only one BP in our subsample had clinically significant levels of sleep disturbance. Affectional expression and dyadic consensus scores were within the normal range for married couples; however, the dyadic satisfaction subscale (M=32.4, SD=9.15), was lower than that for married couples (M=40.5), indicating a minor degree of dissatisfaction in the relationship.

Conclusion: Although PTSD/MDD patients report that their bed partners identify a number of breathing, movement, and confusional events in their sleep, preliminary data indicate that BPs may not sleep poorly. These data are consistent with previous findings indicating a tendency for veterans with PTSD to over-report symptoms. Ongoing work will provide valuable information about whether sleep indices between bed partners correlate and if BP sleep quality correlates with relationship satisfaction.

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SLEEP QUALITY IN RECENTLY SOBER ALCOHOLICS

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Introduction: Impaired sleep quality and the factors associated with it in recovering alcoholics are not clearly understood. The aim of this study was to evaluate the sleep quality in recently sober alcoholic veterans, and to explore its relationship with covariates previously known to be associated with sleep disorders.

Methods: 10 out of the 16 recruited male alcoholic subjects were assessed further. Subjective assessments included: Sleep Quality (Pittsburgh Sleep Quality Index, PSQI), Sleepiness (ESS), Depression (PHQ-9), Anxiety (Beck's Anxiety Inventory, BAI), Alcohol Use (Timeline Follow Back measure). Objective assessments included: polysomnogram (2nd night of overnight in-laboratory PSG) and daytime neurobehavioral performance (10-minute psychomotor vigilance task, PVT).

Results: Subjects were sober for 46 ± 32 days, prior to which they drank 18 ± 9 standard alcoholic beverages a day. The PSQI global score was 11.5 ± 3.8, ESS score was 7 ± 5, PHQ-9 score was 10 ± 5.4 and BAI score was 9.4 ± 10.7. PSG indices were significant for a Total Sleep Time (TST) of 5.2 ± 1.6 hours and 3.3 ± 0.9 REM episodes through the night. On the PVT there were 5 ± 6 lapses and 10% of the fastest reaction times were 222.86 ± 56 ms. Correlates of subjective sleep quality were TST (r = - 0.79, p < .01), number of REM episodes (r = - 0.69, p < .05), total PHQ-9 score (r = .84, p < .005), total BAI score (r = .69, p < .05) and Drinks per Drinking Day (r = .72, p < .05). No correlation of sleep quality with any other measure was seen.

Conclusion: The inadequate quality of sleep in these subjects was associated with polysomnographic sleep abnormalities, depressive and anxiety symptoms and prior intensity of drinking, but not with daytime sleepiness, daytime neurobehavioral performance or the duration of sobriety from alcohol use.

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INSOMNIA AND NIGHTMARES AS PREDICTORS OF ELEVATED SUICIDE RISK AMONG PATIENTS SEEKING ADMISSION TO EMERGENCY MENTAL HEALTH FACILITY

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Introduction: Sleep complaints are now listed among the top 10 warning signs of suicide by SAMHSA, and appear to confer risk for both suicidal ideation and behaviors. Sleep and mood disturbances are tightly coupled, and depression is the single best predictor of suicide. Even so, few investigations have evaluated whether poor sleep predicts suicidality above and beyond depression. Furthermore, a study has yet to examine this link among at-risk populations, including patients in acute psychiatric crisis.

Methods: Data were collected among 82 men and women (aged 18-66) presenting at a community mental health hospital for emergency psychiatric evaluation. Evaluations determined eligibility for crisis stabilization unit inpatient admission. Patients awaiting admittance were invited to participate, and completed: the Disturbing Dreams and Nightmare Severity Index; Insomnia Severity Index (ISI); Beck Depression Inventory (BDI); Beck Scale for Suicide Ideation (BSS). We hypothesized that sleep disturbances, controlling for depression, would predict elevated suicidal symptoms.

Results: Results revealed mean symptom scores in the severe range across measures. Hierarchical linear regressions were employed to test hypotheses. Consistent with past research, DDNSI [t=1.56, β= .19, p=.12] and ISI total scores [t=2.64, β=.33, p=.01] were associated with greater BSS scores. After BDI scores were entered as a covariate, ISI

and DDNSI scores jointly predicted BSS [$F(3,76)=21.6$, $p<.01$]; however, only DDNSI scores [$t=1.84$, $\beta=.19$, $p=.06$] independently predicted higher BSS scores, as a non-significant trend. After accounting for BDI symptoms, ISI scores [$t=-1.21$, $\beta=1.16$, $p>.05$] were no longer associated with BSS scores.

Conclusion: Self-reported nightmares uniquely predicted elevated suicidal symptoms, whereas insomnia did not. To our knowledge, this is the first examination of sleep and suicide risk among patients seeking emergency admission to a community hospital. Based on these initial findings, a more thorough assessment of sleep in acutely-ill patients is warranted and may provide an important opportunity for intervention.

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SLEEP STAGING BASED ON AUTONOMIC SIGNALS - A MULTI-CENTER BLINDED VALIDATION STUDY

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Introduction: One of the most important caveats of level 3 ambulatory devices is the inability to record and stage sleep. In the current study we sought to validate a previously developed and published algorithm to detect sleep stages based on autonomic signals (derived from a Watch_PAT100 device), utilizing epoch-by-epoch comparisons to standard polysomnography (PSG). A previous algorithm to only distinguish sleep and wakefulness has already been published on this cohort. The current study is a validation of a novel advanced algorithm determining 4 different stages: Wake, light sleep, deep sleep and REM sleep based on peripheral arterial tone, actigraphy, heart rate, and oxygen saturation.
Methods: Design: Application of a novel algorithm on a previously published prospective multi-center blinded cohort study. Setting: Three university hospital sleep laboratories. Methods: 38 normal subjects and 189 patients with obstructive sleep apnea (OSA) from three centers (Skara, Boston, Haifa) underwent simultaneous recording of PSG and Watch_PAT100. The PSG was manually scored by a blinded experienced scorer, while the Watch_PAT100 data was automatically scored by the embedded algorithm (zzzPAT). For the purpose of agreement between the PSG and the Watch_PAT100, stages 1 and 2 of the PSG were classified as light sleep.
Results: The agreement in detecting deep vs. light sleep ranged from 87.1±5.1% in the normal subjects to 86.4±4.5%, 87.5±6.0% and 93.5±4.9% in the mild, moderate and severe OSA patients, respectively. The agreement in detecting REM vs. NREM sleep was similar for all OSA subgroups and averaged 88.7±5.5%. There was a good agreement between PSG and Watch_PAT 100 in quantifying sleep latency (56.8 ± 31.4 vs 43.3 ± 45.4 epochs, NS), sleep efficiency (78.4 ± 9.9 vs 78.8 ± 13.4%, NS), REM latency (236.5±147.8 vs 224.9±159min, NS), REM percentage (14.4± 6.5 vs 19.3± 8.7%, NS) and total sleep time (690 ± 152 vs 690 ± 154 epochs, NS) respectively.
Conclusion: These data demonstrate acceptably accurate sleep staging in normal subjects and patients with varying severity of OSA, based on recordings from the Watch_PAT100. These results are of substantial importance in the era of a shift toward unattended ambulatory sleep recordings.

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ACTIGRAPHY AND FUNCTIONAL DATA ANALYSIS FOR OBJECTIVE MEASUREMENT OF FATIGUE: A CASE STUDY IN HIV/AIDS

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Withdrawn

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VALIDATION OF A STATE FATIGUE SCALE

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Introduction: There are currently no scales assessing state fatigue levels. Such an instrument would enable multiple measurements of fatigue within a shorter time frame. The aim of this study is to validate a state Fatigue Scale (FS).
Methods: The 7-item FS, similar in format to the SSS, consists of 7 statements ranging from "Full of energy; enough to manage my usual physical activities" to "Totally physically exhausted: unable to undertake the least activity". Respondents are asked to pick the statement that best describes their current level of fatigue. The FS, Brief Fatigue Inventory (BFI), Fatigue Severity Scale (FSS), Fatigue Assessment Inventory (FAI) and the FACES fatigue adjective checklist were administered in the morning (between 7 and 8am) to 195 sleep clinic patients. For test re-test analysis, 133 other patients were asked to complete the FS scale twice within 10 days. Statistical tests for discriminate validity, correlations with other measures of fatigue and test, re-test stability were conducted.
Results: 178 completed questionnaires were collected: the mean FS score was 3.6±1.5. Using the FSS as the gold standard, scores indicative of normal and abnormal fatigue levels on the FS were found to be 2.4±1.3 and 4.2±1.3, respectively, with FSS-defined abnormal values on the FS significantly different ($p<0.0001$) from the normal FS values. The FS was moderately correlated with the BFI, FAI, FSS, and FACES, r= 0.54, 0.39, 0.51 and 0.47, respectively. The Reliability Correlation Coefficient indicated good test, re-test stability (alpha=0.74).
Conclusion: The FS is the first state fatigue scale. It is easy to use and shows modest levels of correlation with trait fatigue scales. A higher correlation between state and trait scales would not be expected. Further, the FS is able to distinguish fatigued from non-fatigued individuals and shows strong test re-test validity despite the FS being a state scale. The FS should prove extremely useful for future studies.

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COMPARISON BETWEEN ACTIGRAPHY AND POLYSOMNOGRAPHY IN A REAL WORLD ENVIRONMENT

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Introduction: The detrimental extent of sleep restriction in society is becoming increasingly prevalent. Actigraphy has been widely deployed to estimate sleep metrics in real-world situations where polysomnography (PSG) is not suitable. Its use for sleep assessment provides quantitative statistics, although PSG remains the gold standard for sleep measurement. The logistics of research in field settings may require the use of longer epochs to maximize the length of data collection in remote locations (e.g., during spaceflight). The aim of this analysis was to examine the accuracy of the sleep/wake algorithm provided by the Minimitter 'Actiware® - Sleep' scoring program with data collected using different epoch lengths.
Methods: Four PGY-1 medical residents working extended duration shifts wore two Actiwatch-Ls for at least 4 days (Mini-Mitter, Bend, OR); one was set to collect data in 1-minute epochs and the other in 2-minute epochs. Ambulatory PSG was also measured simultaneously (Vitaport, TEMEC Instruments, The Netherlands).
Results: PSG sleep duration was consistently underestimated by 4.16%±6.07% SD in actigraphy data collected using 1-minute epochs

whereas the actigraphy data collected using 2-minute epochs overestimated sleep duration by 6.05%±8.09% SD. Actigraphy-estimated sleep durations were consistently longer using data collected with 2-minute epochs compared with those data collected with 1-minute epochs (10.21%±8.33% SD).

Conclusion: In this small pilot study, sleep duration measured by actigraphy was underestimated by four percent using one-minute epochs and overestimated by six percent as compared to PSG scored every 30 seconds. Results from this limited study population suggest that actigraphy is a reliable estimator of sleep duration in a field environment and two minute epochs can be used when logistics demand long continuous collection episodes.

Support (optional): Data collection was supported by a grant from NIOSH (RO1 OH07567) and was conducted in a General Clinical Research Center (NCRR M01 RR02635). LW was supported by the Irish Research Council for Science Engineering and Technology (IRCSET) and FÁS Ireland.

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QUANTITATIVE CHANGES IN HIGH AND LOW FREQUENCY SPECTRAL DOMAINS IN PRIMARY INSOMNIA DISTRIBUTED IN TWO HOUR INTERVALS ACROSS THE ENTIRE NIGHT

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Introduction: Automated scoring of sleep has been shown to have high interscorer reliability compared with human scoring. Different frequency domains may correlate with wake/sleep states of the brain and quantify the pathology of sleep disorders. This study assesses signal processing outcomes using adaptive segmentation in adults identified with primary insomnia. Morpheus® is a system that performs automated analysis of sleep staging using a multidimensional mathematical analysis of EEG applying adaptive segmentation and fuzzy logic with Markov models.

Methods: 40 adults with a diagnosis of primary insomnia underwent a post-hoc analysis studying 2 nights using a cross-over design with 4 compounds. Patients received 3 different medications or placebo denoted by A, B, C and P(placebo). This represents first night analysis. Advanced spectral parameters were analyzed in 2 hour time intervals for each group and compared with the placebo group including % high frequency activity (HF) and % low frequency activity (LF).

Results: Means and standard deviations are measured as % of TST. For HF% hours 1-2: P=11.70(9.77); A=7.91(5.30); B=5.67(3.98); C=8.64(5.57). Hours 3-4: P=19.71(11.15); A=2.39(2.23); B=4.35(2.78); and C=4.88(4.16). Hours 5-6: P=12.17(13.19); A=2.58(2.31); B=6.31(4.51); and C=4.41(2.48). Hours 7-8: P=12.4(12.11); A= 3.58(3.41); B=8.98(5.91); and C=6.36(4.68). For LF% hours 1-2: P=2.89(2.72); A=4.17(3.05); B=6.12(3.65); C=3.69(3.12). Hours 3-4: P=4.47(3.55); A=8.08(3.55); B=5.10(2.66); and C=5.23(2.68). Hours 5-6: P=1.83(1.74); A=4.67(3.19); B=2.15(1.95); and C=3.59(2.49). Hours 7-8: P=1.34(2.6); A= 1.78(1.59); B=0.61(0.82); and C=1.47(1.81). T-tests of 2 hour intervals of HF% comparing the placebo group with other groups were significant $p<0.05$ except: hours 1-2 for HF% groups A, C and hours 7-8 group C. For LF% except: hours 1-2 group A,C; hours 3-4 group B, C; hours 5-6 group B; and hours 7-8 group C. A significant reduction in HF and increase in LF signal domains was seen with compound A ($p=<0.00001$).

Conclusion: Differences in the time distribution of the pharmacodynamic response in treated primary insomnia patients (HF and LF domains) is effectively demonstrated using spectral analysis.

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THE RELIABILITY OF THE FACTOR STRUCTURE OF THE PEDIATRIC DAYTIME SLEEPINESS SCALE IN BOTH A SPANISH-COLOMBIAN AND FRENCH-CANADIAN VERSIONS

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Introduction: Daytime sleepiness is characterized by an increased likelihood of falling asleep and adversely impacts youth's academic performance, behavior, and mood. The National Sleep Foundation Survey (2006) found almost 50% of youth sleep 1 to 2 hours less than the recommended 9 hours per night and 60% report daytime sleepiness. The Pediatric Daytime Sleepiness Scale (PDSS; Drake et al., 2003) is a self-report questionnaire used to evaluate the likelihood of youth falling asleep in various everyday situations. The original PDSS was developed with an English-speaking American sample (M_{age}=11.8; *SD*=.6 years), and the measure was thought to assess a uni-dimensional construct: daytime sleepiness. The PDSS has previously been translated into a Spanish version for an Argentinean sample (M_{age}=13.3; *SD*=1.5 years).

Methods: The current study evaluated the factor structure of the PDSS in two distinct samples: the first sample included 420 Spanish-speaking students from Bogota, Colombia (M_{age}=9.49, *SD*=.67 years). The second sample included 377 French-speaking students from Montréal, Québec (M_{age}=12.73; *SD*=.67 years) as part of the larger AdoQuest Study. The PDSS was translated into Spanish and French using back translation procedures and administered to their respective sample.

Results: Generalized least-squares method and varimax rotation were used; items with factor loadings >0.40 were retained. Exploratory factor analyses on both the Spanish and French versions revealed two factors: *daytime sleepiness* and *lark/morning preference*, which explained 49% and 56% of the variance, respectively. Daytime sleepiness included questions about feeling sleepy with factor loadings of .59 to .73 (Spanish version) and .73 to .91 (French version). Lark/morning preference included items about feeling alert after being awakened with factor loadings of .49 to .73 (Spanish) and .41 to .71 (French).

Conclusion: The original PDSS may tap into multiple constructs related to sleepiness, such as circadian phase/morningness/eveningness and sleep propensity. Differences in cultural and lifestyle behaviors (e.g., bed/wake-times, school start times, daytime napping) as well as interindividual differences in preferred timing of sleep/wake cycles may also play a role in the multiple constructs identified. Future research should further evaluate the validity of these subscales within the PDSS to determine their validity in relation to objective measures of circadian phase angle and sleep propensity.

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CLAIMS-BASED CASE-FINDING FOR INSOMNIA AND THE INSOMNIA SEVERITY INDEX

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Introduction: Administrative claims studies examine illnesses, comorbidities, and treatment patterns and rely on case-finding rules to identify patients with target diagnoses. For insomnia, it is not known if these techniques are accurate, or what degree of insomnia is reflected. The current analyses use a hybrid of claims and Insomnia Severity Index

(ISI) data to assess the validity and characteristics of 4 different insomnia case-finding rules.
Methods: Health plan enrollees completed the ISI by telephone. Case-finding rules were identification of a claim in the past year for: 1) any insomnia prescription, 2) any insomnia diagnosis, 3) either rule 1 or 2 or 4) both rules 1 and 2. Logistic regression assessed the association between the ISI score and presence of insomnia for each case rule. Group means for ISI were compared for each rule, and ROC analyses were conducted to identify corresponding classification trade-offs.
Results: 2,086 ISI respondents were included. Between-group mean differences and logistic models were significant for all rules. For rules 1-4, mean (SD) ISI scores for non-cases were 8.88 (6.05), 9.86 (6.41), 8.74 (6.00), 9.93 (6.43), respectively, and 12.95 (6.57), 14.20 (6.39), 12.95 (6.57), 15.27 (6.08) for cases. Increase likelihood of identification by claims case-finding rules was significantly associated with increasing ISI score. However, R-Square was low (0.07, 0.05, 0.07, and 0.07 for rules 1-4, respectively). Area under ROC curves was 0.68, 0.69, 0.68 and 0.73, respectively.
Conclusion: There is considerable noise in the discrimination of cases and non-cases with case-finding rules, with overall classification accuracy in the poor to fair range. However, all methods showed significant separation of more severe from less severe insomnia, with corresponding trade-offs of resulting case population size and different predictive error. Treatment effects are likely to have attenuated the ISI scores, but severity differences still remained.

1128

MORPHEE: AN ELECTRONIC PATIENT RECORD WITH AUTOMATED POLYSOMNOGRAPHIC AND CPAP DEVICES DATA TRANSFER

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Introduction: Diagnosis (polysomnography) and therapy (Positive Airway Pressure) devices differ from one manufacturer to another and use different reporting formats. Improving data management will help clinicians to exchange patient information, assess compliance and evaluate therapy efficiency. Thus, there is a need to standardize data and allow their automated transfer and processing into a secured web based server.
Methods: In the sleep laboratory, the polysomnographic analysis software (Cidelec) exports the results in XML CDAR2 format in full and summarized formats. At the home care providers, the therapy devices (Respironics) export the technical data, settings and compliance results in a standardized XML format too. These files are automatically sent via https transfer into the corresponding patient file. The data are then incorporated in the structured patient file which is operated and hosted by Santeos (Atos Origin). The securely shared access is open to affiliated professionals via a simple internet explorer. The exported data include standardized results and additional optional data for each device.
Results: MORPHEE is an internet network for medical data of sleep patients aimed at sharing patient care among sleep health professionals in order to achieve better clinical outcomes. It has included more than 2000 patients since its opening in 2006 in the Paris area.
Conclusion: These internet applications are suited for all sleep data analysis software and therapeutic devices following standard XML format (HL7 rel2).
Support (optional): Supported by ANR "Usages de l'Internet" Contrat Morphée N°04L594,Cidelec and Respironics

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CLASSIFICATION OF STAGE-1 IN A SINGLE CHANNEL WAKE-SLEEP DETECTION SYSTEM

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Introduction: A multi-year effort has been dedicated to the development of an automated wake-sleep detection system that uses a single differential recording of the mastoid EEG channel to facilitate in-home cognitive behavioral therapy for insomnia (CBTI). Previous abstracts reported on the ability of the system to accurately discriminate wake versus Stages 2-4 and REM. This abstract reports on the performance of the system in the classification of Stage-1.
Methods: 100 paid volunteers underwent an overnight laboratory PSG. One subject dropped out of the study and was excluded from analysis. PSG studies from the 99 remaining subjects (52F/47M, 18-60 years, median age 32.7) were independently scored by three or four certified polysomnographic (PSG) technologists whose results were combined into a single score file using a majority voting rule.
Results: Overall the automated system classified 34.4% (1389-epochs) of Stage-1 as wake and 65.6% (2644-epochs) as sleep. However, before sleep onset (defined as the beginning of the period in which 20 of 24 epochs were classified as sleep) 73.4% (491-epochs) of Stage-1 is classified as wake and 26.6% (178-epochs) as sleep. After sleep onset 26.7% (898-epochs) of Stage-1 is classified as wake and 73.3% (2466-epochs) as sleep. For 3 contiguous epochs of Stage-1 (i.e. unequivocal sleep), overall 32.0% (582-epochs) are classified as wake and 68.0% (1239-epochs) as sleep; before sleep onset 70.2% (287-epochs) of Stage-1 is classified as wake and 29.8% (122-epochs) as sleep; after sleep onset 20.9% (295-epochs) of Stage-1 is classified as wake and 79.1% (1117-epochs) as sleep.
Conclusion: The asymmetry in classification performance appears well suited for the automated implementation of CBTI, especially Stimulus Control Rules, as the system would be more likely to alert the subject to leave bed when they have not transitioned beyond wake and Stage-1 prior to sleep onset. Similarly, the system would be more likely to allow the subject to remain in bed after sleep onset has been achieved.

1130

PSYCHOMETRIC VALIDATION OF THE ASSESSMENT OF SLEEP QUESTIONNAIRE

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Introduction: Although many insomnia scales exist, few of these focus on qualitative aspects of sleep as defined by patients. The Assessment of Sleep Questionnaire (ASQ) is a new instrument assessing the sleep experience from the perspective of the person with insomnia. The current study examines the psychometric properties of the ASQ. Beginning with 29 items generated from insomnia patient focus groups, cognitive debriefing, and expert consensus, the current study's aims included item analysis, identification and assessment of subscales, assessment of internal consistency reliability, construct validity and known-groups validity.
Methods: A multi-site, single visit study was conducted among 104 patients diagnosed with primary insomnia and 50 non-insomnia controls. Psychometric analyses included examination of item performance using factor analysis and item response theory (IRT) analysis, Cronbach's al-

pha, and known-groups validity by comparison to the Insomnia Severity Index (ISI) and physician ratings.
Results: Item analysis resulted in a final scale of 21 items covering patient experience over the prior 7 days. Based on factor analysis, three subscales emerged covering 1) sleep onset and maintenance, 2) qualitative sleep experience, and 3) awakening experience. Internal consistency reliability was excellent for each (0.94, 0.94 and 0.95 respectively). Each demonstrated excellent known-groups validity between those with and without insomnia determined by ISI score, with mean (SD) differences of -2.44 (0.7), -2.06 (0.8), and -1.85 (0.8), respectively ($p < 0.001$ for all subscales). Finally, all three subscales were able to distinguish between patients with mild versus severe insomnia as rated by a physician ($p<0.05$), while the Qualitative Sleep Experience and Awakening Experience subscales were able to differentiate between moderate versus severe ($p<0.05$) physician-rated insomnia severity.
Conclusion: The ASQ is a valid and reliable measure of the sleep and awakening experience, providing additional opportunity to quantify important aspects of patient-reported sleep quality in insomnia.

1131
DETECTION OF SLEEP MICROSTRUCTURAL ELEMENTS FROM FRONTAL EEG

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Introduction: Most patients in intensive care unit (ICU) are not able to sleep in the ordinary sense of the word. Yet, it has been suggested that the mere existence of certain microstructural elements of natural sleep in patients' EEG would have positive prognostic value. Furthermore, optimizing the quality of sleep is expected to facilitate the recovery of ICU patients.
Methods: Polysomnography and standard sleep staging methods are too cumbersome for routine use in ICU. In this work we developed algorithms to detect arousals, spindles, and K-complexes from any single EEG derivation. Using these detectors, we explored the possibility to create indices for the incidence of the above-mentioned microstructural events using forehead EEG alone. The most important signal processing techniques applied were adaptive segmentation, discrete wavelet transformation, matching pursuit decomposition, and spectral entropy analysis.
Results: The experimental results were based on polysomnography with additional forehead EEG electrodes on healthy volunteers. The sensitivities and specificities of the developed detection algorithms were 0.62 and 0.79 for arousals, 0.78 and 0.87 for spindles and 0.87 and 0.84 for K-complexes, respectively. Comparison between forehead and central EEG derivations revealed systematic differences in the incidence of arousals, spindles, and K-complexes, linear regression coefficients being 0.56, 0.74, and 0.99, respectively.
Conclusion: Our results suggest that consistent indices for the incidence of arousals, spindles and K-complexes can be based on forehead EEG alone, even though the incidence of detected arousals and spindles may be systematically smaller than that from central derivations.

1132
ASSESSMENT OF A WIRELESS DRY SENSOR TO DETECT SLEEP IN HEALTHY VOLUNTEERS AND SUBJECTS WITH SLEEP DISORDERS

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Introduction: A simple, easy-to-use portable device to detect sleep stages could have many applications in sleep research and clinical practice. We assessed a device with dry fabric sensors that require no skin preparation and are integrated into a simple headband for wireless transmission to a separate bedside monitor. Sleep stages are scored automatically by a neural network. Our aim was to compare sleep scored by the wireless system (WS) to manual scoring of concurrent polysomnography (PSG) in both healthy volunteers and subjects with sleep disorders (obstructive sleep apnea (OSA) and insomnia).
Methods: 30 subjects (10 healthy volunteers, 10 OSA patients, 10 insomniacs) participated. Each subject was setup for a standard PSG and the investigational wireless system for concurrent overnight recordings in our sleep laboratory. WS data were sampled by a 12-bit A-D for automated scoring of 30-second epochs of Wake, Light Sleep (N1+N2), Deep Sleep (N3), and REM sleep. Each PSG record was manually scored using recommended AASM criteria by 2 registered sleep technologists blinded to the results of the wireless system (M1 and M2). Sleep onset latency to 10 minutes of persistent sleep (LPS), total sleep time (TST), and sleep efficiency (SE) were derived from the records for comparison in addition to sleep stage agreement and Cohen's κ using a confusion matrix.
Results: PSG and WS data were available for 29 subjects for a total of 24,138 epochs. Sleep staging (all subjects) agreements/κ were: WS-M1: 68%/0.50, WS-M2: 68%/0.48, M1-M2: 88%/0.79. Sleep staging (healthy volunteers, n=10) agreements/κ were WS-M1: 73%/0.58, WS-M2: 72%/0.51, M1-M2: 89%/0.81. Sleep staging (sleep disordered subjects, n=19) agreements/κ were WS-M1: 65%/0.45, WS-M2: 66%/0.44, M1-M2: 88%/0.81. Mean LPSs (all subjects) were WS: 15±14, M1: 48±83, M2: 48±84 minutes. Mean TSTs (all subjects) were WS: 349±76, M1: 331±84 and M2 329±89 minutes. Mean SEs (all subjects) were WS: 86±17%, M1: 79±19% and M2: 79±20%.
Conclusion: Results for healthy volunteers were consistent with previous findings demonstrating reasonable correlation with full PSG. The device performed better on healthy volunteers than on sleep disordered subjects. The system shows promise as an easy to use wireless system for recording and scoring sleep.
Support (optional): Support for this study provided by Philips Respironics. Wireless Systems were kindly provided by Zeo, Inc (formerly Axon Labs, Inc).

1133
DEVELOPMENT OF STATISTICALLY VERIFIED METRICS FOR CHARACTERIZING THE INTERACTION OF A BODY AND A SLEEP SURFACE

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Introduction: The use of pressure mapping systems to evaluate the interface pressure between a human subject and a sleep surface is well known in the sleep community. Given the complexity of the most advanced systems (10,240 sensors), little attention has been given to developing metrics that are demonstrated to be robust and statistically meaningful. A detailed effort to develop these metrics and to provide statistical characterization of these metrics will be presented. The resulting metrics can now be used to quantify the quality of the sleep interface and may be used as a contributing factor in analyzing sleep behavior.
Methods: Several metrics are evaluated by a Brown & Forsythe's test for homogeneity in addition to other statistical evaluations for items such as the average pressure, median pressure, maximum pressure, percent of contacts above 32mmHg and percent of contacts below 20mmHg (to name a few). Analysis of method error, pad-to-pad variation, and time dependence are provided as well. A series of sleep surfaces were evaluated using subjects selected to represent BMI ranges typical of the North American population. Test subjects were measured on sleep surfaces of varying composition (viscoelastic foam, latex, inner spring and hybrid constructions) using an Xsensor X3 pad containing 10,240 sensors.
Results: Metrics such as maximum pressure, median pressure and average pressure fail the Brown & Forsythe's test for Homogeneity and therefore have been abandoned as metrics for characterizing sleep inter-

actions. The remaining statistics were used to compare the performance of a series of well characterized subjects with BMI's representative of average, overweigh and obese body types. Methods for calculating support and for comparing body types (statistical basis) have been developed and can quantify difference in performance independent of the bed's construction. For example, many beds constructed of memory foam show a degradation in performance over time when compared to other constructions.
Conclusion: A set of metrics; percent of contacts above 30mmHg, below 20mmHg, percent of contact area that distributes pressure below 20mmHg and several others have demonstrated their ability to quantify the quality of a sleep surface.

1134
USING QUALITATIVE METHODS TO STUDY SLEEP IN HOME CONTEXTS
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Introduction: A vast amount of the studies conducted with the aim to improve sleep focus on a population with clinical conditions or sleep disorders. However, many people without consistent sleep complaints also desire to improve their sleep. This study aimed at understanding issues surrounding sleep in healthy people's lives.
Methods: A context mapping study was set up, supplemented by focus groups, both qualitative methods. Context mapping studies, conducted in participant's homes, provide participants with tools to express their routines, experiences and worries. The focus groups served to increase the validity and reliability of the context mapping findings. Prior to the home visits and focus groups, all participants (aged 30-55, with a busy lifestyle, wanting to improve their sleep) completed a booklet with exercises about their relaxation behavior, sleep processes and disturbances. The context mapping study involved 7 couples in the Netherlands. The focus groups involved 32 (4 x 8) English participants.
Results: We identified several common sleep routines, experiences, and environmental and psychological sleep thieves. First, many people experience problems sleeping with even the smallest amount of light. Second, every little noise alerts them. Third, cold feet are detrimental for falling asleep. Fourth, many people have difficulties switching off their minds before sleep. Counter-measures include distraction by watching TV, preparation for the next day, and practicing relaxation exercises. Fifth, especially women have difficulties sleeping due to an 'unsafe' feeling such as the worry about potential burglars. Sixth, people prefer waking up 'naturally' without an alarm. No major differences between the nationalities were found in sleep routines, experiences, and thieves.
Conclusion: Context mapping and focus groups appeared useful qualitative methods to gain insight into sleep of healthy people in home contexts. Further, the results showed that even people without consistent sleep complaints would like to improve the quality of their sleep.

1135
PSYCHOMETRIC VALIDATION OF THE DAYTIME CONSEQUENCES OF INSOMNIA QUESTIONNAIRE
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Introduction: The Daytime Consequences of Insomnia Questionnaire (DCIQ) is a new instrument assessing the impact of insomnia on next-day functioning. The current study examines the psychometric properties of the DCIQ. Beginning with 33 items generated from insomnia patient focus groups, cognitive debriefing interviews, and expert input, the current study's aims included item analysis and reduction, identification and assessment of subscales, and assessment of internal consistency, construct validity and known-groups validity.
Methods: A multi-site, single visit study was conducted among 104 patients diagnosed with primary insomnia and 50 non-insomnia controls. Psychometric analyses included examination of item performance using factor analysis and item response theory (IRT) analysis, reliability using Cronbach's alpha and known-groups validity by comparison to the Insomnia Severity Index (ISI) and physician global ratings.
Results: Item analysis resulted in a final scale of 22 items covering insomnia's daytime consequences over the past 7 days. Factor analysis identified four subscales (Fatigue/malaise, Attention impairment, Mood disturbance, and Motivation/activities). Internal consistency reliability was very good, with Cronbach's alpha of 0.96, 0.93, 0.96 and 0.95 respectively. Each subscale demonstrated excellent known-groups validity between those with and without insomnia, with mean (SD) subscale score differences of -1.74 (1.0), -1.37 (1.0), -1.54 (1.0), and -1.65 (0.9), respectively (all with $p < 0.001$). All subscales also demonstrated differences in daytime consequences corresponding with the different severity levels of the ISI (none, sub-threshold, moderate, severe; all with $p<0.05$). In addition, each distinguished between patients with mild versus severe insomnia according to physician rating ($p<0.05$), and three (Fatigue/Malaise, Mood Disturbance, and Motivation/Activities) distinguished between physician ratings of moderate and severe insomnia ($p<0.05$).
Conclusion: The DCIQ is a valid and reliable measure of the daytime impairments associated with insomnia, and allows quantification of the specific concerns important to insomnia patients.

1136
A USER-FRIENDLY DEVICE FOR HOME MONITORING OF SLEEP DISORDERS
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Introduction: With increasing demand for diagnostic sleep studies comes a need for more efficient, cost-effective and convenient methods of screening for sleep related breathing disorders, especially obstructive sleep apnea. A portable monitoring device, the Alice PDx (Philips-Respironics, Inc.), provides a user friendly diagnostic system that can be used in the home, hospital or laboratory setting.
Methods: Given no device instruction, five PSG naïve participants, ranging in age from 29 to 59 years, were given the portable monitoring device and asked to read the user manual instructions and set up the device independently in their home. Participants were required to apply abdominal and chest effort belts, pulse oximeter, nasal cannula and oral thermistor. After rising, all participants completed a questionnaire related to the ease of use, functionality and acceptance of the device. On a subsequent night in the laboratory, participants applied the device and accessories in the presence of a sleep professional. In addition to the respiratory sensors, ECG, EEG, EOG and EMG sensors were applied by the sleep technician.
Results: Data analysis shows the device was properly set up on all 10 nights with only one application error; however, all studies were successfully read and scored. Overall, participants liked the device and all agreed that it was easy to use and apply all sensors. Further, this small sample suggests a strong, though not statistically significant, correlation between home and lab measures of AHI ($r=0.842$, $p=0.073$) and RDI ($r=0.852$, $p=0.067$), despite inherent night to night differences.
Conclusion: This new portable monitoring device gathers reliable diagnostic data and allows patients to easily and accurately set up a sleep study in their own home with minimal instruction from a sleep professional.

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ACTIGRAPHY FOR THE ASSESSMENT OF SLEEP AND WAKE IN PARKINSON'S DISEASE

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Introduction: Sleep disturbances are common in Parkinson's disease (PD). Although polysomnography (PSG) remains the gold standard for studying sleep, actigraphs are often used as convenient, inexpensive, and reliable tools to provide information about sleep/wake activity in a variety of populations. Although validated in many populations, actigraphy has not been validated in (PD), a condition characterized by motor disturbances. As part of a larger study on sleep in PD, we examined the relationship between PSG and actigraphy for determining sleep/wake activity in PD patients.
Methods: Nine patients with mild-moderate PD had their sleep assessed simultaneously by PSG and actigraphy. Actiwatches (Actiwatch-L, Mini Mitter, Respironics) were configured to record in 30 second epochs reflecting the PSG scoring epochs. Total Sleep Time (TST) was estimated from actigraphy data using Actiware 5.0 software set to varying sensitivity thresholds (amount of activity per epoch required for a "wake" score - 1,2,3,4,5,10, 20, 30, 40). A Spearman's Rank Order correlation was performed comparing TST estimated by actigraphy (TST-A) with that from PSG (TST-P). One-tailed t-tests were used to assess the significance of correlations.
Results: TST-A correlated significantly with TST-P at all thresholds tested. The strongest correlation resulted from using a threshold of 3 (r_s=0.88, p=0.001) while a threshold of 40 generated the weakest correlation (r_s=0.65, p=0.029).
Conclusion: Although preliminary, these results suggest that actigraphy may be a valid tool for assessing sleep and wake variables in patients with mild-moderate PD, particularly at lower thresholds. The optimal threshold varies between different populations. The collection of additional data will allow better assessment of the effect of threshold and disease severity on sleep/wake assessment accuracy in this specific patient population.
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1138

PRIMING AFFECTS POOR SLEEPER RESPONSES BUT NOT NORMAL SLEEPER RESPONSES ON AN AMBIGUOUS INSOMNIA TASK

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Introduction: As research on insomnia progresses within the cognitive domains of attention and perception, the impact of a priming bias on results should be examined and subsequently accounted for. The aim of the present study was to examine whether a priming bias exists and the extent to which this can impact the results when examining differences between normal sleepers and poor sleepers.
Methods: One hundred and eighteen first-year undergraduate psychology students, blinded to the aims of the experiment, were randomly allocated to either receive the Dysfunctional Beliefs About Sleep scale (DBAS-10) and Insomnia Severity Index (ISI) before completing Ree and Harvey's (2006) Insomnia Ambiguity Task (IAT), or afterwards.
Results: There was an overall priming difference, with those receiving the DBAS-10 and ISI first reporting higher insomnia ambiguity than those who received the IAT first ($t = 2.26$, $df = 116$, $p<0.05$). However, when the sample was split further into those who reported a significant sleep disturbance (ISI <8) against those that did not (ISI >8) the results showed that priming only affected the responses of the sleep disturbed group ($t = 2.88$, $df = 57$, $p<0.006$) and not the normal sleeper group ($t = 0.69$, $df = 57$, n.s.). Additionally, there were no overall, or by sleeper status, priming effects on scores on the DBAS-10.
Conclusion: These findings suggest that completing a diagnostic questionnaire before an ambiguity task results in increased levels of insomnia sensitivity, albeit minimally (3 points on the IAT), in poor sleepers but that a distal questionnaire does not. Additionally, this priming effect is not evident for normal sleepers. Therefore, care should be taken when designing studies using samples of poor sleepers as the order in which diagnostic and distal measures are taken can artificially inflate responses.

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TYPES OF MEMORY COMPLAINTS IN COMMON SLEEP DISORDERS

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Introduction: Excessive daytime sleepiness (EDS) has been frequently associated to subjective cognitive impairment, but it is unknown exactly which types of sleep disorder induce increases in memory complaints, and what types of memory are affected. Here we sought to clarify the relations between sleep disorders, evaluated objectively (polysomnographic recordings) and subjectively (validated questionnaires), and metamemory.
Methods: We conducted a population based survey adopting a probabilistic three-stage cluster sample of the metropolitan city of Sao Paulo, Brazil, that represented the local population according to gender, age (20-80 years), and socioeconomic status. Of the 1042 individuals surveyed we excluded those that had scores above cut-off in the Beck depression and anxiety inventories, used psychotropic drugs or had a history of psychiatric or neurologic disorders, factors that can be related to memory impairment. In the remaining 662 individuals we investigated the occurrence of metamemory complaints in subjects with and without sleep problems using the "Prospective and Retrospective Memory Questionnaire", which includes items related to long- and short-term memory complaints, as well as to memory for past event (retrospective) and for future intentions (prospective memory), the latter having been found to be a sensitive criterion for discriminating elderly people with a high risk of having obstructive sleep apnea syndrome (OSAS).
Results: EDS (assessed through the Epworth Sleepiness Scale), poor sleep (Pittsburg Sleep Quality index), and high risk of insomnia (Insomnia Severity Index) increased complaints of prospective and short-term memory. People with Periodic Leg Movement Syndrome (PLMS) also had larger prospective complaints. None of the latter effects were explained by EDS. Age and schooling did not interact with memory and sleep parameters.
Conclusion: Prospective and short-term memory are perceived as being impaired in people with EDS and common sleep disorders, except those with confirmed OSAS. Therefore, questionnaires that evaluate these types of memory should be used in clinical settings.
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COMPARISON OF PIEZOELECTRODE BELTS TO RESPIRATORY INDUCTIVE PLETHYSMOGRAPHY

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Introduction: Before 2007 piezoelectrode belts were commonly used to measure respiratory effort during polysomnography. Newer and more expensive respiratory inductive plethysmography (RIP) belts became the recommended monitoring device in the 2007 AASM sleep scoring guidelines based on a few studies which demonstrated concordance of RIP with esophageal pressure monitoring or pneumotachography in the measurement of respiratory events. There have been no trials comparing piezoelectrode and RIP belts. We postulated that these methods are equivalent for the detection of respiratory effort during pathological events.
Methods: Ten consecutive adult patients referred to a university sleep lab for evaluation of suspected sleep apnea were monitored using both piezoelectrode and RIP belts. Overnight polysomnography data was obtained while the subjects wore piezoelectrode and RIP belts simultaneously. The first 25 respiratory events were analyzed and scored with both belts by measure of a pre-event baseline breath and measure of the signal nadir during the event. All amplitude measures were taken from peak to peak at the same point in all channels. A ratio of baseline to event amplitude was calculated. Readers were blinded to the mode of respiratory effort measurement. Results for each subject were compared with regard to concordance of respiratory event detection between the piezoelectrode and RIP belts by Pearson Product Moment correlation calculation.
Results: All subjects had 25 events evaluated. Correlation between piezoelectrode and RIP belts was $r = 0.56$ for chest belts and $r = 0.81$ for abdominal belts, both $p < 0.05$. Cardiac artifact was seen in 7 of 10 subjects in either one or both types of belts, but did not affect overall measurements.
Conclusion: There is a strong correlation of respiratory events measured during polysomnography by piezoelectrode and RIP belts. For abdominal movement, the piezoelectrode belts offer a reasonable and more economical alternative to RIP belts. Though also statistically significant, correlation of chest measurement is less impressive and requires further investigation.

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DEVELOPMENT AND VALIDATION OF A NEW SCALE FOR EVALUATION OF SLEEPINESS

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Introduction: The Epworth Sleepiness Scale (ESS) is widely used to screen patients with excessive sleepiness. In an initial study, we tested the applicability of ESS in 202 Indian subjects and found that 50% of subjects could not answer 3 or more questions. The common inapplicable items were driving (42%), reading (13.4%) and resting in the afternoon (5.4%). Some of the other limitations of ESS are: most situations are passive, respondents experience difficulty in giving graded responses (0-3) and equal weight is given to all situations. Hence we developed a new scale to overcome these limitations.
Methods: A 13 item questionnaire relating to sleep history and activities of daily living (critical and non-critical) was developed. Responses were either discrete or yes/no. The questionnaire was administered along with ESS by a technologist to two sub-groups:(1)250 non-sleepy subjects to test for applicability of questions and (2)70 patients referred for evaluation of sleepiness, out of which 38 underwent polysomnography(PSG). A weighted score was assigned and applied after subjects answered the questionnaire. A cut-off score of 10 was used for the new scale in the second group for further analysis.
Results: In the non-sleepy sub-group, 102 (31.8%) and 216 (67.5%) were able to answer all items in the ESS and new scale respectively, indicating that the new scale was more applicable than ESS. Among the sleepy patients who underwent PSG, the sensitivity was 77.1% for the new scale and 57% for ESS. The specificity of both scales was 33.3%. Positive predictive values were 93% and 90.9% for the new scale and ESS respectively. Accuracy of the new scale was 73.7% as opposed to 55.2% for ESS.
Conclusion: The new sleepiness scale performed better than ESS with respect to applicability, sensitivity and accuracy. The next step is to test the scale in a larger population of apneic and non-apneic sleep disorders.

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CARDIOPULMONARY COUPLING, A NOVEL METHOD TO ASSESS SLEEP QUALITY: VALIDATION IN PATIENTS SUSPECTED WITH SLEEP DISORDERED BREATHING

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Introduction: There is need for new sleep diagnostic strategies. To assess automated sleep quality analysis software using cardiopulmonary coupling (CPC) from one EKG channel, polysomnographs from 69 patients suspected of sleep disordered breathing (SDB) were used. All studies were reviewed by a board certified sleep medicine physician, and retrospectively analyzed using the Beth Israel Medical Center CPC analyzer. The results were compared to the RemLogic CPC analyzer (Embla, Broomfield, CO).
Methods: Comparison was based upon CPC measures of sleep quality generated in mean percent of the windows analyzed for high frequency coupling (HFC), low frequency coupling (LFC), very low frequency coupling (vLFC), and other frequencies. Calculation of CPC variables in increments of 256 samples (2.1 minutes) from 3 overlapping subwindows of 512 samples within each 1024 sample (8.5 minutes) window and then advanced by 256 samples resulting in approximately 200 windows analyzed per study.
Results: Pearson R correlation was performed on the CPC values for HFC, LFC, vLFC and Other. The quantified results were 0.81, 0.84, 0.57 and 0.35, respectively and all significant at $p < .01$ level. Additionally, a t-Test: Paired Two Sample for Means was calculated. HFC mean % was 43.19 and 42.71 ($p = .78$); LFC mean % was 35.82 and 36.01 ($p = .89$); vLFC mean % was 17.68 and 18.64 ($p = .36$); Other mean % was 3.31 and 2.64 ($p = .16$) for Beth Israel and RemLogic CPC analyzers, respectively.
Conclusion: HFC and LFC correlation values between Beth Israel and RemLogic are excellent. Both HFC and LFC values are used to determine sleep quality. The RemLogic CPC analyzer accurately reproduces sleep quality results from Beth Israel and is comparable to the work of Thomas et al. 2007. It has potential as a diagnostic tool to quantitatively assess sleep quality.

