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Effects of Modafinil on Attentional Processes During 60 Hours of Sleep Deprivation

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The present study investigates the effects of modafinil (300 mg/24 h) versus a placebo on the performance of a visual search task during 60 h of sleep deprivation. Modafinil was administrated in doses of 100 mg three times per day during sleep deprivation. Six healthy volunteers participated in a double-blind experiment including two experimental sessions of 7 days each. The experiment used the visual search paradigm for an 'O' target among 'Q' distractors and the reverse. The speed and accuracy in detecting the target were measured by RTs slopes (i.e. search rates) and the number of errors (i.e. error rates), respectively. Many authors attribute rapid search rates obtained for 'Q' targets (low RTs slopes) to parallel/automatic processes and slow search rates obtained for 'O' targets (high RTs slope) to serial/attentional processes. The results revealed an asymmetrical search pattern for the detection of 'Q' versus 'O' targets across the sleep deprivation period (i.e. parallel versus serial search, respectively). Rapid search rates for 'Q' targets remained unchanged between placebo and modafinil conditions during sleep deprivation. However, slow search rates for 'O' targets increased linearly in placebo condition, but remained at the same level as the control-test in modafinil condition. Error rates and search rates also increased. For 'O' and 'Q' targets, the number of errors increased in the placebo condition, but remained stable in the modafinil condition. In summary, we can conclude that the administration of modafinil (300 mg/24 h) during sleep deprivation prevents the slowing of serial processes (attentional shifts) and the increasing of errors. © 1998 John Wiley & Sons, Ltd.

KEY WORDS — sleep deprivation; modafinil; early vision; spatial attention

INTRODUCTION

The debilitating effects of sleep deprivation on behavioural performance in many prolonged work situations are now well documented in the literature (for a review, see Krueger, 1989; Riback, 1983). Many studies have shown that the disruption of sleep–wake cycles impairs psychomotor and mental performance (Angus and Heslegrave, 1985; Heslegrave and Angus, 1985; Haslam, 1982; Opsad *et al*., 1978). Methods used to prevent the negative effects of sleep deprivation fall into two categories. The first includes non pharmacological procedures based on the training of subjects and on sleep management with strategically placed small naps used in sustained work situations (Naitoh and Angus, 1989; Angus *et al*., 1992). Such procedures rapidly proved to be insufficient to recuperate and overcome the effects of sleep loss (Naitoh, 1981). The second category includes pharmacological methods based on the administration of alerting substances used as a complement to sleep management. Lagarde (1990) divided those substances into three categories: amphetaminic, xanthines derivatives and new synthetic substances. Although these substances keep you awake, amphetamines and xanthines are frequently inapplicable because they induce decrements in mental performance and adverse side effects such as euphoria, loss of appetite, increases in heart rate and blood pressure. In addition, greater Rapid Eye Movement (REM) sleep disturbances were observed with amphetamines than with modafinil (Buguet *et al*., 1995). Not to mention that d-amphetamines can be addictive. The third category is a new family of chemical molecules discovered by the Lafon Laboratory (adrafinil, modafinil, etc.). They have the same wakening properties but without side and rebound-effects (Buguet *et al*., 1995; Pigeau *et al*., 1995). Such substances belong to a new class of psychostimulants called eugregoric (eu = good, gregor = wakefulness) because of the good

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wakefulness they induce. The quality of wakefulness is assessed by mental performance in cognitive tests (Lagarde and Batejat, 1995), whereas drowsiness is assessed by the theta/alpha spectral powers ratio (Pigeau *et al.*, 1987; Bastuji and Jouvet, 1988). Modafinil, whose structural formula is diphenylmethyl-sulfinyl-2 acetamide, has been largely studied. Its eugregoric effect is mediated by an agonist effect of central post-synaptic $\alpha 1$ adrenergic receptors (Duteil *et al.*, 1990) and probably by dopaminergic mechanisms (Mignot *et al.*, 1994). Modafinil administrated per os to healthy young volunteer adults is tolerated until 400 mg/24 h. Up to this dose, EEG effects (increases in EEG alpha rhythm and decreases in slow theta and delta activities) confirm the hypothesis of a higher level of wakefulness without toxic effects. Finally, psycho-behavioural studies on modafinil show that the most appropriate posology for us to obtain a good wakening effect varies between 200 and 400 mg every 24 h in adults (Lafon Laboratory, 1994).

