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Creatine supplementation, sleep deprivation, cortisol, melatonin and behavior

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Abstract

The effect of creatine supplementation and sleep deprivation, with intermittent moderate-intensity exercise, on cognitive and psychomotor performance, mood state, effort and salivary concentrations of cortisol and melatonin were examined. Subjects were divided into a creatine supplementation group and a placebo group. They took 5 g of creatine monohydrate or a placebo, dependent on their group, four times a day for 7 days immediately prior to the experiment. They undertook tests examining central executive functioning, short-term memory, choice reaction time, balance, mood state and effort at baseline and following 18-, 24- and 36-h sleep deprivation, with moderate intermittent exercise. Saliva samples were taken prior to each set of tests. A group × time analysis of covariance, with baseline performance the covariate, showed that the creatine group performed significantly ($p<0.05$) better than the placebo group on the central executive task but only at 36 h. The creatine group demonstrated a significant ($p<0.01$) linear improvement in performance of the central executive task throughout the experiment, while the placebo group showed no significant effects. There were no significant differences between the groups for any of the other variables. A significant ($p<0.001$) main effect of time was found for the balance test with a linear improvement being registered. Cortisol concentrations on Day 1 were significantly ($p<0.01$) higher than on Day 2. Mood significantly ($p<0.001$) deteriorated up to 24 h with no change from 24 to 36 h. Effort at baseline was significantly ($p<0.01$) lower than in the other conditions. It was concluded that, during sleep deprivation with moderate-intensity exercise, creatine supplementation only affects performance of complex central executive tasks.

Keywords: Cognition; Central executive; Short-term memory; Cognitive effort; Intermittent exercise; Adenosine-tri-phosphate; Dynamic balance; Choice reaction time; Random number generation; Prefrontal cortex

Sleep deprivation has been shown to affect physiological and psychological functioning [1,2] and probably increases the organism's demand for energy [3]. In the brain, this energy is required for neural transmission [4] and the synthesis of cyclic adenosine-mono-phosphate (cAMP), which is a messenger involved in hormone synthesis [5]. Energy is dependent on the hydrolysis of adenosine-tri-phosphate (ATP) to adenosine-di-phosphate and inorganic phosphate. The re-synthesis of ATP is dependent upon phosphorylcreatine, which may become depleted when energy demand is increased. The muscle store of phosphorylcreatine can be increased by dietary supplementation with creatine monohydrate [6]. Moreover, creatine monohydrate supplementation has been shown to result in significant increases in creatine concentrations in the human brain [7]. Therefore, based on the evidence, one would expect creatine supplementation to aid cognitive performance. Also, psychomotor tasks, which have both cognitive and motor factors, could also be aided by increased creatine concentrations in both the brain and musculature. If increased creatine concentrations result in more energy available, it is logical to expect mood to be affected.

McMorris et al. [3] provided some support for a beneficial effect of creatine supplementation on cognitive and psychomotor performance, and mood following 24-h sleep deprivation, which was accompanied by mild intermittent exercise. However, not all tasks demonstrated a positive effect of creatine supplementation. A complex central executive, working memory

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task benefited from creatine supplementation, as did four-choice reaction time and performance on a static balance test. However, there were no beneficial effects on performance of a more simple number recall task. Mood state showed a limited beneficial effect of creatine supplementation.

Although McMorris et al. [3] provided evidence for a significant effect of creatine supplementation on cognitive and psychomotor performance, and mood state following sleep deprivation with intermittent exercise, the stress placed on the subjects in that study was limited. Some authors have shown detrimental effects of 24-h sleep deprivation on cognitive and psychomotor performance [1,2], but the majority of studies have covered periods of ≥36 h [8–11]. Overall, the literature suggests that 24-h sleep deprivation is not particularly stressful. Mood has also been shown to deteriorate following 30-h [12] and 37-h sleep deprivation [13]. Therefore, we decided to examine the effect of creatine supplementation on cognitive (working memory and short-term memory tasks) and psychomotor performance (choice reaction time and dynamic balance), and mood during and following 36-h sleep deprivation. We also decided to include moderate-intensity exercise rather than the mild exercise used by McMorris et al. [3]. Thus, the protocol used in the present study placed greater demands on ATP resynthesis and greater psychological stress on the subjects than did the protocol of McMorris et al. [3].