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HRV ANALYSIS DURING SLEEP: CLINICAL INTEREST OF A NEW AUTOMATIC SLEEP ANALYSIS

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Introduction: The study of the autonomic balance can be explored by a non invasive heart rate variability (HRV) analysis, using standardized stand-tests. These tests may nevertheless expose severe dysautonomic patients to a fall risk. The study of HRV during sleep constitutes a safe alternative. Indeed, a vagal predominance is normally observed during slow wave sleep (SWS), whereas a phasic sympathetic activation occurs during REM sleep. The contrast is maximal when stable episodes of SWS and REM are compared. In return, this approach needs a lengthy sleep scoring step. ASEEGA, a single-channel based automatic scoring algorithm, was developed and validated (SLEEP 2007; 30: 1587-95) to provide a reliable sleep scoring-aid with minimal required equipment. The aim of the present study was to assess its ability to identify stable episodes of SWS and REM, prior to a HRV analysis.
Methods: Twenty healthy young male volunteers (29.4 years ± 4.6) had polysomnography for 4 nights, leading to 80 recordings. Stable episodes of SWS and REM were identified independently, both manually (R&K) and automatically (single EEG C4O2). The corresponding parts of ECG signals went through a HRV analysis. The R-R interval, pNN50, HFn and LF/HF parameters were computed for each identified episode. The SWS/REM ratios were calculated for each parameter. The ratios obtained via the automatic and manual scoring were compared.
Results: The relative differences between visual and automatic ratios for R-R interval, pNN50, HFn and LF/HF were of 0.1%, 2.5%, 3.0% and 1.3% respectively.
Conclusion: These results suggest that HRV diagnosis is not modified by automatic sleep scoring. Further studies in patients are needed to evaluate whether this new algorithm could, as a screening aid, provide an objective and more comfortable alternative to the stand-test.

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FEASIBILITY OF USING CARDIAC OUTPATIENT TELEMETRY TO IDENTIFY PATIENTS AT HIGH RISK OF SEVERE SLEEP-DISORDERS

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Introduction: Common sleep disorders (SD) include apnea/hypopneas (AHs) and periodic limb movements (PLMs). Cyclic variation of heart rate (CVHR), a sinus rhythm of brady-tachy changes, indicates presence of PLMs or repeated AHs. Mobile Cardiac Outpatient Telemetry (MCOT, CardioNet) is an ambulatory 2-channel ECG system for continuous ≤21 day arrhythmia monitoring. We examined the feasibility of using MCOT heart rate (HR) to automatically identify CVHR during sleep.
Methods: Complex patients (Pts) referred to a tertiary sleep center for 2nd and 3rd opinions on their SDs were enrolled and wore MCOT devices during an overnight polysomnogram (PSG). An MCOT automatic analysis (AUTO) searched for clear CVHR (amplitude ≥10bpm with regular cycles) quantified its duration. The analysis was blinded to PSG results. CVHR% was measured for each pt as total CVHR time/ total time-in-bed (TIB). TIB was from baseline PSG, excluding any continuous positive airway pressure (CPAP) titration periods. SD index (SDI) was defined as AH index + PLM index from baseline PSG. Pts were categorized as having true SD30 (PSG SDI ≥30) or positive SD30 (CVHR%≥30%). Similar categories (true and positive SD60) were also created. Sensitivity (SS), specificity (SP), and positive predictive value (PPV) of positive compared to true SD were calculated for both categories of SDI.
Results: N=80 pts (F/M:18/62, age 49±13yr, TIB 295 ±187min, SDI 40±38) were assessed. AUTO CVHR% correlated r=0.66 with SDI. In both groups, SD30 (33/80) and SD60 (17/80), AUTO had SP=98% and PPV≥92% compared to PSG measures. CVHR was observed declined or was abolished after CPAP initiation.
Conclusion: Automated identification of clinically relevant CVHR is feasible in a system like MCOT. Such system may provide an efficient platform for identifying pts with severe SD in a large population.

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EFFECTS OF MANUAL ARTIFACT-REJECTION ON NON-REM SLEEP EEG SPECTRAL ANALYSIS

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Introduction: Spectral analysis of the sleep EEG has been widely employed in sleep research. However, studies vary substantially in methodology, especially regarding the handling of artifacts in EEG data. The impact of this methodological difference has not been evaluated. We sought to determine the effects of manual artifact rejection on non-REM EEG spectral indices.
Methods: Analysis was carried out with data from 63 PSGs obtained from 43 insomnia patients participating in a study evaluating insomnia diagnosis. PSGs were obtained two consecutive nights with Grass-Telefactor equipment using a standard NPSG montage. Spectral analysis on 2 second segments yielded absolute and relative power estimates in Delta, Theta, Alpha, Sigma, Beta, and Gamma bands, as in our prior work (Krystal et al., 2002). Manual artifact rejection was carried out on each 30 second epoch of PSG by A.K. as previously described (Krystal et al., 2002). Thirteen studies were excluded for absence of artifact-free sleep data. Spectral indices were generated for artifacted and unartifacted versions of the 50 available studies and compared using multivariate repeated measures ANOVA as well as intraclass correlation coefficients.
Results: Statistically significant differences between artifacted and non-artifacted spectral indices were found for 10/17 spectral measures. Intraclass correlation coefficients for these measures varied from 0.38 for Relative Gamma to 0.93 for Absolute Alpha.
Conclusion: Our results suggest that manual artifact rejection has a significant impact on several spectral measures of interest in research studies (e.g. absolute beta and gamma and relative delta, beta and gamma activity). These findings speak to the need for manual artifact rejection in studies employing non-REM EEG spectral analysis examining these measures. Other measures such as absolute delta and theta activity appear to be less affected by artifacts, however, this needs to be verified in further studies with PSG data collected in circumstances where other types of artifacts may be present.

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A COMPARISON OF AUTOMATICALLY-DETECTED AND MANUALLY OVERREAD DETECTION OF CYCLIC VARIATION OF HEART RATE FROM CARDIAC OUTPATIENT TELEMETRY FOR THE IDENTIFICATION OF PATIENTS WITH SEVERE SLEEP-DISORDERS

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Introduction: Common sleep disorders (SD) include apnea/hypopneas (AHs) and periodic limb movements (PLMs). Cyclic variation of heart rate (CVHR) indicates their presence. Mobile Cardiac Outpatient Telemetry (MCOT, CardioNet) is a 2-lead ECG for continuous ≤21 days monitoring of ECG signals. We compared an automatic algorithm (AUTO) with human tachogram overreading (HUMAN) to identify clear CVHR patterns during sleep.

Methods: N=80 complex pts referred to a tertiary sleep center for polysomnography (PSG) were enrolled. Pts wore MCOT during PSG. AUTO measured "clear" CVHR (amplitude>=10bpm with regular cycles) and HUMAN identified "clear" (large amplitude) or "subtle (lower amplitude) CVHR using HR tachograms generated from MCOT instantaneous HR. Subtle CVHR was not considered in the current analysis, which was blinded to PSG results. CVHR% was clear CVHR time/TIB (time-in-bed from start of study to beginning of any continuous positive airway pressure [CPAP] titration). SD index (SDI) was (AH + PLM index) from PSG and before any CPAP. Pts were categorized as true SD30 (PSG SDI ≥30) or positive SD30 (CVHR%≥30% by either method). Similar categories (true/positive SD60) were also created. Sensitivity (SS), specificity (SP), and positive predictive value (PPV) of positive compared to true SD were calculated. HUMAN excluded pts without HR changes or usable HR data.

Results: N=80 pts (F/M:18/62, age 49±13yr, TIB 295 ±187min, SDI 40±38) were assessed. AUTO and HUMAN CVHR% correlated r=0.66 and r=0.69 with SDI respectively and correlated r=0.85 with each other. In both groups SD30 (33/80) and SD60 (17/80), AUTO had SP=98% and PPV≥92% compared to PSG category (similar in HUMAN). AUTO had SS of 41% and 61% respectively. Excluding 10 who lacked HRV and 2 with unusable data, AUTO and HUMAN CVHR% had SS of 65% and 71% for true SD60 and 45% and 65% for true SD30.

Conclusion: Clear CVHR associated with SD can be detected from automatic assessment, suggesting that outpatient telemetry may efficiently screen for referral to PSG. Sensitivity may depend on preserved autonomic function as well as on SD severity.

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CORRELATION VERSUS AGREEMENT OF THE SPANISH AND ENGLISH VERSIONS OF THE SHHS SLEEP HABITS QUESTIONNAIRE INSOMNIA SUBSCALE

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Introduction: Creating equivalent English and Spanish versions of health questionnaires involves more than English to Spanish translation and analysis of internal consistency. The process is particularly challenging for questionnaires with multi-dimensional subscales. This investigation describes the development of a Spanish version of the Sleep Heart Health Study (SHHS) Sleep Habits Questionnaire (SHQ) and proposes methods to assess parallelism of forms across subgroups. Specifically, the level of correlation and agreement between the Spanish and English versions of the insomnia subscale (Difficulty Initiating and Maintaining Sleep, DIMS) of the SHQ was examined.

Methods: Bilingual Mexican Americans (N=50) completed the SHQ in Spanish and English one week apart in counterbalanced order. Total and category scores on the DIMS were correlated for subgroups defined by order of assessment, gender, age, education, language facility, acculturation, or health condition.

Results: The Spanish version was generally highly correlated and in good agreement with the English version. For example, correlation between versions was 0.87 for both men (n=24) and women (n=26). Women on average scored 0.3 points higher on the English versus Spanish version (95% CI includes 0), while men on average scored 0.3 points lower on the English version (95% CI <0>). The exception was acculturation. The correlation between versions was 0.89 for Traditionals (n=25; strongly identified with Mexican culture) and 0.94 for Biculturals (n=11; identified equally with Mexican and Anglo cultures). Traditionals on average scored 0.4 points lower on the English versus the Spanish version (95% CI <0>), while Biculturals on average scored 0.7 points higher on the English version (95% CI=0.05-1.41).

Conclusion: This Spanish version of the SHHS SHQ insomnia subscale is equivalent to the English instrument and is suitable for use with Mexican American adults; however, controlling for level of acculturation in samples is warranted.

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SCREENING OF SLEEP DISORDERS USING ENTERTAINMENT RECORDERS

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Introduction: There are no easy and cheap screening methods for sleep disorders (RLS, snoring, sleep apnea). Cheap electronic entertainment devices (MP3 player/recorders, mobile phones) have capacity to record and store even hundreds of hours of high quality sound signal. Millions of people own and use these devices. We have developed, tested and validated the method to record and analyse sounds and voices associated and generated by movements in bed using these devices.

Methods: The recording of snoring is easy to perform with a small MP3 device. The microphones are sensitive and the device is easy to use. For recording of leg and foot movements the device is fixed to the sock, pajamas, foot or leg. The sounds generated by the movements of the feet may be amplified using a plastic sheet around the device or beneath the feet. The recorded audio signal is fed into PC and analyzed for detection of snoring, heavy and periodic snoring (associated with apneas). In RLS screening the sound signals associated with movements are detected, the periodic pattern is recognized and the indices are calculated by the software. As the raw signal is stored it is possible even to listen to the signal (e.g. snoring) in real-time or in faster mode.

Results: In 26 snore / apnea patients ten had AHI > 20 in ambulatory PSG. They all had periodic snoring for more than 10% of the MP3 recording. The amount of snoring was calculated in minutes and as percentage of recording time. In RLS the detection accuracy of PLMS was very high (sensitivity 95%, specificity 94%) compared to EMG in PSG.

Conclusion: Screening of snoring, sleep apnea and RLS is possible using small, cheap and common entertainment devices. Repeated home recordings are easy to perform and transfer to PC for quantitative auto-

matic analysis even in areas and countries with no sleep recording facilities. In addition to the screening e.g. the effect of RLS treatment, follow up of patients and assessment of the motor activity in insomnia may be easily documented with the present home recording method.

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A HOME MONITORING DEVICE THAT DETERMINES DATA QUALITY IMMEDIATELY

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Introduction: As the popularity of home diagnosis of sleep disorders grows, so does the desire to obtain a good quality study. A home monitoring device, the Alice PDx (Philips-Respironics, Inc.), allows physicians, sleep technicians and patients to determine if a good quality study was obtained before data is downloaded or the patient returns to the sleep center.
Methods: The home monitoring device reports, in the form of a circular pie chart displayed on the LCD screen, the number of hours of good quality data obtained during a sleep study. Nineteen of an anticipated twenty-two PSG naïve participants have completed a trial to determine their accuracy of setting up the device and performing a respiratory sleep study in their home. Thus far, eight participants received full device setup instructions while eleven received no instruction and were asked only to follow the user manual and video to set up the device. After each study, participants reported the number of hours good quality data was collected. Subsequently, participants performed a full PSG study in a sleep laboratory.
Results: For the trial, the desired threshold for a "good quality study" is defined as one in which 4.5 hours of readable data is collected and all applicable sensors are properly attached. Of the eleven participants who did not receive full device application instructions, nine achieved a good study on the first night; the remaining two participants collected greater than three hours of quality data. Further, all eight participants who received full instruction collected a good quality study. Importantly, the average time it took to explain the device configuration instructions was less than 15 minutes.
Conclusion: All nineteen participants studied were able to set up the new monitoring device correctly at home and achieve and report a reliable study prior to returning to the sleep laboratory for confirmation.

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VALIDITY OF RESPIRATORY EVENTS COLLECTED FROM A PORTABLE MONITORING DEVICE

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Introduction: With the growing awareness of sleep apnea, portable diagnostic testing for sleep disordered breathing is becoming more and more popular. One dilemma facing sleep professionals is the question of the accuracy of these tests. To answer this question, a home monitoring device, the Alice PDx (Philips-Respironics, Inc.) was compared and validated against the existing Alice 5 PSG diagnostic system.
Methods: Seven of an anticipated twenty total participants have been enrolled thus far in a trial designed to compare event by event and overall respiratory data collected from the two diagnostic devices. Participants reported to the sleep laboratory and were simultaneously hooked up to both the existing PSG device and home monitoring device using bifurcated leads. An advanced PSG configuration, including ECG, EEG, EMG and EOG, was assessed. Upon completion, the two studies were time-aligned and analyzed for correlation and accuracy for each participant.
Results: All studies were centrally scored by a blinded sleep technician. AHI values ranged from 4.3 to 103.5 and RDI values ranged from 4.8 to 104.8. The results demonstrate a statistically significant correlation, AHI ($r=0.949$, $p=0.001$) and RDI ($r=0.953$, $p=0.001$) between the home monitoring device and the PSG device.
Conclusion: Respiratory events, including apneas and hypopneas, detected on the new home monitoring device are statistically similar and correlated highly to those captured on an existing in-lab PSG diagnostic system. Therefore, it can be suggested that the home monitoring device is reliable and accurate in capturing events from sleep studies.

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PRELIMINARY INVESTIGATION OF PROBLEM SOLVING AND COPING STYLES AS PRETREATMENT PREDICTORS OF CPAP ADHERENCE AT 1-WEEK

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Introduction: Attitudes toward CPAP treatment after seven days of use significantly correlate with later CPAP adherence. However, long-term adherence patterns are determined within these initial days of treatment and pretreatment attitude measures have failed to predict variations in adherence. There is need for a method of identifying patients at high risk for non-adherence prior to initiation of CPAP.
Methods: Data were collected as routine pre and post-treatment CPAP follow up in the clinic of a licensed psychologist certified in behavioral sleep medicine. Standard care involved pretreatment standardized questionnaires evaluating problem solving and coping styles and collection of objective 1-week CPAP adherence data. Discriminant analyses were performed on 40 data sets to determine the ability of questionnaire scores to differentiate adherent and non-adherent users. Adherence was defined as use of CPAP for ≥4 hours per night. Adherence categories analyzed include all days, days used, and use ≥70% of nights.
Results: All Days: Strategic planning, avoidance coping, proactive coping, and personal control factors correctly classified 81% of users (Sensitivity 0.85; Specificity 0.75; Wilk's Lambda = .58; $p < .001$; Eigen value = .73). Days Used: Strategic planning and personal control factors correctly classified 86% of users (Sensitivity 0.83; Specificity 0.92; Wilk's Lambda = .60; $p < .001$; Eigen value = .66). ≥70%: Avoidance coping, self-efficacy, personal control, and reflective coping correctly classified 88% of users (Sensitivity 0.86; Specificity 0.90; Wilk's Lambda = .50; $p < .001$; Eigen value = .98).
Conclusion: These questionnaires may be an effective pretreatment method for identifying patients at risk for subtherapeutic CPAP use. Identification of these patients has potential to guide development of interventions targeting relevant attitudes to optimize adherence. Further analysis of predictive models may identify behavioral targets for pretreatment interventions.

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SYNCHRONIZATION BETWEEN FRONTAL, CENTRAL, AND OCCIPITAL SLEEP EEG PARAMETERS TO ESTIMATE SLEEP QUALITY

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Introduction: Variables derived from sleep EEG and from sleep stage evaluation correlate only partially with sleep quality assessed by subjective ratings. There is still a need to find objective correlates in polysomnographic recordings for reported sleep quality. We analyzed an existing data base of sleep recordings using a new method to assess cross modulation between amplitudes and frequencies of the sleep EEG in order to correlate these with subjective sleep quality ratings.
Methods: Sleep recordings from 190 healthy subjects with two nights each were used for this analysis. The sleep recordings were taken from the SIESTA study and covered a broad age range. Six EEG leads (Fp1,

Fp2, C3, C4, O1, O2) were analyzed in terms of frequency bands (low and high delta waves, theta, alpha, sigma, and beta waves). For each frequency band instantaneous amplitudes and frequencies were calculated using the Hilbert transform. Based on these data correlation maps were calculated between instantaneous amplitudes and frequencies, within amplitudes and within frequencies in color coded cross modulation matrices. Subjects sleep quality was assessed from a visual analogue scale in the morning after sleep.
Results: Color coded correlation maps were analyzed for all subjects and for groups of subjects. High correlation was found between low and high delta amplitudes and frequencies. Moderate correlation was found in the frequencies map. There were little age differences and no gender differences. Surprising findings were correlations between delta amplitudes and alpha frequencies in some subjects. These subjects had a lower subjective sleep quality according to visual analogue scale.
Conclusion: This new method to analyze instantaneous frequencies and amplitudes allows to calculate synchronization between different brain regions in selected frequency bands. Most synchronizations found confirm previous knowledge about sleep physiology. Rare patterns like alpha delta sleep and indications of disturbed sleep like frequent arousals appear as marked changes in the colored correlation maps. Changes were more pronounced in a selected set of sleep recordings with low subjective sleep quality. The synchronization analysis may enable the assessment of subjective sleep quality with quantitative parameters.
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NON-INVASIVE MEASUREMENT OF MOVEMENT AND RESPIRATORY ACTIVITY IN RATS USING PULSE DOPPLER RADAR
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Introduction: As an initial step in developing non-invasive methods to determine sleep and wakefulness in small animals, we constructed a non-contact monitoring system to measure cardio-pulmonary activity and gross motor activity (i.e., movement) utilizing a 5800MHz microwave pulse Doppler radar sensor.
Methods: To evaluate respiratory rate detection, data collected with the radar sensor was compared to concurrent electrophysiological recordings in rats of the diaphragm electromyogram (EMGDia). Respiration signals were obtained by applying band pass filters (0.85-3.3 HZ) to the data acquired from the radar sensor and the EMGDia during quiescent periods. Respiratory rate was calculated using a local peak finding algorithm over 60 2-minutes epochs. Evaluation of gross motor activity detection was performed by comparing radar signals during active and inactive periods identified using visual determination.
Results: The respiratory signal derived from the radar sensor was highly correlated ($r=0.841\pm0.136$, $p<0.0001$) with the filtered respiratory signal obtained from EMGDia. The radar sensor had an average sensitivity of 97.51% and a PPV (positive predictive value) of 98.05%. Spectral analysis performed over 20 epochs of activity identified relatively equally distributed power densities on all analyzed frequencies (1-10 HZ) and a significant increase on total power density compared to periods of inactivity. Spectral analysis performed over 60 epochs of inactivity identified relative increases in power density greater in the 1-2.2 Hz range (i.e., the respiratory frequencies of rat). Thus, a linear discriminant function could distinguish inactivity from activity.
Conclusion: Pulse Doppler radar can non-invasively discriminate motion and respiration in small animals and will be useful sensor technology for efforts aimed at non-invasive determination of sleep and waking states.
Support (optional): Supported by NIH research grants RR20816, MH64827 and MH61716.

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ADHERENCE TO THE COMPLETION OF A DAILY SLEEP DIARY OVER 9 MONTHS (252 DAYS)
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Introduction: To assess stability in insomnia, 43 People With Insomnia (PWI; meeting DSM IV criteria for primary insomnia) and 43 controls aged 25-50 were compared over 9 months. The study also provided an opportunity to assess adherence to a subjective sleep diary. Daily sleep diaries (measuring subjective SOL, WASO, TIB, sleep quality & TST), were maintained for 252 consecutive days.
Methods: Daily entries were coded to allow analysis of mean adherence for each 'month' (9 months) and 'week' (35 wks) of data collection. To identify any significant 'week day' effect, data were also coded to allow the mean adherence for each day of the week to be calculated (e.g. Mondays n = 35). Weekend sleep was operationalized as sleep occurring on a Friday (F), Saturday (Sat) or Sunday (Sun) night. Wednesday (W) was selected as the reference weekday. Lastly, data were coded to identify weeks where participants successfully completed >4 days of their diary.
Results: Over 252 days no significant group differences were found in adherence between PWI and controls. However, while the mean 'monthly' adherence fell no lower than 80%, a significant main time effect was found ($F=16.70$, $p<0.001$), with adherence falling from 97.6% in the first month to 81.6% in the ninth. Analysis of mean 'weekly' entries also showed a main time effect ($F=23.44$, $p<0.001$), with adherence decreasing toward the weekend. Mean adherence for Mondays was 89.1% compared to 86.1% on Sundays. Data revealed that on average, adherence per week did not fall below 4 entries over the course of the 9 months, however, the number of missing data per week did increase over the 35 weeks. Subjective sleep measures also showed variability over the week within both groups. SE was consistently and significantly lower among PWI with mean differences of 11.0%, 10.0%, 9.4% and 10.1% for F, Sat, Sun and W (group main effect: $F=35.39$; $p<0.001$). Across days (W thru Sun) SE changed uniformly for both groups, with a noticeable decrease in SE reported on Saturday (time main effect $F=4.3$; $p<0.01$). TIB also showed a significant effect of time independent of group, with highest values (relative to W) reported for Sat and Sun.
Conclusion: Findings reveal no significant difference in adherence/compliance to the daily completion of 'paper and pen' sleep diaries between PWI and controls. Data reveal adherence to be strong across 252 days and with evidence of variability across week days, support the continued utility of the sleep diary tool in measuring variability across time.

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SLOW EYE MOVEMENTS AT THE SLEEP-WAKE BOUNDARY: A QUANTITATIVE ANALYSIS
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Introduction: According to the 2007 AASM scoring manual, in subjects who do not generate alpha rhythm, slow eye movements (SEMs) may be used to stage the onset of N1 sleep. SEMs were defined as "conjugate, reasonably regular, sinusoidal eye movements with an initial deflection usually lasting >500msec", though it was admitted that this definition was based on "limited data and clinical experience" and "initial deflection" was not defined. We sought to define the characteristics of SEMs through a systematic quantitative analysis of these waveforms using a digital polysomnographic acquisition system.
Methods: Polysomnograms (PSGs) from 72 consecutive patients were reviewed for inclusion criteria as follows: occipital-predominant alpha waves which attenuated with eye-opening, ≥3 epochs of N1 sleep at the initial sleep-wake transition, and visually identifiable conjugate, sinusoidal-appearing SEMs. PSGs of patients with concomitant SSRI use were excluded. Initial review of amplitude, slope and wavelength identified

an amplitude of ≥±50 μv and time to initial deflection, as defined by ¼ the duration of the wavelength, to be the critical measurements to define SEMs in the first 3 epochs of N1 sleep.
Results: 53 SEMs from 11 PSGs were analyzed. The median time to initial deflection was 870 msec (range: 515-1630 msec, 25th percentile: 670 msec; 75th percentile: 1.105 msec). The median slopes of the positive and negative deflections were 90.32 and 100.85 μv/sec respectively. The median amplitude was 81 μv (range: 51-174 μv, 25th percentile: 68 μv; 75th percentile: 93 μv).
Conclusion: Quantitative analysis confirms the currently held opinion that the time to initial deflection for SEMs is >500 msec and that the waveforms are roughly sinusoidal. However, the sinusoidal quality of SEMs (in contrast to REMs) makes "time to initial deflection" a less practical construct. Wavelength analysis may be an additionally useful descriptive parameter for SEMs.

1156
AUTOMATIC REM SLEEP DETECTION BASED ON RESPIRATORY PHYSIOLOGY

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Introduction: Many researchers reported that during the REM sleep, it has increasing and irregular pattern highly correlated with the autonomic nervous system. We would like to introduce the REM sleep stage scoring method with this respiratory physiology. Polysomnography is the most reliable method to scoring sleep stage but it is very complicate and troublesome that can interfere the subjects' sleep state changes. This study is a kind of preliminary study to score the sleep stage unconsciously, since the respiration is the one of the most robust signals to acquire non-intrusively.
Methods: We studied 13 healthy volunteers (9 males, 4 females, 28.2±2.7). Polysomnogram data was collected for each subjects and sleep stage was scored by one rater to compare with the automatic REM sleep detection algorithm. To extract the respiratory pattern during the REM sleep, we used nasal airflow signal with a thermocouple. Increasing pattern can be monitored with the smoothed respiratory rate by using regression analysis. Irregular pattern was shown by subtracting the smoothed respiratory rate from the original rate and it is also smoothed to determine the level. To determine threshold level adaptively, we also used smoothed data for the each increasing and irregular pattern but used 10 times larger windows or spans with adding empirical offset level. If the increasing and irregular patterns have the higher values than adaptive threshold level, it means that respiratory pattern is abruptly changed at those periods. We considered those periods are the REM sleep state when both increasing and irregular patterns exceed the threshold level.
Results: We used 6 statistical values to evaluate results such as positive predictive value (PPV), negative predictive value(NPV), sensitivity(SENS), specificity(SPEC), agreement(AGREE) and Cohen's kappa(KAPPA) value. Following values shows final result from the proposed algorithm compared with the rated score with the specialist. PPV:0.73±0.13, NPV:0.93±0.03, SENS:0.70±0.17, SPEC:0.93±0.05, AGREE:0.89±0.04, KAPPA:0.64±0.14. Among the results, Cohen's kappa value indicates that the result from the proposed algorithm is substantially agreed to the manual scoring.
Conclusion: Our proposed algorithm is very simple and effective in computation analysis and we use only one signal, respiration, to detect the REM sleep. Moreover it shows substantial agreement with the manual sleep staging. Adopting this algorithm to the unconsciously measured respiration is our further study.

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WIRELESS FOREHEAD EEG LOGGER AND AUTOMATIC SLEEP STAGE SCORING

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Introduction: Actigraphy is an easy and cost-effective way to obtain objective information about patient's sleep at home. Usually a questionnaire is used to complement the objective but limited information from the motion signal recording. We have investigated ways to automatically provide a more comprehensive picture about patient's sleep.
Methods: We have developed a lightweight EEG instrument, which is attached on a patient's forehead with adhesive electrodes. The EEG Logger acquires two channels of EEG and 3D acceleration signals overnight. Data acquisition starts automatically, when patient attaches the logger on the forehead. The measurement data is stored in the device's internal memory and can be downloaded into a computer for analysis, either directly or via mobile phone the following day.
Results: We also designed algorithms for characterizing different aspects of sleep using the frontal EEG and acceleration signals. Spectral entropy of the EEG signal correlated with the depth of sleep. Our data showed prediction probability of 0.91 (0.00) for EEG spectral entropy to S0-S4 in 140 hours of sleep in 10 healthy volunteers. The algorithm was complemented with separate detectors for REM-sleep, sleep spindles, SWA, and arousals. Patient's posture, head orientation, and movement arousals were extracted from the acceleration signals. Standard sleep parameters, like sleep efficiency and sleep latency, were also derived and compared with polysomnography.
Conclusion: For the patient, data acquisition with the EEG Logger is as easy as actigraphs - with the bonus of no need for manual record keeping. For the physician, the system offers versatile information about patient's sleep. The preliminary performance evaluation against polysomnography and users' experiences suggest that the EEG Logger will be useful tool in initial sleep disorder screening.
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A NEW HOME-MONITORING SYSTEM FOR FETAL MOVEMENT DURING PREGNANT WOMEN'S SLEEP

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Introduction: Pregnant women's sleep disturbance due to fetal movement is well known. Fetal movement is thought to be an index of fetal well-being. However, as there has never been a way to easily and reliably record fetal movement, psychophysiological studies of pregnant women's sleep disturbance and fetal well-being have not been done. In 2008, we introduced a long-term monitoring system for fetal movement during maternal sleep at home using a newly developed sensor (Early Human Dev 84:595-603). We confirmed that the new sensor was more sensitive than maternal subjective evaluation but less sensitive than ultrasound imaging. For this study, we developed a fetal movement recorder that pregnant women can operate by themselves. We also developed a system of analysis based on the proposal made in 2008.
Methods: We developed a small capacitive acceleration sensor with high output power (700mV/0.1G). The recorder (290g, 77mm X 27mm X 140mm) consists of two sensors (one for fetal movement; one for maternal movement), biological amplifier, and SD card drive. The analysis can display both fetal and maternal movements, automatically detect fetal movement, change a threshold of fetal movement, count detected

movement based on time, automatically and manually exclude artifacts coming from mothers, and make a comparison based on gestation weeks. The subjects were four normal pregnant women (26-38 yr) who gave written informed consent. They recorded fetal movement from 24 to 36 gestation weeks every four weeks. They put the fetal sensor on their abdomens and the maternal sensor on their thighs, and recorded fetal movement using the recorder during nocturnal sleep.
Results: Medians counts for fetal movement detected per hour during maternal sleep were 153 at 24 weeks, 166 at 28 weeks, 227 at 32 weeks, and 142 at 36 weeks. Fetal movement per hour was the highest at 32 weeks. This result was similar to our previous result of maternal subjective evaluation in 2008.
Conclusion: The pregnant women were able to easily record fetal movement using the new recorder at night by themselves. We have been collecting data of subjects with a normal pregnant course whether the system of analysis for fetal movement is successful.
Support (optional): The Kanagawa Academy of Science and Technology, and the Ministry of Education, Science and Culture of Japan.

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CLINICAL UTILITY OF THE PEDIATRIC DAYTIME SLEEPINESS SCALE IN CHILDREN WITH OBSTRUCTIVE SLEEP APNEA SYNDROME AND NARCOLEPSY

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Introduction: Excessive daytime sleepiness among children and adolescents has become a concern of health professionals and educational fields over the past decade. There are relatively less researches in the development and validation of tools to assess sleepiness in this population. The Pediatric Daytime Sleepiness Scale (PDSS) was proven to be a reliable and valid tool in measuring sleepiness in school settings. However, the utility of the PDSS in clinical settings remains to be evaluated. This study examined the psychometric properties of the PDSS and its utility as a screening tool for pathological daytime sleepiness in children with obstructive sleep apnea (OSA) and narcolepsy.
Methods: Firstly, we collected 441 children and adolescents from grade 6 to 12 from school settings to assess the reliability of the PDSS scale. Secondly, the PDSS was administered to 28 children and adolescents with OSA, 31 children and adolescents with narcolepsy, and 34 normal controls, to examine the validity and clinical utility of the PDSS in clinical populations.
Results: The PDSS showed good internal consistency (Cronbach's alpha = .81) and test-retest reliability (r = .77). The narcoleptic subjects scored the highest on the PDSS; the OSA subjects scored higher than normal controls. Furthermore, the PDSS score decreased in narcoleptic children after medical treatment. As a screening tool for narcolepsy, ROC curve analysis showed that the PDSS, with a cut-off score of 16/17, had good sensitivity (87.1%) and fair specificity (74.3%) for identifying individuals with pathological sleepiness. However, the differentiating power was not as great when the PDSS was used to screen OSA.
Conclusion: The PDSS is a reliable and valid tool for the measurement of sleepiness in clinical youth populations. When used as a screening tool, it is useful for sleep disorders with more severe pathological sleepiness, such as narcolepsy.

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VARIABILITY BETWEEN SELF-REPORTED AND PARTNER REPORTED IN EPWORTH SLEEPINESS SCORE

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Introduction: Epworth sleepiness scale (ESS) is a simple eight questions validated questionnaire which has been widely used for the assessment of sleepiness. Most of the time in clinical practice, the scale is filled out by the patient with little input from the spouse. We wished to assess variability in Epworth sleepiness Score between patient and their bed-partner.
Methods: Epworth Sleepiness Scale questionnaires were given to 61 patients and their partners who presented to the sleep center In South Texas. Thirty-eight female and twenty-three male patients and their partners completed the questionnaire.
Results: Mean age was 54.13 +/- 13.06, and mean BMI was 35.3 +/- 8.5. Mean ESS self-reported was 10 +/- 5.8, whereas that reported by their partners was 9 +/- 5.7 with a p value of 0.353. 15 out of 62 (24%) patients had a difference of >5 between their self-reported ESS and that reported by their bed-partners. In 14 out of 62 (22.5%) patients, use of self-reported ESS would have resulted in a misclassification of Epworth being normal, using a cut-off of 12 or more as being abnormal.
Conclusion: There is significant variability in ESS score among patients and their partners. As many as 24% of patients may end up being misclassified if ESS is based solely on self-report.

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SLEEP/WAKE CLASSIFICATION USING HEAD ACTIGRAPHY, SNORING AND AIRFLOW SIGNALS

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Introduction: Actigraphy is often used in ambulatory devices to differentiate wakefulness from sleep but its accuracy is limited by the inability to distinguish quiet wakefulness from (quiet) sleep and active wakefulness from disturbed sleep with frequent arousal associated movements. We developed and validated an algorithm that combines head actigraphy, nasal flow and snoring from a forehead-worn recorder (ARES UnicoderTM) in order to more accurately distinguish sleep from wakefulness.
Methods: The algorithm was developed on 25 subjects (RDI=30±26; range:3-109) and cross-validated on 86 subjects (RDI=28±25; range:1-103). Subjects underwent concurrent overnight recording with PSG and ARES. The algorithm classified 30-second epochs as Wake or Sleep based on the intensity and duration of head movements and snoring, and presence of sleep-specific phenomena (e.g.events, flow limitation) in the nasal flow. PSG recordings were manually scored according to the AASM criteria. Epoch-by-epoch comparisons (n=60,698) were performed and sensitivity (Se), specificity (Sp), positive predictive value (PPV), agreement (Ag) and kappa calculated for each subject. PSG-ARES differences in sleep latency (SL), total sleep time (TST) and sleep efficiency (SE) were tested with paired t-test, and impact of RDI on performance with Pearson correlation coefficient and ANOVA.
Results: The algorithm's performance was similar in the development (Se:70%;Sp:91%;Ag:84%;kappa=0.57) and validation group (Se:67% ;Sp:92%;Ag:84%;kappa=0.52). 3.6% of all PSG Wake epochs (1.6% in subjects with RDI<20 and 6.8% in those with RDI>21) contained clear respiratory events and/or snoring. Differences in TST (difference: -0.7±34min; range:-84 to +86min) and SE (difference=-1±10%;range=-

26 to 21%) were non-significant, but ARES slightly underestimated SL (difference=2±6min;range=-13 to 30min;p=0.003). Performance did not deteriorate with increased RDI. The use of snoring and flow increased PPV and specificity as compared to using actigraphy alone (PPV gain:3±7%;range:0-35%) without impairing sensitivity (<1% change in all subjects).
Conclusion: Addition of flow and snoring to actigraphy improved specificity and enabled accurate sleep/wake classification across the whole OSA severity spectrum.
Support (optional): NIH SBIR R44HL068463-05 and 2R44-DE016772-0

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A MODIFIED EPWORTH SLEEPINESS SCALE FOR RESIDENTS IN NEW YORK CITY(A PILOT STUDY)

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Introduction: The Epworth Sleepiness Scale (ESS)is used as a subjective method to evaluate daytime sleepiness. The ESS asks patients to rate how likely they would be to doze off in eight different situations (0 for the lowest and 3 for the highest). Two of these pertain to being a passenger or a driver in a car. There are 3,243,239 drivers' licenses on file in New York City. This accounts for only 40.1% of the population as per a 2006 census. There are many residents using mainly public transportation to which these questions may not be applicable. We postulated that in major urban areas, individuals who regularly use public transportation do not answer these specific questions, and thus may have lower ESS scores, than individuals who regularly spend time in automobiles.
Methods: We distributed questionnaires to consecutive adult patients (age 18-75)undergoing nocturnal polysomnograms, which included the standard ESS(ESSa)plus two additional questions concerning the chance of dozing as a passenger on public transportation for one hour without a break and as a passenger on public transportation for a few minutes (ESSb). We calculated a standard ESSa score as well as a score using our modified questions (ESSb).
Results: Sixteen of 19 patients live in New York City. The average ESSa for all patients was 8.89 (9.19 for city residents and 7.33 for non city residents). The average ESSb for all patients was 8.78 (9.06 for city residents and 8.00 for non city residents). Four of 16 city residents felt that the question pertaining to being a passenger on public transportation for one hour was more relevant than being a passenger in a car for one hour. Seven of 16 city dwellers felt that the question addressing riding public transportation for a few minutes was more relevant than being in a car while stopped in traffic for a few minutes. All of our patients reported having driver licenses while only 6/19 city residents reported driving once or more per week.
Conclusion: This pilot study shows there is a potential use of a modified scale in residents of a major urban area who do not drive, or for a specific type of population that do not drive or use a car as a main source of transportation. For our continued investigation, more subjects and a different patient cohort are required.

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RESPIRATORY IMPEDANCE SENSING TO TRIGGER INSPIRATORY-SYNCHRONOUS STIMULATION OF THE GENIOGLOSSUS MUSCLE

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Introduction: The pharyngeal airway is particularly vulnerable to collapse during the inspiratory phase of the respiratory cycle. Inspiratory stimulation of the genioglossus (GG) muscle may be of therapeutic benefit to individuals with obstructive sleep apnea (OSA). Detection of the respiratory cycle with impedance may be a useful way to trigger such stimulation, synchronously with the inspiratory phase of the respiratory cycle.
Methods: Four healthy volunteers were studied. Respiratory impedance was measured via adhesive skin-surface electrodes. The GG was stimulated with an external stimulator (Apnex Medical) via percutaneously inserted intramuscular fine wire electrodes. Two stimulation delivery modes, triggered and synchronous, were used. Triggered mode used impedance measures to deliver stimulation on every other breath. Stimulation was initiated 1.0 sec after cessation of inspiratory flow and maintained until 1.0 sec after the offset of the next inspiratory flow cycle. Synchronous mode used impedance measures to deliver stimulation on every breath. Stimulation was initiated at the onset of inspiratory flow and maintained until the offset of inspiratory flow. The reliability with which inspiratory offset was detected and stimulation delivered was determined by comparing respiratory impedance-based stimulation with pneumotachograph-derived respired airflow. Reliability was determined by calculating the ratio of successfully detected inspiratory offsets to the number of respiratory cycles.
Results: Three subjects (S1, S2, S3) were stimulated during sleep (stable stage 2) in the triggered mode over periods of 300, 94 and 326 breaths, respectively. The reliability with which inspiration was detected and stimulation delivered was 95%, 87% and 95%, respectively. Two subjects (S2, S4) were tested in the synchronous mode during sleep and awake, respectively, over periods of 546 and 85 breaths. Detection reliability was 100% and 93%, respectively.
Conclusion: Measurements of respiratory impedance via skin surface electrodes can be used to reliably detect spontaneous respiratory cycle during wakefulness and sleep and deliver stimulation synchronous with inspiration. Such a technique may have value in automating the delivery of inspiratory synchronous stimulation of the GG for the purpose of decreasing pharyngeal collapsibility and improving inspiratory airflow in individuals with OSA.
Support (optional): Apnex Medical Inc., St. Paul, Minnesota, USA.

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DETERMINATION OF THE SLEEP ONSET PERIOD VIA DETRENDED FLUCTUATION ANALYSIS

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Introduction: The process of falling asleep marks a period of rapid change involving a progressive reduction in the arousal level until the installment of definite sleep. Determining this period has not been fully studied yet. The purpose of this study was to propose a new method to examine and determine the sleep onset period (SOP) quantitatively. Differences between narcoleptics and controls during SOP were also studied.
Methods: Multiple sleep latency tests were performed to 9 healthy controls (23.8 ± 6.3 yrs.; 6 males) and 11 drug-free narcoleptic patients (19.3 ± 4.4 yrs.; 8 males). Sequential detrended fluctuation analysis (DFA) were applied to each 10s segment of EEG recordings at O1/A2, O2/A1, C3/A2, and C4/A1. The sequences of DFA scaling exponents (SE) of individual in the same group were averaged. The SOP of each group was estimated by fitting the averaged sequences to a parametric curve.
Results: The sequence of DFA SE showed that electrophysiological brain activity was changing rapidly across the SOP. This transition was also verified by a conventional method (i.e., the sequential spectral analysis) in previous literature. The SOP durations of narcoleptics and controls were estimated as 239 ± 25 s and 145 ± 20 s, respectively.
Conclusion: The progressive increase of DFA SE indicated electrophysiological changes of the brain during SOP. The significantly larger SOP of narcoleptics, compared to that of controls, suggested the signatures of narcolepsy could be quantified by the sequential DFA and, therefore, the method could serve as a potential tool to diagnose narcolepsy.

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EXPLORATORY FACTOR ANALYSIS OF THE SLEEP DISORDERS QUESTIONNAIRE (SDQ): A PROPOSAL FOR SHORTENING AND RE-SCALING TO PRODUCE "SDQ2"

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Introduction: The SDQ was created by discriminant function analysis in the 1990s, but has never been factor analyzed by the original authors. The intent was to see if the original 4 subscales of the SDQ (sleep apnea, narcolepsy, periodic limb movements, and insomnia) would be supported in this study with much larger n and a different statistical method. It was also hoped that the SDQ, 176 questions long, could be shortened for ease of use.
Methods: An exploratory factor analysis was performed on the 176-item Sleep Disorders Questionnaire (SDQ) using a sample of 2131 subjects drawn from general sleep disorders clinics plus controls and several special populations such as alcoholism, chronic fatigue, and psychiatric illness.
Results: Four principle factors were found, corresponding to Insomnia, Daytime Sleepiness / Narcolepsy, Substance Abuse, and Sleep Apnea. The first factor had three subfactors: Psychiatric Insomnia, Objective Measure of Insomnia, and Periodic Limb Movements. The second factor had two subfactors: Daytime Sleepiness and Narcolepsy Symptoms. The third and fourth factors were homogeneous. The Eigenvalues were 20.69, 6.70, 6.05 and 5.43 respectively. The variance explained by each factor using an orthogonal rotation was 12.76, 8.89, 6.68, and 6.57 per cent.
Conclusion: While the new factors were not exact duplicates of the original subscales of the SDQ, there was substantial overlap (from 18.5% to 60%). The factors show increased precision compared to the original subscales and several new subscales are proposed. The items that did not load on the four main factors could be discarded and a new scale consisting of the 65 pertinent items will soon be published as the SDQ2.

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LIKENESS-BASED DETECTION OF SLEEP SLOW OSCILLATION

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Introduction: Sleep Slow Oscillations (SSOs) are EEG waves oscillating at 0.3-1Hz, with amplitudes up to 300μV, which synchronize cortical networks by their widespread propagation during sleep. Up-to-date, studies on SSOs have been focused on healthy young individuals, for whom sleep slow activity is notably expressed. Detection methods reside in threshold criteria on waves morphology producing detection of well-expressed SSOs. For applications to wider classes of subjects, amplitude-based criteria could be a weak-point since quality of wakefulness affects slow wave sleep, both in normal and pathological conditions. However, amplitude restrictions are needed to identify patterns sustained by alternating silent and active states of cellular slow oscillation.
Methods: For SSO detection, we propose the likeness-based method: it locates propagating SSO instances recognizing well-expressed SSOs (thresholds on morphology) and select among concurrent EEG channels those showing patterns strongly similar to detected well-expressed SSOs (likeness rule: cross-correlation between phases). SSO detections for an instance are thus composed by a well-expressed SSO (or a set of well-expressed SSOs, if concurrent within 200ms) with its similar concurrent waves.
Results: The likeness-based method identifies SSO instances that, propagating, reach the well-expressed form (ensuring identification of patterns sustained by alternating silent and active neural states) with whatever amplitude evolution over the scalp (i.e., a "waxing and waning-like" behavior). The proposed method was applied on two sleep conditions recordings: sleep with normal delta activity, and altered sleep with mingled macrostructure and generally low amplitude delta waves. At variance with canonical methods tested on the same data, the likeness-based one produced reliable number of SSO detections per instance and effective estimates of propagation speed, also for altered conditions.
Conclusion: The effectiveness of the proposed method allows the analysis of SSOs also in altered sleep conditions, thus representing a new approach for studying pathophysiological correlates of sleep disorders.