Besides the effects of modafinil to maintain a high-level of vigilance, the investigations of the mental abilities in healthy subjects (Lagarde and Batejat, 1995; Pigeau *et al.*, 1995) reveal that performance remains at control level for up to 44 h after an administration of 600 mg of modafinil every 24 h. On the whole, performance scores on most behavioural tasks are not affected by sleep deprivation when modafinil is administered. Since those results are obtained from global performance scores on various mental tasks, they do not indicate the nature of the processes involved in maintaining a high level of wakefulness with modafinil. Since spatial attention is an important component of vigilance, we studied the mechanisms through which modafinil becomes effective in visual attentional processes. Many theories of vision agree with the existence of two visual processing stages involving preattentional processes and attentional processes (Julesz, 1981; Marr, 1982; Neisser, 1967; Treisman and Gelade, 1980; Zeki, 1993). Using an experimental paradigm involving the detection of an 'O' target among a set of 'Q' distractors and the reverse ('Q' target among 'O' distractors), Treisman (1985) observed an asymmetrical processing in the detection of 'O' versus 'Q' targets: a serial/attentional processing versus a parallel/preattentional processing. Most models of human visual processing stipulate that covert shifts of attention play an important role in visual search. The preattentional processing is characterized by the absence of attentional shifts. The search is described as 'parallel' because the search time is not affected by the number of stimuli in the array. Conversely, the attentional processing is characterized by the presence of attentional shifts. The search is described as 'serial' because the search time increases as a function of the number of stimuli in the array (Julesz and Bergen, 1983; Treisman and Souther, 1985; Prinzmetal *et al.*, 1986; Wolfe, 1994).

The purpose of this experiment was to study the effects of sleep loss on parallel and serial processes in early vision (i.e. preattentional vision) and to investigate more precisely the compensatory effects of modafinil in visual operating processes. This study was carried out as part of a more general project whose goal was to investigate whether the administration of modafinil in doses of 100 mg three times per day could maintain the subject's cognitive abilities at a high level during sleep deprivation of 60 h.

MATERIALS AND METHODS

Subjects

Six adult male volunteers (age 20–30) participated in the experiment. Their eyesight was normal or corrected to normal. Medical and psychological examinations were normal, without psychiatric antecedent nor sleep disturbance. Results of the Horne and Ostberg (1976) questionnaire revealed that subjects were not markedly categorized as being of the morning or evening type, and that they experienced normal anxiety according to the Cattell anxiety scale (Rickels and Cattell, 1965). The number of subjects was limited to six for technical reasons: (i) the constant supervision of subjects to maintain their wakefulness or to ensure their security was time consuming, (ii) some experimental settings for other tests and psychophysiological recordings in the experiment do not allow more than six subjects in each testing period. After the protocol was approved by the Ethical Committee for the protection of persons involved in biomedical research, subjects were medically screened and were provided with detailed information on the experiment. Each subject signed an informed consent and received payment for their participation.

General experimental design

The experiment took place in the psychology laboratory during the winter in Grenoble to avoid

seasonal effects. Each subject underwent two sessions of 7 days, with a control test before each period of sleep deprivation, and nights followed by continuous activities — i.e. free time between the experimental tests was occupied by interactive video games and parlor games; moreover an experimenter had the specific task to speak to the subjects and to control that nobody was trying to sleep — and medical supervision during 3 nights and 4 days, ending with one recovery night and day with a second control test. Electroencephalographic (EEG) recordings were taken by physiologists during the first night before the experiment to make sure that they had no sleep disturbance (i.e. REM sleep and non-REM sleep alterations), also during the recovery night after sleep deprivation. The other parameters were taken on separate channels: electrooculogram, electromyogram, electrocardiogram and body surface temperature. Polygraphic traces were scored blind as to subjects and drug condition in 20 s epochs following classical criteria for the scoring of wakefulness, Stages 1, 2, 3, and 4 of non REM sleep, Stages 3 and 4 constituting slow-wave sleep (SWS), and REM sleep (Rechtschaffen and Kales, 1968; Buguet *et al*., 1995).

Subjects were kept under constant supervision in the lab with a physician and a supervisor to monitor their wakefulness. They had their meals in the lab. Alcohol, caffeine or theine were not permitted. A typical day (24 h) included two periods of 4 h (24:00–4:00 and 13:00–19:00) to carry out cojointly the visual search task and the physiological measures (ECG, pulse, blood pressure, rectal temperature, etc.). We did not postulate any correlation between the physiological measures and the performance scores on the visual processing task. This paper therefore only presents the investigations on visual search in early vision.