We also examined the effect of creatine supplementation on changes in salivary concentrations of cortisol and melatonin, or 5-methoxy-*N*-acetyltryptamine, during sleep deprivation. Cortisol is indicative of perceptions of stress [14], while melatonin is related to alertness [15] and is an important measure with regard to cognitive and psychomotor performance, and mood state. Therefore, there may be a significant effect on the concentrations of these hormones due to the action of creatine. This may be particularly so because the synthesis of cortisol and melatonin is dependent on the synthesis of cAMP, which is in turn ATP dependent [16].

As it is thought that cognitive effort, often referred to as effort, can ensure optimal performance even under high levels of stress [17], we measured effort using the effort sub-scale of the National Aeronautics and Space Administration–Task Load Index (NASA-TLX) [18]. According to Kahneman [19], as stress increases so does arousal, which results in greater neural excitability. At high levels, this is detrimental to performance unless effort can harness the arousal by allocating neurotransmitters to the task. No previous research examining sleep deprivation has employed this measure but it may account for the equivocal nature of results from previous studies [3,11,20].

We also tested the ability of changes from baseline (Δ) in concentrations of cortisol and melatonin to predict changes in cognitive and psychomotor performance, and mood state. Under many forms of stress, cortisol has been shown to be related to mood and cognition [14,21,22]. Therefore, one would expect significant correlations between Δ cortisol concentrations and Δ performance on the cognitive and psychomotor tests, and Δ perceptions of mood. Similarly, one would expect Δ melatonin concentrations to correlate with Δ cognitive and psychomotor performance, and Δ mood, given the role of melatonin in alertness.

To summarize, in this study we examined the effect of creatine supplementation on cognitive performance, and mood state during 36-h sleep deprivation, with intermittent moderate-intensity exercise. The cognitive tests were a central executive working memory task and a short-term memory task. The psychomotor tasks were four-choice visual reaction time and dynamic balance. Also, salivary concentrations of cortisol and melatonin were examined.

1. Methods

1.1. Subjects

Subjects were paid volunteer male (N=20) sports science majors. Mean (S.D.) age was 21.11 (1.85) years, height 1.79 (0.03) m and mass 72.28 (13.53) kg. Ethical approval was obtained from the University Ethics Committee; and subjects signed informed consent forms and completed a medical questionnaire prior to beginning the experiment.

Subjects were divided into two equal groups (n=10). One group was the creatine supplementation group and the other the placebo group. One subject, in the placebo group, withdrew on the morning of the experiment due to influenza. Subjects took 5 g of creatine monohydrate (Creapure, Deguss AG, Düsseldorf, Germany) or a placebo (Maxijoule, SHS International, Liverpool, UK), dependent on their group, four times a day for 7 days immediately prior to the experiment, as in previous research [3,23]. The study was double blind. Subjects did not take creatine or placebo on the day of the test. Participants were requested not to eat meat or fish products or to take drinks that contained caffeine 24-h prior to the testing. They were also instructed to undertake their normal weekly exercise routines and their normal diet, apart from the restrictions outlined above.

1.2. Cognitive tests

Central executive, working memory performance was measured by a written version of the random number generation task [24]. Subjects were instructed to write down numbers from one to nine in a totally random fashion. Based on the recommendations of Brugger [25] subjects were told to imagine how they would have to respond if they were guided by picking numbers out of a hat. The test lasted for 1 min and participants had to make a response every second and a metronome was used to provide timing. The dependent variables were the random number generation index (RNG), devised by Evans [26], and a measure of redundancy (RED) [27]. The dependent variable RNG is the index of frequency of repetition of response alternatives, while RED is a measure of the response alternative frequency. The results were analyzed by the computer programme RgCalc [27]. Towse and Valentine [28] have shown that there is no learning effect in random generation tasks when feedback is not supplied. However, as we were using a written form, reliability was