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VALIDITY OF PATIENT VERSUS OBSERVER EPWORTH SCORE IN THE ASSESSMENT OF A PATIENT'S DAYTIME SLEEPINESS

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Introduction: Excessive daytime sleepiness (EDS) is common but is often unrecognized. All the tools available to assess EDS have shortcomings. The Epworth Sleepiness Scale (ESS) is most commonly used to quantify sleepiness, while the gold standard is the Multiple Sleep Latency Test (MSLT). However, the patient ESS correlates poorly with the MSLT. The psychomotor vigilance task (PVT) is an objective measurement of alertness which has been shown to correlate well with the MSLT. A close observer's ESS assessment can defer significantly from that of the patient. We hypothesized that the patient ESS (ESS_pt) and observer ESS (ESS_obs) will correlate poorly and the ESS_obs may be a more accurate assessment of EDS as measured either by the MSLT or PVT. We further hypothesized that one or two specific questions in the ESS may be more indicative of the objective findings than the total ESS.
Methods: We studied 21 patients, 12 males and 9 females, aged 47+/-13.9 years, BMI 31.5+/-7.8 kg/m2, with complaints of EDS. We asked them and their close observers to complete the ESS questionnaire without conferring with each other. Patients had a 10 minute PVT, 30 minutes before and after their Polysomnography (PSG). The patients who were scheduled for MSLT had a PVT trial 30 minutes prior to each MSLT nap. Results are presented as means+/-SD. Comparisons were made using correlations and the significance level was < 0.05.
Results: Correlation was poor between the patient and observer ESS r=0.34; p=0.13. ESS_pt correlated poorly with the PVT mean reaction time (RT) r=-0.2; p=0.42, total lapses (TL) r=-0.27; p=0.28, and false responses (FR) r=0.06; p=0.82. ESS_obs similarly correlated poorly, RT r=-0.01; p=0.95, TL r=0.02; p=0.95 and FR r=0.18; p=0.47. Correlation between ESS_pt and MSLT was poor r=0.18; p=0.60 and ESS_obs r=-0.23; p=0.49. However, there was a better correlation between the observer's estimate of sleepiness watching TV and MSLT, r= -0.5 than the same correlation using the patient's score r=-0.31. PVT RT (r=-0.64, p=0.07) and TL (r=-0.68, p=0.04) had good correlation with MSLT.
Conclusion: As hypothesized, there is poor correlation between ESS_pt and ESS_obs. There was poor correlation between overall subjective and objective measures, though the observer's estimate of sleepiness watching TV was better correlated than the patient's. Additionally, there was good correlation between certain PVT variables and MSLT. A larger study is needed to validate these results because of the small sample size.

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VALIDITY OF SEVEN-ITEM RLS DIAGNOSTIC QUESTIONNAIRE (RIBECA-7Q) IN THE RESTLESS LEGS SYNDROME IN THE BALTIMORE EPIDEMIOLOGIC CATCHMENT AREA (RIBECA) STUDY

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Introduction: While several epidemiologic studies have utilized various short diagnostic instruments to assess the prevalence of RLS in the community, few of them examined validity of these instruments. Recently, the RiBECA study utilized the seven-item RLS diagnostic questionnaire (RiBECA-7Q) to report 4.1% prevalence of RLS (41 out of 1024 participants) in East Baltimore. We examined the criterion validity of the RiBECA- 7Q against clinical assessment by a trained specialist.
Methods: Of 1024 original participants, 164 participants (38 with RLS and 127 without RLS based RiBECA-7Q) were examined face-to-face by a trained clinician based on the Johns Hopkins Telephone Diagnostic Interview for RLS and underwent a structured neurological and psychiatric examination. Diagnosis of RLS was further adjudicated by consensus of an expert panel of three RLS specialists who were blind to the group status based on RiBECA-7Q.
Results: Kappa value between the RiBECA-7Q and consensus clinical diagnosis of RLS was 0.81. With consensus clinical diagnosis of RLS as the "gold standard," sensitivity and the specificity of the RiBECA-7Q were 0.88 and 0.95 respectively. Positive- predictive value of the RiBECA-7Q was 0.82 and negative- predictive value was 0.97.
Conclusion: The RiBECA-7Q demonstrates acceptable criterion validity for diagnosis of RLS in the community.

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DESCRIPTION OF SLEEP-RELATED TIME VARIABLE RESPONSES IN THE COMBINED PROMIS DATASET ON SLEEP/WAKE FUNCTIONING

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Introduction: The initial NIH Patient-Reported Outcome Measurement Information System (PROMIS) sleep and wake disturbance scales include qualitative, quantitative, and time-based items. Integrating responses to quantitative and time-based items may be valid options in constructing assessment instruments.
Methods: Fifteen time-variable items were given to 1993 subjects in an internet-polled sample through Polimetrix, Inc., and to 259 subjects recruited at the University of Pittsburgh's PROMIS site. Data collection used standardized pull-downs on computer screens. Conventional quantiles of the time-related variables were computed, along with demographic summaries.
Results: The sample (mean age 51, SD 16, range 18-88 years) included 1167 men and 1085 women. Subjects with college degrees comprised 48%, while 1.6% had less than a high school education. The full-time employed comprised 40%, the retired 25%, the part-time employed 9.5%, the homemakers 7%, and the disabled 7%. Subjects were obese (mean BMI = 32.6, SD = 8.9, range 12-83). Half (49%) reported 15 minutes for sleep onset or less, and 71% less than 30 minutes, while 13% took more than 60 minutes. Key 5th, 50th, and 95th quantiles were: usual bedtime (9:00 PM, 11:00 PM, 3:30 AM); time spent in bed (285, 450, 615 minutes); sleep time (270, 405, 1260 minutes); and usual time out of bed (4:55 AM, 7:00 AM, 11:00 AM). Across the main quantiles, subjects wanted more time in bed than they usually obtained. Comparisons of back-calculations from reported clock times to derive quantitative sleep variables against subjects' categorical responses indicated more bias to underreport time in sleep than time in bed.
Conclusion: This sample is not fully representative of community populations. Yet its data provide some indication of population norms for key sleep-related time-variables. While diagnostically useful when considered individually, these variables may not be amenable to integration into self-report severity scales using traditional psychometric methods.
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1170

VALIDATION OF AN SPANISH VERSION OF THE SLEEP MEDICAL OUTCOMES SCALE FOR MEXICAN POPULATION

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Introduction: There is a high prevalence of sleep disorders among general population. In some countries the reported incidence of sleep disorders is about 30 percent of population. In underdeveloped countries, as Mexico, there are no reliable epidemiological data on sleep disorders. Moreover, there is a lack of reliable instruments to assess the impact of sleep disorders on general population. Therefore, there is a need for fast, self-rated scales to allow us to obtain reliable, epidemiological data on sleep disorders in Mexican population. In the present study, a Spanish version of The Sleep Medical Outcomes was standardized and statistically validated for Mexican population.
Methods: The Sleep Medical Outcomes is a 12 item scale, published in 2004, which assess the presence of the most common symptoms associated with sleep disorders. After the translation to the ordinary Mexican Spanish, pilot observations were made to evaluate comprehension of the items and the proper modifications were made. Thereafter, the scale was applied to 700 young adults (18 -35 years old, both sexes) and the statistical analysis was done.
Results: In the reliability analysis, the Cronbach alpha obtained was 0.744. Concerning sleep features, 40.8 % of the sample report symptoms of sleep disorders. The main complain was excessive diurnal sleepiness (12.5 %) and this symptoms was reported by 68.8 % of women. Symptoms link to insomnia were detected in 6 % of the sample and the women showed the higher incidence.
Conclusion: The results obtained are similar to those reported for population in other countries. The Spanish version showed a high level of reliability. Thus, this scale is a valuable tool to rapidly assess the presence of symptoms suggesting sleep disorders. In the future it is necessary to increase the sample to other populations of different ages.

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EXCESSIVE DAYTIME SLEEPINESS SCALE FOR MEXICAN CHILDREN AND TEENAGER POPULATION

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Introduction: Excessive daytime sleepiness (EDS) is a symptom easily assessable in adults by subjective scales and Multiple Sleep Latency Test (MSLT). However, these procedures are not used to assess the same symptom in children or adolescents. This may be due to two facts: first, in adults the EDS is reflected by the tendency to falling asleep in different situations, while in a child that can reflected with cognitive, behavior and mood disorders; the second fact is that some situations that exacerbate the EDS in adults, like watching television, in children generate activation. Since the Adult drowsiness scales are not effective in chil-

dren and MSLT is impractical and inaccessible, it is necessary to have a standardized scale for children and teenagers in Mexican population. The Pediatric Daytime Sleepiness Scale (PDSS) has recently developed and assesses through 8 items, the possibility to falling asleep in different circumstances, difficulties in concentration and changes in mood.
Methods: The PDSS was translated and adapted to Mexican Spanish. To assess the understanding of the item a first application was made to 200 subjects. From this pilot observation, a new item was inserted as well as four item to a assess sleep habits. Subsequently, a second application to 356 students (age between 8 and 17 years old, both genders), was done.
Results: A reliability analysis was performed obtaining a Cronbach Alpha of 0.701 Maximum score obtained was 34, minimum was 9 and the average was 17.8 (SD 4.7) There was a significant negative correlation (0.01) between hours of sleep on weekdays and total score.. In addition, 28% of the population obtained values higher than 20 points.
Conclusion: The results suggest that this Spanish version of the scale is reliable tool for detecting sleepiness in childhood and adolescent of Mexican population.

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ACTIGRAPHIC ASSESSMENT OF A POLYSOMNOGRAPHIC-RECORDED NAP: A VALIDATION STUDY

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Introduction: Validation studies comparing actigraphy and PSG-recorded nocturnal sleep show a high level of agreement on sleep measures. These results suggest that actigraphs may be a more economical and efficient technique for some sleep studies. One less validated condition, however, is daytime sleep. This study aims to determine if an actigraph can accurately detect a nap. Here we compare actigraph and PSG sleep variables (TIB, TST, SL, WASO, SE) for both an afternoon nap and control period (interval of rest).
Methods: Sixty-three subjects were randomized to either the nap (N=30; ~90min sleep) or control rest condition (N=33; 90min reclining while listening to classical music). All subjects wore sleep watches while simultaneously hooked up to PSG. The automatic minor rest interval (AMRI) option of the Respironics Actiware 5.5.0 program was used to score the actigraph data. We examined three AMRI sensitivity levels (high, medium, low) and three interval duration minimums (15, 40, 65 min). Linear regressions were performed with Bonferroni corrections.
Results: The actigraph accurately predicted TST, SL, WASO, and SE for the napping condition. The most effective parameters were: high sensitivity/15 and 40-minute minimums for TST (R^2=0.74, p<0.001) and SL (R^2=0.52, p<0.001) and medium sensitivity /15 and 40-minute minimums for WASO (R^2=0.29, p=0.01) and SE (R^2=0.73, p<0.001). The actigraph did not accurately predict TIB. No rest intervals were identified as sleep, but 0-20 were identified as rest (depending on parameters).
Conclusion: The results of this study are consistent with validation studies examining nocturnal sleep. The control period of rest demonstrates that an episode of immobility will not be scored as sleep. Furthermore, it appears that different sensitivity levels are more effective for certain sleep measures (high sensitivity for detecting sleep and medium sensitivity for detecting wake). This study validates the ability of the actigraph to detect daytime naps.
Support (optional): Respironics, Co. supplied the sleep watches for this study Dr. Mednick's NIMH K01MH080992-01

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STATE TRAIT SLEEPINESS INVENTORY, A NEW INSTRUMENT FOR MEASURING DAYTIME SLEEPINESS

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Introduction: The aim of this research is characterize psychometrically a small sample by using state-trait sleepiness inventory which is a self report instrument that measures in two-dimensions and several factors of daytime sleepiness as approximations to validate the scale used.
Methods: A cross-sectional study on a sample of 451 university students, ages of 17 and 52 at the Cooperative Colombia University and the University of Antioquia was conducted and of which the ones that presented snoring symptoms were left out. They took a self report questionnaire where the State trait sleepiness inventory was used, a sleeping habit questionnaire, and the Epworth sleepiness scale (ESE). The questionnaire is the result of the review of the theoretical model of state-trait sleepiness, the different sleepiness questionnaires, and assessments by experts.
Results: An analysis of the scale characteristics given by the sample was done, the reliability coefficient of the trait sleepiness scale (TSS) giving back a Cronbach alpha of 0.72 and the state sleepiness scale (STSS), 0.70. These results properly showed an internal consistency. After, the scores of each scale were obtained where the sleepiness scale average was 22.1 with a standard deviation of 7.3, and the TSS averaged 20 with a standard deviation of 7.4. After this analysis, a factorial-analysis was conducted where it showed STSS explains 70.5% of the total variance and the TSS is a 70.7%. Each scale can be explained by the 5 factors that were used in the initial construction of the scale. These factors are warning, motivation, soporific situations, sleep regulating factors and sleep deficit factors.
Conclusion: The inventory shows proper psychometric characteristics when its statistical behavior was analyzed, and both scales showed a good internal Cronbach alpha consistency. The sensitivity of the scales obtained from pathological populations is discussed; in this first approach, the patients and snorers yielded interesting, similar results with those obtained from the ESE scale. In short, this is a new instrument that addresses the phenomenon of excessive daytime sleepiness from several aspects.

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AUTOMATED SLEEP STAGING IN REAL TIME USING A SINGLE EEG CHANNEL (FP1-FP2) ON THE FOREHEAD

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Introduction: Cognitive impairments caused by chronic sleep deprivation can be ameliorated by frequent brief naps, but the effect depends on accumulated sleep debt and timing, duration and sleep architecture of the naps. Naps would likely be more effective if their sleep architecture, timing and duration could be tailored with respect to the accumulated sleep debt and previous naps. Real-time assessment of sleep architecture using a minimal number of EEG channels and dry electrodes is a pre-requisite for such an approach. With an intention of developing a device for optimizing naps in operational environments, we developed algorithms for real-time sleep staging using a single (Fp1-Fp2) EEG channel.
Methods: EEG (C3-A2, Fp1-Fp2), EOG and chin EMG were recorded from thirteen healthy sleep-deprived subjects during a 2-hour nap. Automated scoring evaluated each second of Fp1-Fp2 EEG and classified it into Wake, Light (LS, corresponding to NREM1 and 2), Deep (DS,

corresponding to NREM3) and REM sleep on the basis of a beta-alpha-slow-wave index (a ratio of EEG power at high and low frequencies) and slow-wave-sleep index (%time with the EEG central frequency <4Hz). Visual scoring was done in 30 second epochs according to the AASM criteria (gold standard-GS), and each second within an epoch was assigned the same stage as the whole epoch. Second-by-second comparisons were performed between GS and automated scoring.
Results: Overall agreement between GS and automated scoring on 92,230 seconds of sleep was 77% (Wake:58%;LS:83%; DS:86%;REM:64%). The algorithm tended to score light sleep too early during transitions from wakefulness into drowsiness, and often overlooked brief (15-30s) awakenings. REM was often confused with wakefulness or light sleep.
Conclusion: Automated assessment of sleep architecture from the Fp1-Fp2 EEG in real time is feasible although more work is needed in order to achieve accurate separation among wakefulness, early drowsiness and REM sleep.
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RELIABILITY OF SLEEP STAGING USING ELECTRODES LOCATED BELOW THE HAIRLINE IN THE CONTEXT OF OPTIMIZATION OF NAPPING

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Introduction: Brief naps dispersed throughout the day can ameliorate cognitive impairments caused by chronic sleep deprivation but the effect depends upon their timing, duration, sleep architecture, accumulated sleep debt and susceptibility to sleep deprivation. More efficient mitigation of cognitive deficits could be achieved by tailoring timing and durations of subsequent naps based on the sleep architecture of previous naps and accumulated sleep debt. Ideally, sleep architecture should be assessed using minimal EEG channels and no-prep electrodes. With a goal of developing a device for optimizing naps in operational environments, we studied the reliability of visual sleep staging using electrodes located below the hairline where no-prep electrodes could be applied.
Methods: Thirteen healthy subjects (7 females) took a 2-hour nap while EEG (C3-A2, Fp1-Fp2), EOG and chin EMG were recorded. Sleep was scored in 30-second epochs according to the AASM criteria (gold standard-GS), and repeated by the same scorer using only EOG or Fp1-Fp2 channels. Scoring sessions were two weeks apart to minimize the memorization effect. Epoch-by-epoch comparisons were performed between GS and scoring based on EOG or Fp1-Fp2.
Results: Agreement with the GS was better for EOG (Wake:75%; NREM1:54%;NREM2:82%; NREM3:85%;REM:82%) than for Fp1-Fp2 (Wake:67%;NREM1:52%;NREM2:84%; NREM3:82%;REM:69%). Wake vs. early NREM1, and REM vs. NREM1 were frequently confused. Recognition of wakefulness was hampered by the lack of alpha activity in the EOG and Fp1-Fp2 channels. REM sleep was difficult to recognize with Fp1-Fp2 because differential recording attenuated the amplitudes of ocular artifacts.
Conclusion: Solid NREM sleep, essential for regenerating naps, is reliably recognized from either EOG or Fp1-Fp2. Distinction between Wake and NREM1 is less accurate, but not critical in the context of optimizing naps. A system combining EOG with Fp1-Fp2 could provide sufficient detection of the sleep stages required to optimize napping and maintain the design goal of using only no-prep electrodes.
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COMPARISON OF TWO SCORING METHODS TO DETERMINE APNEA HYPOPNEA INDEX

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Introduction: Recently, the American Academy of Sleep Medicine produced new scoring criteria for identifying breathing events during polysomnography. We evaluated the impact of the new scoring criteria to the previous criteria
Methods: PSG results were first obtained following the AASM 2007 "Recommended" methods (M1). Subsequently, the same PSG's were scored following methodology described in the 1999 AASM guidelines (M2) without knowledge of the M1 results. All PSG's were scored by the same reviewer for each scoring method. Results were analyzed by comparing the mean values of the AHI and its components. Diagnostic Agreement (using the results of the M1 technique as the reference technique) was determined.
Results: PSG results for 34 patients are included. There were 8 females (23.5%). The (mean ± SD) age was 45.7 ± 11.3, BMI was 35.3 ± 8.2, ESS was 14.2 ± 3.9. The average AHI using the 2007 AASM criteria was 40.4 ± 33.9 events per hour. All data are presented with the M1 results listed first followed by (± SD). The AHI values were 40.4 ± 33.9 vs. 56.7 ± 30.7 and differed significantly ($p < 0.0001$). The Obstructive Apnea Index values were 35.1 ± 41.4 vs. 33.2 ± 39.1 and did not differ significantly ($p= 0.4098$). Hypopnea Index values differed significantly (22.5 ± 29.5 vs. 57.9 ± 44.5, $p< 0.0001$) Diagnostic agreement (both methods with AHI ≥ 40 or if AHI< 40, difference between scoring methods is < 10), overscoring (both AHI's < 40, M2 AHI ≥ M1 AHI +10) and underscoring (both AHI's < 40, M2 AHI ≤ M1 AHI - 10) were determined. Using M1 as the reference, diagnostic agreement (i.e. both AHI's >40 or difference less than 10) was present in 22 of 34 cases (67.4%). M2 resulted in overscoring (M2 AHI > M1 AHI + 10) in 12 cases (35.3%). There were no cases of underscoring. 13 of 17 with M1 AHI between 5 and 30 (mild to moderate) were overscored.
Conclusion: There are substantial differences in AHI results obtained with the two scoring methods. Slightly more than one third of patients were classified as having a higher AHI with the 1999 AASM criteria compared to the 2007 recommended criteria.
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NOVEL METHOD TO IDENTIFY THE MECHANISMS MEDIATING ENDOTHELIAL ACTIVATION IN SLEEP APNEA

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Introduction: Mechanisms underlying endothelial activation in obstructive sleep apnea (OSA) remain poorly understood. In contrast to previous studies that examined pathways known to be involved in atherogenesis, we aimed to identify proteins that mediate endothelial activation in OSA without pre-existing notion about the nature of protein interactions.
Methods: Endothelial cells (EC) were harvested from a forearm vein using 3 guidewires sequentially inserted through 20-gauge angiocatheter. EC were purified using magnetic beads coated with endothelial-specific antibody and divided in 3 aliquots. The first aliquot of harvested EC was incubated with a library of $2x10^{11}$ phage-displayed peptides. Each phage contains a single DNA sequence that encodes its displayed peptide which binds to ligand on the EC membrane. Unbound phage was washed away. EC-bound phage was eluted, amplified with E. coli, incubated with 2 remaining EC aliquots for 2 additional binding/amplification cycles, and plated with E. coli on agar medium that allows selective growth of transfected E. coli colonies. Each colony contains a single DNA sequence that encodes for a single peptide. Clones from individual colonies were characterized by DNA automated sequencing.

Homologous analysis of all consensus peptide sequences was performed using BLAST (ncbi.nlm.nih.gov/blast).
Results: We sequenced 270 individual colonies from 3 otherwise healthy OSA patients and 3 healthy controls matched for age and waist circumference. Peptide motifs ENW, HHKHPLK, and TLFESF were identified in controls but not OSA patients. Homology search revealed shared motifs with zinc-finger RAN binding domain containing 1 protein, histidine-rich glycoprotein, and oncostatin M receptor respectively. These proteins mediate inflammatory response in human endothelium.
Conclusion: Phage display peptide library can be used to profile protein interactions in freshly harvested venous endothelial cells in OSA. This approach may uncover previously unknown mechanisms that mediate accelerated atherogenesis in OSA, and may identify novel therapeutic targets in OSA-related vascular diseases.
Support (optional): American Sleep Medicine Foundation 21YI03, Irving Center for Clinical Research RR-0645, and American Lung Association CU-52259701 (S.J.)

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COMPARISON OF A NEW TYPE 3 PORTABLE MONITOR FOR OSA DETECTION VS. IN-LAB POLYSOMNOGRAPHY

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Introduction: A new, compact (3.6 x 1.25 x 2.1in) and lightweight (80g) 6-channel (nasal pressure, effort, snoring, SpO2, pulse rate, body position) portable monitor (PMP-300E, Pacific Medico Co., LTD) was comparison tested against conventional in-lab polysomnography (PSG) for detection of sleep-related breathing parameters.
Methods: Eleven subjects 18 yrs and older suspected of having OSA were recruited, and after informed consent, they underwent a clinical evaluation including EKG. The subjects were instructed on the use of the PMP-300E and wore it at home for 1 night. They returned for 2 consecutive in-lab nights and wore both the PMP-300E and the usual PSG sensors. The subjects completed the Epworth sleepiness scale (ESS), an attitude toward device use questionnaire, a sleep quality questionnaire, sleep logs, and bedtime and morning questionnaires. The 5th and final visit consisted of reviewing the results and discussing treatment options. The PMP-300E data were compared against PSG data (scored using AASM rules) by Wilcoxon matched-pairs tests, and only the data from the second in-lab night was compared to eliminate first-night effects. In order to determine the baseline accuracy of the scoring of respiratory events by the device against gold standard PSG, the automated scoring program was used and the raw downloaded data from the device was reviewed but not manually modified.
Results: Seven men (mean age 43.4, BMI 28.0) and 4 women (mean age 39.8, BMI 22.8) were enrolled in the study. The mean ESS score was 8.1. The mean AHI was 15.2 from the PMP-300E vs. 22.4 from PSG ($p<.05$), with a mean difference of 8.6. The mean AI was 10.0 vs. 8.7, respectively ($p=.44$). The scoring of hypopneas was responsible for the discrepancy in AHI; with a mean HI of 3.6 vs. 13.6, respectively ($p<.05$). The attitude toward device use questionnaire results, scored as 1=disagree completely to 5=agree completely, revealed the following mean scores: confident in using device at home (4.9), confident in applying nasal cannula (4.8) or finger probe (4.8), and can strap on chest belt without difficulty (4.6).
Conclusion: The PMP-300 represents an easy-to-use, compact, and lightweight Type 3 portable monitor that generates sleep respiratory data which has a smaller mean AHI difference (8.6) between PSG and automated portable monitor scoring as reported in the literature (10.7-24.0). Manual review of each patient's data by sleep technologists according to AASM standards should only improve the diagnostic accuracy of the device.
Support (optional): This study was supported by a research grant from Pacific Medico Co., Ltd.

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RELATIONSHIP OF CENTRAL SLEEP APNEA-TYPE CYCLIC VARIATION OF HEART RATE PATTERNS AND THE DEVELOPMENT OF ATRIAL FIBRILLATION AFTER CARDIAC SURGERY

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Introduction: In patients with at least somewhat preserved cardiac autonomic function, sleep-disordered breathing is associated with brady-tachy cyclic variation of heart rate (CVHR). The tachycardia portion of the CVHR is associated with an arousal. We have observed that central sleep apnea (CSA) is associated with a characteristically different CVHR pattern than is obstructive sleep apnea (OSA). With OSA, the HR arousal is usually sharp and the CVHR pattern has a somewhat rectangular or triangular outline. When CSA is present, the CVHR is of far lower amplitude, with a flatter, semi-oval shape, representing a longer time to peak HR and a longer time to return to baseline. Patients with CSA are at increased risk for atrial fibrillation (AF) after cardiac surgery.
Methods: Pre-surgical overnight Holter recordings were obtained on an outpatient basis in 30 patients (aged 67±10 yrs, 23 M) Post-op AF occurred in 63%. Beat-to-beat heart rate (HR) tachograms were plotted from instantaneous HR after research quality Holter scanning.
Results: N=4 tachograms were excluded because of abnormal/uninterpretable HR patterns. CSA-type CVHR patterns were noted in 5 tachograms (4M) and all had post-op AF. Although all CSA had valve repair surgery (3 with CABG), none had a previous diagnosis of sleep apnea. Valve repair per se was not significantly associated with AF ($p=0.3$).
Conclusion: CSA patterns from HR tachograms obtained from overnight Holter recordings might identify a previously-undiagnosed subset of patients at especially elevated risk for AF after cardiac surgery. Presence of such patterns on Holter recordings might also be useful in identify other higher risk patient groups.
Support (optional): BJC Foundation, St. Louis, MO

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ACCURACY OF PRESSURE TRANSDUCER AIRFLOW FOR THE DIAGNOSIS OF UPPER AIRWAY RESISTANCE SYNDROME

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Introduction: Upper airway resistance syndrome (UARS) is a sleep disorder characterized by airway resistance to breathing during sleep. The gold standard in diagnosing UARS is establishing respiratory effort related arousals (RERAs) using esophageal pressure (Pes) manometry. Pressure transducer airflow (PTAF) has been used but sensitivity and specificity compared with the gold standard has not been established.
Methods: Thirteen patients (ages 25-52 years; 6 males and 7 females) suspected of having UARS received the standard NPSG monitoring with simultaneous recording of esophageal pressures. RERAs using Pes were identified by crescendo changes with a nadir of -10 cm H20 followed by arousals. RERAs using PTAF were identified by sequence of breaths lasting at least 10 seconds characterized by increasing respiratory effort or flattening of the nasal pressure waveform leading to an arousal from sleep. The indices of each method were computed by the number of RERAs divided by total sleep time in hours. The diagnosis of UARS is made if RERA index is greater than 5/hour. The sensitivity of PTAF test was computed by dividing the number of patients with RERA index > 5/hour using PTAF with the number of patients with RERA index >5/hour using Pes. The specificity of PTAF test was computed by the number of patients with RERA index < 5/hour using PTAF divided by the number of patients with RERA index < 5/hour using Pes method.

Results: The following results were obtained: PTAF sensitivity(100%); specificity(67%); false positive(33%); false negative(0%). The Pearson correlation of RERA indices of both methods was 64.1($p<0.05$).
Conclusion: The PTAF method of assessing RERAs is good but may lead to over diagnose UARS compared with the gold standard Pes manometry.

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CAUSAL RELATION BETWEEN EEG AND ECG DURING SLEEP OF CHILDREN

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Introduction: Sleep is a complex process showing various activities in the brain and other organs, such as the heart. Although these activities are widely monitored by polysomnography (PSG), relations between these activities are not fully studied yet. The purpose of this study is to quantify the relations between the brain and the heart in terms of coherence and causality.
Methods: A single night PSG was performed to 16 children (5.9 ± 2.2 yrs.; 9 boys) who were free of sleep disorders. Each 30s epoch was scored by standard criteria. To characterize brain activities during sleep, detrended fluctuation analysis (DFA) was applied to epochs of EEG recordings at O1/A2, O2/A1, C3/A2, and C4/A1. Time courses of DFA scaling exponents (SE) were obtained. Cardiac rhythm was quantified by mean RR intervals in 30s epoch. Relations between DFA SE and mean RR intervals were studied via the coherence and Granger's causality methods.
Results: The DFA SE tended to increase as subject fell into deeper sleep states. Similarly, mean RR intervals also increased in deeper sleep states. The coherence of two measures was 0.45. We also found that causal relations of EEG to ECG (0.03) were much smaller than those of ECG to EEG (0.14).
Conclusion: The significantly smaller causal relation of EEG to ECG, compared to that of ECG to EEG, implied that the heart operated autonomously during sleep (i.e., the heart is independent of the brain).

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EVALUATION OF A PORTABLE MONITOR FOR STAGING SLEEP

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Introduction: An accurate tool for the objective collection of sleep data over many nights in a wide population could have important implications in sleep research and clinical practice. The ability to discriminate between sleep stages beyond simple sleep/wake measures may be especially useful in the objective assessment of sleep quality. A simple, easy-to-use portable device for detecting sleep stages has been developed. The system utilizes dry fabric sensors that are integrated into a headband that wirelessly transmits sleep data to a base station for processing in real time. Sleep stages are scored automatically by a neural network. The aim of the current analysis was to compare the sleep stage measures derived from polysomnography (PSG) with measures from the wireless system.
Methods: Ten healthy volunteers (age range 22 to 51) were co-monitored in a sleep lab for a total of 16 nights by the wireless system and standard PSG. Each PSG record was manually scored according to Rechtschaffen & Kales by two trained technicians (M1 and M2) blinded to the results of the wireless system. Total Sleep Time (TST), Time in Deep (Stages 3 and 4), and Time in REM were derived for comparison.
Results: Average TST for all subjects was (Mean ± SEM): WS 310.4±18.0, M1 303.3±17.7, M2 296.2±16.6. Average Deep for all subjects was: WS 49.3±4.7, M1 24.7±4.6, M2 52.4±6.7. Average REM for all subjects was: WS 59.9±9.6, M1 62.4±7.0, M2 56.6±6.7.
Conclusion: Results derived from the wireless system were similar to those derived from PSG. The system shows promise as an easy to use method for measuring sleep stages related to sleep quality.
Support (optional): Support for this study provided by Zeo, Inc.

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SLEEP FRAGMENTATION INDEX: AN USEFUL MEASURE FOR OBSTRUCTIVE SLEEP APNEA

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Introduction: Obstructive sleep apnea (OSA) is characterized by episodes of complete or partial airway obstruction during sleep, which yields subsequent arousal and sleep fragmentation (SF). Severity of OSA is usually determined by the respiratory disturbance index (RDI) assessed via polysomnographic (PSG) measurement during nocturnal sleep. The purpose of this study is to demonstrate relations between the occurrence of apnea/ hypopnea and SF.
Methods: One thousand and seven hundred OSA patients, registered at Seoul National University Hospital, were studied. A single night of PSG was performed for each subject. 30 s epochs were scored following standard criteria. SFI was defined as the number of transitions from a sleep stage S2-S4 or REM to a S1 or Wake stage per hour of sleep time. Analysis of variance and covariance of all indexes were done, yielding correlation between SFI and RDI. SFI during sleep time with apnea/ hypopnea was also compared with SFI during sleep time without apnea/ hypopnea.
Results: We found a linear relation between SFI and RDI (RDI = 1.7 SFI + 10.1, correlation r = 0.56). The correlation measure (r) further increased when a few outliers were excluded. SFI during sleep time with apnea/ hypopnea (37.2) is significantly larger ($p<0.001$) than that without apnea/ hypopnea (20.4), which implies that SF occurs more frequently during sleep time with apnea/ hypopnea (1.6/min) than that without apnea/hypopnea (2.7/min).
Conclusion: Our results of (i) strong correlation between SFI and RDI, and (ii) significantly larger SFI during sleep time with apnea/ hypopnea than that without apnea/ hypopnea, suggest that SFI could be an alternative diagnostic measure to determine severity of OSA.
Support (optional): Australian Research Council

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THE RELIABILITY OF SHORT SLEEP DATA - IMPLICATIONS FOR THE VALIDITY OF DIAGNOSTIC AND TREATMENT DECISIONS

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Introduction: First night effect and natural variance alter sleep parameters leading to difficulty assessing the clinical meaning of first night data. Short sleeps (<3 hr) occur even when patient is given a full night to sleep, but is the norm in split-night studies. In the latter situation, decisions regarding long-term treatment are always made on short sleep data. How valid are these decisions? This is a study on the reliability of short sleep data compared to repeat study results.
Methods: Prospective, randomized, own control study. All PSGs from Feb. 2004 to Oct. 2008 with TST < 3 hours (n=71) were repeated. Data

were analyzed for clinical and statistical significance. Studies were scored according to standardized criteria.
Results: Demographics - male (45), female (26), average BMI (31), age (60), Epworth (9.14), daytime sleepiness (6 VAS). TST: PSG1 = 123 min, PSG2 = 259 min, PSG1 sleep time: < 60 min (8), 1-2 hr (21), 2-3 hr (42). Changes in RDI between PSG1 and PSG2 as follows: Whole group: - <5 to ≥ 5 (48%); mild/moderate to: < 5 (18%), ≥ 30 (20%); severe to: < 5 (17%), to mild/moderate (50%); ≥ 5 to < 5 (18%). Patients with < 2 hr TST: <5 to ≥ 5 (50%); mild/moderate to < 5 (21%), to severe (26%); severe to < 5 (50%), to mild/moderate (50%). Patients with 2-3 hr TST: < 5 to ≥ 5 (46%), mild/moderate to < 5 (16%), to severe (16%), severe to <5 (0%), to mild/moderate (50%).
Conclusion: Short sleep studies misidentify many patients. Significant results become insignificant in 1 in 6 patients; insignificant results become significant in 1 in 2 patients. The shorter the sleep, the greater the change. This has implications for patient management and raises questions about the validity of split-night studies.

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COMPARISON OF SUBJECTIVE SLEEP POSITION PREFERENCE VS. OBJECTIVE AMBULATORY DATA

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Introduction: Body position influences upper airway configuration and lung volumes. Increased frequency of respiratory events is documented among some OSA patients when sleeping in the supine position. Relatively little data is available on how the subjects' preferred sleep position is reflected on objective ambulatory recordings. The primary purpose of this study was to evaluate if favored sleep position is corroborated on objective recordings of head position during sleep.
Methods: Subjects participating in a study evaluating therapies for snoring were screened to have no clinical evidence of excessive sleepiness and to be in stable medical condition with no clinical evidence of OSA. They were asked to complete a Sleep Medicine questionnaire, including the Time of Day Sleepiness Scale (ToDSS), which measures sleepiness in the morning (AM), afternoon (PM), and evening (EVE). Subjects were asked to identify their preferred sleep position during the medical assessment. Participants (n=49) took home a modified Apnea Risk Evaluation System (ARES), which enabled recording of snoring, oxygen desaturation and head position. The study evaluated baseline home recordings. Subjects' favored position for sleep was categorized: supine (S), lateral (L), or prone (P). Reliable snoring and position data was available for 35 subjects on 2 nights (ns =15, 16, 4 respectively).
Results: Groups did not differ demographically (age 46±11; 32 males, 3 females), and did not differ in average oxygen desaturation index (3%) at 10±11. The 3 groups did not differ on ToDSS scores; an increasing level of sleepiness across the day was documented (2 ±2 AM, 5±5 PM, 7±5 EVE; all significantly different to each other). Repeated-measures analysis with percentage of the night spent supine on both nights by reported sleep position had a significant main effect of position (p =.04). S participants spent approximately half of the night on their backs (51±27%); L participants (28±25%), and P participants (17±9%) spent significantly less time supine. There was no effect of time and no interaction.
Conclusion: The study confirmed differential levels of subjective sleepiness across the day in subjects with primary snoring. In addition, preferred position during sleep was found to reflect differential time spent in the supine position during ambulatory recordings. Thus, the data show the importance of these subjective reports to the accurate clinical assessment of people with complaints of snoring.
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THE GREAT DIVIDE BETWEEN GENDERS: SPLITNIGHT POLYSOMNOGRAPHY TESTING

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Introduction: Although split night polysomnography (SN-PSG) algorithms can diagnose and allow for early treatment initiation for Obstructive Sleep Apnea Syndrome(OSAS) for many patients, there is no published data concerning gender difference in the performance of SN-PSG. This study evaluated the split differences between females and males when it comes to algorithms and to pre-set providers' orders.
Methods: Medical records were reviewed for all OSAS patients with available PSGs. Data collected from 11,2006-1,2008 included: patient demographics, split protocol orders and PSG variables. Gender differences were compared in two groups: 1)SN-PSG according to algorithms (having AHI>30 in 2 hours of sleep) and 2) pre-ordered SN-PSG at lower AHI levels. Descriptive, T-test and Chi-square tests were conducted using SPSS 12.0 software.
Results: Three hundred seventy four consecutive OSAS patients [223(59.3%)male and 151 (40.2%)females]that underwent PSG evaluations were included. Mean age was 48.5+/-13.13. Of the 374 73 (19%) had SN-PSGs. The rate of SN-PSG was 43% in patients who had an overall AHI of >30, reasons for not splitting were delayed sleep onset, underscored AHI by the night techs and poor sleep efficiency. In this group we found no significant differences in baseline characteristics between the two genders. In this group males were significantly split more than females (41/82 vs. 15/46; LR=3.678, p=0.05) There were no significant differences in baseline characteristics of 184 patients included in group 2. Of the group 13/97 males and 1/73 females(LR=8.5, p=0.004) underwent SN-PSG according to pre-set provider orders in this group.
Conclusion: Significant differences were found between genders undergoing split-night studies even when following pre-set splitting algorithms. This indicates that females may be delayed in their treatment when compared to males.

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USE OF A DRIVING SIMULATOR TO ASSESS FUEL INEFFICIENCY AS A DOWNSTREAM EFFECT OF DRIVER SLEEPINESS IN CONTROLLED LABORATORY EXPERIMENTS

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Introduction: Sleepiness impairs real-world driving, which may be reflected in increased fuel use. In transportation and emergency response operations, it is common to limit sleep time and work extended hours to reduce costs. However, inefficient fuel use due to sleepiness may offset savings from extended work hours. High fidelity driving simulators may be used for studying the effects of sleepiness on fuel efficiency in laboratory experiments. We explored the usefulness of such a device for assessing fuel efficiency under a variety of controlled conditions.
Methods: We used a PatrolSim IV driving simulator (MPRI, Salt Lake City) for which we developed software to collect driving performance measures. We prepared eight different 2-mile simulated driving scenarios, which involved steady driving at 30mph, 60mph or 120mph; full acceleration followed by coasting; driving 60mph with breaking for a pedestrian; uphill and downhill driving; and city driving. Six research assistants each practiced driving the simulator and then drove all eight scenarios in a controlled laboratory setting. Average fuel efficiency was

extracted from the simulator, which logged fuel consumption at a 72Hz rate. Fuel efficiency was compared among conditions using mixed-effects ANOVA.
Results: Fuel efficiency differed significantly among the eight driving scenarios ($F[7,35]=600.5$, $P<0.001$), while between-subject differences were not significant ($Z=0.75$, $P=0.23$). Driving uphill consumed 3.1 times as much fuel as driving the same course downhill, the latter being the most fuel-efficient scenario. Steadily driving 120mph and stop-and-go city driving consumed 1.9 and 1.8 times as much fuel, respectively, as steadily driving 60mph. Breaking for a pedestrian during the 60mph drive resulted in a 1.2-fold increase in fuel use across the 2-mile course.
Conclusion: Using driving scenarios for which the impact on real-world fuel efficiency would vary, we found that the PatrolSim IV driving simulator yielded a priori expected estimates of fuel efficiency. Even with the small sample size of the present preliminary work, we were able to differentiate fuel efficiency among selected driving conditions. The observations suggest that driving simulators may provide ecologically valid laboratory measures of sleepy-driver fuel efficiency and attendant economic costs.
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MICRO ARCHITECTURE OF SLEEP A PILOT STUDY TO ASSESS SLEEP STATE VARIABILITY

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Introduction: Subjective daytime sleepiness and polysomnography results are not well correlated. Unfortunately, standard scoring methods of sleep EEGs, which result in hypnograms of macro-architecture (R&K), incompletely represent sleep physiology. The dynamic biological state of sleep is obscured by the smoothened and cyclical pattern that is often suggested by a macrohypnogram.
Methods: Micro Epochs were defined to segment 30 second epochs into 2 second epochs which recapitulate R&K scoring. Electrode montage consisted of : C3-A2, C4 -A1, O2-A1, A1-T3, T3-C3, C3-CZ, CZ-C4,C4-T4, T4-A2, Chin EMG and EOG. Two second epochs were categorized by frequency and pattern distribution. REM was identified by rapid eye movements and lack of EMG activity. Movement was scored when EMG was elevated in EEG leads. Wake was defined as 200ms or greater duration of alpha or sustained beta not spindle frequency. Low Voltage Non Rem was defined as low voltage theta without delta, spindle, or vertex waves. Delta epochs consisted of more than 400ms of a single delta wave (1-2 hz activity) or one second of 1-4 hz activity. Spindle epoch was defined if more than 200ms of 12-15 hz activity was identified. K Complex was scored if spindle and delta activity occurred in the same epoch. Vertex epochs were scored if delta phase reversed over the vertex.
Results: Comparison of macro vs microepic scoring are demonstrated for two normal and one sleep apnea subjects. The micro-architectural hypnogram established by the scoring of 2 second windows, although showing greater variance, was a course reflection of the macro-architectural hypnogram. The waterfall plots demonstrate the overlap and increased variability of correspondence between micro-architecture based on 2 second scoring and macro-architecture based on 30 second scoring. Visual comparison of the macro and micro hypnogram demonstrated less variability during the first half of nights sleep when sleep typically has a greater degree of stationarity (Penzel et al., 2003). During the latter half of night, a greater amount of variance was indicated in both hypnograms but the microhypnogram displayed greater variance.
Conclusion: Micro architecture characterization of sleep provides a means to explore the properties of the hypnogram and adds valuable detail to our understanding of sleep state variability. Application of this method to assess the effect of disease states and correlate subjective sleepiness will help to validate this method.

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PERFORMANCE OF A WIRELESS DRY SENSOR SYSTEM IN AUTOMATICALLY MONITORING SLEEP AND WAKEFULNESS

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Introduction: A cost-effective, portable method for effectively monitoring sleep stages and wakefulness would be useful in the sleep medicine and research communities. One such system, which utilizes a single dry fabric sensor to monitor EEG, EOG, and EMG, wirelessly transmits a signal to a base station. A neural network then automatically assesses sleep stages and wakefulness. The aim of the current study was to compare the sleep and wake measures derived by this wireless system (WS) against polysomnography (PSG) and actigraphy (ACT).
Methods: Ten healthy subjects (4 female), ages 22-51, slept in a sleep lab for a total of 16 nights. Subjects were co-monitored by PSG, ACT, and WS each night. WS data were captured at 128Hz, sampled with a 12-bit A-D converter and automatically staged. PSG records were visually analyzed by two sleep technicians (T1 & T2), who were blinded to WS and ACT data, according to Rechtschaffen & Kales sleep scoring criteria. Actigraphy data were collected on the Phillips Respironics Actiwatch-64 and scored automatically by Actiware 5.0 software at medium wake threshold sensitivity. Parameters derived and compared between the three systems were (using 30s epochs): Sleep onset latency to 3 continuous epochs (SOL), latency to persistent sleep of 10 continuous min (LPS), wake after sleep onset (WASO), sleep efficiency (SE), and the number of awakenings after LPS lasting at least 4 continuous epochs (NA).
Results: Mean sleep/wake measurements between the three systems appeared to be similar: SOL(min±SEM) = T1:31.8±16.0, T2:22.3±9.3, WS:7.5±2.5, ACT:3.4±0.8; LPS(min±SEM) = T1:33.0±16.5, T2: 36.4±16.3, WS:31.8±16.1, ACT:34.7±15.8; WASO(min±SEM) = T1: 27.8±3.7, T2:47.1±8.5, WS:41.7±13.4, ACT:48.5±9.7; SE(%±SEM) = T1:84.5±4.0, T2:82.6±3.6, WS:86.7±3.4, ACT:86.4±2.4; NA(#±SEM) = T1:2.2±0.4, T2:2.2±0.4, WS:2.6±0.7, ACT:3.3±0.6.
Conclusion: This new wireless system shows promise as a way to effectively determine sleep and wakefulness over the course of the night. Further evaluation of the system is needed.
Support (optional): Support for this study was provided by Zeo, Inc.