Drug administration and medical surveillance

Double-blind random assignment was used to determine the order of modafinil and placebo in a session and consisted of either a placebo pill or 100 mg of modafinil every 8 h (300 mg/24 h). During a session, subjects always received seven pills: one every 8 h (i.e. 8 p.m. on Tuesday, followed by 4 a.m., 12 a.m., 8 p.m. on both Wednesday and Thursday). The T_{max} of modafinil is about 4 h and the $T_{1/2}$ is 13·6 h when administered at intervals throughout the day. Sessions were separated by a wash-out period of 15 days to ensure a complete elimination of the drug.

An observation chart was filled in every 8 h to assess side effects. Blood pressure, pulse, body temperature and ambient temperature were measured.

Specific experimental design

The visual search task. The visual search task consisted of detecting a target letter 'Q' among a varying number of distractor letters 'O' and the reverse (see Figure 1). This visual search task used by Treisman (1985) reveals that the detection of a 'Q' target involves parallel processing (i.e. response times are identical whatever the number of distractors), while the detection of an 'O' target involves serial processing (i.e. increasing of response times as a function of the number of distractors). This asymmetrical search pattern ('parallel versus serial') is used to identify the two processes involved in early vision.

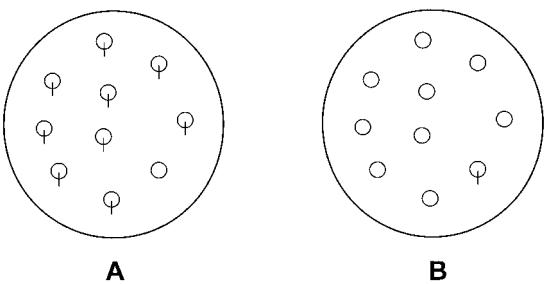

Figure 1. Examples of the letter arrays. (A) 10 items with 'O' target present among 'Q' distractors; (B) 10 items with 'Q' target present among 'O' distractors

The 'Q' target pops out among 'O' distractors because it is the only item with a vertical line segment (target-distractor dissimilarity). Conversely, the 'O' target requires a longer visual searching time among 'Q' distractors because the 'O' target shares all its characteristics with the 'Q' distractor (target-distractor similarity).

Apparatus and stimuli. The stimuli arrays were generated by a computer and displayed in a dark room on an oscilloscope screen (P31-1311A Hewlett Packard Display). Displays consisted of 4, 10, 16 letters arrays ('O' and/or 'Q'). There were 16 displays of each set size with the target present and 16 without target. The position of the targets

and distractors on the screen was different on each display. The positions of the targets were preset so that four would appear in each quadrant of the display at $4{\cdot}5^{\circ} \pm 0{\cdot}4$ eccentricity. The angular distance between two neighbouring letters was more than the size of a letter, and distractor letters were randomly distributed over the whole visual field.

Procedure. Each display was preceded by a central fixation dot (displayed for 800 ms) and followed by a random line mask (displayed for 1·5 s). Arrays remained on the screen until a response was provided by the subject. Subjects were required to respond as quickly and accurately as possible and asked to specify whether or not the target was present with a trigger control in each hand.

Two counterbalanced blocks (i.e. one with a 'O' target among 'Q' distractors and one with a, 'Q' among 'Os') consisted respectively of 24 practice trials followed by 96 experimental trials whose half were with target present. The trials blocks were presented in random order with the constraint that subjects could not give the same answer more than three times in a row. Response times diverging from the mean by more than $\pm 2\sigma$ were considered as erroneous responses and were discarded.

Statistical analysis. The dependent variables were the slope of the best fitted linear regression of the RTs as a function of the number of elements (search rates) and the mean response errors rate (error rates). The former measured the search rates in milliseconds per letter, the latter measured the error rates in percentage. The response data computed concerned only the arrays with target present because the fatigue of sleep loss often involved strategies of verification to find the target in absent-target arrays (re-examination). The time of verification did not correspond exactly to the visual search time.