Table 1
Diagrammatic representation of procedure

Cycle 1	Cycle 2	Cycle 3	Cycle 4	Cycle 5	Cycle 6
0–1 h Saliva sample tests	1–2 h Stair climbing [a]	2–3 h Step-ups [a]	3–4 h Walk [b] Snack ~ 150 kcal	4–5 h Stair climbing [a]	5–6 h Step-ups [a]
6–7 h Walk [b]	7–8 h Stair climbing [a]	8–9 h Step-ups [a]	9–10 h Walk [b] Meal ~ 600 kcal	10–11 h Stair climbing [a]	11–12 h Saliva sample step-ups [a]
12–13 h Walk [b]	13–14 h Meal ~ 1000 kcal	14–15 h Stair climbing [a]	15–16 h Step-ups [a]	17–18 h Walk [b]	18–19 h Saliva sample tests
19–20 h Stair climbing [a] Snack ~ 200 kcal	20–21 h Step-ups [a]	21–22 h Walk [b]	22–23 h Stair climbing [a]	23–24 h Step-ups [a]	24–25 h Walk [b]
25–26 h Saliva sample tests	26–27 h Stair climbing [a] Snack ~ 250 kcal	27–28 h Step-ups [a]	28–29 h Walk [b]	29–30 h Stair climbing [a]	30–31 h Step-ups [a]
31–32 h Walk [b]	32–33 h Meal ~ 600 kcal	33–34 h Stair climbing [a]	34–35 h Step-ups [a]	35–36 h Walk [b]	Post-test Saliva sample tests

[a] 2 × 5 min at 65% estimated maximum heart rate with 3 min rest interval.
[b] 15 min continuous at 65% estimated maximum heart rate.

examined in a pilot study using similarly aged and experienced subjects ($N = 35$). Test–retest reliability coefficients of 0.79 for RNG and 0.74 for RED were found.

The verbal short-term memory test was a written version of Baddeley et al.'s [24] number recall test. The experimenter read out a series of numbers and, when the experimenter stopped, the subject had to write them down immediately. The experimenter began with three numbers and increased the amount by one every trial. The dependent variable was the amount of numbers repeated in the final successful trial. Although reliability has been shown previously [3,24], as this was a written version, reliability was examined in the pilot study. A test–retest reliability coefficient of 0.79 was demonstrated.

The choice reaction time test was a classical four-choice visual reaction time test, the same as used by McMorris et al. [3]. Subjects undertook 40 trials. There were 10 trials on each of the four stimuli as movement time can differ between fingers. Order of presentation differed between tests and foreperiods were randomized between 0.5 s and 2 s. The dependent variable was speed of response. Previous research has shown that the test is reliable as long as subjects undertake a habituation period of 160 trials [3].

The psychomotor test was a dynamic balance test. The subject attempted to balance on a stabilometer for 1 min. The dependent variable was the percentage of time in balance. In balance was considered to be when the stabilometer was at angle of $<15°$. A test–retest reliability coefficient of 0.92 was demonstrated.

1.3. Mood state

Mood state was examined by an inventory developed by Hemmings [29], which is a shortened version of the Profile of Mood States questionnaire [30]. The inventory measures the individual's perceptions of fatigue, vigor, anger, depression and tension. A composite mood score was calculated from the sub-sets. The measurement scale for all five variables is from 0 to 5, with lower scores on fatigue, anger, depression and tension being positive and lower scores on vigor being negative. Therefore, scores ≤ 0 on the composite scale are indicative of positive mood and scores ≥ 0 indicate negative mood state.

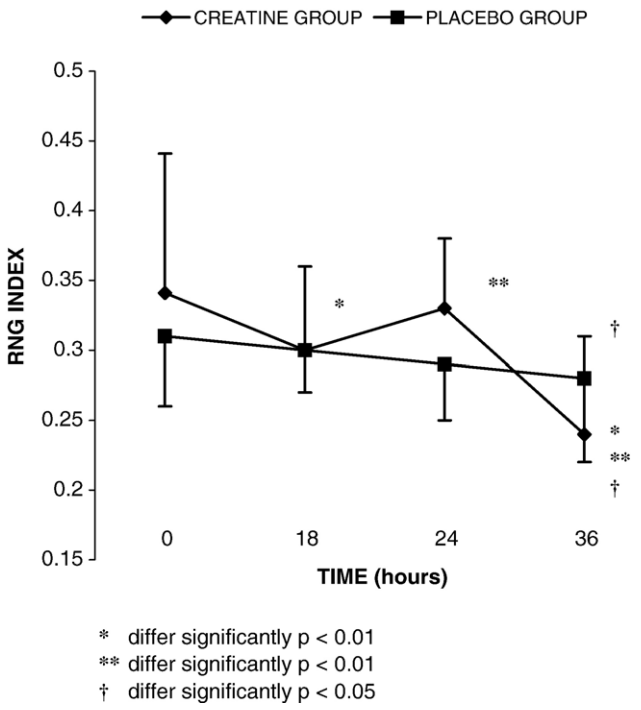

Fig. 1. The mean (S.D.) random number generation index scores (RNG) for both groups at each time point.