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QUANTIFICATION OF THE SLEEP EEG VIA WAVELET ANALYSIS

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Introduction: Spectral analysis, the most common quantitative EEG technique used to assess the sleep EEG, provides information about what frequencies and their amplitude are found in the EEG, but provides little information about where the frequencies are occurring in time. We studied wavelet analysis, a signal processing technique that provides information about the frequencies found in the EEG and where those frequencies occur in time. Furthermore, unlike traditional power spectral analysis, wavelet analysis does not assume signals are stationary. The aim of this research is to test the usefulness of the wavelet transform in modeling the sleep EEG.
Methods: Seven healthy subjects (5 men, 2 women), aged 22.43±4.76 (Mean±SD), participated. Sleep was monitored via actigraphy for one week prior to the laboratory visit. The first night in the laboratory served as habituation and sleep disorders screening. Sleep EEG from night two was included in the current analysis. Sleep episodes were visually scored

using standard criteria. Artifact free EEG samples of quiet wakefulness, stage 2 sleep, REM sleep, and SWS were selected for analysis using the Morlet wavelet transform. EEG signals were resolved at intervals of 2sec and 0.5Hz steps. Frequencies from 0.5Hz to 15Hz were examined.
Results: Preliminary results show that the Morlet wavelet transform detected significantly more power in the delta and theta frequencies during SWS compared to wakefulness, stage 2, and REM sleep ($p<0.05$). The Morlet also detected more power in theta frequencies during stage 2 sleep compared to wakefulness ($p<0.05$), but not REM. During quiet wakefulness the Morlet detected more power in the alpha frequencies, especially ~10 Hz, compared to sleep ($p<0.05$).
Conclusion: The Morlet wavelet transform detected differences in EEG activity among visually scored sleep stages. Additional analyses are required to confirm these preliminary findings and to compare the Morlet to other quantitative EEG techniques, such as spectral analysis.
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MARKOV ANALYSIS OF HYPNOGRAMS

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Introduction: Sleep is a dynamical process showing frequent transitions across various levels of sleep states. Understanding the underlying mechanisms of these transitions can facilitate diagnosis and monitoring sleep-related disorders. Hypnograms are commonly used to represent sleep states symbolically, including REM, Wake, S1, S2, SS(=S3+S4). The purpose of this study is to suggest a new mathematical method to represent key features of human sleep, such as sleep structures and transition probabilities of sleep stages, which give new insights into dynamical evolution of sleep. The method is further discussed in a view of a potential application in sleep clinics, such as monitoring effectiveness of continuous positive airway pressure (CPAP) treatment on obstructive sleep apnea (OSA).
Methods: One hundred and thirteen OSA patients (54.0 ± 11.7 yrs., 16 females), registered at Seoul National University Hospital, were studied. Polysomnography (PSG) was performed twice for each subject, one without CPAP and the other with CPAP titration. Hypnograms were obtained by scoring 30 s epochs following standard criteria. Markov processes were constructed by determining transition probabilities of sleep stages from statistical analysis of clinical hypnograms of controls (hypnograms of subjects without CPAP) and treated group (hypnograms with CPAP). Differences of two groups were statistically analyzed (e.g., paired t-test).
Results: We found that CPAP treatment greatly increased probabilities of remaining in the same stage (e.g., Prob. of S2->S2 is 0.88 with CPAP, while that is 0.86 without CPAP, $p<0.01$), which implies that subjects could sleep with less sleep fragmentation. This stabilization of sleep was further verified by comparing the amount of Stage 1 of two groups (18% with CPAP and 32% without CPAP, $p<0.01$).
Conclusion: Our results showed that the new Markov method was an advanced tool to characterize properties of hypnograms and it successfully monitored effects of CPAP on OSA.
Support (optional): Australian Research Council

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QUANTIFICATION OF SLEEP MICRO-ARCHITECTURE USING MULTIPLE TOOLS OF ANALYSIS

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Introduction: To avoid the complexities of EEG readings, the subjective nature of R&K sleep scoring, we present methods for quantitative analysis of sleep microstructure. Our goal to start a path towards the analysis of sleep micro-architecture. Analytical methods for signal decomposition and feature extraction may provide methods for quantification of the microstructure of sleep.
Methods: Power spectra were computed from consecutive 2 sec segments of EEG using the Fast Fourier Transform routine in MATLAB (The Mathworks, Natick, Massachusetts) resulting power spectra : 1-4Hz, 4-8Hz, 8-12Hz, 12-15Hz, and 15-30Hz. Principle eigenvalues were calculated using 2 second windows. Wavelet decomposition of 2-second EEG windows was performed utilizing a Daubechies4 wavelet (levels 3,4,5). The squared mean of the wavelet coefficients was summed over each window to yield the total wavelet power at each level of decomposition.
Results: Wavelet power corresponded with some micro-architectural findings in the EEG signal. Cluster analysis of wavelet power did not differentiate the 8 micro-architectural categories. The principle eigenvalue which was scored for every 2 second window mirrored the macro-architectural hypnogram to a greater extent than micro-architectural hypnogram. The graph of principle eigenvalues over time is shown to be inversely related to the macrohypnogram and may, in the near future, serve as a gross depiction of a standard sleep hypnogram. Visual inspection of frequency banded power spectra derived was successful in identifying macrostages for Stage 3 and Stage 4 sleep from 1-4Hz banded power, Stage 2 sleep, and Wake from 8-12 Hz banded power. The normal subjects had a higher density and greater cyclic regularity than the sleep apnea patient in the 1-4 Hz banded power. There was also greater smear of the 4-8 Hz banded power for the sleep apnea subjects.
Conclusion: This study suggest the 3 metrics used may be partly successful at identifying the macro structure of sleep and may have diagnostic value. Power spectra demonstrated greater variability for 2 sleep apnea vs. 3 normal subjects. Further analysis must be performed to quantify the observations related to the structural detail of sleep EEGs. Future directions include comparing a measure of variance between of sleep architecture between normal and sleep apnea subjects, use of different sized windows, and quantitative measure of variance within subjects throughout the night, using the metrics described in this study.

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THE ROLE OF SLEEP AND SLEEP DISORDERS IN THE THERAPEUTIC ENCOUNTER: AN IPA STUDY OF COUNSELLING PSYCHOLOGISTS IN THE UK

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Introduction: It is often the case that individuals enter into a therapy during, or directly following, a stressful life event. Considering one of the most consistent events during this time is an acute disruption in sleep, it is important to know how this is assessed and managed within the therapeutic encounter. Furthermore, a lack of training in sleep medicine within the UK questions what advice and support is provided when a client presents with a sleep complaint, either acute or chronic. The aim of this study was to examine how counseling psychologists addressed sleep medicine within the therapeutic encounter.
Methods: Semi-structured interviews were carried out with a sample of eight chartered counseling psychologists recruited through their registration with the British Psychological Society (BPS). The study examined in-depth the perceptions, attitudes, and beliefs of counseling psychologists about sleep and sleep disorders, how this applied to their therapeutic practice, and what had informed this understanding. The interviews were recorded and transcribed. The transcripts were analyzed using an Interpretative Phenomenological Analysis approach, based on the constant comparison technique.
Results: Four core themes emerged from the data. The first encompassed sleep disruption as a symptom of an underlying illness or pathology; the second, a sleep disorder as an index of psychological well being. The third category was practice-based evidence, and the final category was called non-intention to treat. In each case, the category was informed by levels of exposure to supplementary courses, previous 'trial and error' attempts, and personal experiences.
Conclusion: The results suggest that levels of knowledge about sleep medicine in the UK, amongst counseling psychologists, varies widely, and this is mainly informed by media interpretations and lay beliefs, as opposed to a taught evidence base. Future directions, in terms of training in sleep medicine are forwarded, and areas of misinformation are identified.

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THE IMPACT OF SLEEP QUALITY ON HEALTH-RELATED QUALITY OF LIFE IN ADOLESCENCE WITH BLINDNESS

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Introduction: The purpose of this research was (1) to assess the relationship between sleep quality and health-related quality of life in adolescence with blindness, and (2) to examine the effect of sociodemography, body mass index (BMI), and sleep quality on the health-related quality of life in this population.
Methods: Subjects included 109 adolescents with blindness aged 12-18 years old. Sleep disturbances were evaluated using Pittsburgh Sleep Quality Index (PSQI), and health-related quality of life was assessed by the 36-Item Short Form Health Survey (SF-36). Multiple hierarchical regression analysis was used to determine the relative significances of sociodemographic, sleep quality variables, and BMI in explaining their quality of life.
Results: Sleep quality account for 43% of the variance in the health-related quality of life after adjusting for sex, age, and BMI ($p<.001$). All subscales of PSQI, including subjective sleep quality (Beta=-.259, $p=.005$), sleep disturbance (Beta=-.31, $p<.001$), usage of sleeping medication (Beta=-.211, $p=.003$), and daytime dysfunction (Beta=-.30, $p=.003$), accounted for a significant amount of the health-related quality of life.
Conclusion: The results demonstrate that sleep quality alone, rather than sex, age, and BMI, contribute significantly to the decreased overall health-related quality of life in adolescence with blindness. The findings indicate the importance to develop strategies to improve sleep quality in this group that might potentially improve their health-related quality of life.

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SECULAR TRENDS OF SLEEP COMPLAINTS IN SAO PAULO, BRAZIL, BASED ON PROBABILISTIC SAMPLE SURVEYS PERFORMED IN THREE CONSECUTIVE DECADES

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Introduction: Previous epidemiological studies showed potential methodological limitations which can produce less precise sleep disorders complaints prevalence estimates and impair the evaluation of the secular trends. However, estimates of morbidity/mortality associated with sleep disorders across several population cohorts have emerged. The aim of this study was to compare the prevalence of sleep complaints and to estimate de secular trends through three population-based surveys carried out in 1987, 1995, and 2007, in the general adult population from Sao Paulo city - Brazil.
Methods: Surveys were performed using the same three-stage cluster sampling technique on three consecutives decades (1987, 1995, and 2007) in order to obtain a representative sample of the inhabitants of Sao Paulo city according to gender, age (20-80 years), and social classes. Sample sizes were of 1,000 in the 1987 and 1995 surveys and of 1,056 volunteers in the 2007. UNIFESP Sleep Questionnaire was face-to-face applied in each selected household.
Results: Difficulty initiating sleep (weighted frequency %; 95%CI) (13.9%(11.9-16.2) vs. 19.15%(16.8-21.6) vs. 25.0%(22.5-27.8)), difficulty maintaining sleep (15.8%(13.7-18.2) vs. 27.6%(24.9-30.4) vs. 36.5%(33.5-39.5)), and early morning awakening (10.6%(8.8-12.7) vs. 14.2%(12.2-16.5) vs. 26.7%(24-29.6)) increased in the general population among surveys, mostly in women. Habitual snoring was the most common reported complaint across decades, higher in men than in women. There was no statistically significant difference in the snoring complaint between 1987 (21.5%;19.1-24.2) and 1995 (19.0%;16.7-21.6) but it was significant increased in 2007 (41.7%;38.6-44.8). Nightmares, bruxism, leg cramps, and somnambulism complaints were significantly higher in 2007 than 1987 and 1995. All of then were more frequent in women than men.
Conclusion: This is the first study comparing sleep complaints in a probabilistic populational sample using the same methodology across three consecutive decades. There was a trend of increased sleep disorders complaints, higher in 2007 than in 1987 and 1995.
Support (optional): AFIP, FAPESP, CNPq

1196

ATTITUDES ABOUT SLEEP LOSS AND FATIGUE IN MEDICAL RESIDENTS: IMPACT OF THE 2003 RESIDENCY WORK HOUR REGULATION CHANGES

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Introduction: Numerous studies have demonstrated that sleep loss and fatigue associated with medical training negatively impact the lives of residents. In 2003, the ACGME instituted new work hour regulations. This study compared residents' perception of fatigue and attitudes about sleep loss before and after the institution of work hour regulations.
Methods: Residents were asked to complete a survey at surveymonkey.com consisting of 17 statements regarding the impact of sleep loss on their personal and professional functioning. Participants rated their agreement on a 5-point scale from 1 (strongly disagree) to 5 (strongly agree). This survey was administered to 34 pediatric residents (18 women; mean age, 28.7; 62.8% interns, PRE) between October 2001 and August 2003 and to 34 pediatric residents (23 women; mean age, 28.8; 41.1% interns, POST) between April 2006 and November 2008 in an academic medical center.
Results: Overall, the two samples agreed that fatigue affects their personal and professional lives. More POST residents disagreed that their bodies had adapted to fatigue (35% vs. 15%, p=.046) and that they had effective sleepiness countermeasures (53% vs. 24%, p=.026); more agreed that they had heard of sleep-related medical errors (91% vs. 82%, p=.044) than PRE residents. Women in both samples perceived fatigue as having a greater impact on their functioning (p=.052), with fewer reporting having effective sleepiness countermeasures, having chosen their field because they function well on little sleep, or that their bodies have adapted to less sleep. No differences were found based on training year.
Conclusion: Residents continue to perceive fatigue as having a major impact on their functioning. Women continue to report higher levels of perceived impact than men. Similarities between the two groups may indicate that the 2003 work hour regulations have had a minimal effect on perceptions of the effects of sleep loss on functioning among residents.

1197

RACE/ETHNIC VARIATION IN EXCESSIVE DAYTIME SLEEPINESS: THE MULTI-ETHNIC STUDY OF ATHEROSCLEROSIS (MESA)

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Introduction: Race/ethnic variation in sleep duration and disorders may be mediator and consequence of health disparities. This study evaluated contributors to race/ethnic variation in excessive daytime sleepiness (EDS).
Methods: Data were drawn from The Multi-Ethnic Study of Atherosclerosis (MESA). Participants included 5,173 men and women (average age 66.4 years). Race/ethnicity was 40.7% White, 11.3% Chinese, 26.2% African-American, and 21.3% Hispanic. Measurements included: demographics, health behavior (e.g. exercise and smoking), physical health and medications (e.g. BMI and hypertension), sleep (self report sleep time, diagnoses and sleep disturbance symptoms), depression, social support and chronic burden (e.g. areas of ongoing stress). Analyses were conducted defining EDS with two measures: 1) self report of EDS frequency > 5 days per month or 2) Epworth Sleepiness Scale (ESS) > 12.
Results: Prevalence for EDS was 16.3% for EDS > 5 days/ month and 9.5% for ESS > 12 in the total sample. White participants were more likely to report EDS > 5 days/month (White 18.4% (ref), Chinese 12.1%, p < .001 , African-American 14.3%, p < .001, Hispanic 16.8%, p < .001). After controlling for potential covariates (demographics, health behavior, health and medications, sleep time, diagnoses, and symptoms, depression, social support and chronic burden, African American (OR= .57, p < .001) and Hispanic participants (OR= .62, p< .001), remained less likely to report EDS > 5 days/month. Results using the ESS indicated higher rates of EDS in African Americans (White 7.9% (ref), Chinese 7.7%, p = ns, African-American 13.0%, p < .001, Hispanic 9.3%, p = n.s.). Odds of EDS on the ESS in African-American participants were attenuated but remained significant after controlling for potential covariates (OR= 1.53 p <.01).
Conclusion: Race/ethnic variation in EDS depends on whether frequency or severity of EDS is measured. African-Americans were more likely to report EDS on the ESS above clinical cutoffs even after controlling for physical health, depression, and aspects of the social environment.
Support (optional): T32 HS00078

1198

EVALUATION OF SLEEP DISORDERS IN THE PRIMARY CARE SETTING: HISTORY-TAKING COMPARED TO QUESTIONNAIRES

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Introduction: Sleep disorders are highly prevalent, though the majority of patients remain undiagnosed. In the primary care setting, it is believed that little time is spent screening for sleep disorders. We hypothesized that primary care providers (PCPs) do not routinely evaluate for sleep disorders in new patients and that validated questionnaires could efficiently identify individuals warranting further sleep evaluation.
Methods: New adult (ages 18-65) patients seen in a primary care clinic at an urban academic institution were recruited. Patients were approached during checkout and asked to complete the Cleveland Sleep Habits questionnaire (CSHQ) (includes Berlin questionnaire and Epworth Sleepiness Scale or ESS) and the STOP questionnaire. Patients were timed while completing each questionnaire. The new patient encounter was reviewed for elements of a sleep history, sleep review of systems, and/or sleep workup.
Results: 101 of 111 patients approached agreed to participate. Demographics: 57% female, age 38 +/- 12.9 years old, Body Mass Index (BMI) 29.5 +/- 8.3 kg/m2, (BMI > 30 kg/m2 in 44%), and ethnicity: 46% Caucasian, 38% African American, 11% Hispanic, 5% others. 51% were smokers and 93% consumed caffeinated beverages. Co-morbid conditions included: 23% with hypertension, 9% with diabetes, and 3% with hypothyroidism. Housestaff evaluated 58% of the patients; the remaining patients were seen by faculty. A limited sleep history was found in 21% of encounters. 2% of all patients were referred to Sleep Clinic for suspected or diagnosed obstructive sleep apnea (OSA) and 6% to Psychiatry for insomnia/depression. The ESS was greater than 10 in 28%. OSA risk assessment found 33% (Berlin) and 34% (STOP) of patients at high risk for OSA (22% by both). The CSHQ suggested the following sleep disorders: 30% insomnia, 22% restless legs syndrome, 8% narcolepsy. Time to complete each survey: CSHQ 302 +/- 97 seconds and STOP 24 +/- 12 seconds.
Conclusion: Sleep disorders appear common but are not routinely screened for in the primary care setting. The use of validated questionnaires may be able to efficiently identify common sleep disorders in these patients.

1199

ETHNIC DIFFERENCES IN SLEEP-HEALTH KNOWLEDGE

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Introduction: Deficiencies in the knowledge of sleep disorders may preclude adequate treatment and lead to poor health. Little is known about ethnic differences in sleep-health knowledge. We explored the differences in sleep-health knowledge between Hispanics of Mexican descent (HMD) and Non-Hispanic Whites (NHW).
Methods: We performed a population-based random digit dialing telephone survey on sleep-health in San Diego County. Surveys were offered in English or Spanish and acculturation to the US life style was assessed.
Results: We surveyed 2336 (1061 HMD and 1275 NHW, gender ratio 1:1) adults. HMD were younger (40.9±15.6 vs.54.5±17.3 years, $p<0.001$), and 53.4% of HMD chose the Spanish language survey. HMD were less likely than NHW to report ever hearing about obstructive sleep apnea (OSA) (38.9% vs. 91.5%), restless leg syndrome (RLS) (39.5% vs. 84.3%) or insomnia (83.1% vs. 97.6%), all $p<0.001$. When provided with descriptions of OSA and RLS the knowledge differences between HMD and NHW decreased but remained significantly different (OSA 63.6% vs. 69.4%, $p=0.05$; RLS 33.8% vs.51.7% $p<0.001$). Of 1061 HMD, 394 scored as highly acculturated and 663 were less acculturated. Less acculturated HMD were older (41.7±15.7 vs. 39.7±15.7 years, $p=0.05$) and less likely to have completed high school or higher education (38.3% vs. 90.7%, $p<0.001$). Less acculturated HMD were less likely to report ever hearing about OSA (23.1% vs. 65%), RLS (23.7% vs. 65.5%) or insomnia (78.3% vs. 91.1%), $p<0.001$. When provided with descriptions of OSA and RLS, the difference disappeared for OSA, but not for RLS (27.8% vs. 43.9%, $p<0.001$) for less acculturated and highly acculturated HMD, respectively.
Conclusion: There is a significant difference in knowledge of common sleep disorders between less acculturated-HMD, highly acculturated-HMD, and NHW. Deficiencies in sleep health knowledge in HMD appear to be related to less education and less acculturation.
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1200

DIAGNOSING AND TREATING SLEEP DISORDERS: DO PHYSICIANS HAVE THE TRAINING THEY NEED?

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Introduction: Although up to 75% of Americans complain of sleep problems, they often go unrecognized and untreated by physicians of all specialties. This raises the question of whether a physician's training is directly related to his/her ability to detect, diagnose and treat sleep disorders.
Methods: A self-administered, confidential questionnaire was electronically distributed to all physicians, both staff and trainees, in the Cleveland Clinic Healthcare System (n = 2624).
Results: Of the 395 respondents (15.1%), 33.9% were trainees and 29.6% were practicing for 10 years or less. Forty-one percent had no sleep disorder lectures in medical school. Of those who did have sleep lectures in medical school, 78.1% reported having <3 lectures. Additionally, 86.6% of respondents did not participate in a sleep-related clinical rotation during their training. Another 57.2% had never read a journal article or attended a lecture on sleep disorders. Of the staff physician respondents, 71.6% had never attended a continuing medical education (CME) course or lecture on sleep disorders. Of those who did not have sleep lectures in medical school, sleep-related clinical rotations, or a CME course or lecture on sleep disorders, respectively, only 52.8%, 50.6%, and 46.3%, inquired about sleep problems during their typical review of systems. Only 20.5%, 18.5%, and 12.8% of the respective respondents were confident in their ability to treat sleep disorders. In comparison, of the physicians who had a sleep rotation or >2 sleep-related CME lectures or courses, 65.9% and 81.0%, respectively, asked sleep-related questions on their typical review of systems. Additionally, in the same groups of respondents, 47.7% and 71.4%, respectively, were confident in their ability to treat sleep disorders.
Conclusion: While the lack of recognition, and therefore, treatment of sleep disorders continue to be problematic, in general, the physician's sleep exposure and education remain inadequate. This inadequate training appears to directly affect the physician's awareness and comfort in treating sleep disorders.

1201

PRIMARY CARE PHYSICIAN KNOWLEDGE, AWARENESS, AND COMFORT IN TREATING SLEEP DISORDERS

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Introduction: As the initial point of contact for most patients, the primary care physician (PCP) plays an essential role in detecting, diagnosing and treating many sleep disorders. The goal of this survey was to assess, in a sample group of PCPs, their knowledge of and comfort in treating sleep disorders.
Methods: A self-administered, confidential questionnaire was electronically distributed to 402 PCPs, both staff physicians and trainees (residents or fellows) in the Cleveland Clinic Healthcare System.
Results: Of the 100 respondents (24.8%), 30.2% were trainees and 38.1% were in practice for 10 years or less. 34.3% of the PCPs reported having had no lectures on sleep disorders during medical school, and only 13.1% had a training rotation in sleep medicine. Of the PCPs who felt that sleep medicine was relevant to their medical practice, 40.2% agreed that they spent as much time discussing sleep issues with their patients as they did other common health issues such as diet, exercise, and smoking cessation. Only 53.6% included a sleep history in their typical review of systems. Another 26.8% reported addressing their patients' sleep problems only when the patients brought it to their attention first. When a sleep history was included, PCPs most often asked about insomnia (69.1%) and obstructive sleep apnea (60.8%). Only 26.8% reported being confident in treating sleep disorders. PCP respondents most commonly treated the sleep disorders of insomnia (66.0%) and obstructive sleep apnea (49.5%). 74.0% of respondents reported that they had never attended a CME course or lecture on sleep disorders. Only 59.0% read journal articles or attended lectures to stay updated on sleep disorders.
Conclusion: As sleep disorders have gained increasing recognition as a significant burden on individuals and society, the role of the PCP has been identified as essential for screening and treating sleep disorders during patients' regular exams. Yet, this survey indicates that the PCP's awareness of and comfort in treating sleep disorders remain unacceptable. This appears to be directly related to a lack of exposure and education in sleep disorders.

1202

SLEEP PATTERNS AMONG HEALTHCARE PROVIDERS AT AN ACADEMIC NEUROLOGY PRACTICE

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Introduction: Sleep patterns of resident-physicians and its relationship to occupational accidents have been widely documented. However, there

have been few studies documenting the sleep patterns and disturbances among attending physicians and other healthcare providers.
Methods: We conducted a survey about healthcare providers' sleep patterns and described preliminary findings. The inclusion criteria included physicians, nurses and allied health providers who work at the NYU Comprehensive Epilepsy Center.
Results: There were 22 full-time healthcare providers included in the study. There were 9 physicians (7 neurologists, 2 neuropsychiatrists), 8 nurses, and 5 allied-health professionals. The mean age was 41.5 years, and 18 were women. Two nurses worked overnight or mixed shifts, along with three allied-health providers. Twenty respondents (91%) reported using caffeine during the day. On average, nurses (2.4 cups/day) and allied-health providers (3 cups/day) drank more caffeine than physicians (1.9 cups/day) did. Six respondents (27%) reported a history or diagnosis of a sleep disorder, with insomnia, restless legs, snoring, and bruxism being reported most frequently. None of the respondents reported having sleep problems develop before professional school. Three (14%, 1 physicians and 2 nurses) reported developing problems during professional school, and four (18%, 2 physicians and 2 nurses) reported developing sleep problems (mostly insomnia) after professional school. Physicians reported an average of 7 hours of sleep on working nights, and an average of 12 minutes to fall asleep. Nurses reported 5.9 hours of sleep, and an average of 21 minutes to fall asleep. All groups reported that they think that they needed longer sleep hours. Sixty-three percent of respondents reported as least some snoring during sleep, with nurses (86%) most likely to have this complaint. Five respondents (23%) reported very often feeling fatigued during the day, with another 14 (64%) reporting occasionally feeling fatigued during the day. Eight respondents (36%) reported using some sort of medication to help them fall asleep. The most commonly used sleep aid was Tylenol PM, followed by Benadryl, melatonin and Ambien.
Conclusion: Attending physicians, nurses and allied-health providers reported a high percentage of sleep problems, daytime fatigue, and insufficient sleep. These problems may affect patient care.

1203

FATIGUE AND CLINICAL DECISION SELF-EFFICACY AMONG CRITICAL CARE NURSES

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Introduction: Nurses play a pivotal role on the healthcare team, monitoring hemodynamic status, making patient care decisions and delivering high quality nursing care. Yet fatigued nurses may make errors in clinical judgment or medication administration, or fail to intercept errors made by others. Inadequate sleep, an inevitable consequence of extended work hours, may contribute to deficits in situational awareness, problem-solving, and vigilance, further jeopardizing patient safety. This study examines the relationships between sleep quality, daytime sleepiness, sleep debt, fatigue, and intershift recovery with clinical decision self-efficacy (confidence, satisfaction, and regret) among full-time critical care nurses (CCNs). The model of impaired sleep provides the conceptual framework for this investigation.
Methods: A descriptive study was conducted using a random sample of 3500 CCNs who are members of the American Association of Critical Care Nurses. Data were collected using a demographic questionnaire, the Pittsburgh Sleep Quality Index, Epsworth Sleepiness Scale, Occupational Fatigue, Exhaustion, and Recovery Scale, and other self-report instruments for sleep debt calculation and clinical decision self-efficacy assessment. A total of 605 usable (17%) questionnaires were returned.
Results: The majority (73%) of the CCNs were sleep-deprived (1-36 hours deficit). Twenty-nine percent (n=157) of the CCNs reported making a clinical decision while fatigued that they later regretted. CCNs who experienced decisional regret had significantly more daytime sleepiness, poor sleep quality, inadequate intershift recovery, and fatigue impairment than those who did not experience decisional regret. In addition, CCNs with regret were significantly less confident and satisfied with the clinical decisions they made when fatigued.
Conclusion: The presence of fatigue-impaired nurses has serious implications for the delivery of high quality healthcare to critically ill patients. The identification of factors that may ensure a more alert nursing workforce and maximize the safety and outcomes of these vulnerable patients is imperative.

1204

THIRTY-FOLD SPIKE IN ADVERSE EVENT REPORTING ASSOCIATED WITH ZOLPIDEM USE IN AUSTRALIA WAS MOST LIKELY CAUSED BY THE MEDIA

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Introduction: Zolpidem, a non-benzodiazepine hypnotic member of the so-called Z-class of hypnotics, has been licensed for the short-term treatment of insomnia in Australia since 2001. In only the past 3 years and only in the United States and Australia have dangerous parasomnias been attributed to zolpidem use.
Methods: We retrieved all free-to-air televised media stories broadcasted in the Sydney metropolitan area mentioning insomnia or zolpidem between May 2005 and May 2008 and classified them according to their broadcasting date, general reporting tone, duration and the patients and expert testimonials employed. We also retrieved zolpidem-associated adverse event reports collected by the Australian drug regulatory agency between Feb 2001 and August 2008.
Results: Sections of the Australian media have run a deliberate campaign to have zolpidem withdrawn from market (38 televised stories beginning Feb 2007). They were aided by the communication of patient testimonials by the head of the consumer-focused Adverse Medicine Events Line- the existence of which is supposed to improve the detection of rare adverse events caused by pharmaceuticals. This intensely hostile media interest is the most likely cause of the number of adverse events climbing from an average of 4-8 per month over the preceding 7 years to 189 reports in April 2007. Two further smaller peaks were associated with renewed media interest in June 2007 and with the unrelated death of the actor Heath Ledger in Feb 2008 which the media chose to link to zolpidem.
Conclusion: Hostile and unchecked media coverage of zolpidem has caused one of the largest media-induced surges in adverse event reporting ever recorded. This may have been amplified by the collusion of a patient-centered adverse event line whose funding was threatened. There is currently little high-quality evidence that links indicated use of zolpidem to these side-effects.
Support (optional): Australian National Health and Medical Research Council Centre for Clinical Research Excellence in Respiratory and Sleep Medicine

1205

AN INTERNET SURVEY ON THE SLEEP PROBLEMS, QUALITY OF LIFE, AND HELP-SEEKING BEHAVIOR IN COLLEGE STUDENTS IN TAIWAN

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Introduction: Sleep problems are common in college students and may affect different aspects of their quality of life. However, the majority of

them did not seek for help. The aims of this study were to 1) survey sleep problems in college students, 2) examine the effects of their sleep problems on the quality of life, and 3) investigate their preferred treatment options in related to their readiness for a change.
Methods: A total of 2185 college students (72.9% females; age: 19.81 ±1.49) responded to a survey administered through internet. The survey consists of three parts: 1) a questionnaire to assess study participants' sleep schedule, perceived sleep problems, and preferred treatment options; 2) the SF-36 to assess the quality of life; 3) a questionnaire based on transtheoretical model to assess the stages of behavior changes in related to their sleep problems.
Results: The results showed that 86.5% of the participants reported experiencing sleep problems, with insufficient sleep as the most common complaint (57.3%). Participants without sleep problems had better quality of life than participants reported sleep problems ($F= 55.77 \sim 180.85$, $p < .001$, ES: $d= .37 \sim .68$). In terms of preferred mode of treatment, 97.7% of the poor sleepers preferred non-pharmacological treatment than medication. When given the treatment options to chose, the highest percentage of sufferers (34.7%) preferred internet-based therapy followed by preferred assistance from clinical psychologist (24.3%). In addition, the stages of their help-seeking behavior centralized at precontemplation stage (39.6%). Chi-square test revealed that the stages of change is not associated with the preferred treatment options ($\chi 2=24.96$, $p= .07$).
Conclusion: As expected, sleep problems are highly prevalent among college students and may have detrimental effects on their quality of life. Based on their preference and the high accessibility of internet, internet-based treatment may be a potential way to help them coping with their sleep problems.

1206

PATIENT SATISFACTION WITH SLEEP STUDIES: A COMPARISON OF COMMUNITY AND TERTIARY CARE FACILITIES

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Introduction: Sleep studies are traditionally conducted in hospital/institution-based sleep laboratories (IBL) or independent diagnostic and treatment facilities. However, there has been a growing interest in providing these tests in the community in hotel-based laboratories (CBL). To our knowledge, there have been no previously published studies comparing patient experience in CBL with IBL. We aimed to compare patient satisfaction in 4 Cleveland Clinic Sleep Disorders Center (CCSDC) outreach CBL (beds= 16) and our main campus tertiary care IBL (beds= 9) using a questionnaire-based approach. We hypothesized patients presenting to CBL will have a greater total satisfaction than those who are studied in IBL.
Methods: Patients needing a routine multi-channel PSG or PAP titration were free to choose their preferred test location via centralized scheduling. Sleep technicians were rotated at all sites per their annual roster. Questionnaires were collected from July-October 2008 on all patients the morning after the test as part of quality control. Of 9 items, 5 were scaled to give a total satisfaction score of 5-25. We excluded studies run preferentially at the IBL (age <18 y; medically unstable patients; special order studies), and for those traveling >100 miles. We discarded incomplete questionnaires.
Results: 512 (IBL=124; CBL= 388) of 630 questionnaires were analyzed. While satisfaction overall was high, IBL patients traveled 8.5 more miles on average and were more likely to be dissatisfied with distance traveled (10.5%) than CBL patients (1.8%; $p<0.003$). Total scaled satisfaction scores (mean +/- standard deviation) were higher for CBL (24.3 +/- 1.7) than IBL (23.8 +/- 1.8; $p< 0.05$).
Conclusion: At CCSDC, CBL provides a more satisfying patient experience when compared to IBL for non-complex sleep studies. This may, in part, be due to the availability of testing closer to the patient's homes.

1207

WORK HOURS, SLEEP, AND PERFORMANCE IN MEDICAL RESIDENTS WORKING NIGHT FLOAT VS. DAY SHIFT

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Introduction: We studied the effect of working night float vs. day shift on the sleep and performance of medical residents. Night float is an extended night shift (typically from 17:30 until 07:00), usually with some opportunity for sleep while on shift. We hypothesized that residents working night float would have less daily total sleep time and poorer waking neurobehavioral performance compared to day shift, due to truncated daytime sleep and working at an adverse circadian phase.
Methods: 17 medical residents (PGY1, PGY2; 4 women) participated in a field study, each serving as his/her own control. Their work schedules during the study consisted of a week or more of day shift, a month of night float, and a week or more of day shift. Residents were studied for 5-6 days during the last week of day shift before night float, for 6-8 days during the first week of night float, for 6-8 days during the last week of night float, and for 5-6 days during the first week of day shift after night float. Shift duration was assessed by self-report and hospital records. Sleep/wake patterns were recorded continuously using actigraphy (Ambulatory Monitoring, Inc.). Performance was measured at shift onset and shift end using mean reaction time (RT) on a 10min psychomotor vigilance test (PVT).
Results: Residents worked longer hours on night float (13.4±0.2h per 24h) than on day shift (9.0±0.2h per 24h) ($F=506.4$, $P<0.001$). Actigraphic estimates of sleep showed no significant difference between night float (6.9±0.2h per 24h) and day shift (6.9±0.3h per 24h) ($F=0.08$, $P=0.78$). Furthermore, mean RT on the PVT did not differ significantly between night float (393±28ms) and day shift (382±28ms) ($F=2.50$, $P=0.11$), nor between shift onset (382±28ms) and shift end (392±28ms) ($F=1.97$, $P=0.16$; interaction with shift: $F=0.78$; $P=0.38$).
Conclusion: Medical residents worked longer hours on night float than on day shift. Contrary to our hypotheses, they slept approximately 7h per 24h on both night float and day shift, and did not show a significant difference between night float and day shift in PVT mean RT as measured at shift onset and shift end. Further research with testing at frequent intervals while on shift is needed to determine whether performance is maintained at day shift levels throughout the night float.
Support (optional): USAMRMC award W81XWH-05-1-0099.

1208

PERCEIVED RISKS AND SELF-RATINGS OF DROWSINESS AND INATTENTION IN YOUNG NOVICE DRIVERS: A COMMUNITY-BASED STUDY

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Introduction: Drivers under the age of 25 years old are a known high-risk group, but it is unclear what the role and magnitude of sleep-related impairment is in the context of other risk factors. The purpose of this study was to evaluate prevalence of drowsy and inattentive driving and awareness of sleep-related risks in adolescents and young adults.
Methods: 36 novice drivers (20M, 16F, mean age 17.2) with learner's permits attending driver's training classes in Toronto completed this study, which received approval by the University of Toronto Research Ethics Board. A questionnaire consisting of quantitative and qualitative

data was used to assess excessive daytime sleepiness (EDS) and inattentiveness and to examine attitudes regarding sleep and inattention. The questionnaire included the Epworth Sleepiness Scale (ESS), the Toronto Hospital Alertness Test (THAT) and part A of the Adult ADHD Self-Report Scale (ASRS v 1.0) Symptom Checklist, as well as a number of questions regarding perceived risk factors of driving safety in self and others.

Results: 60% of males and 75% of females had ESS scores greater than 10, indicating EDS. 50% of males and 37.5% of females had THAT scores greater than 30, indicating decreased alertness. 36.8% of male participants and 31.3% of female participants had self-ratings of inattention sufficient to meet criteria for ADHD on the ASRS v1.0. There was a very high awareness of alcohol as a collision cause, but only a moderate awareness of EDS and distraction as collision causes. Females were more aware than males of the risks of drowsy and distracted driving.

Conclusion: There was a high prevalence of EDS and inattentiveness in young novice drivers in this community survey. Public health policy targeting elevated collision risk in young novice drivers should consider the role of both self-imposed sleep loss and the overlap in symptoms related to drowsiness and attention sleep disorders in this high-risk population.

1209

RACIAL/ETHNIC DIFFERENCES IN SLEEP COMPLAINTS: AN ETHICAL CONCERN

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Introduction: The process and outcome of investigating whether race/ethnicity and culture influence sleep have ethical implications for population-based medicine. This prompts exploration of two important research questions: 1) Do blacks reporting fewer sleep complaints experience verifiably fewer sleep problems than whites? 2) Is the finding of fewer sleep complaints among blacks a function of greater utilization of positive reappraisal?

Methods: We examined data from adults (average age: 59.36 years) in Brooklyn, NY who participated in two multi-factorial community-based studies completed in 1999 and 2004. Recruitment was based on stratified, cluster-sampling techniques. Data were obtained by trained interviewers administering several questionnaires during face-to-face interviews. Our analysis focused on reports of sleep complaints: difficulty initiating sleep (DIS), difficulty maintaining sleep (DSM), and early morning awakenings (EMA).

Results: In study I (n=1118), 41% of whites reported DIS, 75%, DMS; and 46%, EMA. Among blacks, 14% reported DIS; 37%, DMS; and 17%, EMA. In study II (n=1279), 42% of whites reported DIS; 64%, DMS; and 53%, EMA. By contrast, 16% of blacks reported DIS; 40%, DMS; and 27%, EMA. Overall, trends indicated that blacks had greater sleep satisfaction (r_s=0.20, $p<0.001$), better sleep quality (r_s=-0.11, $p=0.02$), and longer sleep (r_s=-0.10, $p=0.04$). We observed race/ethnic differences in self-regulation, the ability to repress negative affect. Highly regulated black women reported significantly fewer sleep complaints compared with low regulators: 28% vs. 70%; $p<0.0001$, as did highly regulated white women (54% vs. 77%; $p<0.001$).

Conclusion: Findings suggest that blacks report fewer sleep complaints because of greater reliance on positive reappraisal as a coping strategy. Positive reappraisal has been necessary to weather hardships from social stressors (racism, segregation, poverty). Care should be exercised that an inappropriately pragmatic oversimplification of these findings does not lead to wholesome disregard for inquiries of sleep problems among blacks, who are paradoxically at greater risk for sleep apnea.

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SUPPRESSION OF OREXIN NEUROTRANSMISSION IN LOCUS COERULEUS FACILITATES REM SLEEP OCCURRENCE

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Introduction: The locus coeruleus (LC) is heavily innervated by orexinergic neurons. Orexins excite LC neurons via the type I orexin receptor (OxR1). Since LC is thought to regulate sleep/wakefulness, especially REM sleep, we used small interfering RNAs (siRNAs) to reversibly knock down OxR1 in the LC in rats to assess its effect on vigilance state.
Methods: A pool of 3 siRNAs against OxR1 was used (siRNA-OxR1) to knockdown OxR1 in the LC of male Sprague-Dawley rats, and a corresponding pool of 3 siRNAs with no homology to known rat genes (siRNA-scrambled) was used as control. The extent of knockdown was assessed qualitatively by immunofluorescence histochemistry for OxR1 and TyH protein and quantitatively by performing real time PCR to exam OxR1 and TyH mRNA levels. For sleep studies (N=13), either the target siRNAs or scrambled siRNAs were bilaterally microinjected into the LC on two consecutive days. Baseline sleep was first recorded for 24hr and then the rats were divided into two groups to be injected either with target siRNAs or scrambled siRNAs. EEG/EMG data was recorded for at least 6 days following injections, and scored visually offline.
Results: Immunohistochemical staining revealed selective knockdown of OXR1 but not TyH after OXR1 siRNA injection in LC. This observation was confirmed by real-time RT-PCR. A single OxR1-siRNA injection induced a 26% reduction of OxR1 mRNA in LC ($N=11$, $P<0.01$). In contrast, there was no significant change in non-targeted TyH mRNA levels. Microinjection of OxR1 siRNA into LC (2 injections over 2 days) increased REM sleep during the dark period by over 30% ($N=7$, $P<0.05$) on the second night compared to the baseline. This increase was mainly due to increased number of REM sleep episodes. Neither the REM sleep duration nor the REMS-REMS cycle duration were appreciably altered.
Conclusion: Our results indicate that a modest knockdown of OxR1 was sufficient to induce observable sleep changes. Data are as predicted by a model in which orexin acting on LC gates the probability of the REM sleep oscillator being turned on without modifying the fundamental properties of the oscillator, such as cycle duration and REMS episode duration.
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CENTRAL CORTICOTROPIN-RELEASING HORMONE OVEREXPRESSION ENHANCES REM SLEEP IN CONDITIONAL TRANSGENIC MICE

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Introduction: Impaired sleep is a morbid symptom that often associates with depression. However, its mechanism remains unclear since all stress hormones are elevated in patients and known to affect sleep. So far, it has been technically difficult to separate the effects of corticotropin-releasing hormone (CRH), an initial mediator of acute stress responses, from the following others on sleep-wake regulation. To investigate an impact of central CRH on sleep, we used recently generated conditional mouse mutants that chronically overexpress CRH in the entire central nervous system (CRH-COE-Nes) or only in the forebrain including limbic structures (CRH-COE-Cam) without neuroendocrine disturbances under basal conditions.
Methods: Baseline polysomnographic recordings of CRH-COE-Nes and -Cam mice were performed first to detect differences in spontaneous sleep-wake patterns among control, heterozygous and homozygous littermates. Then, the mice were subjected to 6-h sleep deprivation (SD). Effects of SD on recovery sleep, plasma levels of corticosterone were compared across these genotypes. Separately, CRH receptor type 1 (CRHR1) antagonist DMP696 (30 mg/kg orally) and muscarinic antagonist atropine (2 or 6 mg/kg ip) were tested during SD in CRH-COE-Nes mice.
Results: During baseline, both homozygous CRH-COE-Nes and -Cam mice showed constantly increased REM sleep, whereas slightly suppressed non-REM sleep was detected only in CRH-COE-Nes mice. In response to SD, elevated levels of REM sleep became evident also in heterozygous CRH-COE-Nes and -Cam mice, which was reversed by treatment with DMP696 and the high dose of atropine. Plasma corticosterone concentrations were indistinguishable across genotypes at baseline and even after SD.
Conclusion: Since peripheral stress hormones were not altered, sleep changes occurring in this model, especially REM sleep enhancement, are most likely induced by forebrain CRH via activation of CRHR1. In CRH-COE mice, cholinergic activity seems to be higher than in control mice, suggesting CRH-ACh interaction on enhanced REM sleep in this model.