Results were subjected to non parametric tests for dependent samples. The Wilcoxon matched-pairs signed-ranks test was used to verify the absence of any learning effect in the two sessions or a rebound effect comparing the control tests before and after sleep deprivation, and to compare the substance effect ('modafinil versus placebo'). The Friedman test was used to evaluate the effect of sleep deprivation. The null hypothesis was rejected at the level of $p < 0{\cdot}05$.

RESULTS

Control data

Because of the few subjects number, before and after each experimental session, control measurements were done to assess the stability of mental performance. The control data (search rates and error rates) obtained before sleep deprivation and after one recovery night, respectively, were not significantly different between the two sessions. Therefore, in the following analyses and in the data plotted in Figure 2, we used as control data the mean values of the responses obtained before sleep deprivation in the two sessions. We confirmed the usual observation of the asymmetrical search pattern for 'O' versus 'Q' targets both on search rates and error rates. The slopes were 12·7 ms/letter for 'O' targets and 0·8 ms/letter for 'Q' targets (Wilcoxon Test, $z = 2{\cdot}82$; $p < 0{\cdot}004$). The percentage of errors was 4% for 'O' targets and 1·5% for 'Q' targets (Wilcoxon Test, $z = 2{\cdot}53$; $p < 0{\cdot}01$).

Sleep deprivation data

Overall data observed under sleep deprivation shows that mean slopes were respectively 16·12 ms/letter for 'O' targets and 4·13 ms/letter for 'Q' targets (Wilcoxon Test: $z = 4{\cdot}88$;

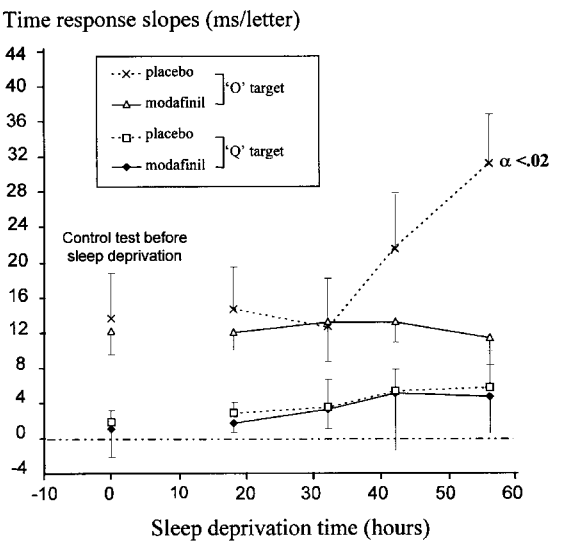

Figure 2. Evolution of the mean search slopes for 'O' and 'Q' targets during sleep deprivation with modafinil and with the placebo. The graph shows the only significant effect of sleep deprivation observed with placebo for 'O' targets search

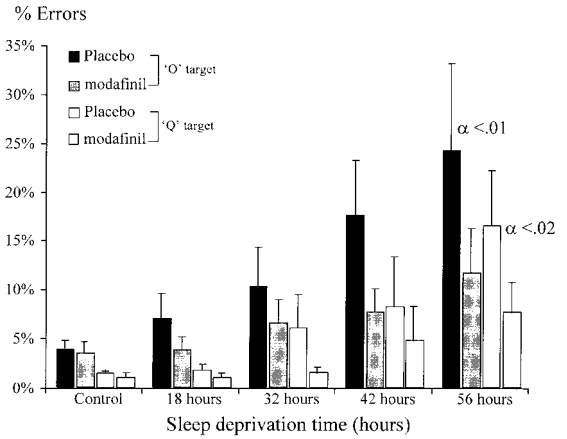

Figure 3. Evolution of error percentages for visual search for 'O' target among 'Q' distractors and the reverse during sleep deprivation with modafinil and with placebo. The graph shows a progressive increase of error during sleep deprivation; however, there are significant differences only with the placebo whatever the processing — serial for 'O' target or parallel for 'Q' target

$p < 0{\cdot}0001$), confirming the asymmetrical search pattern between 'O' targets (serial processing) and 'Q' targets (parallel processing).

For 'O' target trials, mean slopes were respectively 12·36 ms/letter with modafinil and 19·87 ms/letter with the placebo (Wilcoxon Test: $z = 2{\cdot}17$; $p < 0{\cdot}02$). For 'Q' target trials, mean slopes were respectively 3·97 ms/letter with modafinil and 4·29 ms/letter with the placebo ($z = 0{\cdot}74$; n.s.). Thus, the substance effect (i.e. modafinil versus placebo) was significant for the serial processing ('O' target search), but it was not for the parallel processing ('Q' target search).