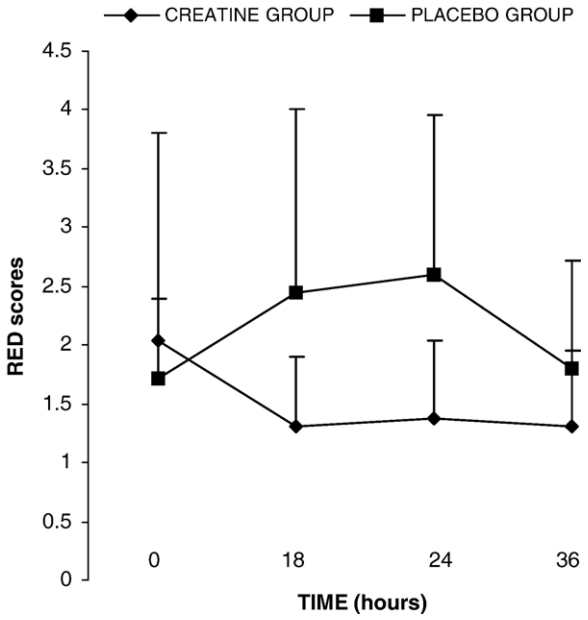

Fig. 2. The mean (S.D.) redundancy scores (RED) for both groups at each time point.

1.4. Cognitive effort

Cognitive effort was measured using the effort sub-scale of the National Aeronautics and Space Administration Task Load Index (NASA-TLX) [18]. The measurement scale is from 0 to 20, with higher scores indicative of greater effort.

1.5. Saliva samples

Saliva was directly collected from mouth to tube (International Scientific Supplies, Bradford, UK), ≥15 min after stimulation with water as recommended in the instruction manuals of the assay kit manufacturers (DRG Instruments GmbH, Marburg, Germany and Bühlmann Laboratories AG, Schönenbuch, Switzerland) . Samples were stored at −20 °C before analysis. Following thawing, the samples were centrifuged for 5 min at 1000×*g*. Cortisol samples were assayed using DRG Instruments GmbH (Marburg, Germany) kit and melatonin with Bühlmann Laboratories AG (Schönenbuch, Switzerland) kit prior to analysis using solid phase enzyme-linked immunosorbent (ELISA) assay.

1.6. Procedure

All subjects undertook a habituation session in which they practised all of the cognitive and psychomotor tests. They had three trials on the random number generation task, with no feedback; three trials on the number recall task, also with no feedback; and 160 trials on the choice reaction time task, as recommended by McMorris et al. [3]. The pilot study had shown that ten trials were necessary on the dynamic balance test in order to reach a plateau, therefore this amount was given. Again there was no feedback.

The experiment began at 0900 h on Day 1. Subjects arrived 20 min before testing was due to begin and sat in a quiet room. They provided a saliva sample and then undertook the cognitive and psychomotor tests. The order of testing was random number generation, number recall, choice reaction time and dynamic balance. They then completed the mood state inventory and the effort sub-scale of the NASA-TLX. Subjects then undertook six 6-h cycles of testing and exercise (see Table 1). Testing at the beginning of Cycle 1 was termed the baseline condition. Subjects were also tested at 0300 h on Day 2 (the 18-h time point), 0900 h on Day 2 (the 24-h time point) and 2100 h on Day 2 (the 36-h time point). Saliva samples were taken before each set of testing. Although there was no cognitive, psychomotor or mood testing at 2100 h on Day 1, saliva samples were taken then so that creatine and melatonin concentrations at 2100 h on Day 1 could be compared to those at the same time on Day 2.

Three types of exercise were undertaken; stair climbing and step-ups, each for 2×5 min with a 3 min rest interval, and 15 min continuous walking (see Table 1). Subjects were instructed to maintain 65% estimated maximum heart rate during exercise ((220−age/100)×65) [31]. During exercise 5000 Sports Tester heart rate monitors (Polar Electric, Kempele, Finland) were worn. Heart rates were continually monitored by the experimenters and participants were fed once every 6-h cycle (see Table 1).