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THE EFFECTS OF CAFFEINE ON SLEEP IN DROSOPHILA REQUIRE PKA ACTIVITY, BUT NOT THE ADENOSINE RECEPTOR

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Introduction: Caffeine is one of the most widely consumed stimulants in the world, and its effects on sleep are thought to be mediated by antagonizing adenosine receptor function. In contrast to mammals which have 4 adenosine receptors, there appears to be a single adenosine receptor (dAdoR) in fruit flies. To investigate the mechanisms by which chronic caffeine administration acts in Drosophila, we generated null mutants of dAdoR and tested their response to chronic caffeine administration.
Methods: Sleep was measured using standard methods with the DAMS monitoring system in D:D and 12:12 L:D cycles in tubes containing 5% sucrose with or without drugs. 5-9 day old female or male flies (wild-type, dAdoR, or PKAR-overexpressing) were tested. All lines were outcrossed into a common wild-type background at least 5 times before behavioral testing.
Results: Chronic administration (2 days) of caffeine (0.1-0.5 mg/ml in the food) reduces and fragments sleep in flies. In addition, chronic feeding of caffeine also lengthens circadian period (0.9 hr/day for males and 0.5 hr/day for females with 0.5 mg/ml caffeine). Feeding of isobutylmethylxanthine (0.03-0.1 mg/ml) (IBMX), a non-specific phosphodiesterase inhibitor, also reduces sleep and lengthens circadian period in flies. Flies lacking dAdoR exhibit a similar amount of baseline sleep to controls. In addition, sleep rebound following sleep deprivation by 6 hr mechanical stimulation or 2 days of caffeine administration is not significantly altered in dAdoR mutants compared to controls. Surprisingly, dAdoR mutants and wild-type controls are similarly sensitive to the effects of caffeine on sleep. In contrast, the effects of caffeine on sleep are blocked in flies overexpressing a regulatory subunit of PKA (PKAR) in neurons.
Conclusion: These results suggest that chronic administration of caffeine may promote wakefulness not via dAdoR, but rather a PKA-dependent mechanism, such as inhibition of cAMP phosphodiesterase activity.

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FATTY-ACID BINDING PROTEINS MODULATE SLEEP AND IMPROVE LONG-TERM MEMORY IN DROSOPHILA

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Introduction: Brain-type fatty-acid binding protein (Fabp7) mRNA and protein follow a diurnal rhythm, and the cycling pattern is coordinated globally throughout the murine brain. The ethological function for the synchronized oscillation of Fabp7 is unknown. Using the fruit fly Drosophila melanogaster, we examined the effect of Fabp7 over-expression on sleep and long-term memory formation.
Methods: Transgenic flies were generated that either overexpress the mouse Fabp7, the endogenous fly fatty-acid binding protein (dFABP), or conditional knock-down of dFABP via RNAi. Drosophila sleep was assessed according to standard procedures, using the Drosophila Activity Monitoring System (DAMS) developed by Trikinetics (Waltham, MA). Drosophila learning and memory was tested using the olfactory-avoidance classical (Pavlovian) conditioning protocol, with automated and repetitive training regimens using 3-octanol (OCT) and 4-methylcyclohexanol (MCH) odors.
Results: Overall there was a reduction in daytime sleep in flies over-expressing the mouse Fabp7 or the Drosophila Fabp7 homologue (dFABP), as compared to control flies. Interestingly, RNAi knock-down of dFABP decreased rest behavior during the night-time, suggesting dFABP regulates normal sleep in Drosophila. Given the putative functional role for sleep mechanisms contributing to memory formation, we also monitored sleep in these flies following training in the olfactory avoidance conditioning paradigm. Both Fabp7 and dFABP over-expressing flies had a statistically significant enhancement of long-term memory (LTM) formation, compared to control flies. Following LTM training, control flies exhibited an increase in rest which was completely abrogated in mFabp7-tg and dFABP-tg flies. The LTM enhancement observed in mFabp7-tg and dFABP-tg was resistant to short-term (4hrs) but sensitive to long-term (12hrs) sleep deprivation following training.
Conclusion: This evidence implicates lipid-binding proteins and lipid-signaling pathways in the regulation of sleep and LTM formation, and provides a novel role for a specific gene product in regulating memory consolidation during sleep.

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EFFECTS OF CHRONIC HYPOXIA MIMICKING SLEEP RELATED V/Q MISMATCH ON GENE EXPRESSION IN THE RIGHT VENTRICLES IN SPRAGUE DAWLEY AND BROWN NORWAY RATS

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Introduction: There are physiologic differences in the response of Sprague Dawley (SD) and Brown Norway (BN) strains of rats to daily hypoxia (DH) (8 hours of hypoxia/day for 2 weeks). The BN strain was found to develop a significantly higher degree of right ventricular (RV) hypertrophy than the SD strain. The purpose of this study was to describe differences in gene expression in the RV between the two rat strains in response to daily hypoxia exposure.
Methods: SD and BN rat strains were exposed either to hypoxia (10% O2 and balance N2) 8 h/day for 2 weeks (N= SD 5, BN 6) or to room air (N= SD 5, BN5) in an identical chamber and cycle. Total RNA was extracted from right ventricles and prepared for use on Affymetrix gene expression microarrays. Statistical analysis done with Baysian analysis of variance for microarrays (BAM).
Results: Both BN and SD rats when exposed to daily hypoxia overexpressed an array of genes that belonged mainly to three Gene Ontology (GO) biological process groups: development including myofibroblast development, cell motility, and intracellular mechanisms. The hypoxia conditioned BN rats were characterized by predominantly augmented gene expression when compared to hypoxia conditioned SD, irrespective of the fold-change threshold. Among 43 identifiable genes with >2-fold significantly altered expression, 26 belonged to the previously mentioned GO groups. GO cellular constituent assignment resulted in the highest degree of over representation in oxireductase genes, one of which included Nox4, identified previously to play a role in hypoxia reperfusion responses. In addition, there was eight-fold increase in the myristoyal alanine protein kinase and myrosine heavy polypeptide 7, genes previously been found to play a direct or indirect role in oxidative stress.
Conclusion: We conclude that the two strains respond to chronic steady state hypoxic stress with similar but quantitatively different genomic expression of molecules in large part previously known to act in hypoxic sensing and oxidative responses.
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IDENTIFICATION OF "SLEEP GENES" FROM NATURAL AND PHARMACOLOGICALLY INDUCED SLEEP STUDIES

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Introduction: Previous studies have supported the hypothesis that macromolecular synthesis occurs in the brain during sleep as a response to prior waking activities and that prostaglandin D2 (PGD2) is an endogenous sleep substance whose effects are dependent on adenosine A2a receptor-mediated signaling. We compared gene expression during PGD2- and adenosinergically-induced sleep to recovery sleep (RS) after sleep deprivation (SD) because pathways common to both natural and chemically-induced sleep may provide insights into the function of sleep.
Methods: Wistar rats were surgically prepared, recorded, and subjected to SD as described (Terao et al., 2006, Neuroscience 137(2): 593-605). Rats were randomly assigned to one of four groups: (1) SD from light onset (ZT0) to ZT6; (2) control rats for the SD group; (3) SD from ZT0 to ZT6 followed by RS from ZT6 to ZT8; (4) control rats for the RS group. SD and their control animals were sacrificed at ZT6; RS and their control animals were sacrificed at ZT8. Another sets of Wistar rats were surgically prepared, recorded, and subjected to drug infusions as described (Terao et al., 2008, J. Neurochem 105(4): 1480-1498). Rats were randomly assigned to one of three groups: (5) Saline infusion group; (6) PGD2 infusion (200 pmol/min) group; (7) CGS21680, a selective adenosine A2a agonist (20 pmol/min) group. All animals were sacrificed at ZT14. All brains were dissected into cortex (Cx), basal forebrain (BF), and hypothalamus (Hy) and total RNA was extracted. cRNA probes were prepared for hybridization to duplicate Affymetrix rat U34 Neurobiology arrays. Candidate genes from the arrays were verified by quantitative real-time PCR.
Results: In pharmacologically induced sleep studies, changes in gene expression were more similar in comparisons of BF to Hy than in comparisons of either region to Cx. However, Cx were more similar to BF in response to SD than either region was to Hy. We found that gene expression during PGD2- and CGS21680-induced sleep showed surprisingly limited similarity to that observed during RS. Of the genes that were up-regulated in one or more brain regions by both PGD2 and CGS21680, 10 were also up-regulated during SD and 5 during RS.

Conclusion: Gene expression induced in the brain after PGD2 or CGS21680 treatment was distinct from that described during RS after SD and apparently involves glial cell gene activation and signaling pathways in neural-immune interactions.
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GENOME-WIDE ASSOCIATION STUDY OF NARCOLEPSY IDENTIFIES A SUSCEPTIBILITY VARIANT LOCATED BETWEEN *CPT1B* AND *CHKB*

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Introduction: Narcolepsy, a sleep disorder characterized by sleepiness, cataplexy and rapid eye movement (REM) sleep abnormalities, is tightly associated with HLA-DRB1*1501 and HLA-DQB1*0602. Susceptibility genes other than those in the HLA region are also likely involved.
Methods: To search for additional susceptibility and/or resistance genes to narcolepsy, we conducted a genome-wide association study using 500K SNP microarrays in 222 Japanese individuals with narcolepsy and 389 Japanese controls, with replication of top hits in 159 Japanese individuals with narcolepsy and 190 Japanese controls, followed by the testing of 424 Koreans, 785 individuals of European descent and 184 African Americans. Expression of each gene was measured by a real-time quantitative RT-PCR using RNA purified from leukocyte.
Results: SNP rs5770917 located between the carnitine palmitoyltransferase 1B (*CPT1B*) gene and the choline kinase beta (*CHKB*) gene was associated with narcolepsy in Japanese (rs5770917[C], odds ratio (OR) = 1.79, combined $P = 4.4\times10^{-7}$) and other ancestry groups (OR = 1.40, P = 0.02). A meta-analysis in the four populations provided $P = 5.9\times10^{-8}$, with an OR of 1.63. The association was genome-wide significant. Moreover, real-time quantitative PCR assays in white blood cells indicated decreased *CPT1B* and *CHKB* expression in subjects with the C allele, suggesting that a genetic variant regulating *CPT1B* or *CHKB* expression is associated with narcolepsy.
Conclusion: Either of these genes is a plausible candidate. CPT1B is the rate-controlling enzyme of long-chain fatty acid β-oxidation in muscle mitochondria. CPT1B catalyzes the transport of long-chain fatty acyl-CoAs from the cytoplasm into the mitochondria through the carnitine shuttle. Several reports have implicated fatty acid β-oxidation and carnitine system in sleep regulation. CHKB is an enzyme involved in the metabolism of choline, a precursor of the REM- and wake-regulating neurotransmitter acetylcholine.

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DO CAUCASIAN AND ASIAN CLOCKS TICK DIFFERENTLY?

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Introduction: The Per3 and Clock genes are important components of the mammalian circadian system. Studies have shown association between polymorphisms in these clock genes and circadian phenotypes in a variety of population samples. Nevertheless, differences between the pattern of allele frequency and genotyping distributions are systematically observed in studies with different ethnic groups. To investigate and compare the pattern of distribution in a sample of Asian and Caucasian populations living in Brazil, we evaluated two polymorphisms in the clock genes: The VNTR in Per3 and The T3111C in Clock.
Methods: We selected 109 Asian and 135 Caucasian descendents. The subjects were visually observed and answered an ancestry questionnaire comprising two generations. DNA sample collection was performed from the buccal cells and extracted using a commercial kit. The polymorphisms were genotyped by PCR (Polymerase Chain Reaction) and Real Time method.
Results: The genotype and allele distributions for both gene polymorphisms are different between the two ethnic groups .The allele frequency of 4 repeats in the Per 3 gene is much higher in Asians than Caucasians, while the 5-repeat variant is much less frequent in the Asian population. Likewise, the Clock gene T3111 allele frequency is higher in Asians than Caucasians.
Conclusion: Our results directly confirm the different distribution of these polymorphisms in the Asian and Caucasian ethnicities. Given the genetic differences between groups and considering that such differences may have implications for the interpretation of results in association studies, we suggest that ethnic variations in polymorphisms should be analyzed carefully and considered in research of clock gene variation and circadian phenotypes. It is becoming clear that polymorphisms identified in a given ethnic group cannot be extrapolated to another.
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PLASMA KISSPEPTIN LEVELS IN PATIENTS WITH OBSTRUCTIVE SLEEP APNEA HYPOPNEA SYNDROME

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Introduction: obstructive sleep apnea hypopnea syndrome(OSAHS) is a highly prevalent disease with an estimated incidence of 4% in men and 2% in women. The 7-years mortality of patients with untreated severe OSAHS is reported to reach 30% or higher. The most important factors in death in OSAHS are cardiovascular risk factors such as leptin, insulin resistance. These factors all play a critical role. These factors that are involved in the onset and pathological condition of metabolic syndrome also have implications in OSAHS. Recently, GPR 54 and a bioactive peptide newly identified as a ligand for GPR 54 have been identified as kisspeptin. Kisspeptin was initially reported as metastin, a substance that controlled cancer metastasis, but subsequent studies suggested its role as a sex hormone. Also, like peptides such as leptin, kisspeptin has been reported to have a close relationship to food consumption and energy metabolism. The relationship between OSAHS with leptin and orexin-A has already been shown in previous reports. We, therefore, hypothesized that kisspeptin may also be related to the sleep and energy balance in OSAHS, and examined the correlation between the plasma kisspeptin level and sleep disorder.
Methods: The subjects were 122 patients who had a documented diagnosis of OSAHS by PSG performed to confirm OSAHS and 7 non-OSAHS volunteers who were enrolled as controls. Plasma kisspeptin was measured in all subjects and compared with the results of the PSG data and patients' backgrounds.
Results: Plasma kisspeptin levels were significantly lower in patients with OSAHS than in controls. The plasma kisspeptin levels in significantly correlated with the percentage of Stage N3 in PSG. Also, no dif-

ference was seen between the plasma kisspeptin levels of the controls and patients in which the percentage of slow wave sleep was maintained. These patients were grouped into Group A (preserved slow wave sleep), and the other 80 patients who had fragmented sleep due to apnea events and impaired sleep architecture were grouped into Group B (impaired slow wave sleep). The plasma kisspeptin level in Group B was significantly lower than that in Group A. Correlation analysis of plasma kisspeptin levels with physical findings and PSG data in Groups A and B revealed a significant correlation only with %Stage N3 in Group A.
Conclusion: The results of this study suggest that kisspeptin is linked not only to the feeding behavior and sex hormones but also to sleeping, especially the percentage of slow wave sleep.

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MICRO-RNA (MIRNA) SIGNATURES IN MOUSE ADIPOSE TISSUE FOLLOWING ACUTE SLEEP FRAGMENTATION

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Introduction: Sleep apnea induces sleep fragmentation (SF), and leads to significant metabolic morbidity. Adipose tissues play major metabolic functions and produce hormones with important physiological effects. MicroRNAs (miRNAs) are small noncoding RNAs that bind to multiple target mRNAs, and have been implicated in multiple biological processes, including cellular differentiation, apoptosis and proliferation. We hypothesized that changes in miRNA expression in adipose tissues may occur in SF, and contribute to altered metabolic homeostasis. Furthermore, the miRNAs expressions patterns in mouse adipose tissues are unknown.
Methods: Adult CB57BL mice were exposed to either acute SF (arousals every 2 min for 6 h; n=8)) or time-control conditions (n=7). Visceral and subcutaneous fat tissues were harvested, and 100 ng miRNA and total RNA were extracted, and hybridized onto a miRNA microarray containing probes for 570 mouse miRNAs (replicate features per miRNA 20-40).
Results: Of 570 miRNA in the array, 114 miRNA in visceral, 84 miRNA in subcutaneous fat tissues expression levels that exceeded at least 3-fold increased levels compared to control background expression levels in the array. Of these, significant changes following SF emerged among 15 miRNA in subcutaneous fat (3 down regulated and 12 up-regulated), while expression of 39 miRNA (13 down-regulated and 26 up-regulated) were significantly altered by SF in visceral fat. The expression of these miRNAs awaits validation by quantitative PCR, after which putative biological pathways that may potentially activated by SF will be delineated.
Conclusion: Expression of specific miRNAs is restricted to a subset of known mouse miRNAs. Furthermore, expression of a selective group miRNAs is altered following acute sleep fragmentation in adipose tissues, particularly in visceral fat. These findings highlight the potential role of miRNAs is regulating metabolic and biological responses in the context of sleep disorders.
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PLASMA KISSPEPTIN CONCENTRATIONS IN FEMALE PATIENTS WITH OBSTRUCTIVE SLEEP APNEA HYPOPNEA SYNDROME (PLASMA KISSPEPTIN STUDY - PART 2)

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Introduction: We have submitted the subject of a poster presentation in this congress that the relationship between 122 Obstructive Sleep Apnea Hypopnea Syndrome (OSAHS) patients of men and 7 non-OSAHS volunteers as controls of 5 men and 2 postmenopausal women with plasma kisspeptin concentrations. As a result Plasma kisspeptin concentrations were significantly lower in patients with OSAHS than in controls, the plasma kisspeptin concentrations in significantly correlated with the percentage of Stage N3 in PSG data and in addition the plasma kisspeptin concentration in Group of impaired slow wave sleep (SWS) with OSAHS was significantly lower than that in Group of preserved SWS with OSAHS.
Methods: Consequently based on these result, this study aims to clarify that women's plasma kisspeptin may also related with sleep depth or sleep disorder as well as our another reports of men's study of plasma kisspeptin concentration. The subjects were 27 patients who had a documented diagnosis of OSAHS by overnight polysomnography (PSG) performed to confirm OSAHS and 7 non-OSAHS volunteers who were enrolled as controls.
Results: Plasma kisspeptin concentrations were significantly lower in patients with OSAHS than in controls. But no difference was seen between postmenopausal with control and with OSAHS versus significantly lower in patients with prior to postmenopausal OSAHS than controls. And comparison of impaired and preserved with SWS, the plasma kisspeptin concentration in Group of impaired SWS with control and OSAHS was significantly lower than that in Group of preserved SWS with control and OSAHS.
Conclusion: Consequences of this study suggest that the plasma kisspeptin concentration may be affected by sleep depth or sleep disorder, play an important role in our construction of sleep and raise the possibility of plasma kisspeptin will become a marker to ascertain whether maintaining or not.

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CO-REGULATED TRANSCRIPTIONAL NETWORKS CONTRIBUTE TO NATURAL GENETIC VARIATION IN *DROSOPHILA* SLEEP

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Introduction: Sleep is conserved throughout the animal kingdom, and is thought to affect processes as diverse as energy conservation and synaptic plasticity. Using *Drosophila* as a model for the study of mammalian sleep, recent studies have implicated genetic pathways and neural tissues in sleep regulation. The suite of genes that maintain genetic variation for sleep in natural populations remains unknown, however. We hypothesized that the genetic variation in transcript abundance of a

panel of wild-derived inbred lines would reflect their genetic variation in sleep propensity.
Methods: We measured sleep in male and female virgins from 40 homozygous wild-derived inbred lines. We measured whole-body transcript abundance in the same lines using Affymetrix *Drosophila* 2.0 whole-genome microarrays. 3,136 probe sets contained single feature polymorphisms which we tested for their association with sleep. We used linear regression on the remaining 10,096 differentially expressed genes to determine the association between transcript abundance and sleep phenotypes. Residuals from the regression analysis were used to compute genetic correlations among transcripts, and statistically correlated transcriptional modules were identified using graphical mapping procedures.
Results: We observed abundant and sex-specific genetic variation in the duration and architecture of sleep. Sequences of the gene *Catacholamines up*, a gene involved in the negative regulation of tyrosine hydroxylase, confirmed a polymorphism that affected day sleep. Using *P*-element insertional mutations in the regression candidate genes *bin3*, *Akt1*, *CG17574*, and *Tsp42Ef*, we independently demonstrated that altered gene expression affected sleep duration. Statistically correlated transcriptional modules revealed biologically meaningful networks, implicating genes involved in fundamental cellular processes. We confirmed positive inter-correlations within a module for night sleep duration using RT-PCR.
Conclusion: Our analysis revealed novel gene networks impacting sleep. Thus, quantitative genetic analysis of natural phenotypic variation in sleep and gene expression is an efficient method for revealing novel candidate genes and pathways.
Support (optional): This work was supported by National Institutes of Health grants R01 GM 45146, R01 GM 076083 and R01 AA016560 to T.F.C.M., and the National Sleep Foundation Pickwick Fellowship to S.T.H.

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GENOME WIDE EXPRESSION CHANGES IN MURINE ADIPOSE TISSUE FOLLOWING ACUTE INTERMITTENT HYPOXIA

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Introduction: Obstructive sleep apnea (OSA) is associated with a variety of cardiovascular and metabolic complications that appear to be mediated by mechanisms involving intermittent hypoxia (IH). Adipose tissue is now recognized as a biologically active compartment with multiple biological functions. However, the gene pathways recruited by IH in visceral and subcutaneous fat are not well understood. We hypothesized that exposure to IH would lead to changes in global gene expression in adipose tissues.
Methods: Adult CB57BL6 mice (n=7) were exposed to either acute IH (cycling of 5.7% or 21% oxygen every 3 min) for a period of 6 hours from 1pm-7pm (last six hours of light period), or to room air as control (RA; n=7). Adipose tissues (subcutaneous and visceral fat) were harvested and snap frozen and total RNA was extracted, and hybridized onto whole mouse genome long-oligonucleotide microarrays. Gene ontology (GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway analyses were used to identify significant functionally-related groups of genes, and hierarchical cluster analyses were used to visualize expression changes between control and IH conditions.
Results: A comparison of gene expression profiles from subcutaneous fat in IH and RA identified 1,373 significantly altered genes (p-value <0.01). Most prominent pathways modified among these genes involved insulin signaling pathway, oxidative phosphorylation, glycolysis, and calcium signaling. Similarly, gene expression in visceral fat identified 1,294 genes with statistically significant changes in IH (p-value <0.01). These genes involved p53 signaling pathways, apoptosis, insulin signaling pathways, MAP signaling, VEGF signaling, and adipocytokine pathways.
Conclusion: These findings provide initial steps toward improved understanding of the dynamics of gene regulatory networks in the context of IH in fat tissues, and may identify specific genes within biological pathways in adipose tissues that play a central role in metabolic and vascular dysfunction associated with OSA.
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1223

AROUSAL RESPONSES TO FASTING ARE BLUNTED IN GHRELIN KNOCKOUT MICE

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Introduction: Intrahypothalamic microinjections of ghrelin and neuropeptide Y (NPY) enhance wakefulness and feeding in rats. The first hours of the behaviorally active phase are characterized by eating and increased arousal; in nocturnal rodents, they constitute the dark onset syndrome. Short-term fasting accentuates the sensitivity to metabolic signals and the dark onset syndrome. The hypothalamic circuit formed by ghrelin-, NPY- and orexin-producing neurons integrates metabolic and circadian clock signals. We hypothesized that the activation of this circuit plays a key role in triggering wakefulness and eating during the dark phase in mice.
Methods: Sleep, motor activity and body temperature of WT and ghrelin KO mice (n = 12 for each group) in response to fasting were determined. After a baseline day, animals were fasted from the beginning of dark for 24 hours.
Results: Fasting induced increased wakefulness during the dark period in both genotypes. The response in the ghrelin KO mice was significantly attenuated as compared to WTs (WT, baseline: 442 ± 11 vs. fasting: 510 ± 22 min/12 h, $p < 0.05$; KO, baseline: 433 ± 15 vs. fasting 478 ± 12 min/12 h, $p < 0.05$). Increased wakefulness was accompanied by decreased NREMS in both groups of mice. During the light phase, NREMS returned to baseline in the KO mice while NREMS was increased in WT animals. Although NREMS was suppressed during the dark phase, EEG SWA during NREMS was enhanced in WTs then returned to normal during the light. WT mice showed increased motor activity from h 3 to 8 during the dark. The activity response was completely absent in the KOs. During fasting body temperature of WT mice was suppressed for 5 h in the light.
Conclusion: Results support the hypothesis that the product(s) of the preproghrelin gene play a role in behavioral activation during the dark phase in mice.
Support (optional): NIH NS27250

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IDENTIFICATION OF A NOVEL ZINC FINGER DOMAIN-CONTAINING SLEEP GENE IN *DROSOPHILA*

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Introduction: The fruit fly, *Drosophila melanogaster*, continues to prove itself useful in the search for the molecular mechanisms of sleep.

In the course of a large scale screen to investigate the underlying genetic mechanisms of sleep we identified a mutant fly that sleeps only 40% of the time wild type flies sleep. Molecular analysis indicated that gene affected in this mutant fly strain a novel zinc finger domain-containing gene.
Methods: Over 2,000 P-element lines were screened using the Drosophila Activity Monitoring System (DAMS) and the resulting behavioral data were analyzed with custom software. We next used RT-PCR to characterize the expression of candidate genes. Transgenic GAL4/UAS lines were then prepared to study promising candidates in *Drosophila* brains.
Results: In the course of our screen we identified two P-element insertion lines (P1 and P2) that both disrupt sleep duration in both males and females to 40% of the wild type level. Precise P-element excision from line P1 restored sleep duration to the wild-type level. P1 also failed to exhibit any sleep rebound after a 12-hour bout of nighttime sleep deprivation. The P-elements of lines P1 and P2 both map to the same candidate gene, and their presence reduces gene expression as confirmed by RT-PCR. Heterozygotes (P1/Df, P2/Df, P1/P2) failed to complement the short sleep phenotype. Repression of this candidate gene expression in the mushroom bodies via RNAi causes a similar sleep phenotype. A zinc finger domain is the only recognizable feature in this novel gene, which must now be characterized.
Conclusion: This study identified a novel zinc finger domain-containing gene that affects sleep duration in *Drosophila*. The mutant sleep profiles will be discussed.

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NEW BIOMARKERS OF SLEEPINESS IDENTIFIED IN HUMANS AND *DROSOPHILA*

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Introduction: Reliable identification of sleepiness is useful for both clinical and real-world applications. Currently assays that objectively measure sleepiness, such as the multiple sleep latency test, are labor intensive and expensive. Therefore, there is a need for a simple, inexpensive, and non-invasive tool that can detect sleepiness. Previously, we have shown that salivary *Amylase* is responsive to sleep loss and thus is a candidate biomarker in humans. However genes are notoriously pleiotropic and thus a panel of multiple genes from different gene ontology categories may be required to effectively and objectively measure sleepiness. To address this issue, we have used markers identified in *Drosophila* to interrogate the salivary transcriptome of sleep deprived human subjects.
Methods: Humans saliva samples from eight human subjects were taken after 24 and 30 hours of wakefulness. Quantitative RT-PCR was used to evaluate changes in expression levels. Each subject served as their own circadian-matched, untreated control. Follow-up studies were conducted in sleep deprived flies to evaluate potential conservation between species.
Results: We identified 5 genes that were increased after 24 and 30 h of waking. Of the 5 genes, 2 had *Drosophila* homologues that were also responsive to sleep deprivation in wild-type flies. Follow up genetic studies in mutants indicated that these genes were only responsive to waking-conditions that are followed by a homeostatic response.
Conclusion: Our results indicate that the salivary transcriptome can be mined to identify genes that are responsive to sleep loss. These candidate genes, along with, *Amylase*, bring us closer to defining a panel of genes that can be used to reliably identify and track sleepiness in the laboratory, the clinic and real-world settings. In addition, these results reveal a surprising conservation of genes associated with sleepiness between humans and flies.

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GENETICS OF SLEEP PHENOTYPES IN THE NHLBI'S FRAMINGHAM HEART STUDY OFFSPRING COHORT

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Introduction: Many of the genetic loci responsible for the control of sleep are unknown. Association of NPSR1 to weekday bedtime and PDE4D to sleepiness as represented by the Epworth Sleepiness Scale (ESS) score has been demonstrated in a subset of approximately 700 Framingham Heart Study (FHS) Offspring Cohort participants using an Affymetrix 100K SNP GeneChip. We now have analyzed a larger sample of the Framingham Offspring.
Methods: The FHS Offspring Cohort is a community-based cohort unascertained for sleep phenotypes. The cohort is nearly entirely composed of white Americans of European descent. Sleep phenotypes from 2,848 participants were collected through a sleep habits questionnaire administered by the Sleep Heart Health Study between 1995 and 1998. Genotyping was performed using an Affymetrix 550K SNP GeneChip platform. Heritability and linkage analyses on age- and sex-adjusted standardized residual traits were performed in SOLAR. Linkage analysis was implemented with 4,157 SNPs and identity-by-descent computed every 1 centiMorgan using Haldane maps. Association analysis was implemented with a genome-wide association analysis pipeline created for the NHLBI's SNP Health Association Resource project.
Results: Heritability for the ESS score was 26%, for weekday bedtime was 25% and for weekday sleep duration was 24%. Linkage for the ESS score (LOD 1.67, chrom 3), weekday bedtime (LOD 3.24, chrom 9), and weekday sleep duration (LOD 1.96, chrom 4) did not parallel prior FHS results. Top linkage results were found for weekday mid-sleep time (LOD 3.77, chrom 9), weekend mid-sleep time (LOD 3.33, chrom 9), and weekday rise-time (LOD 4.37, chrom 3).
Conclusion: Genome-wide significant linkage was found for weekday rise-time on chromosome 3q with a two megabase 1-LOD support interval which contains several genes with potential relevance to sleep and metabolic factors. Additional linkage peaks were also observed and further details of these genes including genome-wide association results will be presented.

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LIPOPOLYSACHARID-INDUCED ALTERATIONS OF SLEEP IN CORTICOTROPIN-RELEASING HORMONE TYPE 2 RECEPTOR KNOCKOUT MICE

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Introduction: The onset of acute bacterial infection is typically associated with the increased synthesis and release of cytokines which act in the brain to alter sleep-wake behavior by the enhancement of NREM sleep (NREMS). The expression of cytokines can be mediated by two corticotropin-releasing hormone (CRH) receptors, CRHR1 and CRHR2. To elucidate the contribution of CRHR2 to sleep-wake regulation during immune activation we investigated the sleep response in CRHR2 knockout mice (CRHR2 KO) subjected to acute systemic infection via peripheral administration of lipopoplysacharid (LPS), a small immunogenic unit of the cell wall from gram negative bacteria.
Methods: CRHR2 KO mice and their wild-type littermates (wt) habituated into 12:12-h light-dark cycles were implanted with electrodes to record EEG/EMG signals. After recovery from surgery mice were injected

i.p. with 0.2 ml vehicle (pyrogen-free saline; PFS), and on separate days with vehicle containing 0.1, 1 or 10µg LPS 15-min prior to the onset of the dark period. Vigilance states and power spectra of EEG signals were analyzed to display dimensional presentations of frequency, time, and amplitude relations, respectively.

Results: NREMS of both genotypes was increased in a dose-related fashion during the first 6h following i.p. administration of LPS, but with opposed trends to the amount of LPS between examined genotypes. In the end of the light period, LPS suppressed REMS of wt mice, but not of mice lacking CRHR2 receptors. Spectral analysis revealed differences in frequency distribution between groups (vehicle). After i.p. LPS administration, the power spectra within the slower frequencies increased radically in CRHR2 KO mice compared to that in wt mice.

Conclusion: The results demonstrate that CRHR2 KO mice show greater sleep response to LPS. Therefore, CRHR2 would be necessary to control the manifestation of sleep-immune interactions, likely affecting the expression or production of inflammatory cytokines.

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CRH-R1 AND CRH-R2 ARE INVOLVED DIFFERENTLY IN EFFECTS OF CRH ON SLEEP AND WAKE REGULATION

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Introduction: Corticotropin-releasing hormone (CRH) is reported to promote wakefulness or increase arousal and to suppress sleep. Up to now only few studies investigated the different contribution of the two CRH receptors (CRH-R1 and CRH-R2) to the regulation of rapid-eye-movement (REMS) and nonREM (NREMS) sleep. We therefore compared the effects of exogenous CRH on sleep in CNS-specific CRH-R1 (CRH-R1 KO) and conventional CRH-R2 (CRH-R2 KO) deficient mice with their corresponding wildtype littermates (WT).

Methods: Under isoflurane anaesthesia, four EEG-electrodes, two EMG-electrodes, and an intracerebroventricular (ICV) cannula were implanted in each mouse. Three doses of CRH (0.3, 1.0, and 3.0µg) were administered ICV 30 min prior to the light period. Vigilance states were visually scored from EEG and EMG recordings.

Results: CRH caused dose-dependent increases in wake and suppression of sleep in all WT and CRH-R2 KO mice immediately after injections if compared to vehicle control. After 2-h postinjection elevated waking levels gradually declined, returning dose-dependently to baseline levels. Decreases in NREMS reflected wake reversely. However, in CRH-R1 KO animals no significant changes in wake or NREMS amounts could be induced by exogenous CRH. Contrariwise, REMS levels were dose-dependently decreased similarly seen in WT and CRH-R2 KO mice and almost totally blunted after the highest dose of CRH in all mice, whereas during the dark period a more or less distinct rebound in REMS could be observed.

Conclusion: As previously shown in C57BL/6J mice, CRH increased wakefulness and reduced NREMS and REMS in WT and CRH-R2 KO mice. In CRH-R1 KOs, however, only REMS was affected by exogenous CRH. This suggests that central CRH-R1 in contrast to CRH-R2 is essentially involved in the regulation of wake and NREMS but not REMS.

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PERSISTENT BRAIN INFECTION OF PR8 INFLUENZA AT 48 AND 96 HOURS POST-INFECTION

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Introduction: Profound changes in sleep occur in mice after viral challenge. PR8 influenza virus induces upper respiratory tract infections. Previously we showed that mouse-adapted PR8 influenza virus also invades the olfactory bulb (OB) of mice within hours of intranasal challenge and that there is an association between the occurrence of viral antigen and up-regulation of somnogenic cytokines such as interleukin-1 and tumor necrosis factor at the time sleep and temperature responses are initiated. Viral RNA is present in the olfactory bulb at 4, 7, 10 and 15 hours post-viral challenge, however, the sleep responses persist for days. We now analyze OB and somatosensory cortex (Sctx) from PR8 infected mice at 48 and 96 hours post-infection to resolve whether the virus is present and replicating at later time points.

Methods: C57Bl/6J mice were intranasally inoculated with purified PR8 or heat-killed virus as control (n=8 each condition). OBs and Sctx were collected at 48 and 96 hours post-infection. cDNA was synthesized from extracted RNA using gene specific primers for plus or minus viral nucleoprotein (NP) strands. The cDNAs were amplified using a nested PCR reaction and PCR products were analyzed using agarose gels; NP bands migrated as 450 bp products.

Results: OB extracts from 48 and 96 hour samples contained minus and plus viral RNA strands, indicating viral replication. In contrast, the Sctx contained no NP plus strand RNA, indicating that blood in the brain is not the source of replicating virus.

Conclusion: It is posited that the presence of viral RNA and associated up-regulation of cytokines in the brain at 15 h post-inoculation triggered sleep responses and that within 1-2 days after inoculation virus-enhanced lung production of cytokines maintained the sleep responses over the course of the infection. In light of current evidence this hypothesis will have to be revised.

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MICRO RNAS THAT CHANGE WITH SLEEP PROPENSITY TARGET KNOWN SLEEP REGULATORY SUBSTANCES IN VITRO

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Introduction: MicroRNAs (miRNAs) are a class of non-coding RNA strands capable of regulating gene expression via degradation or translational repression of mRNA transcripts. Previously we showed that brain levels of the let-7b miRNA vary with sleep propensity and preliminary data suggest that analogs of specific miRNAs locally alter EEG power during NREM sleep when applied directly to the cortex in rats. We hypothesize that these miRNAs are targeting known sleep regulatory substances (SRSs). Here we present in vitro data suggesting that let-7b targets SRSs such as NGFβ and IL-13 and may play a role in sleep regulation.

Methods: Potential miRNA targets were identified via bioinformatics techniques and chosen based on their capacity as SRSs or as modulators of SRS signaling pathways. The rat target gene 3' UTR was synthesized and cloned into the pMir-Report Ambion expression vector. H19-7 immortalized rat neurons were co-transfected with an expression vector and control vector in the presence or absence of either a miRNA analog, inhibitor or nonsense control oligonucleotide. After 48 hours luciferase expression was assayed using the Dual-Glo Luciferase Assay System. Reporter vector activity was normalized to the control vector. An expression vector containing a binding site for p250Gap, an established target of mir-132, was used as a positive control in a separate experiment to validate the plasmid conduction, transfection and assay protocols.

Results: Cells transfected with an analog of let-7b showed a 3-fold decrease in expression of the reporter vector containing an IL-13 3' UTR sequence compared with cells transfected with a nonsense control oligonucleotide. Cells transfected with an inhibitor of let-7b showed a 0.7-fold increase in expression of the reporter vector containing an NGFβ 3'

UTR sequence compared with cells transfected with a nonsense control oligonucleotide.
Conclusion: NGFβ and IL-13 are targets of miRNA let-7b.
Support (optional): NIH NS25378 and NS31453

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MICROINJECTION OF MICRO RNA ANALOGS CAUSES CORTICAL ELECTROENCEPHALOGRAPHIC ASYMMETRIES IN THE RAT

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Introduction: MicroRNAs (miRNAs) are regulators of mRNA stability. They are small (~22 nucleotide) strands with the capacity to hybridize with the RNA-induced silencing complex and target mRNA for degradation or inhibiting its translation. Previously we showed that miRNAs in the brain change with sleep propensity. Moreover, many of these miRNAs have sequence alignments with sleep regulatory substances (SRS) mRNAs. We hypothesize that manipulating miRNA levels in the brain will affect the sleep EEG and thereby establish causality between miRNAs and changes in a sleep phenotype.
Methods: Male Sprague-Dawley rats 275-325 g were maintained on a 12 hr light/dark cycle and instrumented with bilateral supracortical cannulae and differential EEG electrodes over the somatosensory cortex. At light onset, naked (IDT) or cholesterol-conjugated oligonucleotides (50 µmoles; Ambion) for miR-132 were delivered to one side of the brain while saline or a scrambled sequence was delivered to the other side (all in 2 µl over 5 min). EEG was recorded from both hemispheres for two baseline days and five post-injection days. Power analyses of NREM sleep were performed using two hour time blocks and compared with recordings from the contralateral hemisphere.
Results: Naked or cholesterol-conjugated miR-132 analogs significantly decreased EEG slow-wave activity during NREM sleep 14-20 hours post-injection as compared with saline- or scrambled sequence-treatments.
Conclusion: This is the first indication that in vivo delivery of miRNAs changes a sleep phenotype. Our laboratory is currently engaged in identifying the target SRSs that underlie this response. It seems likely that miRNAs acting on known SRS mRNAs are important components in the long-term regulation of sleep.
Support (optional): NS25378 and NS31453

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INTERLEUKIN 1-BETA TREATMENT UP-REGULATES PURINE TYPE 2 RECEPTOR MRNAS IN RAT SOMATOSENSORY CORTEX

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Introduction: Sleep is regulated in part by a central nervous system molecular network. Interleukin-1β (IL1β) is strongly implicated in non-rapid eye movement sleep (NREMS) regulation. Systemic administration, or intracerebroventricular injection of IL1β, or microinjection of IL1β into specific brain regions enhances NREMS in rats. In contrast, anti- IL1β antibodies, or the naturally occurring IL1β receptor antagonist, or the soluble IL1β receptor inhibit spontaneous sleep and sleep rebound after sleep deprivation. Brain IL1β mRNA levels, and cerebrospinal fluid levels of IL1β protein, correlate with sleep propensity. Adenosine triphosphate (ATP) releases cytokines, including IL1β, from immunocytes and glia via purine type 2 receptors (P2Rs). Purine receptor (P2Y1 and P2X7) mRNAs are associated with IL1β release and have a diurnal rhythm in the rat somatosensory cortex (Sctx). In the current experiments we determined SSctx P2Rs mRNA responses to IL1β treatment using real-time RT-PCR.
Methods: Male Sprague-Dawley rats (280 - 350 g) were provided with a guide icv cannula under anesthesia. Six groups (n=8 each) of rats were used. After recovery, human recombinant (hr) IL1β (0, 2.5 and 25 ng) was injected icv at 1 h before dark onset and rats were sacrificed 2 h or 5 h later. The Sctx was dissected and quickly frozen. Total RNA was extracted using Trizol reagent and P2X1 and 7 and P2Y1, 4, 5, 13, and 14 receptor mRNAs were determined using real-time RT-PCR.
Results: One way ANOVA indicated that Sctx P2X7 and P2Y1, 4, 5, 14 mRNAs were significantly increased at 2 h after IL1 β (2.5 and 25 ng). By 5 h after treatment they had returned to baseline values. P2X1 and P2Y13 receptor mRNA expressions were not affected by IL1β treatment.
Conclusion: Results are consistent with the hypothesis that IL1β-induced up-regulation of P2Rs form part of the biochemical processes leading to sleep.
Support (optional): NIH NS25378 and NS31453

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EXPRESSION OF PLASTICITY-RELATED GENES DURING ESZOPICLONE-INDUCED SLEEP

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Introduction: The "synaptic homeostasis hypothesis" predicts that synaptic strength should change in many brain circuits during sleep. We studied whether the expression of plasticity-related genes changes during drug-induced sleep.
Methods: We first characterized sleep induced by eszopiclone in C57BL/6 male mice (n=27) during baseline conditions and during the recovery from sleep deprivation, and then compared the expression of 18 genes critically involved in synaptic plasticity during sleep induced by eszopiclone to that observed during physiological sleep. The expression of these genes was assessed by TaqMan RT PCR and correlated with sleep parameters in mice.
Results: Eszopiclone reduced latency to NREM sleep, increased NREM sleep amounts, and did not change REM sleep amounts. Eszopiclone had no effect on slow wave activity when it was injected during baseline conditions. Analysis of gene expression revealed three distinct patterns: (1) four genes had higher expression in the group of mice with the largest amounts of wakefulness either in the cortex or hippocampus (Arc, Egr1, Egr2, and Egr4), (2) a large proportion of plasticity-related genes had higher expression during recovery sleep after sleep deprivation in the cortex (BDNF, Egr3, grp78, grp94, homer, narp, and Scg2) but not in the hippocamus and (3) six genes had no changes across all conditions (CaMKII, Fra2, MMP9, Neurogranin, Syt4, and tPA). Eszopiclone did not interfere with the expression of plasticity-related genes during recovery sleep period after sleep deprivation in the mouse cortex even at a relatively large dose (20 mg/kg).
Conclusion: This result suggests that synaptic plasticity changes can efficiently occur in the cortex in the presence of eszopiclone.
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CHOLINE ACETYLTRANSFERASE EXPRESSION DURING SPONTANEOUS SLEEP-WAKE BOUTS OVER 24H

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Introduction: There is general agreement that sleep is a time of restoration. The available data indicate that the expression of proteins as-

sociated with energy metabolism, cytoskeletal integrity and oxidation state are associated with sleep that occurs during the latter portion of the day. We hypothesized that the maintenance of critical cellular activities occurs during sleep at different times over a 24 h period. To test this hypothesis, we examined acetylcholine (ACh) synthesis, based on the differential release of ACh across sleep-wakefulness and the role of ACh in a number of higher order behaviors. The activity of choline acetyl¬transferase (ChAT), the protein that synthesizes ACh, was monitored in the entorhinal cortex (EC) across spontaneous sleep-wake bouts over a 24 h period.

Methods: Sprague Dawley rats were instrumented with a femoral catheter and electrodes to record brain and muscle activities. Rats were sacrificed after timed bouts of waking (W), slow wave sleep (SWS) and rapid eye movement sleep (REM) that occurred in three time frames over a 24 h period- at the beginning of the lights-on period, across the middle of the lights-on period and during the lights-off period. A group of freely behaving rats sacrificed within the same time periods served as behavioral and time of day (TOD) controls.

Results: ChAT activity in the EC across individual sleep-wake bouts was dependent on both the time of day and the state of sacrifice. ChAT activity during W bouts was highest during the lights-off period ($p<0.05$). ChAT activity across W/SWS/REM bouts, was highest during REM compared to W at the beginning of the lights-on phase. No changes in ChAT activity were monitored within SWS states across time or when SWS was compared to W or REM sleep states.

Conclusion: Our results support a role for sleep in the maintenance of essential molecules.

Support (optional): HL069706 and NS045791

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OXIDATIVE STRESS IN AN OBSTRUCTIVE SLEEP APNEA POPULATION

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Introduction: Obstructive Sleep Apnea (OSA) is a risk factor for cardiovascular diseases. Patients with OSA have endothelial dysfunction and reduced Nitric Oxide (NO) bioavailability. The expression of endothelial NO synthase (eNOS) in patients with OSA has not been evaluated. Additionally, increased superoxide in the vascular environment may interact with NO producing peroxynitrite, thereby reducing the available NO.

Methods: Patients with OSA (AHI >10) and no clinically manifested cardiovascular disease along with healthy controls were enrolled. Volunteers (n=5) underwent measurement of flow mediated dilation (FMD) of the brachial artery for assessment of NO dependent endothelial function at baseline and 8 weeks after treatment. Percutaneous biopsies were taken from the forearm for measurement of eNOS activity at baseline and conclusion and for nitrotyrosine staining. Endothelial cells were extracted by Laser Microdisection Pressure Catapulting. eNOS expression pre and post treatment was controlled to endogenous b-actin and 18s rRNA primers and to two control volunteers (AHI<5). Immunohistochemical staining for peroxynitrite was done with an anti-nitrotyrosine antibody stain. Slides were scanned digitally and analyzed by a blinded observer using imaging software.