Moreover, the effect of sleep deprivation — from $t_0 =$ control-test to $t_{56h} =$ the 56th hour of sleep deprivation — was significant with the placebo for 'O' target (Friedman Test: Chi-square (4) = 11·46; $\alpha < 0{\cdot}02$), whereas it was not with the modafinil (Chi-square (4) = 0·26; n.s.). No effect of sleep deprivation was observed for 'Q' target search. The data plotted in Figure 2 show not only the slope differences between parallel and serial processing — asymmetrical processing pattern for the 'O' versus 'Q' — but also the evolution of the slope values during the sleep deprivation for placebo and modafinil.

In sum, the effect of sleep deprivation was observed only with the placebo for 'O' target search (serial processing). The search rates for 'O' targets remained at the same level as that of the control test with modafinil during sleep deprivation.

Overall data observed under sleep deprivation show significant differences on error rates between the target types 'O' versus 'Q' (Wilcoxon Test: $z = 4{\cdot}6$; $p < 0{\cdot}0001$). Moreover, a significant effect on error rates were found between modafinil and placebo respectively for 'O' targets (Wilcoxon Test: $z = 3{\cdot}49$; $p < 0{\cdot}0005$) and for 'Q' targets (Wilcoxon Test: $z = 2{\cdot}95$; $p < 0{\cdot}003$). Mean percentages of errors show that the errors on 'O' target detection during the sleep deprivation were 3·66% for the control test, 7·42% with modafinil and 14·71% with the placebo, and the errors of 'Q' target detection were 1·22% for the control test, 3·77% with modafinil and 8·11% with placebo (Figure 3). The administration of modafinil decreased by half the mean percentage of errors with respect to the placebo.

Furthermore, the effect of sleep deprivation — from $t_0 =$ control test to $t_{56h} =$ the 56th hour of sleep deprivation — was significant with the placebo for the two types of targets (Figure 3), respectively for 'O' targets (Friedman Test: Chi-Square (4) = 11·96; $\alpha < 0{\cdot}01$) and for 'Q' targets (Friedman Test: Chi-Square (4) = 11·23; $\alpha < 0{\cdot}02$), but was not significant with modafinil for any targets ('O' target: Chi-Square (4) = 6·83; n.s.; 'Q' targets: Chi-Square (4) = 6·23; n.s.). Thus, with the modafinil, error rates did not increase significantly during sleep deprivation for any targets, while with the placebo they significantly increased for both 'O' and 'Q' targets.

DISCUSSION AND CONCLUSION

Figure 2 shows that search rates are higher for 'O' target detection than for 'Q' target detection throughout the period of sleep deprivation. This suggests that search time for 'O' targets steeply increased as a function of the number of distractors and very smoothly for the 'Q' targets.

Visual search results for detecting a 'Q' target among 'O' distractors of variable number and the reverse 'O' target among 'Q' distractors, are characterized by an asymmetrical search pattern observed throughout the sleep deprivation period. This search asymmetry was attributed by Treisman (1985) and Wolfe (1994) to the existence of two visual stages. The preattentional stage is characterized by the absence of attentional shifts. Such search processing is described as 'parallel' because it is not affected by the number of stimuli in the configuration. The preattentional stage is supported by parallel processes which operate

automatically across the whole visual field. Conversely, the attentional stage is characterized by the presence of attentional shifts. The search processing is described as 'serial' because the search time increases as a function of the number of stimuli in the configuration. The attentional stage is supported by serial processes which scan sequentially the visual field (Treisman and Gelade, 1980; Bergen and Julesz, 1983). This model of vision can account for the data obtained during sleep deprivation. It is thus plausible to assume that disorders and fatigue provoked by sleep loss are more disturbing for complex high level processes (serial) than for automatic low level processes (parallel).

In summary, we observed that sleep deprivation does not disturb the parallel processes of the first visual stage but slows down the serial processes of the second visual stage. The effect of modafinil appears clearly after the 32nd hour. Its administration prevents a decrease in performance during sleep deprivation. It maintains search rates approximately at the same level as in the control test. The performance improvement observed at the 56th hour is not significant and can probably be attributed to an overlearning of the task. Though this kind of search task is not affected by learning, a small learning effect can be observed after blocks of several hundreds of trials.