1.7. Statistical analysis

Performance on the random number generation, number recall, choice reaction time and dynamic balance tests at 18, 24 and 36 h were compared by separate Group×Time analysis of covariance (ANCOVA), with baseline performance as the covariate. Effect sizes were measured by the η^2 method. Post hoc planned comparisons for the time main effect were undertaken by Tukey's Honestly Significant Difference (HSD) tests; and where there were interaction effects, within-group effects were measured by HSD and between-group effects by the Tukey–Kramer variation of HSD for unequal sample sizes.

Cortisol and melatonin concentrations at each time period were compared by Group×Time ANOVA. Post hoc planned comparisons were carried out as for the cognitive tests. In

Table 2
Mean (S.D.) scores for both groups on the forward number recall, choice reaction time and balance tests at baseline, 18, 24 and 36 h

	Baseline		18 h		24 h		36 h	
	CRE	PLAC	CRE	PLAC	CRE	PLAC	CRE	PLAC
Forward no. recall	6.70 (1.57)	7.00 (1.80)	6.90 (1.60)	6.89 (1.17)	7.40 (1.17)	7.67 (1.12)	6.90 (1.37)	7.33 (0.87)
Choice reaction time (ms)	353 (29)	350 (36)	346 (23)	347 (36)	342 (35)	342 (41)	337 (17)	336 (36)
Balance (% in balance)	44.30 (11.03)	44.93 (10.80)	50.93 (15.14)	46.34 (10.62)	55.34 (15.23)	50.91 (10.80)	62.96 (13.98)	61.07 (10.11)

CRE=creatine group; PLAC=placebo group.

Table 3
Mean (S.D.) mood state and effort scores for both groups at baseline, 18, 24 and 36 h: mean (S.D.) Δ scores for mood state and effort at 18, 24 and 36 h

	Baseline		18 h		24 h		36 h	
	CRE	PLAC	CRE	PLAC	CRE	PLAC	CRE	PLAC
Mood	−1.98 (0.92)	−1.03 (0.68)	2.38 (1.86)	1.81 (1.29)	4.48 (0.85)	3.83 (0.58)	4.68 (1.02)	4.17 (0.67)
Δ Mood			4.45 (1.42)	2.83 (1.68)	6.45 (2.36)	4.86 (1.78)	6.65 (2.88)	5.19 (2.00)
Effort	9.00 (3.59)	9.33 (5.94)	13.30 (3.06)	12.89 (4.28)	14.40 (3.06)	14.22 (4.29)	15.00 (3.97)	15.78 (3.27)
Δ Effort			4.30 (3.89)	3.56 (4.13)	5.40 (4.38)	4.89 (4.37)	6.00 (4.00)	6.44 (4.13)

addition, trend analyses were undertaken by ANOVA contrasts in order to ascertain whether creatine supplementation and/or sleep deprivation affected diurnal patterns.

As the mood state and effort scores are ordinal data, they were examined using non-parametric tests. As there are no two-way non-parametric tests nor any tests that utilize covariates, Δ scores were examined by separate within- and between-group tests. To examine the main effect of time the groups' combined Δ scores were examined by Friedman's test and where appropriate follow-up Wilcoxon tests. Between-group data at each time period were compared by Mann–Whitney tests.

A series of multiple regression analyses were undertaken with Δ cortisol and melatonin concentrations as the independent variables and Δ cognitive and psychomotor performance and Δ scores on the mood inventory as the dependent variable separately. As each individual's Δ scores at 18, 24 and 36 h were used, a correction factor for within and between-plot information was applied [32].

2. Results

Figs. 1 and 2 show the mean (S.D.) scores for the RNG and RED variables on the random number generation test, respectively, for both groups at each time point. Group × Time ANCOVA for the RNG variable found no significant main effects but a significant group × time interaction effect ($F(2,32)=4.21$, $p<0.05$, $\eta^2=0.26$). Tukey's HSD showed that for the creatine group performance at 36 h was significantly ($p<0.01$) better than at the other times. The Tukey–Kramer test showed that the only significant ($p<0.05$) between-group effect was at 36 h with the creatine group performing the better. The results for the RED variable demonstrated a significant main effect for group ($F(1,16)=11.12$, $p<0.005$, $\eta^2=0.70$), with the creatine group being better than the placebo group. There were no other significant effects.

Table 2 shows the mean (S.D.) results for number recall, balance and choice reaction time for both groups at each time point. Group × Time ANCOVA demonstrated a significant main effect for time on the balance test ($F(2,32)=9.46$, $p<0.001$, $\eta^2=0.59$). Post hoc HSD tests demonstrated that performance at 18 h was significantly ($p<0.001$) poorer than that at 24 h and 36 h. There were no interaction effects nor were there any significant effects for number recall and reaction time.