Results: At baseline, OSA patients had FMD of 5.8% (0.3) vs. 10% (0.8) in controls ($p<0.001$). Post treatment FMD increased to 7.4% (0.5) ($p<0.05$). Average Nitrotyrosine Stain density ratio was 36.6 (1.4) in OSA patients vs. 23.3 (1.2) in controls ($p<0.001$) and decreased following treatment to 32.3 (1.3) ($p<0.05$ vs. pre). At baseline, eNOS expression ($\Delta\Delta Ct$) was 6.76 (2.19) fold more than control and decreased post-treatment to 0.77 fold (1.79) ($p<0.05$).

Conclusion: After 8 weeks of treatment, patients with OSA had an improvement in their endothelial function. The improvement in endothelial function was associated with reduced scavenging of NO by super oxide. eNOS levels were elevated at baseline and reduced with treatment. Endothelial dysfunction in OSA is not due to reduced eNOS expression.

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STEM CELL DIVISION IN THE DROSOPHILA TESTIS IS ACTIVATED IN RESPONSE TO SEVERE SLEEP LOSS

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Introduction: It is now well established that quality sleep is absolutely necessary for the performance of various cognitive tasks in higher animals, and roles of sleep are likely to extend far beyond central nervous system. Experimental rats that were forcedly devoid of sleep died and showed multiple pathological signs in different organs among which were the tissues with active cell-renewal, skin and intestine. Tissue homeostasis in multicellular organisms is supported by the set-aside populations of so called stem cells that undergo multiple rounds of mitotic divisions in response to a cell loss in surrounding tissues. Our present work aims to address possible effect of sleep on spermatogonial stem cell function using Drosophila melanogaster as a model object.

Methods: Locomotor activity is monitored for individual flies in DAMS monitors (Trikinetics) and calculated using Matlab software. Testes are dissected out of adult male flies and immunostained using fluorescently labeled antibodies against cell specific and mitotic markers.

Results: We genetically engineered flies that had elevated level of cAMP signaling in the brain and because of this lost 50% of their normal daily sleep amount over one week period of time. We monitored stem cell mitotic activity in their testes and found that there was no change mitotic compare to control flies. However, more significant decrease in daily amounts of sleep characteristic for recently discovered in our lab sleepless mutant led to a 1.5-2 fold activation in number of dividing stem cells. Similar effect on stem cell division was observed after 6 hrs of nighttime sleep deprivation the population of wild type flies.

Conclusion: Severe reduction in total amount of daily sleep stimulates stem cell divisions in the Drosophila testis. In future we plan to look at additional mutant lines that have strongly reduced sleep durations in order to confirmed the results observed in the sleepless mutants.

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SLEEP-DEPENDENT EXTRACTION & CONSOLIDATION OF EPISODIC MEMORY DETAILS

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Introduction: Although the benefit of sleep on procedural-skill consolidation is well established, the role of sleep in declarative memory processing remains incomplete. Using a nap paradigm, here we investigated the impact of wake and sleep on the offline consolidation of ITEM versus CONTEXT memory.
Methods: Participants (n=27) studied two lists of words at 12noon, which were each associated with a different set of contextual cues. Post-learning, subjects were assigned to either a Nap group (n=13), obtaining a 90min sleep opportunity, or a No-Nap group (n=14) which remained awake. Six hours post-learning (6PM) subjects performed a recognition test. For each recognition trial, subjects made two possible responses indicating 1) whether the item was old or new (ITEM-memory), and 2) if old, which study list the item came from (CONTEXT-memory).
Results: No offline difference in ITEM-memory was found between the two groups. In contrast, a significant consolidation benefit for CONTEXT-memory occurred following sleep in the Nap group ($p=0.04$). Furthermore, within the Nap group, the extent of CONTEXT-memory retention was positively correlated with the amount of stage-2 NREM sleep ($r=0.57$, $p=0.04$). Most interestingly, CONTEXT-memory not only correlated with Stage-2 NREM, but a specific electrophysiological signature of NREM-sleep spindles, especially in prefrontal regions ($r=0.72$, $p<0.01$).
Conclusion: The findings clarify the role of sleep in declarative memory processing, indicating that sleep preferentially benefits more hippocampal-dependent aspects of episodic representations (contextual details). Moreover, sleep does not appear to represent a passive time of minimal interference, but a proactive state modulating episodic memory by way of specific electrophysiological oscillations.

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BOLD ACTIVITY ENHANCEMENT DURING NREM SLEEP FOR CONSOLIDATION OF PERCEPTUAL LEARNING

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Introduction: While a growing body of evidence suggests that sleep is beneficial for visual learning, its mechanisms are not clear. Here, we investigated consolidation-related brain activation during sleep subsequent to training of a visual task using fMRI concurrently with measurements of EEG, EOG and EMG to obtain polysomnogram.
Methods: We employed a texture discrimination task (Karni & Sagi, 1992, Nature). Perceptual learning of this task activates only the region in the primary cortex (V1) corresponding to the trained location (Yotsumoto, Watanabe & Sasaki, 2008, Neuron). The experiment consisted of 2 nights' sleep adaptation sessions, the pre-training sleep session for 90 min on the 3rd night, intensive training of the texture discrimination task 6 hours prior to the post-training sleep session for 90 min, followed by the re-test session of the task. To estimate brain activation in the pre- and post-training sleep, we contrasted BOLD signals during NREM sleep before and after training to during wakefulness before each sleep. NREM sleep periods were identified by the standard sleep scoring criteria on the obtained polysomnogram.
Results: The results indicate that brain activation in the trained region of V1 was significantly higher than in the untrained region of V1 in the post-training sleep, but not in the pre-training sleep. Significant performance improvement was obtained in the re-test session after the post-training sleep and was highly correlated with the brain activation in the trained region of V1 in the post-training sleep. Furthermore, the left dorsolateral prefrontal cortex (DLPFC) was significantly more highly activated than the right DLPFC in the post-training sleep and was correlated with activation of the trained region in V1.
Conclusion: These results suggest that during early NREM sleep after training, consolidation of learning occurs in the trained region of V1 under a control by the prefrontal cortex.

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DIFFERENTIAL DISRUPTION OF EXECUTIVE FUNCTION, ON WAKING FROM MORNING AND AFTERNOON NAPS, IN SLEEP RESTRICTED SUBJECTS

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Introduction: The effects of inertia resulting from morning and afternoon naps were assessed by contrasting the post-nap working memory performance of subjects who had taken a nap with waking controls.
Methods: Twice, 1 week apart, 32 healthy subjects (18-30y) restricted their sleep to 6 hours before an 08:30 arrival at the sleep laboratory, when sleep-schedule compliance was assessed using actigraphy. At 09:30, having performed a declarative learning task, subjects performed the Psychomotor Vigilance Task (PVT) and Karolinska Sleepiness Scale (KSS). Subjects were randomized to napping or continuous wakefulness in a parallel group design. Counterbalanced 90-minute Polysomnography (PSG) monitored nap opportunities were scheduled for 10:00 or 15:00. As each subject slept, a yoked-control remained awake at leisure. After napping, both subjects performed blocks of 1-, 2- and 3-back working memory tests 25 minutes apart.
Results: Subjects allocated to the napping and continuous waking conditions reported similar levels of sleepiness (KSS) and were indistinguishable on all PVT measures. PSG showed that sleep propensity was greater in the afternoon: Latency to Stage 2 sleep was shorter (11mins vs 18mins, $p<.05$); Total sleep time was longer (77mins vs 65mins, $p<0.005$), sleep efficiency was higher (86% vs 72%, $p<0.005$) and SWS expressed as a percentage of TST was larger (39 vs 13%, $p<0.005$). Soon after waking, napping subjects performed worse than waking controls but had recovered to waking-subject-levels by the second assessment ($p<0.01$). Separate analyses of the napping group showed sleep inertia was evident only for executive functions tasks (i.e. 2- & 3- back, but not 1-back) and then only following afternoon naps, when sleep pressure was greatest.
Conclusion: Inertia following daytime naps impairs executive function, particularly when naps are taken in the afternoon when sleep pressure is greatest. Subjects who do not sleep show no such variation in performance.
Support (optional): Biotechnology and Biological Sciences Research Council (UK, BBSRC) Air Force Office of Scientific Research (US, AFOSR)

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SLEEP SELECTIVELY ENHANCES HIPPOCAMPUS-DEPENDENT MEMORY IN MICE

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Introduction: Recently, sleep has been implicated in playing a critical role in memory consolidation. Emerging evidence suggests that reactivation of memories during sleep may facilitate the transfer of explicit memories from the hippocampus to neocortex. Prior rodent studies have

utilized sleep-deprivation to examine the role of sleep in memory consolidation.
Methods: The current design uses a novel paradigm to study the effect of sleep on rodent Pavlovian fear conditioning, a task with both hippocampus-dependent and -independent components (contextual vs. cued memories). Mice were trained an hour prior to their inactive/sleep phase or active/wake phase, then tested for contextual and cued fear 12 or 24 hours later.
Results: We found that hippocampus-dependent contextual memory consolidation was enhanced if tested after a sleep period within 24 hours of training. This enhancement was specific to context, not cued, memory.
Conclusion: These findings provide the first behavioral evidence of a role for sleep in enhancing hippocampus-dependent memory consolidation in rodents, and detail a novel paradigm for examining sleep-induced memory effects.

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SLEEP DEPRIVATION AFFECTS MULTIPLE DISTINCT COMPONENTS OF COGNITIVE PROCESSING

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Introduction: The nature of cognitive impairment caused by sleep deprivation is hotly debated. We used a two-choice numerosity discrimination task and applied cognitive modeling to examine sleep deprivation effects on distinct components of cognitive processing. We used the diffusion model, which posits that in the course of response time, noisy information from a stimulus accumulates (drifts) to one of the two decision criteria of the two-choice task. Parameters governing this central cognitive mechanism can be separated from peripheral nondecision components (e.g., motor response), and interpreted in terms of distinct cognitive processes.
Methods: 25 healthy adults (22-38y; 13 women) participated in a laboratory study. After 2 baseline days (10h TIB), subjects were randomized to 62h sleep deprivation (n=12) or a control condition (10h TIB each night; n=13), which was followed by 2 recovery days (10h TIB). At 17:00 during baseline, 48h later after 57h sleep deprivation (or control), and again 48h later after 2 recovery nights, performance was tested on a two-choice numerosity discrimination task. Subjects rated the number (<50 or >50) of a random distribution of 31-70 asterisks in a 10x10 array. Response times and accuracy across 1,200 trials per test were analyzed using the diffusion model.
Results: Mixed-effects ANOVA showed that during sleep deprivation, compared to baseline and recovery and compared to controls, central processing drift rates were significantly decreased. Additionally, sleep deprivation resulted in larger separation between decision criteria; greater variability in decision starting point; more random guesses; and longer and more variable peripheral nondecision components (all $P<0.05$).
Conclusion: Changes in diffusion model parameters revealed that sleep deprivation caused substantial degradation in cognitive processes extracting an estimate of numerosity in the two-choice numerosity discrimination task. When sleep-deprived, subjects also adopted more conservative decision criteria (requiring greater accumulation of information before deciding). Furthermore, they made more random guesses. They were more variable in the peripheral nondecision processes of stimulus detection and/or response execution as well. These results indicate that sleep deprivation affects central cognitive processes and peripheral nondecision processes, with impaired central processing and reduced attentional arousal combining to produce an overall decline in cognitive functioning.
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SDB AND COGNITIVE FUNCTIONS IN THE TUCSON CHILDREN'S ASSESSMENT OF SLEEP APNEA (TUCASA) STUDY; 5 YEARS AFTER INITIAL ASSESSMENT

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Introduction: Sleep disordered breathing (SDB) has been shown to be negatively associated with mental flexibility and other cognitive functions in school-aged children. However, it is currently not known how SDB affects different cognitive functions over time. In this study, we examined how respiratory disturbance index (RDI) and disturbed sleep affect cognitive functions over a five year period.
Methods: 261 children (133 boys and 128 girls, 174 Caucasian and 87 Hispanic) in the TuCASA study (mean age 13.7, SD ± 1.8) underwent in-home polysomnography (PSG) and completed the Wechsler Abbreviated Scale of Intelligence (WASI) an average of 1668.9 (± 288.3) days after their first PSG. RDI (RDI3%) was the number of 3% oxygen desaturation events per hour of sleep. Disturbed sleep (N1) was percent of N1 sleep/total sleep time (TST). Partial correlation analysis was conducted with WASI subscale scores, RDI3% and N1 while controlling for body mass index percentile-for-age (BMI) and TST.
Results: WASI verbal IQ was the only subscale to decrease from time 1 to time 2 (109.3 ± 13.5 vs 106.9 ± 13.8, p=0.001). TST did not change, while RDI3% decreased from 1.09 (± 2.2) to 0.48 (± 0.8); (p< 0.001), and N1 decreased from 4.6 (± 3.3) to 3.9 (± 2.3); p=0.011. BMI increased from 58.5 (± 31.9) to 61.6 (± 31.7); p=0.04. RDI3% at time 1 was negatively correlated with WASI performance IQ (-0.15, p=0.15) and Matrix Reasoning subscale t-score (-0.14, p=0.03) at time 2. N1 at time 2 was negatively correlated with WASI Verbal IQ (-0.15, p=0.015) Performance IQ (-0.15, p=0.017) and Full Scale IQs (-0.17, p=0.006).
Conclusion: SDB may have a lasting negative affect on measures of mental flexibility and cognitive performance. Disturbed sleep at time of testing also has negative effects on measures of cognitive function in school-aged children.
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THE DREAM REPETITION CONTINUUM AND ITS RELATIONSHIP TO WELL-BEING

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Introduction: Studies have shown that people with recurrent dreams, in which the content is always identical from beginning to end, show deficits on measures of psychological well-being. A less extreme form of recurrence is found in the repetition of themes within a series of dreams which are not themselves strict duplicates of each another. We investigated if people who report recurrent dream themes also score lower than non-recurrent controls on tests of well-being.
Methods: Twenty-eight people experiencing "recurrent dreams" in which the content was rated as being rarely or never identical but in which the theme was described as always or often identical were investigated. The control group included 24 subjects who had never experienced recurrent dreams or recurrent dream themes in their adult life. All completed six standard self-report measures of psychological well-being and a 14-day dream log. Dream content reports were scored using the quantitative content analysis instruments of Hall and Van de Castle.
Results: A one-way multivariate analyses of variance (MANOVA) showed that the recurrent theme group had a significantly lower overall level of well-being than the controls. Statistically significant univariate differences existed on four of the six measures of well-being. A one-

way MANOVA on the dream content measures showed that the recurrent theme group had significantly more negative dream content than the control group. Univariate analyses indicated that the dreams of individuals who experienced recurrent dream themes contain a significantly greater proportion of negative dream affect and more dream anxiety.
Conclusion: The data indicate that people who experience recurrent themes show a deficit on measures of well-being, but not to the extent shown by those with recurrent dreams. These results suggest that scores on measures of well-being are inversely related to the position of a dreaming experience on a dream repetition continuum.
Support (optional): Research supported by the Social Sciences and Humanities Research Council of Canada.

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SLEEP PROMOTES LASTING CHANGES IN MEMORY FOR EMOTIONAL SCENES

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Introduction: Here we demonstrate that sleep selectively consolidates emotionally salient components of complex scenes. This effect persists across long delays (24hr and 4mos), but only when sleep follows soon after learning. These long delay conditions provide important controls for circadian and interference influences, because subjects were trained and tested at the same circadian time, and time spent awake and sleeping were equated.
Methods: Subjects encoded scenes with neutral or negative objects on a neutral background. 24hr later, they were tested on memory for objects and backgrounds separately. Forty-five college students (age 18-22) were randomly assigned to the "Sleep-first" group (n=22), which trained and tested on the scenes between the hours of 7PM-9PM, or the "Wake-first" group (n=22), which trained and tested on the scenes between the hours of 9AM-11AM. Four months later, participants were re-contacted and tested again on their memory for the scenes.
Results: Negative, but not neutral, objects were better remembered in the Sleep-First than Wake-First group [$t(42)=2.0$, $p<.05$]. Moreover, the backgrounds associated with negative, but not neutral, objects were more poorly remembered in the Sleep-First than Wake-First group [$t(42)=2.7$, $p=.01$]. Thus, while negative object memory was enhanced in the Sleep-First relative to the Wake-First group, memory for the backgrounds on which they were presented was impaired in the Sleep-First relative to the Wake-First group. Four months later, this pattern persisted, with emotional objects being preferentially retained in the Sleep-First group only ($p<.05$).
Conclusion: The placement of sleep is critical for remembering the components of emotionally negative scenes, but it does not impact memory for neutral scenes. Emotional items are selectively remembered 24hrs and 4 months later, but only if sleep comes soon after learning. Our results suggest that sleep preserves in long-term memory only what is emotionally salient and relevant to future goals.

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COLLEGE STUDENTS' BELIEFS ABOUT THEIR OWN SLEEP CONFLICT WITH SLEEP HYGIENE RECOMMENDATIONS FOR GOOD SLEEP

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Introduction: This study examined college students' beliefs about behaviors and environments that affect their sleep, and their ratings of how easily they could comply with sleep hygiene recommendations for good sleep. The goal was to identify student beliefs that may lessen students' receptiveness to sleep hygiene education.
Methods: Participants were 499 (355 female) students at a Canadian college. Mean age was 21.21 (SD = 5.50). Participants completed online a questionnaire designed for this study that asked how 29 factors affected the student's own sleep (positive, negative, no effect, or do not know), and how difficult it would be to comply with recommendations for good sleep. Items were adapted from the Sleep Hygiene Index and the International Classification of Sleep Disorders' criteria for inadequate sleep hygiene.
Results: Student beliefs about their own sleep were inconsistent with sleep hygiene recommendations in that students were likely to believe that their sleep was not worsened by intense physical exercise at bedtime, getting extra sleep on weekends, doing important or alerting work at bedtime , or using their beds for waking activities such as studying (OR = 1.32 to 2.58). Consistent with sleep hygiene advice, students reported that their sleep was worsened by irregular sleep schedules, by thinking, problem-solving, or worrying in bed, or by going to bed stressed, angry, upset or nervous (OR = 1.83 to 17.44), but that it would be difficult to avoid doing so (OR = 1.17 to 6.69).
Conclusion: Students' beliefs about their own sleep may undermine the effectiveness of sleep hygiene education. First, students' beliefs about factors that worsen their own sleep conflicted with sleep hygiene recommendations. Second, students indicated that they would have difficulty complying with some sleep hygiene recommendations, even though they reported that doing so would have a positive effect on their sleep.

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SLEEP MICROSTRUCTURE (CYCLIC ALTERNATING PATTERN) AND COGNITIVE BEHAVIORAL MEASURES IN NORMAL HEALTHY ADULTS

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Introduction: Based on previous findings, we hypothesized that the overall Cyclic Alternating Pattern (CAP) rate is correlated with cognitive performance; we also predicted that CAP A1 is positively correlated with cognitive functions, especially those related to frontal lobe functioning. For this reason, we correlated objective sleep parameters with cognitive behavioral measures in normal healthy adults.
Methods: Eight subjects (mean age 27.75 years) were recruited and 2 nocturnal polysomnographies were carried out after an adaptation night. A series of neuropsychological tests were performed by the subjects in the morning and afternoon of the second day and in the morning of the third day. Raw scores from the neuropsychological tests were used as dependent variables in the statistical analysis of the results. Partial correlations between sleep microstructure parameters and indices of cognitive functioning were performed.
Results: CAP rate was positively correlated with visuospatial working memory, planning and motor sequencing, and the retention of words (HVLT). Conversely, CAP was negatively correlated with visuospatial fluency. CAP A1 were correlated with many of the tests of neuropsychological functioning, such as verbal fluency (COWAT), working memory (Digit Span - Backward test), and both delay recall and retention of the words from the HVLT. The same parameters were found to be negatively correlated with CAP A2 subtypes. CAP 3 were negatively correlated with planning and motor sequencing.
Conclusion: To our knowledge this is the first study indicating a role of CAP A1 and A2 on cognitive performance of healthy adults. The results suggest that a high rate of CAP A1 might be related to higher performances in healthy individuals whereas a high rate of CAP A2 subtypes might be accompanied by lower performances at cognitive testing.

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INCREASE IN REM SLEEP AND MORNING CORTISOL DURING EMOTIONAL LEARNING IN CYBERTHERAPY FOR SPECIFIC PHOBIA

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Introduction: We report on a study of the effects of emotional learning through cybertherapy for specific phobia on sleep and cortisol levels.
Methods: Nine phobic subjects (PS) were recorded for five consecutive nights, and three controls subjects (CS) for four consecutive nights. The first night was for adaptation, the second for baseline (BN). The third and fourth day the PS underwent an intensive therapy using virtual reality (VR) (experimental nights, EN1 and EN2). The CS had only one session of VR (EN1). The follow up night (FN) was the fifth for the PS and the fourth for the CS. Daytime cortisol was measured throughout the study.
Results: All PS exhibited an increase in REM sleep% (REMS%) from BN to EN1. Six out of nine slightly increased REMS% from EN1 to EN2 and seven out of nine from EN2 to FN (overall averages respectively; 21.8%, 26.7%, 27.1%, 28.5%). No systematic changes were noted in other sleep stages. The CS did not show changes in REMS (overall averages respectively; 26.4%, 25.2%, 25.6%). Typical circadian levels of cortisol were maintained for CS. For the PS, there was a major increase about 30 min after bed rise (CS=8.2nmol/l vs PS=19.5nmol/l) on the mornings prior to VR. Moreover, cortisol increased from 4PM to bedtime instead of the usual decrease (CS=2.5nmol/l to 0.6nmol/l; PS=1.5nmol/l to 2.8nmol/l).
Conclusion: Despite this small sample, these results suggest that REMS is involved in the processing of emotionally charged information such as during cybertherapy for specific phobia. Moreover, the increases in REMS did not seem to be due to the VR novelty nor the increase in visual stimulation since the CS did not exhibit any REMS changes. Whether the prior increases in cortisol in the PS enhanced emotional learning or is linked to the REMS% increases needs to be further investigated.

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THE UPS AND DOWNS OF MARRIAGE: A BUMPY ROAD FOR SLEEP?

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Introduction: Epidemiological studies have shown that married individuals sleep better than unmarried individuals. However, these studies typically assess marital status cross-sectionally, and reveal little about how relationship histories or the stability of relationships influences sleep. We examined how relationship transitions, including the gain or loss of a partner, may impact sleep.
Methods: Participants were 291 middle-aged, African American and Caucasian women (M age= 51 years) enrolled in the Study of Women's Health Across the Nation (SWAN) Sleep Study. Participants reported their current relationship status at annual visits. In-home polysomnographic (PSG) sleep studies were conducted over 3 successive nights (6 to 8 years after baseline). Participants also wore actigraphs for approximately one month. PSG- and actigraphy-assessed sleep efficiency (SE), and subjective sleep quality (PSQI) served as the primary outcomes. We examined the cross-sectional association between marital status (married/ unmarried) and sleep outcomes. We also examined the association between relationship histories and sleep, by analyzing sleep differences between women who were always married, always unmarried, or those who experienced a relationship status transition (gained or lost a partner) over the follow-up period. Covariates included age, ethnicity, and depressive symptoms.
Results: Cross-sectionally, married women had better subjective sleep quality and PSG SE sleep compared to unmarried women ($p < .05$). Significant differences were found among the relationship history categories, with the "lost a partner" group showing the lowest subjective sleep quality and the "gained a partner" showing the highest quality ($p's < .05$). There was a marginal difference in PSG SE, with the "lost a partner" group showing the poorest SE and the "always married" showing the highest ($p = .08$).
Conclusion: These findings highlight the utility of examining the cross-sectional and cumulative effects of relationship histories on women's sleep. Being stably married or gaining a partner is associated with better sleep than being unmarried or losing a partner.
Support (optional): The Study of Women's Health Across the Nation (SWAN) has grant support from the National Institute on Aging, the National Institute of Nursing Research (NINR), and the NIH Office of Research on Women's Health (ORWH) (Grants NR04061, AG012505, AG012554, AG012546, AG019360, AG019361, AG019362, AG019363) and by the National Institutes of Health (NIH) (RR00056 and RR023506). The content of this abstract is solely the responsibility of the authors and does not necessarily reflect the official views of the NIA, NINR, ORWH, or the NIH.

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EDUCATIONAL MESSAGE FRAMING IMPROVES ADHERENCE TO CPAP AT 30 DAYS

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Introduction: Continuous positive airway pressure (CPAP) is known to be highly efficacious in mitigating the acute physiologic responses to OSA. However, CPAP treatment is associated with suboptimal and variable rates of adherence. Importantly, patterns of CPAP use are established quickly, often within the first week of therapy, and are not easily altered after that initial exposure. To date, no reliable or modifiable variables or technological advancements have been shown to consistently improve CPAP use.
Methods: 55 patients with pre-existing cardiovascular disease, newly diagnosed with OSA, and with no previous CPAP experience were enrolled at the time of the second PSG. Validated instruments on sleepiness, dispositional optimism, depression, and self-efficacy were administered. Following completion, participants were randomized to receive supplemental education about CPAP, from either positive (focusing on good outcomes associated with using CPAP) or negative (emphasizing the consequences of untreated OSA) framing formats. After 30 days of home CPAP use, the instruments were re-administered, and adherence data was retrieved from the device.
Results: Participants receiving negative educational messages were more adherent to CPAP at 30 days ($p=0.015$). When examining the interaction effects of message framing and time, those randomized to negative messages had statistically significant reductions in sleepiness and improvements in optimism and self-efficacy, compared to the positive message framing group.
Conclusion: Patients routinely make decisions about treatment recommendations based simply upon how information is presented to them. Negative message framing appears to be a viable and straightforward approach to improving adherence to CPAP.

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SLEEP AND THE RELATIONSHIP TO MOOD IN A HEALTHY ADULT SAMPLE

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Introduction: Mood depends on all kinds of events and impressions. We hypothesize that a person's mood is related to the sleep of the night before. Studies that found evidence for this hypothesis often rely on single measurements of mood, whereas mood may fluctuate during the day. Therefore, we measured mood throughout the day. In addition, most studies investigate between-subject effects, whereas we also studied within-subject effects to increase the study's reliability. Following people for more than one night and day combination allows to control for individual differences, for example in sleep need.
Methods: Twenty-four participants (9 female, aged 30-55, without sleep problems, no shift-workers) took part in the study which lasted one week, including weekend days-off. During the night participants wore a SenseWear PRO3 Armband. Each morning the participants filled out a sleep diary. Eight times a day a mood survey was completed on a PDA. The independent variables TST, SOL, and WASO were measured both objectively (SenseWear) and subjectively (diary). Subjective Sleep Quality (SQ) was rated on a seven-point scale, ranging from very bad to very good. Mood was measured using six bipolar mood items (e.g., agitated-calm). Mixed linear models were used to analyze the data both between-subjects and within-subjects.
Results: Subjective and objective measurements of the same sleep parameter correlated, but were not the same. Above all, day-to-day variations in subjective SQ, TST, and SOL affected mood. Between subjects, subjective SQ and WASO related to mood. Contrary, objective measurements practically did not relate to mood. Further, sleep quality was better during nights preceding a day off than during nights preceding a working day.
Conclusion: A person's sleep affects day-to-day fluctuations in mood, despite all kinds of events and impressions that also influence mood during the day. Further, we found that subjective perceptions of sleep are more important for mood then objective parameters.

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DIURNAL PATTERNS OF RISK TAKING: PRELIMINARY RESULTS

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Introduction: Extensive research has shown that cognitive functioning in adults shows a distinct circadian pattern. Recent work has shown that sleep deprivation affects risk taking behavior; however, no research to date has examined whether there is a diurnal or circadian pattern to risk taking.
Methods: As part of an ongoing study, 40 subjects (26 females; mean age 18.7, SD = 1) completed the Balloon Analog Risk Task (BART) at two time points: approximately four hours after awakening and approximately 16 hours after awakening. These time points were chosen to approximate high and low points in the wakeful portion of the sleep-wake circadian rhythm. In the BART, subjects earn money for each time they pump a virtual balloon up, but with each pump the risk of the balloon popping (resulting in no money earned) increases. The main outcome measure for the BART is the adjusted total number of times the balloon was pumped up.
Results: A repeated measures ANOVA revealed a trend towards subjects pumping the balloon up more during the night-time session (16 hours after awakening) than during the daytime session (4 hours after awakening; $p = 0.07$). This result represents a small to medium effect size (Cohen's $d = 0.28$).
Conclusion: While these data are preliminary, results indicate that subjects are more likely to take risks after 16 hours of wakefulness (as the circadian phase declines), than after 4 hours of wakefulness (during the height of their circadian phase). Two time points may be insufficient to fully elucidate the circadian pattern of risk taking. Future research should assess the effect of circadian phase of risk taking across multiple time points. In a society in which individuals are awake and working at all hours of the day, identifying a circadian pattern of risk-taking has important implications for public health and safety.
Support (optional): This research was supported by a grant from the Social and Behavioral Sciences Research Institute at the University of Arizona.

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THE EFFECTS OF AN IMMEDIATE NAP VERSUS A DELAYED NAP ON DECLARATIVE MEMORY CONSOLIDATION

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Introduction: We previously showed that a 90-min daytime nap immediately following learning facilitated the consolidation of declarative memory. Here, we examined the importance of the timing of the nap episode relative to the end of the learning session, i.e. an immediate nap vs. a delayed nap, in subsequent recall performance and the speed of memory retrieval over a 7.75-hr retention interval.
Methods: Thirty-two participants (mean age = 22.50; SD = 2.98) attended two laboratory sessions where each time, they learned 40 semantically related and 40 unrelated word pairs, and baseline cued recall performance was measured 0.25hr after learning. In one session, immediately after baseline assessment, the nap group ($n = 16$) was given a 90-min nap opportunity, while the wake group ($n = 16$) remained awake prior to a second memory assessment. In the other session, the nap / wake treatment was delayed until 5.50hr after learning (preceded by a second assessment). A third cued recall test was administered at the end of the 7.75-hour retention interval. Note that while one quarter of the word pair stimuli were included in all three recall tests (repeated pairs), the rest were presented just once during the retention interval (unique pairs).
Results: If the nap / wake treatment was administered soon after learning, the wake group demonstrated reliable forgetting of unique related word pairs across the 7.75-hour retention interval (mean ± SD: 9.00 ± 1.21 in first recall vs. 8.19 ± 1.22 in third recall, $t(15) = 3.90$, $p < .01$). Such forgetting was negligible in the nap group (8.69 ± 0.66 vs. 8.63 ± 1.75, $t(15) = .14$, $p > .05$). Furthermore, the amount of NREM sleep of the immediate nap episode was related to greater reduction in reaction time for the correct recalls of unique unrelated word pairs, i.e. faster retrieval, across the entire retention interval ($r(11) = .69$, $p < .01$). These beneficial effects of daytime napping, however, were not observed if the nap had been delayed to several hours after the end of learning.
Conclusion: A daytime nap immediately following learning, relative to a delayed nap, provided more benefits on subsequent declarative memory retrievals, pointing out the importance of the timing of the nap episode in maximizing the effects of sleep in declarative memory consolidation.

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THE EFFECT OF THE FAST AND SLOW TEMPO MUSIC ON SLEEP INERTIA AND AROUSAL

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Introduction: Sleep inertia (SI) is a transitional state occurring immediately after awakening from sleep and producing sleepiness, less alertness and decrement in subsequent performance. It has been suggested that SI may be due to a decline in arousal level. Therefore, it was hypothesized that factors likely to increase arousal would reduce the effects of SI. Previous studies showed that fast-tempo music may enhance the level of arousal. The present study was conducted to clarify the role of arousal in SI by exposed to music with different tempos.
Methods: Twelve healthy young adults, aged 18 to 31 years, participated in the study. All the subjects participated in three conditions: fast-tempo music, slow-tempo music, and control (no music) condition. Musical stimuli were applied after a 20-mins nap, and the subjects were given an addition task and asked to rate their level of subjective sleepiness and arousal on the Karolinska Sleepiness Scale (KSS), visual analog scales (VAS) and the Self-Assessment Manikin (SAM) 6 times during an hour.
Results: The effects of SI on cognitive throughput and subjective ratings were evident. Subjective sleepiness was significantly reduced and subjective arousal level measured by SAM was elevated when the participants were exposed to fast-tempo music. However, cognitive throughput was not influenced by musical stimuli.
Conclusion: The present findings suggest that increased arousal level during SI by manipulating music stimuli may decrease subjective sleepiness but have no impact on cognitive performance. This dissociative effect suggests that the dissipation of sleep inertia may not be a function of a general arousal level. Rather, there may be multiple underlying processes that are responsible for different aspects of SI.

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MEMORY CONSOLIDATION DURING SLEEP AND EEG SPECTRAL ANALYSIS IN PRIMARY INSOMNIA

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Introduction: Compelling evidence indicates that healthy sleep contributes to the consolidation of new memories. The aim of this study was to test the hypothesis that ongoing hyperarousal processes during sleep as indexed by EEG beta activity mediates previously shown deficits in memory consolidation during sleep in patients with primary insomnia.
Methods: General neurocognitive and memory performance (procedural mirror-tracing task, declarative visual and verbal learning task) was assessed before and after one night of polysomnographic monitoring in 18 patients with primary insomnia (7 men, aged 45.5±4.5 years) and 34 sex, age and IQ matched healthy subjects. EEG spectral analysis was performed for epochs of NREM sleep.
Results: Insomnia patients showed a significantly increased EEG beta activity during NREM sleep (16-32 Hz), decreased overnight procedural memory consolidation (MANOVA, $p<0.05$, large effect size), and a non-significant attenuation of declarative verbal and visual memory consolidation (MANOVA, medium effect size) compared to healthy subjects. In the current sample, no significant correlation between EEG spectral power in the standard frequency bands, including EEG beta activity, and overnight memory consolidation was observed.
Conclusion: The results suggest that primary insomnia is associated with a significant impairment of procedural memory consolidation and a less pronounced impairment of declarative memory consolidation during sleep. The observed increased EEG beta activity in insomnia patients compared to healthy subjects is consistent with the hyperarousal hypothesis of insomnia. It seems plausible that ongoing hyperarousal processes during sleep disrupt sleep-related memory consolidation. The absence of a significant correlation between these parameters may be due to the small homogeneous study sample.

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EXTENDED SLEEP IN SLEEPY NORMALS IS ANALGESIC

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Introduction: Variations, both increasing and decreasing, in bed time and associated sleep time directly impacts level of daytime sleepiness. We have shown that decreasing sleep duration is hyperalgesic, so we sought to determine whether or not sleep recovery in sleepy, healthy adults is analgesic.
Methods: Eighteen healthy adults, 18-35 years old, with sleep efficiencies >85% on a 8-hr screening NPSG, no sleep disorders, and an average MSLT of < 7 min participated. They were randomly assigned to a sleep extension (EXT) or a habitual sleep (HAB) group. The EXT group spent 10 hrs in bed each of four nights and the HAB group maintained their one-week diary reported sleep schedule for four nights. Standard MSLTs (1000, 1200, 1400 1600 hrs) and pain assessments were done on baseline (Base) and experimental day 4 (Exp4). Pain sensitivity assessments were done at 1030 and 1430 hrs using a radiant heat stimulation method. At each assessment finger withdrawal latency in seconds (FWL) was measured for 5 randomly presented heat intensities directed to the index finger pad of each hand.
Results: MSLT increased in EXT (Base= 4.7 ± 2.72; Exp4=10.1 ± 4.43 min), but not HAB subjects (Base= 4.6 ± 3.77; Exp4=5.0 ± 3.48 min) (group x day interaction, $p<.02$). As hypothesized, FWL increased as a function of extended time in bed in the EXT group, but not in the HAB group. Mean daily FWL in EXT subjects was Base=7.8 ± 1.83 and Exp4=10.0 ± 2.98 sec and in HAB subjects Base=8.5 ± 2.20 and Exp4=8.5 ± 1.76 sec (group x day interaction, $p<.03$).
Conclusion: These data are the first to show the analgesic effects of improved alertness as a result of sleep extension in sleepy pain-free normals. It suggests that pain sensitivity is modulated by level of sleepiness/alertness.
Support (optional): The Fund for Henry Ford Hospital, B10914 awarded to Dr Roehrs

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A FOUR-NIGHT SLEEP EXTENSION NORMALIZES MSLT IN SLEEPY NORMALS

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Introduction: About 20% of the population is sleepy, as defined by MSLT, mostly due to mild chronic sleep restriction. In previous studies, we showed that 7-14 nights of increased sleep by extending bedtime increased MSLT, but only 70% of the subjects improved. This study attempted to replicate and extend our previous results by assessing nightly sleep over 4 nights of extended bedtime.
Methods: Twenty-four healthy adults, 18-35 years old, with normal sleep participated. Each underwent a screening 8-hr NPSG and standard MSLT (1000, 1200, 1400, 1600 hrs) the following day. All had sleep efficiencies of >85% on their NPSG and MSLT of <7 min. They were randomized to extension (EXT: 4 nights of 10hrs bedtime) or habitual sleep (HAB: 4 nights of 1-week diary-reported bedtimes) groups. Standard MSLTs were done after the 8-hr bedtime nights (Base) and after the fourth night of bedtime manipulations (Exp).
Results: The MSLT was increased in the EXT group, Base=4.53 ± 0.71 min, Exp=9.58 ± 1.32 min, but not in the HAB sleep group, Base=4.09

± 0.98 min, Exp=5.30 ± 1.07 min, (group by day interaction: F=5.56, p<0.03). The average nightly hours between EXT (8.90 ± 0.12 hrs) and HAB groups (7.14 ± 0.18 hrs) differed (p<0.01). Not all EXT subjects (n=3) improved and some in the HAB group (n=3) improved, (MSLT increase >2.5 min). Regardless of group assignment the average nightly sleep of the MSLT improved group differed from those not improving (8.58 ± 0.25 vs 7.46 ± 0.27 hrs, p<0.01), respectively. The correlation between change in MSLT and average nightly sleep was (r=.41, p<0.05).
Conclusion: These data show that four nights of increased sleep will normalize MSLTs, but 25% do not benefit. Those improving get 1 hr of additional nightly sleep.
Support (optional): The Fund for Henry Ford Hospital, B10914 awarded to Dr Roehrs

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THE IMPACT OF UPLIFTS ON SLEEP QUALITY

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Introduction: Psychological literature has focused on how stress and psychopathology affect sleep quality. Recently, there has been a growth of interest in positive psychology and factors that play a protective role in sleep. Uplifts (events appraised as pleasant) are thought to positively influence health. However, the impact of frequency and intensity of uplifts on sleep quality is poorly understood. We examined the relationship between daily uplifts and sleep quality.
Methods: 104 healthy adults were recruited as part of a larger study examining the relationship between stress, health and sleep. The frequency and intensity of daily hassles and uplifts was measured with the Combined Hassles and Uplifts Scale (CHUS) and sleep quality was assessed with the Pittsburgh Sleep Quality Index (PSQI). Candidate predictors {depressed mood, body mass index (BMI), socioeconomic status (SES), age, ethnicity, gender, frequency and intensity of daily hassles and uplifts} were assessed. Those predictors that had a simple significant correlation with PSQI global score were included in subsequent hierarchical regression analysis.
Results: Older age, higher BMI, lower SES, higher depression scores, and more reported daily hassles were all related to higher PSQI. Increased levels of Uplift Intensity was related to lower PSQI. With PSQI as the dependent variable, the overall hierarchical regression model was significant (R2 = .44, p< .01). Age, ethnicity and BMI explained 12% of the variance in sleep quality (p=.02); depression and SES explained an additional 25%, (p< .01) and Uplift Intensity explained an additional 6% (p< .01). After controlling for covariates, depression scores (p<.01) and Uplift Intensity (p<.01) remained significant individual predictors of PSQI.
Conclusion: Results suggest that higher scores of Uplift Intensity are significantly related to better sleep quality even after controlling for a number of covariates. Future research should examine whether these results can be integrated into treatment regimens for poor sleep.
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IMAGING MOTOR LEARNING BEFORE AND AFTER SLEEP

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Introduction: Acquisition of skilled motor task performance is enhanced by sleep. Early learning has been hypothesized to depend on a large frontal, parietal, striatal and cerebellar network, while consolidated learning is codified in a reduced network involving cerebellar, motor and parietal cortices. As sleep consolidates learning, we tested the hypothesis that similar shifts in network activations appear in learned task performance following sleep.
Methods: Healthy, right-handed volunteers participated in 2-evening functional magnetic resonance imaging (fMRI) of a serial reaction time (SRT) task with re-testing 24 hours later. Stimuli consisted of 4 squares arranged horizontally on a screen to which subjects responded in 45-second blocks by button press with the right hand (a repeating tap block) alternating with the left hand (2 random blocks, 8 fixed sequence, 2 random). The subject was cued to begin learning the fixed sequence. Learning was assessed by reaction time (RT) increase between the final random and the last learned sequence blocks.
Results: All subjects (9/13 retained, 5 male) reported normal sleep quality (PSQI; 3.4±2.7, n=10) and duration (7.78±0.96 hours) in agreement with actigraphy obtained between scans (7.83±1.09, p=0.85). Task performance (RT) improved within session (p<0.005), but did not differ significantly across days. Within-session learning was marginally greater during day 1 (p>0.1). Final performance on day 1 versus initial performance on day 2 was unchanged (p=0.15); so knowledge of the learned sequence was retained following sleep. Consolidated task performance resulted in increased motor and parietal activity, a decrease in cerebellar activity, and no change in striatal activation.
Conclusion: In keeping with the tested hypothesis, consolidation resulted in increased motor and parietal activity. However, neither striatum nor cerebellum followed this pattern. Thus, consolidated task performance relied heavily on a parietal-motor network.

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GENDER DIFFERENTIALS IN SLEEP DISORDER: AN ANALYSIS USING KOREAN TIME DIARY DATA

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Introduction: In this study, we claim that sleep needs to be recognized as one of the important social product. In order to gather some insights of sleep as social phenomena, our study focused on the gender differentials in sleep patterns. We assumed if we can examine gender differences, where gender role is still a critical factor in charting men and women's life course, the inequality might reflect into individual sleep hours. Using the representative data, we investigated the sleep pattern by gender and tried to explain the difference. Not only we examined the average sleep hour differences, but we also compared the prevalence of short sleep and over sleep pattern, in order to estimate the health effect.
Methods: From the original data of 2004 Korea Time Diary Survey from KNOS (Korean National Office of Statistics), we constructed a data set of 37,406 respondents (women, 50.2%), between age 25 to 60. In the orginal data respondents were asked to write the 24 hours time diary, during two days. Dependent variable was night time sleep and we tested the sleep pattern dividing into short sleep(less than 6 hours), over sleep(more than 9 hours), and mid-range sleep. We tested diverse analysis including regression and multinomial model. Socio-demographic variables, activity times as well as work and family variables were employed as a independent variables to the model.
Results: According to our results, women slept less than men by average of 10 minutes (t=11.06, p<.001). Estimating the sleep disorders, women were more likely to be classified to short sleepers rather than over sleepers. The difference was diverse in terms of age and the date. The 10 minutes gap remains during weekdays but not on Sunday. We could observe U shape pattern in women's case, which was not apparent in men's case. The gender gap widened when women and men reach their 40's. Results of the regression and multinomial regression showed that the gender difference in sleep pattern could be explained partly by

the varied effects of time schedules, and the social roles that men and women hold throughout their life course.
Conclusion: Gender inequality in sleep hours and sleep disorder were apparent in our study. Also other structural and social factors were related in this gendered reality. The results imply that "gendered" course of life can be stretched out, even when people are asleep.