The error rates increased as a function of sleep deprivation in the same way as the mean search rates, except for the 'Q' target where error rates increased significantly in the placebo condition. There is no evidence for a shift in the speed-accuracy trade-off. Subjects who are more efficient in their visual search do not make more errors. Errors rates increase as a function of sleep deprivation time for 'O' and 'Q' targets in the placebo condition. But, the most striking result was observed in the modafinil condition where error rates do not increase significantly during sleep deprivation and are not significantly different from control error rates. Errors of detection are attributed to a dysfunction of identification processes due to an erroneous perceptual decision making. According to Schwartz *et al.* (1977) and to the models of McCann and Johnston (1992), this processing stage matches the stimulus features with the template of the target loaded in visual short term memory (VSTM). The successful analysis of similarities between the letters and the target template involves an accurate identification (Duncan and Humphreys, 1989, 1992). As a consequence, sleep deprivation seems to disturb these processes, while the administration of modafinil protects the visual system against such degradation. Total mean errors decrease by 50% with modafinil as compared to placebo. The analysis of error rates as a function of sleep deprivation time shows the positive effect of modafinil beyond the 42nd hour of sleep deprivation (Figure 3).

In summary, this study shows the positive effects of modafinil on attentional processes when administered in doses of 100 mg three times per day during a sleep deprivation of 60 h. Its administration does not increase performance scores, but maintains the speed of attentional scanning and the performance of identification processes at a mean level which enables the subject to perform cognitive tasks without major disturbance.

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REFERENCES

Angus, R. G. and Heslegrave, R. J. (1985). Effects of sleep loss on sustained cognitive performance during a command and control simulation. *Behavior Research Methods, Instruments and Computers*, **17**, 55–67.

Angus, R. G., Pigeau, R. A. and Heslegrave, R. J. (1992). Sustained-operations studies: from the field to the laboratory. In *Why We Nap: Evolution Chronology and Function of Polyphasic and Ultrashort Sleep*, Stampi, C. (Ed.), Birkhauser, Boston, pp. 217–241.

Bastuji, H. and Jouvet, M. (1988). Successful treatment of idiopathic hypersomnia and narcolepsy with Modafinil. *Prog. Neuropsychopharmacological Biological Psychiatry*, **12**, 695–700.

Bergen, J. R. and Julesz, B. (1983). Parallel versus serial processing in rapid pattern discrimination. *Nature*, **303**, 696–698.

Buguet, A., Montmayeur, A., Pigeau, R. and Naitoh, P. (1995). Modafinil, d-amphetamine and placebo during 64 hours of sustained mental work — II. Effects on two nights of recovery sleep. *Journal of Sleep Research*, **4**, 229–241.

Duncan, J. and Humphreys, G. W. (1989). Visual search and stimulus similarity. *Psychological Review*, **96**, 433–458.

Duncan, J. and Humphreys, G. W. (1992). Beyond the search surface: visual search and attentional engagement. *Journal of Experimental Psychology (HPP)*, **18**, 578–588.

Duteil, J., Rambert, F., Pessonnier, J., Hermant, J. F., Gombert, R. and Assous, E. (1990). Central alpha 1 adrenergic stimulation in relation to the awakening activity of modafinil: behavioral studies in laboratory animals. *European Journal of Pharmacology*, **180**, 49–58.

Haslam, D. R. (1982). Sleep loss, recovery sleep and military performance. *Ergonomics*, **25**, 163–178.

Heslegrave, R. J. and Angus, R. G. (1985). The effects of task duration and work-session location on performance degradation induced by sleep loss and sustained cognitive work. *Behavior Research Methods, Instruments and Computers*, **17**, 592–603.

Horne, J. A. and Ostberg, O. (1976). A self-assessment questionnaire to determine morningness-eveningness in human circadian rhythms. *International Journal of Chronobiology*, **4**, 97–110.

Julesz, B. (1981). Textons, the elements of texture perception, and their interactions. *Nature*, **290**, 91–97.

Julesz, B. and Bergen, J. R. (1983). Textons, the fundamental items in preattentive vision and perception of textures. *The Bell System Technical Journal*, **62**, 1619–1645.

Krueger, G. P. (1989). Sustained work, fatigue, sleep loss and performance: a review of the issues. *Work and Stress*, **3**, 129–141.

Lafon Laboratory (1994). Modiodal® Modafinil. *Dossier d'information médicale et pharmaceutique*. Laboratoire L. Lafon, Maisons-Alfort.

Lagarde, D. (1990). Effects of Modafinil on the nocturnal activity and behavioural sleep of rhesus monkeys (*Macaca mulatta*). *Medical Science Research*, **18**, 307–399.

Lagarde, D. and Batejat, D. (1995). Disrupted sleep-wake rhythm and performance: advantages of modafinil. *Military Psychology*, **7**, 165–191.

Marr, D. C. (1982). *Vision*. Freeman, San Francisco.

McCann and Johnston. (1992). Locus of the Single-Channel Bottleneck in Dual Task Interference. *Journal of Experimental Psychology (HPP)*, **18**, 471–484.

Mignot, E., Nishino, S., Guilleminault, C. and Dement, W. C. (1994). Modafinil binds to the dopamine uptake carrier site with low affinity. *Sleep*, **17**, 436–437.

Naitoh, P. (1981). Circadian cycles and restorative power of naps. In *Biological Rhythms, Sleep, and Shift Work*, Johnson, L. C., Tepas, D. I., Colquhoun, W. P. and Colligan, M. J. (Eds), SP Medical and Scientific Books, New York, pp. 553–558.

Naitoh, P. and Angus, R. G. (1989). Napping and human functioning during prolonged work. In *Sleep and Alertness: Chronobiological, Behavioral, and Medical Aspects of Napping*, Dingues, D. F. and Broughton, R. J. (Eds), Raven Press, New York, pp. 221–246.

Neisser, U. (1967). *Cognitive Psychology*, Appleton-Century-Crofts, New York.

Opsad, P. D., Ekanger, R., Numestad, M. and Raabe, N. (1978). Performance, mood and clinical symptoms in men exposed to prolonged severe physical work and sleep deprivation. *Aviation, Space, and Environmental Medicine*, **49**, 1065–1073.

Pigeau, R., Heslegrave, R. J. and Angus, R. G. (1987). Psychophysiological measures of drowsiness as estimates of mental fatigue and performance degradation during sleep deprivation. In *Electric and Magnetic Activity of the Central Nervous System: Research and Clinical Applications in Aerospace Medicine*, NATO Advisory Group for Aerospace Research and Development, Paris, pp. 21.1–21.16.

Pigeau, R., Naitoh, P., Buguet, A., McCann, C., Baransky, J., Taylor, M., Thompson, M. and Mack, I. (1995). Modafinil d-amphetamine and placebo during 64 hours of sustained mental work. 1. Effects on two nights of recovery sleep. *Journal of Sleep Research*, **4**, 212–228.

Prinzmetal, W., Presti, D. E. and Posner, M. I. (1986). Does attention affect visual feature integration? *Journal of Experimental Psychology (HPP)*, **12**, 361–369.

Rechtschaffen, A. and Kales, A. (1968). *A Manual of Standardized Terminology, Techniques and Scoring System for Sleep Stages of Human Subjects*. US Govt. Printing Office, Washington, D.C.

Riback, J., Ashkenazi, J. E. and Klepfish, A. (1983). Diurnal rhythmicity and Air Force flight accidents due to pilot error. *Aviation, Space, and Environmental Medicine*, **54**, 1096–1099.

Rickels, K. and Cattell, R. B. (1965). The clinical factor validity and trueness of the IPAT verbal and objective batteries for anxiety and regression. *Journal of Clinical Psychology*, **21**, 257–264.

Schwartz, S. P., Pomerantz, J. R. and Egeth, H. E. (1977). State and process limitations in information processing: An additive factors analysis. *Journal of Experimental Psychology (HPP)*, **3**, 402–410.

Treisman, A. (1985). Preattentive processing in vision. *Computer Vision Graphics and Image Processing*, **31**, 156–177.

Treisman, A. and Gelade, G. (1980). A feature-integration theory of attention. *Cognitive Psychology,* **12**, 97–136.

Treisman, A. and Souther, J. (1985). Search asymmetry: a diagnostic for preattentive processing of separable features. *Journal of Experimental Psychology: General*, **114**, 285–310.

Wolfe, J. M. (1994). Guided search model: a revised model of visual search. *Psychonomic Bulletin and Review*, **1**, 202–238.

Zeki, S. (1993). *A Vision of the Brain*. Blackwell, Oxford.