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THE TIME OF OUR LIVES: WORK, SLEEP AND TELEVISION

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Introduction: Sleeping less than 7-8 hours daily impairs alertness and is associated with increased obesity, morbidity and mortality. Yet 40% of US adults do so. Population data indicate work time is the primary activity reciprocally related to sleep time. However, reducing work time and its economic benefits in order to increase sleep time may not be feasible for most of the population. Waking activities under discretionary control and adjacent to the sleep period may be a better source for increasing sleep time. We investigated this issue using the American Time Use Survey.
Methods: American Time Use Survey data from 23,791 respondents aged 15 or older were pooled for the years 2003-2006 to explore activities in 2h periods immediately before and after bed time for sleep. Those who worked for compensation were divided into long workers (LW: ≥8h/day) and short workers (SW: <8h/day), and compared to each other and to non-workers (NW).
Results: LW terminated bed time an average of 0.68h earlier than SW ($p<0.0001$) and 1.31h earlier than NW ($p<0.001$) on the interview day, but time of going to bed did not differ among groups (22:37h vs. 22:42h vs. 22:37h, respectively, $p=0.385$). Watching television was the primary activity people engaged in before going to bed, accounting for 55.6min (46.3%) of the 2h pre-sleep period. In the morning, travel time and work time increased steadily towards the end of the post-awakening 2h period, accounting for 14.8% and 12.3%, respectively.
Conclusion: Watching television may be an important Zeitgeber for the time of going to bed. Watching less television in the evening and postponing work start time in the morning were the activities most likely to reduce chronic sleep debt. While the timing of work may not be flexible, giving up some TV viewing in the evening should be possible to promote adequate sleep duration.
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NAP AND RELATIONAL MEMORY - A DAYTIME NAP FACILITATES EXTRACTION OF GENERAL CONCEPTS

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Introduction: Whereas numerous studies provided insight to sleep's effect on declarative, procedural and perceptual memory tasks, we still know little of the fundamental role of sleep in relational memory - the ability to make indirect associations based on items learned in separate occasions, to extract rules and to generalize. The present study investigated the effect of a daytime nap on a relational memory task that requires extraction of a general concept.
Methods: Participants learned English meanings of Chinese characters, consisting of groups that shared the same left components called the radicals. Each radical represents a certain general concept. Characters sharing the same radical have related meanings. After either a daytime nap or a period of wakefulness, participants were first to match the English meaning to a given character in a multiple-choice task (MC task). However, the task consisted some new characters, which the participants had not seen before but shared the same radicals as the old characters. The choices were selected so that if the participants had extracted the concept of the radical, they would have been able to deduce correct answer even if they had not been exposed to that given character before. Then, they were asked to state explicitly the meaning of isolated radicals (radical task).
Results: In the MC task, the nap group performed better than the no-nap group. Importantly, they performed better on the new characters with a near significance ($t=2.04$, $p=0.056$) than the no-nap group. They also performed significantly better on the radical task ($t=2.46$, $p=0.011$).
Conclusion: The results suggest a nap facilitates reorganization of memory networks that underlie the extraction of general concepts from discretely learned items.

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FAMILY INFLUENCE ON ADOLESCENT SLEEP SCHEDULES

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Introduction: Most research on adolescent sleep has focused on the sleep of teens "in a vacuum," not taking into account the family situations and sleep schedules that surround these adolescents. This study explores familial influences, including household composition and sleep patterns of parents and siblings, on adolescent sleep schedules.
Methods: As part of a larger study, data on family sleep patterns were collected from 14 and 15-year old adolescents (N=30, 15 males) during an individual interview about sleep. Bedtimes represent usual weeknight sleep. Data were analyzed in SPSS using bivariate correlations and one-way ANOVA to determine relevant factors and further explored using multivariate analysis.
Results: Mother's bedtime ($r=.560$, $p=.003$), father's bedtime ($r=.551$, $p=.018$), and younger sister's bedtime ($r=.674$, $p=.047$) are positively correlated with adolescent bedtime. Adolescents whose household consists of just a parent and themselves have a later mean bedtime, going to bed 30 minutes later than adolescents in two-parent households, after adjustment for the presence of siblings. Presence of an older sibling shifts adolescent bedtime an average of 33 minutes earlier, while presence of a younger sibling shifts adolescent bedtime 10 minutes earlier.
Conclusion: Although rarely analyzed, family situations and sleep patterns of family members exert an important influence on adolescent bedtime. Though it is possible that parents (and younger sisters) take their bedtime cues from the adolescent in the household, it is more likely that adolescents follow their parents' lead with regard to appropriate sleep timing. In addition, education about sleep in school may benefit children of single parents more than adolescents who live with both parents because they are more likely to control their own bedtime and stay up later. Finally, the sibling effects may be explained by parents enforcing a bedtime for younger children while the oldest child may have more freedom to set their own schedule.

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INFLUENCE OF METEOROLOGICAL AND GEOMAGNETIC VARIABLES, MOON CYCLES, POLLUTANTS AND OTHER ENVIRONMENTAL FACTORS ON SUBJECTIVE SLEEP

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Introduction: This web-based study sought to establish a possible relationship between sleep and environmental factors
Methods: Upon anonymous registration subjects answered a 27-item questionnaire (gender, weight, height, general health status, sleep habits and disorders) and Epworth scale. Every morning during 3 weeks, they

answered a 17-items questionnaire about their sleep.. Parameters collected: 1) Weather (relative humidity H, temperature T, barometric pressure B, wind speed, precipitation, sunshine SL). 2) Pollutants (CO, NO2, NOx, PM-10) 3) Pollen (Birch, Juniper, Pine, Quercus and Sallow) 4) Global and geomagnetic (water tide, moon phase (M), solar winds (SW) and flux (SF), solar spots, geomagnetic radiation).
Results: 125 subjects completed the study (54 men 71 women). T, H, B, M, SF, SW affected dreams occurrence specially in young adults and men. Pleasant dreams had a negative correlation with B (ρ -0.70, P <0.005) but also T and H, and a positive one with M (ρ 0.80 P < 0.005). Pollen increase yielded 24 hours later mainly in women to unpleasant dreams (ρ 0.75 P < 0.005) and awakenings shortly after falling asleep (ρ 0.61 P< 0.005). There was a negative correlation between SL intensity and awakenings (ρ - 0.69 P<0.005) and a positive one between changes in T and sleep latency (ρ 0.52, P<0.05). There was a negative correlation between B changes and feeling refreshed in the morning, specially if changes occurred 24 hours earlier (ρ -0.71, P<0.005), more in men (ρ -0.83, p< 0.005). There was a positive correlation between feeling refreshed and M specially in men (ρ 0.66 P < 0.005). Middle aged, snoring men, with daytime sleepiness, high BMI were more affected by B with more awakenings (ρ 0.57, P< 0.005). Windy weather yielded to awakenings in women (ρ 0.68, P<0.005).There was a positive correlation between SW and increased tiredness specially for men (ρ 0.63, P < 0.005) Changes in weather the 2 or 3 preceding days did not affect sleep.
Conclusion: Environmental factors seem to have an impact on subjective sleep.

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SELF-REPORTED SLEEP DURATION, SLEEP QUALITY AND DAYTIME FUNCTIONING AMONG CHINESE UNIVERSITY STUDENTS

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Introduction: Self-report data suggests that habitual short sleep duration is associated with difficulty initiating or maintaining sleep. In contrast, studies of polysomnographically determined sleep suggest that short sleepers may have more efficient sleep (e.g., reduced sleep latency). We collected self-reports of sleep duration in Chinese students and examined the relationship of sleep duration to perceived sleep quality and daytime functioning.
Methods: The subjects were 1066 first year undergraduate students (male 617 and female 449, age 19.7±0.99 (18-23) years old) at three universities in Xi'an. They were administered a modified Sleep Habits & Problems Questionnaire to collect self-report information regarding sleep habits and quality, and daytime functioning.
Results: Reported mean nightly sleep duration for all students was 6.8±0.9 and 8.1±1.3 h for weekdays and weekends, respectively. Based on sleep duration, the students were divided into short sleepers (SS, ≤ 6 h, 34.4%), intermediate sleepers (IS, 6.1-7.9 h, 48.4%) and long sleepers (LS, ≥ 8 h, 17.2%). Compared to LS and IS, a significantly greater percentage of SS reported having difficulty in falling asleep (SS 39%; IS 17%; LS 9%), being easily awakened, early awakening, morning sadness, daytime sleepiness and problems with focusing. SS students (n=367) were further divided on the basis of reporting difficulty (39%) or no difficulty (61%) in falling asleep. SS with difficulty in falling asleep also reported greater sleep related difficulties (e.g., being easily awakened: 15% vs. 3%; early awakening: 18% vs. 7%; sadness: 18% vs. 10%; and daytime sleepiness: 33% vs. 21%).
Conclusion: Consistent with polysomnographic studies, some SS individuals reported "good" sleep with minimal or no functional impairments. However, a higher percentage of SS individuals also reported greater problems in initiating and maintaining sleep and poorer daytime performance. This suggests that short sleep duration in this population may occur both with and without sleep or performance problems.

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COGNITIVE VULNERABILITY IN THE DEVELOPMENT OF CONCOMITANT PAIN AND SLEEP DISTURBANCES

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Introduction: Reviews of the pain and sleep literature implicate similar cognitive and behavioral processes in the maintenance of symptom reports of chronic pain and insomnia. The present study uses a cognitive behavioral framework to explore the idea that people with concomitant pain and sleep disturbances share a common cognitive vulnerability.
Methods: A longitudinal classification of people (N=592) in a community sample reporting on symptoms of pain and sleep at baseline, 3 and 12 months after the initial survey. Cluster analysis was used to classify people reporting different degrees of symptoms, and their endorsement of cognitive behavioral processes and consequences at each time point. Groups in similar clusters were linked at adjacent time points to document patterns of stability and change. The clusters are described at baseline on a range of psychological indices not used to form them (Perceived Stress, Positive/Negative Affect, Anxiety and Depression). Stability and change was corroborated with the same variables.
Results: Cluster analyses resulted in six homogenous and distinct profiles at each time point. Linking the clusters over time showed partial individual stability in cluster membership at adjacent time points. Elevated levels of Catastrophizing as well as avoidant Safety Behaviors of a cognitive and behavioral orientation were endorsed by a group with the most stable response pattern in the sample who reported both pain and sleep related interference.
Conclusion: The character and partial individual stability of symptom cluster membership suggests that problems with pain and sleep may share mutually maintaining cognitive behavioral processes and consequences. It may be that for some people avoidant strategies during the day as well as at night are enhanced in the presence of concomitant problems with pain and sleep. Future research should examine the utility of identifying mutually maintaining factors in the treatment of concomitant pain and sleep disturbances.

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EPIC DREAMING: A REPORT OF THREE PATIENTS

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Introduction: Epic dreaming (ED) is a disorder of unknown origin that has been reported in two full-length articles and two abstracts. It is characterized by dreams that are experienced as excessive and continuous throughout the night, resulting in daytime fatigue. We report the clinical and polysomnographic features of three patients with ED.
Methods: Three patients with ED were identified out of over 1000 consecutive patients seen in our outpatient sleep clinic. Assessment included a detailed neurological examination and polysomnography (PSG).
Results: Patient 1: A 20-year old woman reported a three-year history of excessive neutral-content dreaming. Dreams had long, complicated plots and involved multiple dream characters that she could interpret from different perspectives. Patient 2: A 24-year old woman had been experiencing exhausting nightmares for two years, in which she would witness violent scenes, such stabbing or fighting, as an observer. Patient 3: A 69-year old man related a 5-year history of excessive dreaming involving his past activity as a cook, in which he would mentally rehearse the sequence of steps involved in the preparation of a meal. Patients 1 and 2 had a history of depression and cardiac arrhythmias, while patient 3 was known for recurrent vertigo, essential tremor and prostate cancer. Neurological examination was normal in patient 1, revealed attention deficits in patient 2 and short term memory loss in patient 3. PSG documented sleep fragmentation in patients 2 and 3 (due to bruxism and

PMLS respectively). All patients had persistent epic dreaming on follow up interviews after 0.5-2 years.
Conclusion: ED appears to be a heterogenous disorder, in which sleep fragmentation might play a major role. Our observations support the existence of at least two subtypes, including "story epic dreaming" and "non-story epic dreaming".

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MISPERCEPTION OF OVERNIGHT SLEEP AND DAYTIME NAPS

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Introduction: The aim of the study was to investigate the correlation between the misperception of overnight sleep and perception of daytime naps.
Methods: A prospective longitudinal study involved a consecutive series of patients (n=106) who underwent an overnight polysomnography with MSLT, and who had completed a set of morning questionnaires including questions querying the subjective perception of their sleep the night prior and the set of questions asking the patients to estimate their daytime MSLT naps. The sample was divided into two subgroups, those who correctly estimated their overnight sleep (CE), and those who either under- or over-estimated their overnight sleep (SSM, at least +/- 1.5 hour difference). The second subgroup was then divided into those with negative (NSSM) and those with positive sleep misperception (PSSM). The paired samples t-test was performed to analyze data.
Results: The CE group (n=27) correctly estimated their daytime naps, and their difference between objective (9.9+/-5 minutes) and subjective nap duration (8.6+/-5.7 minutes) was not statistically significant. On the other hand, as a whole, those with sleep misperception (n=16) underestimated their naps (MSLTobject = 11.5+/-5.2 minutes, MSLTsubject = 6.6+/-5.1 minutes, $p<0.001$). When divided into subgroups, those who underestimated their overnight sleep (NSSM, n=6) also underestimated their daytime naps (MSLTobject = 12.4+/-4.7, MSLTsubject = 9.5+/-5.6, $p<0.05$). However, in spite of their overestimation of night sleep, the PSSM group (n=10) grossly underestimated their daytime sleep (MSLTobject = 10.9+/-5.7 minutes, MSLTsubject = 4.9+/-4.7 minutes, $p<0.05$).
Conclusion: The finding that CE patients are also able to correctly estimate their daytime naps is clinically useful in that, even in absence of MSLT testing, their subjective daytime nap estimate could be used at face value. On the other hand, as previous studies had shown, patients with PSSM present a clinical challenge because of their overestimation of night sleep and the resulting objective daytime sleepiness. The current study shows that these patients, in contrast to their overnight sleep, grossly underestimate their daytime sleep, and thus potentially reduce the chance of being seen by a clinician. The study also showed that patients who underestimate their overnight sleep have tendency to underestimate daytime naps as well.

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DOES HABITUAL STRESS CAUSE SLEEP PROBLEMS AND DAYTIME FUNCTIONING IMPAIRMENTS, OR IS STRESS THE RESULT OF POOR SLEEP?

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Introduction: Like pain, the consequences between stress and sleep are often assumed. However, most research focuses on poor sleep as a consequence of stress or workload. We recently demonstrated a bidirectional effect between these variables in college students. The current study assesses preliminary data in a clinical sleep patient population.
Methods: A total of 271 patients who presented to a Midwestern metropolitan sleep center for diagnostic PSG completed a brief estimate of their state and trait stress. In addition, patients completed subjective sleep measures including the Epworth Sleepiness Scale (ESS), Fatigue Severity Scale (FSS), Clayton Daytime Functioning Scale (CDFS), and the Pittsburgh Sleep Quality Index (PSQI). Inclusion criteria were ages 18-79, no shift work, no prior sleep disorder diagnosis, and no split-night studies.
Results: Trait stress was significantly correlated with habitual sleep time (HST) ($r= -.192$, $p< .01$), global PSQI ($r= .308$, $p< .001$), daytime functioning impairments (CDFS ($r= .393$, $p< .001$); ESS ($r= .248$, $p< .001$)), and the AFNAR index on the PSG ($r= .138$, $p< .05$). Using a forward stepwise linear regression, a model consisting of the CDFS, HST, and age accounted for 20% of the dependent measure trait stress's variance. Dividing the sample into low and high trait stress groups (LtS, HtS, respectively), revealed that the HtS group had significantly less HST ($F= 8.6$, $p< .01$) and more subjective sleep complaints according to the PSQI ($F= 19.3$, $p< .001$). The HtS group also reported more daytime functioning impairments than the LtS group (CDFS ($F= 48.1$, $p< .001$).
Conclusion: Higher habitual stress is associated with reported shorter sleep duration, poorer sleep quality, and daytime functioning impairments. Conversely, daytime functioning impairments and shorter sleep duration demonstrated a predictive relationship with habitual stress complaints. Further work is needed to determine the bidirectional relationship between stress and poor and its consequences.

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ARE STRESSED OUT PEOPLE WITH POORER SLEEP AT HIGHER RISK FOR ADVERSE HEALTH CONSEQUENCES?

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Introduction: Individuals with prolonged stress are susceptible to adverse health consequences, such as cardiovascular disease, affective disorders, and altered immune function. Similarly, poor sleep over time can result in increased health risks. This preliminary study looked at the interaction of these risk factors and adverse health consequences in a clinical sleep patient population.
Methods: A total of 271 patients who presented to a Midwestern metropolitan sleep center for diagnostic PSG completed a brief estimate of their state and trait stress. Patients completed the Pittsburgh Sleep Quality Index (PSQI), sleep habits, and daytime functioning estimates. History of affective disorders, HTN, diabetes, pain conditions, and BMI were obtained from their medical history and used in the analysis. Odds ratios (OR) were calculated comparing trait stress levels (low vs. high (LtS vs. HtS), to either habitual sleep duration (HSD) or sleep quality (SQ) using the PSQI minus component three, which assesses sleep duration.
Results: A total of 259 patients were analyzed for HSD and 99 for SQ in this preliminary report. Comparing to patients with LtS and normal HSD (7-8.5 hrs), HtS patients have higher risk of affective disorders regardless of HSD (OR= 4.5-4.67). Risk for diabetes tends to be related to HSD, but patients with HtS and normal HSD are also at higher risk (OR= 2.11). The OR for elevated BMI is highest in the HtS, <7hr HSD group (OR= 1.29). Controlling for normal HSD, patients with HtS and higher PSQI scores have the highest risk for affective disorders (OR= 13.8) and arthritis (OR= 1.63), and an increased risk for diabetes (OR= 3.0).
Conclusion: Although some adverse health consequences appear solely related to HSD, the interaction of high stress and poor sleep does appear to increase risk for some health problems, especially affective disorders. Further work is needed on larger samples to explore these relationships.

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EFFECTS OF INTERMITTENT BRIGHT LIGHT EXPOSURE DURING DAYTIME ON DAYTIME SLEEPINESS, COGNITION, AND PERFORMANCE

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Introduction: While phase shifting effects of bright light (BL) by the circadian system have been well investigated, relatively less attention has been paid to its direct effects on psychological function. The aim of this study was to understand whether daytime sleepiness and selective attention could be improved by BL exposure. We analyzed the diurnal changes of sleepiness, P300 (an auditory event-related potential that reflects cognitive function), and performance test during the daytime.

Methods: Ten healthy young volunteers (six males and four females, mean age 21.11years: range 18-24 years) participated in the experiment after informed consent. For the 7 days before the experiments, their regular sleep-wake patterns were confirmed by Actiwatch (Respironics, USA). On the experimental day, subjects wore a goggle from their home to the lab to avoid exposure to sunlight. Each of the subjects participated in two experiments: exposure to ordinary room light (RL, <200 lx) and exposure to BL of more than 3,000 lx from 9:00 to 18:00 except during the MSLT and the P300 evaluation. We examined MSLT and P300 every 2 hours using EEG equipments (Nihonkoden, Japan). P300 was computed with a software developed by Miyukigiken, Japan. The subjects estimated their subjective symptoms on visual analog scale and Stanford Sleepiness Scale.

Results: Compared to RL condition, objective and subjective sleepiness measured by the MSLT and Sleepiness Scales significantly decreased under BL condition ($F=6.70$, $p<0.05$; $F=21.19$, $p<0.005$, respectively). The average latency of P300 shortened significantly ($F=33.58$, $p<0.001$), and the amplitude of P300 increased significantly ($F=6.47$, $p<0.05$)under BL condition. Reaction time in oddball paradigm shortened significantly ($F=13.18$, $p<0.01$). Time effect was seen in MSLT and reaction time ($F=7.31$, $p<0.001$; $F=3.66$, $p<0.05$, respectively). Sleep latency and reaction time at 10:00 were significantly shorter and longer, respectively, than those at 18:00.

Conclusion: Intermittent exposure to BL during daytime counteracts sleepiness. The reduction of sleepiness by BL exposure may improve selective attention and prevent mistakes. Time dependent effect of BL exposure may exist, but the training effect of the performance test may also need to be considered.

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THE EFFECT OF CONSOLE/COMPUTER GAME PLAY ON SLEEPINESS AND SLEEP HYGIENE

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Introduction: Research has shown that individuals who spend more time using the Internet and playing computer games delay sleep, spend less time in bed, have longer sleep latency, and shorter REM latency. No research has been conducted investigating computer/console game use and sleep hygiene or daytime sleepiness. Our objective was to examine the sleep hygiene, sleepiness, type of games played, and self-perception of interference and addiction to these game related behaviors.

Methods: 137 university students (M=22.26 years old, SD=6.63, women =86) were recruited from introductory psychology courses. Each participant completed the Sleep Hygiene Index (SHI), Epworth Sleepiness Scale (ESS), and a computer/console gaming and demographic questionnaire. For some analyses excessive gamers (hours played per week >7) were compared to other gamers.

Results: Gamers who reported gaming interfered with their sleep (10.81%) were sleepier (ESS M=11.5 vs 8.4, SD=3.40, 3.44; $t(109)=2.9$, $p<.05$), had more maladaptive sleep hygiene (SHI M=39.7 vs 34.0, SD=9.0, 6.8; $t(108)=2.6$, $p<.05$), and slept 1.6 hours less on weekdays ($t(102)=-3.4$, $p<.05$) compared to other gamers. Gamers who self-identified as being addicted to gaming (12.6%) were sleepier (ESS M=10.2 vs 8.5, SD=3.2, 3.5; $t(132)=1.76$, $p<.05$), and slept 1 hour less on weekdays ($t(124)=-2.2$, $p<.05$) compared to other gamers. Excessive gamers had significantly poorer sleep hygiene ($t(82)=2.00$, $p<.05$) and slept less on weekdays (M=7.27 vs 6.26, SD=1.46, 1.66, $t(79)=-2.69$, $p<.05$) than other gamers. For excessive gamers, there was a significant moderate positive correlation between the hours of play and sleepiness ($r(23)=.365$, $p<.05$).

Conclusion: Computer/console gamers that identified their gaming as an addiction or as interfering with their sleep experienced more sleepiness and slept less. In general, for excessive gamers, more gaming was associated with more sleepiness. Maladaptive sleep hygiene found among the excessive gamers is suggested here as a likely target for intervention.

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NORMAL SLEEP IN AFRICAN AMERICANS AND CAUCASIAN AMERICANS: A META-ANALYSIS

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Introduction: There has been equivocal evidence on the differences in sleep architecture and continuity between normal-sleeping African Americans (AA) and Caucasian Americans (CA). The goals of this meta-analysis were to identify the presence and magnitude of ethnic differences in normal sleep among adults, and any moderating effects on those differences by gender, age, location of PSG, and total nights recorded.

Methods: The research articles included met the following criteria: (a) samples of AA and CA, (b)adult populations, (c)numerical data to compute effect sizes, (d)measures of either subjective and/or objective sleep and (e)were published articles.

Results: A total of 13 studies met criteria. The number of articles per sleep variable ranged from 5 to 7. Using Cohen's d, there was a medium effect size for objective TST such that AA sleep less than CA; however this effect was moderated by age, gender, and total nights recorded indicating greater differences between the groups as age, the percentage of women, and the total nights recorded increased. Small effect sizes were determined for SWS%, stage 2%, subjective TST, SE, and SOL such that sleep continuity was poorer and sleep architecture was lighter for AA compared to CA. Gender moderated subjective TST, SE, and SOL indicating women tend to widen these differences. Age reduced ethnic differences in subjective TST, and in-home PSGs reduced ethnic differences in SE. Neither age nor gender moderated SWS% and stage 2%. However, the greater the total nights recorded, the greater the ethnic differences in SWS. There were no ethnic differences in REM%, stage 1%, RDI/AHI, and insufficient data for WASO.

Conclusion: AA appear to sleep worse than CA; however, women inflate differences in sleep continuity. Sleep architecture differences are free from the influences of age, gender, and location of PSG. It is likely increased age attenuates ethnic differences in self-reported sleep.

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ANALYSIS OF REPORTS OF DIFFERENTS EXPERIENCES OF CONSCIOUSNESS DURING WAKEFULNESS, SLEEP AND TRANSITIONAL STATES

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Introduction: A physiologic and phenomenologic integration of reports of dreams, lucid dreams, imagined dreams, fantasies and near-death experiences is carried out, in the context of contemporary theories of conscious states.
Methods: The collected reports correspond to a control dreams group (A: n=25), Franz Kafka dreams (B: n=85), imagined dreams by Antonio Tabucchi (C: n=20), lucid dreams (D: n=10), fantasies (E: n=10) and near-death experiences (NDEs) (F=10). The Hobson and McCarley form-content analysis (American Journal of Psychiatry, 1977) and a multidimensional approach (MDA) (Kallmeyer RJ and Chang EC, Perceptual and Motor Skills, 1997) were used to characterize those conscious and dream experiences.
Results: Significant changes were obtained within the sensorial evaluation scales with an increase in its perceptive distribution (A: 0.32 +/- 0.34; B: 0.42 +/- 0.31; C: 0.50 +/- 0.26; D: 0.52 +/- 0.26; E: 0.51 +/- 0.26, F: 0.58 +/- 0.30; values were expressed as X+/-SD, AB < CDEF, Friedman and Dunns Test, p less than 0.05). Analysis of contents and the MDA detect significant changes between groups.
Conclusion: 1) Significant changes followed concepts of the activation-synthesis model; 2) Kafka dreams, imbedding of current personal concerns rooted in emotional preoccupations reflected per se continuity and repetition principles; 3) Wish fulfillment and the presence of an autobiographic-self characterized fantasies and, 4) Metacognitives experiences were founded in both, lucid dreams and NDEs. Thus, this type of analysis has proven capacity to detect significant changes following concepts that reconcile different aspects of theories of the conscious processes and dreaming.

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DIFFERENCES BETWEEN MSLT-DEFINED 'MILDLY' AND 'MODERATELY' SLEEPY NORMALS, IN NOCTURNAL SLEEP AND OTHER MEASURES OF DAYTIME SLEEPINESS

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Introduction: 'Mild' and 'moderate' daytime sleepiness are categories of sleepiness defined by MSLT criteria; encompassing latency scores of 5-9min and 12-15min respectively. We wished to see the extent these categories were reflected in nocturnal sleep and extended PVT sessions.
Methods: Twenty healthy, young (mean age 25.9y, 9=male), regular 7-8h sleepers, without complaint of daytime sleepiness (ESS<10, normal KSS), non-nappers, previously categorized via the Standard MSLT as either mildly sleepy (n=13) or moderately sleepy (n=7), underwent one night and one day of testing. This comprised: overnight, home EEG recordings, PVTs extended to 30 min, subjective sleepiness ratings, and further MSLTs undertaken four times, but delayed until 15:30h and then up to 23:00h.
Results: Nocturnal sleep - There was nsd between the two groups for: sleep latency, wake after sleep onset or sleep efficiency. Daytime testing - there was nsd between the two groups for any measure.
Conclusion: Our two groups were carefully selected to fulfill the Standard MSLT criteria for Mild and Moderate sleepiness. The Moderate group comprised participants who regularly slept 7-8h, with no other signs of increased daytime sleepiness, nor differences in nocturnal sleep compared with those categorized as 'Mild'. During the MSLT, there must be a normal distribution in the ability to fall asleep with any given level of sleepiness. Given this normal distribution, then any MSLT-defined Moderately sleepy group will contain more (healthy) people with the ability (but not necessarily the propensity) to fall asleep with lower sleepiness (i.e. 'high sleepability') than a MSLT defined 'Mildly' sleepy group. We find this to be the case, and are exploring the phenomenon of 'sleepability' further in our groups.

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DREAMS AND SMELL - THE IMPACT OF NOCTURNAL OLFACTORY STIMULATION ON DREAMS

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Introduction: Only a limited number of trials is available regarding the impact of external stimulation on dreams. Olfactory stimuli have hardly been investigated in this context, as stimulation is much harder to control and the experimental setting is more delicate compared to e.g. acoustic stimuli. Aim of the present study was to investigate whether olfactory stimuli of different hedonic characteristics are incorporated into dreams and to what extend they influence dream emotions.
Methods: 15 female volunteers were investigated during 30 nights of testing (first night for adaptation). Standardized awakenings were performed during REM sleep. Subjects were exposed against non-odorous control, a positive (PEA, 20%) and a negative odor (H2S, 4 ppm) for 10 seconds each during REM sleep in a randomized fashion. Stimulation was performed with a computer olfactometer in a constant air stream. After awakening, subjects were advised to report dream content in a standardized fashion and to rate dream emotions (positive and negative) on a four digit scale (0 to 3: no to strong feelings). The overall emotional coloration was calculated. Dream content was analyzed by an independent investigator with regard to the incorporation of olfactory stimulation.
Results: Mean emotional coloration after control stimulation was slightly positive (+0.5). After negative stimulation, it was shifted to negative values (-0.4) while the mean emotional coloration was more positive after positive stimulation (+1.2). The differences between the conditions were statistically significant. Direct incorporation was detected in one dream only (neutral condition), indirect incorporation (dream contents associated with smelling) was detected in four dreams without relation to stimulus condition.
Conclusion: With olfactory stimulation the emotional coloration of dreams can be significantly influenced according to the hedonic aspect of the stimulus. In contrast, direct incorporation of olfactory stimuli into dreams does not seem to appear.

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THE IMPACT OF SLEEP AND INTERFERENCE ON MEMORY CONSOLIDATION

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Introduction: Recent evidence indicates that sleep contributes to the consolidation of new memories in comparison to periods of active wakefulness. The authors sought to further determine the specific effect of sleep as contrasted to reduced levels of interference.
Methods: Memory performance (perceptual texture discrimination task, TDT, motor mirror-tracing task, declarative word-pair associate task) and general neurocognitive performance were measured before and after 1 hr of polysomnographic monitoring (1:30 pm to 2:30 pm) containing either sleep or restful wakefulness with maximally reduced sensory and motor activity in 20 healthy subjects (12 females, aged 23±2.3 years) in a randomized, cross-over design.
Results: Polysomnography revealed clear-cut differences between the sleep (NREM sleep 47.4±8.7 min, no REM sleep) and restful wakeful-

ness condition (NREM sleep 0.7±0.2 min, p<0.001). TDT performance improved after sleep but declined after restful wakefulness (p<0.05). However, the retention rate for word-pairs and % improvement in mirror tracing were virtually identical in both conditions (p>0.5). No significant differences in general neurocognitive parameters were observed between the conditions.
Conclusion: Sleep might be of differential importance for distinct types of learning. Whereas local neural refinement in the primary visual cortex underlying perceptual TDT learning seems to be enhanced by sleep-specific neural activity, shorter periods of sleep might provide less additional benefit for complex motor and declarative learning compared to neural activity patterns associated with restful wakefulness.

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CORRELATIONS BETWEEN ACTIVITY AND SLEEP
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Introduction: Total sleep time (TST) and sleep efficiency (SE) may be improved with regular daytime exercise. We examined the effects of total energy expenditure (TEE), exercise energy expenditure (EEE), non-exercise activity (NEA), steps taken, and Body Mass Index (BMI) on sleep.
Methods: Subjects wore actigraphy armbands designed to measure body temperature, ambient temperature, position sense, and accelerometry and programmed to calculate TEE, EEE, NEA, steps taken, TST, and SE. Correlations were performed using t-tests.
Results: 14 subjects (age 37±10y, 4 men, BMI=26.4±4.6 kg/m^2) wore armbands >22h/day for a mean of 23 days. Group TST was 6.1±1.8 hr/night; SE was 0.80±0.10. Group TEE was 2521±657 kcal/day, EEE 399±393 kcal/day, NEA 2122±431 kcal/day, and steps/day were 11946±5189. There were no differences in TST or SE following days with high and low TEE, EEE, or steps taken. However, following days with low NEA (<2000 kcal/day, mean 1732±210 kcal/day) the TST at night was significantly greater (6.5±1.8 hr vs 5.8±1.8 hr, p=0.006) than on nights following days with high NEA (>2200 kcal/day, mean 2529±329 kcal/day), with no difference in SE (both 0.80±0.10, p=0.94). Alternatively, nights with lower TST (<6 hr/night, mean 4.8±1.0 hr/night) were compared to nights with higher TST (>6 hr/night, mean 7.4±1.2 hr/night) for activity level the following day. After low TST, there was greater daytime activity of all categories, TEE 2630±635 vs 2422±640 kcal/day (p=0.002), EEE 421±350 vs 350±348 kcal/day (p=0.05), NEA 2209±451 vs 2072±416 kcal/day (p=0.003), and 12838±4977 vs 10148±4808 steps taken (p<0.001). When sorted by BMI, 7 subjects had normal BMI <25 kg/m^2 (mean 22.4±1.7) and 7 were overweight (BMI >25 kg/m^2, mean 30.0±2.9). The group with higher BMI had higher TEE (3064 vs 2080 kcal/day, p=0.03), and took more steps/day (13896 vs 11292, p=0.05).
Conclusion: Exercise did not correlate with TST in this population. Days of increased NEA were followed by nights with lower TST. Nights with lower TST were followed by increased activities the next day. Increased activities were seen in subjects with greater BMI. These unexpected findings deserve explanation by unmeasured factors such as individual metabolic profiles, stress and changes in circadian rhythm.

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COGNITIVE DETERMINANTS OF SLEEP BEHAVIORS IN SENIOR HIGH SCHOOL STUDENTS: BASED ON THE THEORY OF PLANNED BEHAVIOR
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Introduction: Irregular sleep pattern and insufficient sleep are common among high school students and have been shown to have a negative impact on their daily function. The Theory of Planned Behavior (TPB), that posits that behavioral intention is a function of attitude toward behavior, subjective norm and perceived behavior control, has been shown to predict the intention of health-related behaviors. The current study is to explore the cognitive factors that determine sleep patterns in high school students based on the TPB, and to examine the role of amount of daily activities and time management skill in moderating the intention to more healthy sleep patterns.
Methods: Nine hundred and fifty senior high school students from north Taiwan were included in the study. A questionnaire constructed based on the TPB was administered to assess their sleep beliefs, perceived attitude toward sleep of significant others, their perceived control over their sleep behaviors. Their actual sleep habit, daily activity level, time management skills, and intention for regular and sufficient sleep were also assessed. The model was then verified with the Structure Equation Model.
Results: In terms of regularity in sleep, the attitude about sleep and perceived behavioral control accounted for 40% of the variation of intention of regular sleep, but only 5% of actual behavior. In high daily activity group, adding the factor of time-management increases the explanatory power to 11%. Regarding the amount of sleep, although the model based on the Theory of Planned Behavior does generate acceptable fitting indices, the total explanatory power is very low (3%).
Conclusion: For busy senior high school students, increased positive attitude towards sleep and the controllability of sleep behaviors are associated with intention for regular sleep. The intention may be actualized in those with better time-management skill. Sleep education addressing these issues may be helpful in improving sleep patterns in high school students.

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SLEEP DEPRIVATION AFTER ENCODING IS DETRIMENTAL TO RECALL OF BOTH NEGATIVE AND NEUTRAL WORDS
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Introduction: Work over the last few years has shown that both positive and negative emotional episodes are more strongly consolidated over sleep than neutral episodes. At odds with this, a recent study demonstrated that sleep-deprivation on the post-encoding night impairs the subsequent retrieval of positive, but not negative pictures. We set out to determine whether this unexpected finding generalizes to emotional words.
Methods: 32 healthy volunteers with no history of neurological disorder, depression, or sleep disturbance participated. All spoke English as their first language. During training, they performed a self referential deep encoding task while viewing 244 words (negative and neutral) from the ANEW list. Words were displayed for 2 seconds each in random order. Immediately after training, one group (N=16) experienced a night of total sleep deprivation (TSD) and the other (N=16) a night of normal sleep. 2 nights of recovery sleep were allowed prior to testing.

At test, subjects performed a remember-know (R/K/N) recognition task while viewing trained words and 128 foils. Words were displayed for 1 second, followed by a 2 second delay.
Results: We calculated the recognition accuracy (hits-false alarms) for Remember and Know responses. Know responses were at chance and were therefore excluded. Remember responses were above chance so we performed a 2x2 mixed ANOVA with factors Group (sleep, TSD) and Emotion (negative, neutral) using these data. This revealed a significant impairment in the TSD group ($p<.05$) but no interaction between this effect and emotion.
Conclusion: These data show that sleep deprivation on the post-encoding night has a detrimental influence on the subsequent recollection of both negative and neutral words, with no significant difference between these categories. Our findings replicate the data on emotional pictures and build on this by showing that the apparent protection of negative retrieval against sleep deprivation related deficits extends to the domain of words.

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PERFORMANCE MAY BE MORE IMPORTANT THAN SLEEP PRESSURE TO PERCEIVED QUALITY OF LIFE (FOSQ) IN SLEEP DISORDERED BREATHING

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Introduction: Daytime complaints, including excessive daytime somnolence, are the primary reason for patients to seek evaluation at sleep disorder centers. Various objective and subjective tests have been developed to quantify these complaints. Although multiple studies have shown poor agreement amongst these measures they remain widely used. In an effort to better understand their utility in outcomes studies, we examined the interrelationships between objective and subjective measures of daytime function in a well characterized group of patients with sleep-disordered breathing (SDB).
Methods: 40M/15F, including 7 volunteers, well characterized for symptoms of SDB underwent two nights of limited ambulatory and one laboratory NPSG (AHI4% 0.3-99.2/hr) followed by multiple tests of objective and subjective daytime function. Objective tests included a multiple sleep latency test (MSLT - Four 20 min trials, two hours apart) interspersed with 4 Psychomotor Vigilance Task (PVT) trials. Parameters analyzed were the sleep latency on the MSLT and the Transformed Lapses (XLapses) and Slope of Mean Reaction Time from the PVT. The subjective measures obtained were the Epworth Sleepiness Scale (ESS), Stanford Sleepiness Scale (SSS), and Functional Outcomes of Sleep Questionnaire (FOSQ).
Results: Among the objective tests, only the slope of the PVT reaction time and the sleep latency on the MSLT were modestly correlated($r=.31$, $P< .0001$). For the subjective tests, the FOSQ showed a correlation of 0.46 ($p<.0001$) to the ESS and 0.42 ($p <0.001$) to the SSS, while the ESS and SSS were less well correlated.($r=0.28$). A multiple linear regression model appeared to strengthen the relationship of the ESS and SSS to the FOSQ ($r=0.57$) implying that they measure complementary aspects of a patient's subjective sleepiness. Comparing subjective to objective measures, the best relationship was found between the FOSQ and XLapses on the PVT ($r=0.48$, $p<0.001$). The sleep latency on the MSLT did not show significant correlations to any of the subjective measures. The slope of the PVT reaction time had a modest correlation to the ESS and SSS ($r=0.2$, $P<0.001$).
Conclusion: The FOSQ appears to combine subjective information from the ESS and SSS in a consistent fashion. Because these subjective complaints are more closely correlated to a measure of XLapses than to the sleep latency on MSLT it appears that patient quality of life may be more closely associated with failure to perform than with the tendency to fall asleep.
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SLEEP, REWARD, AND MEMORY

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Introduction: What is the adaptive value of sleep for memory processing? To address this question we examined the impact of stimulus reward value on sleep-related memory processing across a 12 and 24hr interval. "Reward" participants were informed that in addition to the $10 they would be paid for participating, they would receive $1 for each correct answer they gave at retest, which meant that they could earn up to $40. The "no-reward" participants were paid a flat fee ($30) for participating. While most studies have used verbal learning tasks (e.g. paired associates), the present study employed a visual declarative task.
Methods: Participants were 152 Harvard students (63 male, 89 female; 79 12hr, 73 24hr) were trained at 9AM or 9PM on a visual paired associates task (30 Face - Object picture pairs), and were retested either 12 or 24hrs later.
Results: We found that recall was dramatically improved following a 12hr interval that contained a night of sleep compared to a day of wakefulness ($p<.00001$), and that rewarded subjects performed better than non-rewarded subjects ($p=.01$). Across a 24hr interval, we found that if the second 12hrs contained a night of sleep, performance improved relative to the first 12hrs that were filled with wake ($p=.07$). Conversely, when the second 12hrs was filled with wake, performance declined relative to the first 12hrs which contained a night of sleep ($p<.01$). Interestingly, the effect of reward was only sustained across the first 12hr interval.
Conclusion: Sleep imparts a powerful benefit to visual declarative memory regardless of when it occurs within the 24hr interval. The effect of reward, on the other hand, appears to be time-dependent, being most effective over the short term (the first 12hr), but dissipating thereafter.

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REM AND NREM-RELATED MEMORY AND MOOD REGULATION IN HEALTHY ADULTS

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Introduction: REM sleep has been implicated in mood regulatory processes, in emotional memory consolidation and in depression. NREM sleep has been implicated in declarative memory consolidation. The aim of this study was to assess potential contributions of REM sleep to negative mood and emotional memory and NREM sleep to positive mood and memory.
Methods: After one habituation night, 55 healthy young adults were assessed with overnight polysomnography and then awakened from REM and NREM sleep states. Awakenings were counterbalanced across subjects. After each awakening, subjects completed self versus 'significant other' positive and negative trait rankings and were given tests of mood function and autobiographical memory retrieval in the morning.
Results: Significantly higher negative affective scores (as measured by PANAS) were found after awakenings from REM vs. NREM (14.73 ± 0.56 vs. 13.51 ± 0.56, $p=0.03$). Endorsements of positive trait ratings for self vs. a significant other were significantly decreased relative to a pre-sleep baseline after awakenings from REM (1.73, $p=0.05$) but not NREM (0.63, $p=0.38$). Conversely, endorsements of negative trait ratings for self vs. a significant other were significantly decreased relative to a pre-sleep baseline after NREM (1.16, $p=0.04$) and not REM (0.27, $p=0.62$). Negative ratings of self vs. other after awakenings from REM significantly predicted daytime impulse control difficulties ($r=0.42$, $p=0.003$),

limited access to emotion regulation strategies (r=0.37, p=0.01), POMS anger (r=0.32, p=0.03) and daytime depression (r=0.43, p=0.002).
Conclusion: REM specializes in negative emotional memory and REM cognitive processing predicts daytime mood function.
Support (optional): This work was support by NIMH Grant no. 1 R21 MH076916-01A2 to the first author.

1283

EFFECT OF NAPPING ON INTER-SESSION HABITUATION TO EMOTIONAL STIMULI-PRELIMINARY PSYCHOPHYSIOLOGICAL AND SUBJECTIVE RESULTS

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Introduction: Sleep may regulate emotions. Nap effects on inter-session habituation to emotional stimuli were investigated.
Methods: Healthy volunteers, mean age=21.2 (range=18-27) assigned to Nap (N=16, 9 female) or Wake (N=14, 8 female) "Groups" viewed two 35-min "Sessions" of International Affective Picture System digital photographs separated by mean 155 min (SD=19), 13:20-15:55, when Nap subjects had a 120-min PSG-monitored sleep opportunity and Wake subjects viewed non-stimulating videos. Six highly negative "Valence" and 6 neutral photographs were equated for mean arousability. Three 20-photograph sets each contained 2 negative and 2 neutral photographs intermingled and repeated 5 times. One set began both sessions followed by 1 of 2 remaining sets. Six permutations of 3 sets were counterbalanced across subjects. Electrodermal, electrocardiographic, and corrugator electromyographic (EMG) data were recorded with stimulus-onset times. Subjects rated photographs' valence and arousability using the Self-Assessment Manikin (SAM). Stimuli appeared for 6 sec, then SAM screens, then varying 17-29-sec ISIs. Data were separate means for the 2 negative and 2 neutral photographs occupying each ordinal repetition (1st-5th "Trials"). Means during 2 sec before stimulus onset were subtracted from maxima during stimulus presentation for skin-conductance (square-root SCR) and EMG responses or from minima for heart-rate deceleration (HRD). Data were normalized by dividing by session-1's 2-stimulus-mean maximum (SCR, EMG) or minimum (HRD). Stimuli presented at both sessions were analyzed by 4-factor ANOVA (within: Valence, Session and Trials nested; between: Group).
Results: GroupXSession (but not Group's 3- and 4-way) interactions were significant for psychophysiological ($p<0.05$) but not SAM data. From first to second session, SCR and EMG significantly decreased in Nap ($p<0.01$ and <0.05 respectively) but not Wake groups whereas HRD decreased in Wake ($p<0.01$) but not Sleep.
Conclusion: SCR and EMG indicate better inter-session habituation across Nap versus Wake. HRD suggests the opposite. Subjective ratings did not differentiate groups.
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SEX DIFFERENCES IN SLEEP-RELATED MEMORY AND MOOD REGULATION

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Introduction: Both REM and NREM sleep have been implicated in depression and in mood regulatory processes. Because women exhibit higher rates of depression than men, we hypothesized that sleep-related memory and mood regulatory processes would differ as a function of sex.
Methods: After one habituation night in a sleep Lab, 26 male (mean age (range)= 21.1 (18-26)) and 29 female (mean age (range) = 21.1 (18-32), (p=0.93)) volunteers were assessed with overnight polysomnography and then awakened from REM and NREM sleep states to perform cognitive tasks. Awakenings were counterbalanced across subjects. After each awakening, subjects completed self versus 'significant other' positive and negative trait rankings and were given tests of mood function and autobiographical memory retrieval.
Results: Although mood states (as measured by PANAS) did not significantly change across awakenings for men vs. women, 'latency to retrieve a positive memory' was significantly longer for females (mean =19.84 secs (sd=3.66)) than for males (mean= 11.82 secs (sd=3.59)) after REM versus NREM awakenings (p=0.07). For females, negative ratings of self versus other after awakenings from REM significantly predicted impulse control difficulties (r=0.41, p=0.04), mood regulation strategies (r=0.43, p=0.03), and daytime depression (r=0.53, p=0.005). For males, negative ratings of self versus other after awakenings from REM significantly predicted impulse control difficulties (r=0.46, p=0.03), POMS anger (r=0.42, p=0.045) and daytime depression (r=0.39, p=0.06).
Conclusion: In both men and women, REM appears to modulate negative affect. In females, REM may also modulate negative autobiographical memories.
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1285

NIGHTLY SLEEP DISTURBANCE AND DAILY RELATIONSHIP QUALITY IN COUPLES: EVIDENCE FOR BIDIRECTIONAL ASSOCIATIONS

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Introduction: Although many adults share a bed with a romantic partner, most sleep research has focused on the individual, thereby neglecting the impact of sharing a bed on the partners' respective sleep. Furthermore, evidence suggests that a bidirectional association exists between the partners' sleep quality and the quality of their relationship. This study sought to examine the bidirectional impact and cross-partner effects of daily interpersonal interactions and nighttime sleep quality over the course of 7 days.
Methods: Twenty-nine heterosexual co-sleeping couples completed sleep diaries and wore wrist actigraphs for 7 days. Six times a day, participants individually recorded the quality of interactions with their partner (since the previous timepoint) on personal data assistants. Measures of individual well-being (World Health Organization Well-being Scale (WHO-5)) and relationship satisfaction (Relationship Assessment Scale (RAS) were also completed.
Results: Based on correlation analyses of the weekly averages of sleep and relationship measures, a longer actigraphy-based sleep onset latency (SOL) was associated with lower relationship satisfaction (RAS) in women ($r=-.50$, $p<.01$), while a higher diary-based wake after sleep onset (WASO) was associated with lower relationship satisfaction (RAS) and well-being (WHO-5) in men ($r=-.39$, $p=.04$; $r=-.42$, $p=.03$). Regression analyses of the daily data were also conducted. In women, her own and her partner's SOL predicted more negative ratings of partner interactions on the subsequent day (longer SOLs predicted more negative ratings; $\beta=-.14$, $p<.05$; $\beta=-.12$, $p=.10$). Moreover, in women, more positive daytime partner interactions predicted shorter SOLs on the subsequent night ($\beta=-.12$, $p<.01$). In contrast, for men, only their own SOL predicted more positive ratings of partner interaction (longer SOLs predicted more positive ratings; $\beta=.13$, $p=.07$).
Conclusion: Bidirectional associations appear to exist between sleep quality and interpersonal interactions, particularly in women, suggesting novel opportunities for interventions that may improve sleep and relationship problems.

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DIFFERENCES IN DAYTIME SLEEP ARCHITECTURE IN HABITUAL AND NON-HABITUAL NAPPERS

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Introduction: Some people express resistance to napping due to sleep inertia and inability to wake up. Habitual nappers showed differences in sleep quality during a short, 20-min nap (Milner, 2006) (i.e. higher theta, alpha, beta, and delta power, and more refreshed post-nap). Here we examine differences in the architecture of a 60-90min nap, between habitual and non-habitual nappers determined by prior nap history.
Methods: Thirty-one healthy subjects (18-35yrs) kept a sleep diary for 7 nights, including the number and duration of naps. Subjects were categorized as habitual nappers if naps were recorded in diaries at least once during the seven days (65% of subjects). Subjects took a 60-90min, PSG-recorded nap. We examined the influence of the number of naps in the week on nap architecture (i.e., TST, sum of Stg1 & Stg2, SWS, REM (min & %)).
Results: We found a significant interaction between nap groups and sleep stages (p=.005, eta2 =.26), controlling for TST. Habitual nappers showed more time in stage 1 and 2 sleep, whereas non-habitual nappers spent more time in SWS. No differences were found in REM or TST. Furthermore, the more subjects napped during the prior week, the less SWS (r= -.38) and more stage 1 and 2 (r= .35) in the nap.
Conclusion: The present study shows that in the context of a longer nap, where the likelihood of reaching stage 3 and stage 4 sleep is increased, non-habitual nappers spent more time in these stages of deep sleep. Delta activity, the EEG signature of SWS, has been shown to increase following sleep deprivation or sleepiness. This may be the case for our non-habitual nappers. Awakening from these stages of sleep increases the risk of sleep inertia, which may be a reason for people's resistance to napping.
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IMPLICIT HIPPOCAMPAL-RELATED MEMORY IMPROVES WITH PRACTICE, NOT SLEEP

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Introduction: Sleep is shown to facilitate learning on a variety of tasks that require procedural memory. Evidence of replay during sleep of waking experience in rat hippocampus has been proposed as a mechanism of the sleep-dependent learning process in humans. However, behavioral data in humans that support the notion of improved hippocampal-related memory due to sleep has been inconsistent. We asked whether sleep improved hippocampal-related implicit memory in a contextual cueing task.
Methods: Seventy-four subjects were tested twice on the contextual cueing task. Subjects searched for a target (T) amongst distractors (L). In session 1, half of the item configurations are repeated throughout the session (OLD) and half contain random item configurations (NEW). Session 2 tested three conditions 1) OLD configurations from session 1, 2) NEW configurations, 3) and a new set of 12 repeated configurations (NEW/OLD). Subjects were assigned to a 90min Nap, Nocturnal Sleep, or Rest condition between the two sessions.
Results: We found an overall contextual cueing effect for session 1 (i.e. faster RT for OLD configurations compared with NEW), with no group interaction. The GroupXSessionXCondition ANOVA found no differences between groups, indicating that improvement between sessions was similar in subjects who slept and in those who did not sleep. Post-hoc tests showed no differences in session 2 between any of the groups in their retention of session 1 OLD or acquisition of session 2 NEW/OLD. All groups were also at chance in recognition of the OLD configurations.
Conclusion: These results are further evidence of a lack of involvement of sleep in learning involving the hippocampus. Thus, the proposed mechanism of hippocampal replay as a general model for sleep-dependent learning may need to be reconsidered.
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ERROR MONITORING IS IMPAIRED IN OBSTRUCTIVE SLEEP APNEA

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Introduction: The Anterior Cingulate Cortex (ACC) is critical in executive function and error-processing, and activity of ACC may be indexed by an event-related potential (ERP) measure known as the error-related negativity (ERN). Abnormal ERN has been found in sleep deprived neurologically normal controls, and executive dysfunction has been recognized previously in Obstructive Sleep Apnea Syndrome (OSA). To our knowledge, there has been no previous research of error-detection in OSA with the ERN.
Methods: Participants included 9 OSA patients aged 18-60 (mean/SD = 45.1 (10.9) years, 2 women and 8 men) with apnea-hypopnea index mean/SD = 27.3 (11.9) and oxygen saturation nadir mean/SD = 82.8 (5.6), and 9 age/sex-matched controls. ERN was elicited by Eriksen's Flanker Task, measured as the difference between correct and incorrect responses. Averaging and filtering was performed off-line utilizing ERP Statistical Software. Statistical analysis compared average ERN amplitude in patients and controls, utilizing one-way ANOVA and the jackknifing procedure utilizing SPSS software.
Results: There was a significant difference between OSA and control groups in response-locked ERN onset latency (OSA=-178.22 msec, controls=-88.89 msec; p=0.017), and a similar difference in stimulus-locked ERN onset latency (OSA=296.89 msec, controls= 272.89 msec; p=0.044). ERN average amplitudes for OSA and controls were not significantly different, nor was the lateralized readiness potential (LRP) delayed in OSA. P3 component latencies upstream of the ERN were also significantly longer in OSA than controls (p<0.001), but earlier primary perceptual encoding ERP waveforms did not differ between the groups.
Conclusion: Error processing is impaired in OSA patients compared to controls. P3 latency was also delayed in OSA, but earlier processing delays were not seen, nor was the LRP prolonged in OSA, indicating sparing of dysfunction in a temporally parallel cognitive processing pathway. These findings indicate a slowing in processing following encoding but just prior to stimulus classification that further extends to error-processing networks while sparing motor preparation pathways. Future research will expand the sample size and explore potential impact of clinical subgroups of OSA.
Support (optional): The author is grateful for study support by The Nathan and Beth Tross Research Fund for Cognitive Neuroscience, University of Iowa.

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NEXT-DAY TRAZODONE IMPAIRMENTS OF ARM STRENGTH AND MEMORY IN INSOMNIACS

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Introduction: Trazodone (Desyrel) is among the most widely prescribed sleep medications in the United States despite being indicated for depression and not insomnia. The risk of bedtime dosing of trazodone has not been systematically investigated in insomniacs. The primary goal of this ongoing study is to identify surrogates of accident risk with trazodone in chronic insomniacs.
Methods: Thus far four female adults with primary insomnia (mean + SD age 39+5 years) have completed this within-subject, randomized, double-blind three-week study in which seven-consecutive-day administration periods of 50 mg trazodone (TRZ) or placebo (PBO) capsules were separated by a one-week washout period. Following the first and seventh nights of capsule administration, participants completed overnight polysomnography followed by a next-morning test battery that included measures of simulated driving, equilibrium, short- and long-term memory, proximal strength, subjective effects, and daytime sleepiness.
Results: The morning after administration of the first capsule, robust effects were found on the 100-point self-reported impairment scale (TRZ: 54+11, PBO: 23+5; p=0.02). Also on the morning after the first capsule, trazodone significantly reduced upper limb function--reflected in mean total 1-kg lifts per arm in 30 seconds (TRZ: 25+5, PBO: 29+6, p=0.01)--and impaired verbal learning and memory on the Buschke Selective Reminding Test to a near-significant degree (TRZ: 120+11, PBO: 125+8 total words recalled, p=0.07). These three effects were no longer present after one week of dosing. After seven days of trazodone administration, slow wave sleep was increased relative to placebo (TRZ: 28+12%, PBO: 19+8% total sleep time, p=0.02). No statistically significant effects were found on any other measures.
Conclusion: These data suggest that a low starting dose of trazodone may be associated with early subjective and objective evidence of impairment in insomniacs in the absence of efficacy.
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SLEEP QUALITY FOLLOWING HEAVY ALCOHOL CONSUMPTION IN HEALTHY, YOUNG ADULTS: EFFECTS OF GENDER AND BEVERAGE TYPE

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Introduction: Alcohol ingested to intoxication prior to bed severely disrupts sleep quality, but few studies have examined moderators of this relationship. We evaluated whether subjective sleep quality and objective sleep continuity and architecture measures differed by gender and beverage type (high vs. low congener content) following a high dose of alcohol.
Methods: Ninety-five healthy, young adult volunteers (56 women, 24.5 ± 2.8 years) consumed alcohol or placebo at two experimental sessions in a randomized, placebo-controlled, mixed design. Following three days of 8 hours time in bed and screening polysomnography, participants consumed alcohol (high [bourbon] or low [vodka] congener content) to intoxication (maximum BrAC .11 ± .01g%) or matching placebo between 2045 and 2200 hours. Sleep was monitored with polysomnography (PSG) between 2300 and 0700 hours. In the morning, participants completed a validated post-sleep questionnaire.
Results: Morning sleep quality ratings did not differ by gender or beverage type, but sleep was rated as less refreshing (p<.001) and of a worse quality (p=.04) following alcohol. PSG indicated that alcohol increased the number of awakenings (p=.01) and wake after sleep onset (p=.01) and reduced total sleep time (p=.03) and sleep efficiency (p=.03) more in women than in men. Alcohol also increased SWS % (p=.01) and latency to REM sleep (p<.001) and reduced REM % (p<.001) and latency to SWS (p=.02) compared to placebo. Other than a trend for sleep latency (p=.06), no PSG differences in sleep continuity or architecture were found by beverage type. No differences in maximum BrAC were evident by gender of beverage type.
Conclusion: Alcohol consumed to intoxication disrupted sleep both subjectively and objectively. Objective measures of sleep continuity were more disturbed following alcohol for women than for men. The effects of a high dose of alcohol on sleep differ by gender but not by beverage type.
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ASSESSMENT OF THE ADAPTIVE VALUE OF DREAMS

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Introduction: Several lines of evidence indicate that sleep is beneficial for learning, but there is no experimental evidence yet that the content of dreams is adaptive, i.e., that dreams help the dreamer to cope with challenges of the following day. Our aim here is to investigate the role of dreams in the acquisition of a complex cognitive task.
Methods: We investigated electroencephalographic recordings and dream reports of adult subjects (n=22, 5 females and 17 males) exposed to a computer game comprising perceptual, motor, spatial, emotional and higher-level cognitive aspects ("Doom"). Subjects slept two nights in the sleep laboratory, a completely dark room with a comfortable bed and controlled temperature. Electroencephalographic recordings with 28 channels were continuously performed throughout the experiment to identify episodes of rapid-eye-movement (REM) sleep. Behaviors were continuously recorded in audio and video with an infrared camera. Dream reports were collected upon forced awakening from late REM sleep, and again in the morning after spontaneous awakening. On day 1, subjects were habituated to the sleep laboratory, no computer game was played, and negative controls for game-related dream reports were collected. On day 2, subjects played the computer game before and after sleep. Each game session lasted 1 hour, and sleep lasted 7-9 hours. Questionnaires were applied before and after the experiment to assess relevant variables (socio-demographic, pre- and post sleep, Pittsburgh, Fletcher & Luckett, Epworth, Horne).
Results: Several measurements of game performance showed marked overnight improvement in 21 out of 22 subjects; 17 out of 22 subjects reported the intrusion of game elements in their dreams, including potentially adaptive (insightful)strategies. Analysis of dream reports showed that the amount of game-related elements in dreams correlated with performance gains according to an inverted-U function analogous to the Yerkes-Dodson law that governs the relationship between arousal and learning.
Conclusion: The results indicate that dreaming is an adaptive behavior.
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DREAMS DURING PREGNANCY AND POSTPARTUM DEPRESSION: FURTHER EXPLORATION

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Introduction: It has been suggested that dreams during pregnancy could help identify early signs of postpartum depression. Kron and Brosh (2003) reported that postpartum depression was related to low masochistic score and low apprehension levels in retrospectively collected dreams of pregnant women during their third trimester. They suggested that women who developed postpartum depression tended to repress anxiety and apprehension in their dreams, and that they did not do "emotional work" through their dreams. We report on an attempt to further examine this phenomenon with dreams obtained with a morning home dream diary.
Methods: 93 pregnant women maintained a ten-day morning dream diary during their third trimester and one month after the delivery. In addition, they completed the Edinburgh Postnatal Depression Scale (EPDS) during pregnancy and after birth. For each period, one dream per participant was coded by two raters using Hall & Van de Castle scales and Beck Masochistic scale.
Results: We did not observe a significant relationship between postpartum depression and masochistic scores and apprehension levels in pregnancy dreams. However, a t-test revealed a higher frequency of misfortune elements ($p < .01$) and masochistic dreams ($p < .01$) during pregnancy in women who reported depressive symptoms in their third trimester compared to those who did not. Moreover, the postnatal dreams of women with postpartum depressive symptoms contained more misfortunes ($p < .01$) and more elements related to a threat for the baby ($p < .01$).
Conclusion: Our results support the continuity hypothesis and suggest that dreams during pregnancy and postpartum do reflect waking levels of depression. Discrepancy in our results compared to earlier findings may be due to methodological differences, namely our use of actual morning dream diary reports as opposed to retrospective dreams.
Support (optional): This research was supported by the Canadian Institutes of Health Research.

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NOCTURNAL ROAD TRAFFIC NOISE AND SLEEP QUALITY: HABITUATION EFFECTS ASSESSED IN A TEST-RETEST FIELD SITUATION

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Introduction: The impact of nocturnal road traffic noise on sleep has been well documented over the years, but few studies have demonstrated longitudinal effects in the home environment. In this field study, habituation of nocturnal road traffic noise on sleep quality over a period of 1.5 years has been investigated.
Methods: 24 healthy volunteers, living in areas with a high density of road traffic noise in the Brussels area wore an actigraph during 7 consecutive nights. Road traffic noise [LAeq (23h-07h)] was measured inside and outside the bedroom during 7 nights using class 1 & 2 noise measurement devices. The same test protocol was repeated 1.5 years later. Sleep variables Time in Bed (TIB) and Total Sleep Time (TST) during week days were derived from actigraphy measurements to calculate Sleep Efficiency (SE). Mean noise levels inside and outside the bedroom during week days were analyzed.
Results: Repeated measures ANOVAs show no significant change in the noise level inside and outside the bedroom ([$F(8,4)=0.75$;ns], [$F(8,1)=33.91$;ns]; respectively). In parallel with this observation, sleep efficacy evidenced no statistically significant difference between the test and retest after 1,5 years [$F(6,5)=0.31$;ns].
Conclusion: Over a period of 1.5 years, the impact of environmental noise on sleep efficiency did not change in our participants as no improvement, nor a decrement in SE was observed. However, only SE was calculated based on actigraphic recordings. Given the complexity of the different domains involved - sleep and noise, subjectively defined sleep quality, for instance, should also be taken into account in further evaluation.

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THE EFFECT OF SLEEP ON EGOCENTRIC AND ALLOCENTRIC SPATIAL MEMORY PERFORMANCE

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Introduction: Several studies now demonstrate that post-training sleep is beneficial for the retention of hippocampus-dependent memory. It has been proposed that sleep may not only enhance memory performance, but also may function to facilitate systems-level reorganization of memory traces across time. Here, we examined the effects of post-training NREM sleep on qualitative aspects of spatial memory. Additionally, we assessed whether the report of task-related mentation (i.e. thoughts, feelings, dreams) during the retention interval predicted performance at retest.
Methods: Participants (n=39) were trained on a 3D-style virtual maze task at 12:30pm. Following training, subjects either immediately lay down to begin a 1.5 hr nap opportunity (n=18), or else remained awake (n=21). At retest (5:30pm), participants completed recognition tests from an Egocentric Perspective (1st person view) and Allocentric Perspective (overhead map view), regarding critical decision points in the maze. Each participant was also classified as having an egocentric or allocentric spatial representation preference, using the "Tunnel Task" developed by Gramann et al (JEP, 2005).
Results: Rather than exerting a particular effect on egocentric vs. allocentric test performance, sleep was selectively beneficial for the test format which matched participants' spatial representation preference (sleep x preference interaction: $p=.04$). Furthermore, the overall effect of sleep on maze completion times was dependent on whether participants reported mentation (thoughts, feelings, dreams) related to the maze task between learning and retest (sleep enhanced performance only when related cognition was reported: $p=.006$).
Conclusion: These observations suggest that the process of sleep-dependent memory consolidation is contingent upon the specific manner in which a task is encoded, and is correlated with task-related cognition during the retention interval.
Support (optional): This research was supported by NIMH grant #48832 and NIH T32 training grant HL07901-10 to the Harvard Division of Sleep Medicine.

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WHO SLEEPS BETTER? SOCIOECONOMIC DIFFERENCES IN REPORTS OF SLEEP DISTURBANCE

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Introduction: Individuals with lower socioeconomic status are more likely to report short or long sleep duration, which are related to increased

mortality. However, these studies have not examined sleep disturbance, which may better predict health problems. This study examined sleep disturbance from the CDC Behavioral Risk Factor Surveillance System (BRFSS), distributed across socioeconomic factors.
Methods: The present data includes n=159,856 participants who provided complete data. Sleep disturbance (SLEEPDIS) was measured with the item, "Over the last 2 weeks, how many days have you had trouble falling asleep or staying asleep or sleeping too much?" Responses were dichotomized as percentage who reported ≥7 days disturbance. Socioeconomic variables included ethnicity, marital status, education, income, and employment. Cases were weighted to reflect population norms and compared using omnibus chi-square.
Results: All omnibus tests were significant. 18.8% of Americans reported SLEEPDIS. Rates of reported SLEEPDIS were as follows: Ethnicity:White(19.3%), African-American(19.2%), Hispanic/Latino(18.8%), Asian/Other(18.6%), Multiracial(26.8%). Income:<$10,000(26.1%), $10,000-$15,000(22.3%), $15,000-$20,000(18.5%), $20,000-$25,000(16.2%), $25,000-$35,000(13.2%), $35,000-$50,000(11.4%),$50,000-$75,000(9.7%),$75,000+(7.8%). Education: didn't finish(27.4%), high school(21.8%), some college(20.7%), college degree(13.7%). Employment: employed(15.7%), self-employed(16.1%), retired(17.1%), student(21.5%), homemaker(20.5%), unemployed <1yr(31.6%), unemployed >1yr(35.8%), unable to work(51.6%). Marital status: married(16.3%), never married(21.3%), part of unmarried couple(22.8%), widowed(25.4%), divorced(21.2%), separated(30.7%).
Conclusion: These results, from the largest sample to date investigating sleep quality, show several interesting patterns. SLEEPDIS was inversely related to socioeconomic status- SLEEPDIS was associated with less education, lower income, being unmarried or being unemployed. Lower socioeconomic status bestows disadvantages from an early age that may develop over time, and sleep may be part of this. SLEEPDIS was much more likely in Multiracial individuals, but rates in African-American, Hispanic/Latino or Asian groups approached Whites, suggesting that while disparities exist, they are not as prominent as in other disorders. Future research will need to examine interactions between race/ethnicity and other factors to understand what populations are at greatest risk and why.
Support (optional): Supported by 2T32HL007713.

1296

THE EFFECT OF REDUCED SENSORY INTERFERENCE ON DECLARATIVE AND PROCEDURAL MEMORY PERFORMANCE ACROSS TIME

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Introduction: Although it is now well established that post-training sleep is beneficial for both declarative and procedural memory, the underlying processes at work remain unclear. It has been proposed that the mnemonic benefits of sleep might be primarily due to a simple "lack of interference", as sleep unquestionably represents a time when sensory input is reduced to a minimum. To address this hypothesis, we examined the effect of reduced sensory stimulation during wakefulness on memory retention.
Methods: Participants (n=53) were student volunteers between the ages of 18-30. Subjects arrived at the laboratory at 5:00pm and were trained on both a declarative "word pair associates" task, and a procedural "finger tapping" task (counterbalanced). Immediately following learning, subjects assigned to the "Quiet Wake" condition sat, semi-recumbent, in a darkened room for 30 minutes while wearing a blindfold and earplugs. A white noise generator additionally masked ambient noise. PSG data were recorded to ensure wakefulness. Subjects assigned to the "Active Wake" condition watched PG-rated videos during this time. At approximately 7:30pm, all participants were retested on both learning tasks. Sleepiness was measured at both pre- and posttest using the Stanford Sleepiness Scale (SSS).
Results: Subjects were excluded from analysis if they fell asleep during the study, or if they provided SSS scores >4. Memory performance was equivalent in the "Active" (n=13) and "Quiet" (n=18) groups, for both the declarative (p>.9) and the procedural (p>.7) learning tasks.
Conclusion: In the present study, a 30-minute period of reduced sensory simulation had no effect on either declarative or procedural memory, despite the fact that equal or shorter durations of sleep (i.e., brief naps) have been shown to have large mnemonic benefits. These data suggest that reduction of sensory input alone is insufficient to explain the effects of sleep on memory processes.
Support (optional): This research was supported by NIMH grant #48832 and NIH T32 training grant HL07901-10 to the Harvard Division of Sleep Medicine.

1297

CHANGES IN SLEEP ARCHITECTURE FOLLOW THE SUCCESSFUL ACQUISITION OF A MOTOR SKILL USING MENTAL PRACTICE

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Introduction: Previous studies have reported learning related sleep changes after physical practice on a motor task. The present study assessed sleep changes occurring after acquisition of a motor task (rotary pursuit task) using mental practice. Mental practice refers to the cognitive rehearsal of a task in the absence of the physical movements used to perform the task.
Methods: Participants were 22 university students (mean age=20.5). After an acclimatisation night, participants had a baseline night of sleep recording. The following evening participants were randomly assigned to one of three conditions: (1) physical practice (n=8; performed 30 physical trials of the rotary pursuit); (2) mental practice (n=7; performed 3 physical and 27 mental trials); (3) no-practice controls (n=7; performed 3 physical trials). Then, participants had a post-training night of sleep recording. One week later, all participants were given 30 physical trials on the rotary pursuit. Within-group comparisons (baseline vs. post-training) were used to examine learning related changes in sleep stage duration, stage 2 spindle densities and REM densities.
Results: The physical and mental practice groups performed significantly better than the controls on the rotary pursuit at retest (p<.02), indicating that successful learning occurred in both groups. The mental practice group had a significant decrease in slow-wave sleep from the baseline to post-training night (p<.01), with the reduced minutes manifesting primarily as increased REM sleep. None of the groups showed a significant difference between baseline and post-training for stage 2 spindles or REM densities.
Conclusion: The results suggest that mental practice was as effective as physical practice for acquiring a motor skill. Furthermore, the post-learning night of sleep following mental practice appears to be structurally different than that following physical or no-practice. Together, the findings point to a role for sleep in the consolidation of motor learning through mental practice.
Support (optional): This research was supported by a grant from the Natural Sciences and Engineering Research Council (NSERC) of Canada

1298

DISAPPEARANCE OF GENDER DIFFERENCES IN THE DREAMS OF UNIVERSITY STUDENTS

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Introduction: Studies from the 1950s and 1980s have observed significant gender differences in the dream content of American college students. However, it has been suggested that these differences may be affected by significant changes towards homogenization of gender roles in Western society. We examined this hypothesis with an equivalent sample of Canadian students.
Methods: So far, two morning home diary dreams were obtained from each of 100 Canadian university students (50 males, 50 females, age range 18 to 24). Each dream was then coded by two raters using the Hall and Van de Castle scales. Gender differences in dream content were calculated for the variables of characters, social interactions, settings, self-concepts, misfortunes, good fortune, success and failure as well as striving using Cohen's h.
Results: Significant gender differences were found for the male to female ratio of dream characters (M>F, h=-0.25, p=0.012), in the percentage of characters that were animals (F>M, h=+0.23, p=0.003), in the aggression to friendliness ratio of social interactions (M>F, h=-0.29, p=0.039) and the amount of dreams containing sexuality (F>M, h=+0.33, p=0.021). However, significance was not observed for the other variables such as proportion of characters that are friends, familiar or family, amount of physical aggression, indoor or familiar settings, references to the torso or anatomy, failure, success and striving. Therefore, 10 of the 14 gender differences of the American studies were not found in this new sample.
Conclusion: It will be interesting in future studies to determine if the reduction in gender differences is attributable to changes in social roles and/or cultural differences between Americans and Canadians or simply to sample size.
Support (optional): Social Sciences and Humanities Research Council of Canada

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CENTRAL VS PERIPHERAL REPRESENTATIONS IN SLEEP AND OFFLINE CONSOLIDATION OF RHYTHM TIMING

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Introduction: The consolidation of procedural memory during sleep has been increasingly documented in the last decade. However, most studies to date have investigated this phenomenon through the use of low-level perceptual or motor tasks which place a strong emphasis on peripheral (effector-specific) representations. In this paper, we build on recent findings from our lab which have demonstrated that the processing of temporal rhythms consolidates over a period of sleep, by evaluating the extent to which this consolidation transfers from a trained to an untrained effector.
Methods: A rhythm tapping task was used to probe the representation of rhythms, performed by the same subjects over two sessions separated by a 24hr period including sleep. On each trial, participants first synchronized finger taps to an auditory rhythm, then continued to tap the rhythm after the auditory stimulus ceased. Right-handed participants were trained using either their right or left hand, and subsequently tested on both hands in separate blocks after 24hrs. Performance was measured using both coefficient of variation of produced temporal intervals (to measure consistency) and Euclidean distance from the original rhythm (to measure accuracy).
Results: T-tests revealed a significant improvement in consistency across the 24hr period for both hands ($p<0.0001$), with no difference in performance between hands ($p>0.1$), while accuracy showed a significant improvement over the same period for the training hand only ($p<0.01$).
Conclusion: Our results show that both central and peripheral representations of a temporal rhythm consolidate offline over a 24 hour period. The improvement in consistency shows transfer between effectors, and must therefore occur at a central level. The improvement in accuracy does not transfer, indicating a peripheral level representation. In keeping with our previous results which reveal that the consolidation benefit occurs primarily during sleep, these data suggest that sleep consolidation may operate at both central and peripheral levels.

1300

MOTOR SKILL LEARNING AFTER EXPERIMENTAL REDUCTION OF SLOW-WAVE ACTIVITY AND INCREASE OF SPINDLE FREQUENCY ACTIVITY

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Introduction: Previously we found evidence for a causal role EEG slow-wave activity (SWA; power density in the 0.75-4.5 Hz range) in overnight gains of a perceptual skill, by using an acoustic SWA suppression paradigm. In contrast, several researchers have reported improvements in motor skills to be associated with the production of sleep spindles. Here we used the SWA suppression paradigm to examine the role of both SWA and spindle frequency activity (SFA; power density in the 12.25-15.0 Hz range) in motor sequence learning.
Methods: Participants (age 18-30 y) were trained with their left non-dominant hand on a 5-element finger tap sequence task (twelve 30-s trials) following baseline sleep (BL), and were tested 24 h later after a 4-h experimental sleep episode (EX) in Test 1 (four 30-s trials), and again following a night of 8-h recovery sleep (RC) in Test 2 (four 30-s trials). In the Suppression group (N=11) SWA was reduced with acoustic tones (45-100 dBA) during EX, while no tones were presented in the Control group (N=9). SWA and SFA (derivation: F4/C4) in EX were expressed as percentages of the first 4 h of BL. Learning was quantified as the percent increase of correct sequences in Test 1 and Test 2 relative the last 4 trials during the training session.
Results: In the Suppression group, SWA in EX was reduced by 27%, and SFA increased by 21% compared to BL sleep ($p<0.01$ t-tests), while no such changes were found in the Control group ($p>0.47$). Both groups showed learning, but the extent of learning did not differ between groups neither in Test 1 (Suppression vs. Control: +17.0% vs. +19.5%; $p=0.72$) nor in Test 2 (+24.3% vs. +27.2%; $p=0.62$). Performance improvement in Test 1 did neither correlate (Pearson; N=20) with SWA ($r=0.20$, $p=0.38$) nor with SFA ($r= -0.21$, $p=0.36$) in EX sleep. Furthermore, there was no correlation between performance improvement and the product of SWA and SFA ($p=0.83$).
Conclusion: In contrast to perceptual learning, overnight gains in a motor skill appear to be resilient against large reductions of SWA. While not excluding a role for NREM sleep in learning, the data do not support a simple relationship between NREM sleep intensity and overnight improvement of a motor skill.
Support (optional): NARSAD, Milton Fund of Harvard University, NIH grant NCRR-GCRC-M01-RR02635; MM was supported by a NIH postdoctoral training fellowship 5-T35GM12453_03.

1301

ANXIETY AND DEPRESSION MEDIATE THE RELATIONSHIP BETWEEN SLEEP ONSET LATENCY AND EMOTIONAL EATING IN MINORITY CHILDREN

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Introduction: Research suggests that there is a link between sleep and the obesity epidemic that disproportionately affects minority populations. Studies examining the pathways by which this association exists are lacking. Obesity-related behaviors, such as emotional eating, associated with sleep disturbances, such as prolonged sleep onset latency (time to fall asleep), may be involved. This study examined associations between sleep onset latency and eating style in a minority sample of children.
Methods: A cross-sectional school-based study of sleep, psychological constructs, diet and physical activity was conducted in 6 public and private schools in Los Angeles County. An ethnically diverse sample of 356 third through fifth graders completed confidential self-report surveys. Multilevel regression (MLM) analyses were conducted to study associations while controlling for gender, ethnicity, and the random effect of school.
Results: Girls made up 57% of the total sample, which was predominantly Latino (42.6%), followed by African Americans (21.6%) and Asians (19.2%). MLM revealed that there were significant associations between sleep onset latency and emotional eating ($p=.0049$), depressive symptomology ($p<.0001$) and trait anxiety ($p<.0001$). Sobel's test for mediation showed that both depressive symptomology ($p=.028$) and trait anxiety ($p=.018$) were mediators of the relationship between sleep onset latency and emotional eating. Thereby providing a mechanism through which sleep onset latency is related to emotional eating.
Conclusion: These findings suggest that sleep onset latency is associated with increased anxiety, depressive symptoms, and emotional eating. Although causal inferences cannot be drawn from this cross-sectional data, future studies should examine the possibility that problems falling asleep could lead to emotional dysregulation that in turn leads to emotional eating. Emotional eating may be one avenue by which sleep disturbances lead to overweight and obesity.

1302

DOES SLEEP TRANSFER IMPLICIT TRAINING TO EXPLICIT KNOWLEDGE?

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Introduction: Sleep influences learning of the classic serial reaction time task (SRTT). It has been reported that implicit SRTT learning before sleep produces explicit SRTT knowledge after sleep. As part of a larger study of SRTT learning and sleep, we undertook to evaluate this finding.
Methods: Eight subjects were trained on an explicit version of the classic SRTT task, and eight subjects were trained on an implicit version. The two conditions were designed to definitively separate explicit from implicit learning in normal college students. In subjects trained and tested in the same session, without intervening sleep, a significant dissociation of explicit from implicit SRTT learning was achieved. Each subject slept in the laboratory on one adaptation night and one experimental night, at which time he or she received SRTT training before sleep and SRTT testing in the morning after sleep. BIOPAC™ hardware and software were used for data collection and analysis.
Results: After sleep, subjects trained in the implicit condition showed significantly greater reaction times to a novel SRTT sequence than to the implicitly trained target sequence (2-tailed paired t-test, $p = 0.001$). Subjects trained in the explicit condition did not (2-tailed paired t-test, $p = 0.126$). Conversely, implicitly trained subjects could not explicitly reproduce the target sequence (X^2 for goodness of fit = 2.08^{-15}), whereas explicitly trained subjects did so easily (X^2 for goodness of fit = 0.997). In addition, explicitly trained subjects rated the similarity of non-target sequences to the target sequence significantly more accurately than did implicitly trained subjects.
Conclusion: In this study sleep did not transfer implicit SRTT training to explicit SRTT learning. Nor did sleep transfer explicit training to implicit learning. Given a strict dissociation between implicit training and explicit training, the functional boundary between presumed neostriatal and presumed medial temporal lobe processes can be maintained in sleep.

1303

OBJECTIVE TOTAL SLEEP TIME IS LONGER THAN SUBJECTIVE TOTAL SLEEP TIME IN THOSE PATIENTS WITH PRIMARY INSOMNIA AND OBSTRUCTIVE SLEEP APNEA SYNDROME

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Introduction: It is assumed that there is a discrepancy between subjective and objective sleep time in patients with sleep disorders. This study evaluated the difference between the objective total sleep time (TST) and the subjective TST obtained from nocturnal polysomnography (NPSG) and sleep questionnaires completed by patients diagnosed with primary insomnia or obstructive sleep apnea syndrome (OSA).
Methods: The subjects were 311 consecutive patients who were referred to the Center for Sleep and Chronobiology at the Seoul National University Hospital during 2007~2008 and were finally diagnosed with NPSG as primary insomnia or OSA. They were also asked to complete two questionnaires: Pittsburgh Sleep Quality Index (PSQI) including TST of recent 1 month (TST_{PSQI}) and a Morning Questionnaire administered on the morning right after NPSG about the subjective TST during NPSG (TST_{MQ}). ANOVA (with post hoc Tukey B test) and Pearson correlation (each with significance level of $p<0.05$) were used for analyses.
Results: Among the 311 subjects, 77 were diagnosed with primary insomnia (40 males, 37 females) and 234 were diagnosed with OSA (198 males, 36 females). In both diagnostic groups, TST_{NPSG}, TST_{PSQI} and TST_{MQ} significantly differed (primary insomnia: 388.6+68.8 min vs. 297.1+101.9 min vs. 272.0+113.0 min, $F=31.3$, $df=2$, $p<0.01$) (OSA: 411.8+56.4 min vs. 374.0+83.3 min vs. 369.0+107.4 min, $F=18.0$, $df=2$, $p<0.01$). Tukey B test revealed that TST_{NPSG} differed significantly either from TST_{PSQI} or from TST_{MQ} in both diagnostic groups ($p<0.05$, respectively). Differences of TST_{NPSG} and TST_{PSQI} between primary insomnia and OSA (91.5±117.3 min vs. 37.8±99.5 min, respectfully) and of TST_{NPSG} and TST_{MQ} between primary insomnia and OSA (116.7±117.5 min vs. 43.2±100.1 min, respectfully) were all significant ($t=3.9$, $p<0.01$; $t=5.3$, $p<0.01$, respectfully). Differences between TST_{NPSG} and TST_{PSQI} and between TST_{NPSG} and TST_{MQ} were positively correlated with PSQI total scores in both diagnostic groups (primary insomnia: $r=0.62$, $p<0.01$ and $r=0.29$, $p<0.01$, respectfully) (OSA: $r=0.42$, $p<0.01$ and $r=0.25$, $p<0.01$, respectfully).
Conclusion: The subjective TST was shorter than the objective TST not only in patients with primary insomnia but also in patients with OSA. The differences were significantly higher in primary insomnia than in OSA, probably reflecting additional psychological factor. We also noted that the difference between the objective and the subjective TSTs increases, as the subjective sleep quality gets poorer.

1304

COLLEGE ORGANIC CHEMISTRY GRADES CORRELATE WITH VARIABILITY IN SLEEP DURATION

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Introduction: Converging evidence has demonstrated the importance of sleep in the consolidation and enhancement of recently formed memories. But it's relationship to the use of memory in real life scenarios is less clear.
Methods: Twelve Harvard undergraduates enrolled in organic chemistry (Chemistry 17), 18-21 years of age at enrollment, wore wrist actigraphs for a total of 1,259 subject-nights. Eight of 11 completers provided permission for their grades to be obtained, and 7 had complete data sets for analysis of sleep - grade correlations.
Results: Average grades for each student correlated positively, but non-significantly, with their mean total sleep time the night before each exam ($r = .63$, $p = .13$), minimally with their mean total sleep time 2-5 nights prior to each exam ($r = .05$, $p = .90$), but strongly with the standard deviation of mean sleep time 2-5 night prior to each exam ($r = -.92$, $p = .003$), with each hour increase in standard deviation predicting a 17 percentile drop in rank-in-class.
Conclusion: Performance in a rigorous college course was highly correlated with the variability in actigraphically determined total sleep time 2-5 nights prior to exams. Possible sources of this correlation will be discussed.
Support (optional): Support provided by NIMH 48832.

1305

NO SIGNIFICANT EFFECT OF SLEEP DEPRIVATION ON IMPULSIVITY IN A DELAY DISCOUNTING TASK

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Introduction: Executive functioning is thought to be especially vulnerable to impairment due to sleep loss. In previous studies, however, we found that some aspects of executive functioning are resilient to total sleep deprivation (TSD). These studies focused on "cold" cognitive tasks, devoid of affective cognition. In the present study, we consider a delay discounting (DD) task, which requires motivational reasoning and affective or "hot" cognition. In each of 27 trials, subjects choose between receiving two different amounts of imaginary money—one amount is smaller but rewarded immediately, while the other is larger but rewarded after varying time delay. Choices based on reward magnitude and delay are used to estimate how value declines subjectively with delay. This is described with a hyperbola with rate parameter k, which reflects impulsivity. We use the DD task here to examine the effects of TSD on impulsivity in decision making.
Methods: 23 healthy adults (22-38y; 11f) spent 7 consecutive 24h days in a laboratory. 12 subjects were randomized to 62h TSD preceded and followed by 2 days with 10h TIB; 11 controls had 10h TIB each night. The DD task was administered during baseline, at 51h TSD (or control), and after 2 days of recovery, with circadian timing held constant. Different but equivalent versions of the task were presented in randomized order.
Results: Mixed-effects ANOVA showed no effect on k values of test session ($F=1.32$, $P=0.28$), condition ($F=2.05$, $P=0.16$), and condition by session interaction ($F=0.09$, $P=0.92$). The average TSD effect on k values was -0.002±0.006—a non-significant decrease in impulsivity. There was a significant effect on response time (RT) of test session ($F=17.7$, $P<0.001$), with subjects responding progressively faster (practice effect), while there was no effect of condition ($F=1.31$, $P=0.26$) or interaction ($F=2.44$, $P=0.10$). The average TSD effect on RT was an increase of 605±230ms (planned contrast: $t=-2.16$, $P=0.04$).
Conclusion: The effect of TSD on k values was non-significant and negligible compared to effects in studies involving increased working memory load, which documented large increases in k. The present results indicate that under controlled laboratory circumstances, 51h TSD did not alter impulsivity, providing preliminary evidence that some aspects of "hot" executive functioning may be resilient to sleep loss. This finding needs to be interpreted in the context of subjects responding slower on the DD task during TSD.
Support (optional): USAMRMC award W81XWH-05-1-0099 and DURIP grant FA9550-06-1-0281.

1306

INFLUENCE OF ZOLPIDEM AND SLEEP INERTIA ON COGNITION

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Introduction: Sleep inertia and hypnotics are reported to impair cognition. We examined whether the combination of sleep inertia and the hypnotic zolpidem produce greater cognitive impairment than sleep inertia alone. We tested the hypotheses that awakening from sleep would impair cognition, that the sleep medication zolpidem would produce greater impairments than placebo, and that older adults would show greater impairments than young adults.
Methods: Twenty-three healthy, community-dwelling adults, twelve older (8 females, 4 males), aged 67.42±4.23 (mean±SD) and eleven younger (5 females, 6 males), aged 21.82±2.36 participated in a randomized, placebo-controlled, counterbalanced protocol. Participants completed three laboratory conditions. Two conditions were double blind: (a) sleep-placebo, (b) sleep-hypnotic (5mg Zolpidem); and the third single-blind: (c) wakefulness-placebo. Hypnotic/placebo was administered 10 min prior to lights out/wakefulness, scheduled at habitual bedtime. Six minutes following a 110 min sleep opportunity or 110 min wakefulness sitting in bed, cognition was assessed with two executive function tasks: working memory—Mathematical Addition task, and inhibitory control—Stroop Color Word test. Age and condition differences were assessed with Mixed-effects model ANOVA.
Results: Significant effects of treatment condition and age x treatment condition for working memory and of treatment condition for inhibitory control were found ($p<0.05$). Cognition was worse with large effect sizes after sleep-hypnotic compared to sitting in bed wakefulness-placebo. In addition, cognition was worse with medium to large effect sizes after taking sleep-hypnotic compared to sleep-placebo. Cognition was also worse with small to medium effect sizes in older and large effect sizes in young subjects after awakening from sleep-placebo when compared to sitting in bed wakefulness-placebo.
Conclusion: The combination of sleep inertia with a hypnotic produces greater cognitive impairment than does sleep inertia alone, regardless of age. These findings reveal that awakening from sleep after taking the sleep medication zolpidem impairs components of executive function that are critical for decision making.
Support (optional): Research supported by NIH AG024621, NIH M01RR00051, Beverly Sears Graduate Student Grant and a grant from the Undergraduate Research Opportunities Program in collaboration with the Biological Sciences Initiative at the University of Colorado at Boulder.

1307

MEMORY CONSOLIDATION OF SEMANTICALLY RELATED AND UNRELATED WORD PAIR MEMORIZATION INCLUDING EMOTION

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Introduction: Several studies demonstrating the effect of sleep on memory consolidation have used word-pairs (WP) consisting of semantically associated nouns. Some other studies also used unrelated materials to find a similar sleep effect. Putting their results together, some researchers have suggested that memories with a strong semantic association might benefit more from sleep than memories for novel associations. Contrary to previous conclusion, we assess, for the first time, the relative contribution of sleep to the processing of both types of stimuli, semantically related word-pair (SRWP) and semantically unrelated word-pair (SUWP). In addition to this foundation, the WPs which we used conveyed three different kinds of emotions, negative, neutral and positive, to investigate the contribution of emotion to memory consolidation in WP memorization task.

Methods: 66 university students (42 female, age 18-30) were assigned randomly to 4 groups night+SRWP (n=14), night+SUWP (n=14), day+SRWP (n=20) and day+SUWP (n=18). Two lists of SRWPs and SUWPs were generated consisting of 48 WPs including negative, neutral and positive emotions, 18 pairs each. Subjects had to repeat the training phase until they can memorize 60% of the WPs. They then recalled the WPs after a 12-hour delay.

Results: Night group showed better performance than day group ($p<0.001$). There were no difference between the two SRWP and the two SUWP groups after training session, but the performance difference for both SUWP groups was better than the SRWP groups in the test session ($p<0.01$). The number of memorized emotionally neutral, positive and negative WPs for both SRWPs and SUWPs were significantly different at the end of the training phase ($p<0.05$). Memorized emotionally neutral WPs for Day group in the test session was significantly better than emotionally negative and positively WPs ($p<0.05$). Emotionally different WPs were not significantly different in night group ($p=0.5$).

Conclusion: Performance on retrieving SUWPs was better in both day and night groups. It was the SUWPs that showed the greatest performance post-sleep. Our results suggest that sleep benefits the consolidation of newly formed semantic relationships. In addition, non-selectively retain all kind of WPs compared to non-sleep which retain emotionally neutral WPs more.

Key Word Index

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