Table 3 shows the mean (S.D.) results for mood, effort, Δ mood and Δ effort for both groups at each time point. Friedman's test showed a significant effect for time for the mood state variable ($\chi^2=22.24$, $df=2$, $p<0.001$, $N=19$), post hoc Wilcoxon tests demonstrated that Δ mood at 18 h was significantly better than at 24 ($Z=3.69$, $p<0.001$, $N=19$) and 36 h ($Z=3.28$, $p<0.001$, $N=19$): there was no significant difference in Δ mood scores at 24 and 36 h. There was no significant effect of creatine supplementation. Friedman's test showed a significant effect for time for the effort variable ($\chi^2=5.83$, $df=2$, $p=0.05$, $N=19$), post hoc Wilcoxon tests found that Δ effort at 18 was significantly lower than at 24 ($Z=1.66$, $p<0.05$, $N=19$) and 36 h ($Z=2.18$, $p<0.05$, $N=19$), which did not differ significantly from one another. There were no between-group differences.

Fig. 3 shows the mean (S.D.) salivary concentrations of cortisol for each group at 0900 h Day 1, 2100 h Day 1, 0300 h Day 2, 0900 h Day 2 and 2100 h Day 2. Results of the Group × Time ANOVA showed a significant main effect of time ($F(4,68)=35.04$, $p<0.001$, $\eta^2=0.63$). Tukey HSD tests showed that cortisol concentrations at 0900 h Day 1 were significantly ($p<0.001$) higher than those 0900 h Day 2 and concentrations 2100 h Day 1 were significantly ($p<0.01$) higher than those at 2100 h Day 2. There was no interaction effect. The trend test demonstrated a cubic effect ($F(1,14)=14.15$, $p<0.001$).

Due to failure to supply sufficient saliva, we were not able to assay melatonin samples for four subjects in the placebo group. Data were collapsed and concentrations at each time point were compared by a one-way ANOVA. Results were approaching

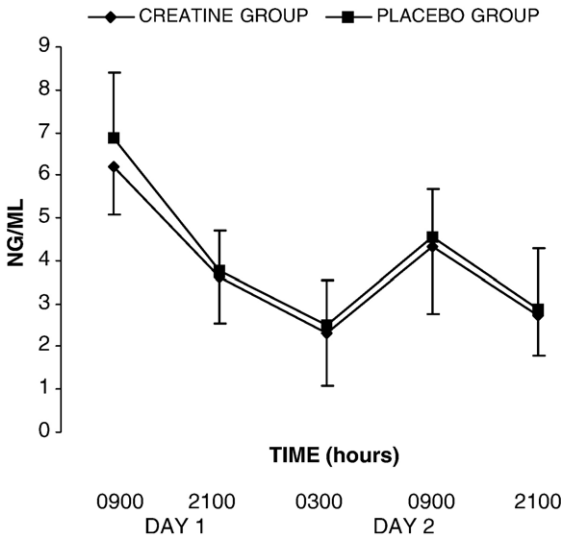

Fig. 3. The mean (S.D.) salivary concentrations of cortisol for each group at 0900 h Day 1, 2100 h Day 1, 0300 h Day 2, 0900 h Day 2 and 2100 h Day 2 for both groups.

significance ($F(4,56)=2.09$, $p=0.09$, $\eta^2=0.15$) with a moderate effect size; therefore, the trend test was undertaken as recommended by Clark–Carter [33]. A significant cubic trend was found ($F(1,14)=14.15$, $p<0.002$).

Multiple regression analyses with Δ cortisol and Δ melatonin concentrations as the independent variables and Δ scores on each of the tests as dependent variables demonstrated that Δ cortisol and Δ melatonin combined were significant predictors of Δ performance on the balance test ($R^2=0.24$, $p<0.005$), Δ RED ($R^2=0.19$, $p<0.01$) and Δ mood ($R^2=0.15$, $p<0.03$). According to Cohen [34], R^2 of 0.13–0.26 is a moderate effect size and >0.26 a high effect size.

3. Discussion

The data provide only partial support for the hypothesis that creatine supplementation would have a positive effect on cognitive and psychomotor performance, and mood state during 36 h of sleep deprivation with moderate-intensity exercise. Creatine supplementation had a positive effect on the random number generation task only. Tukey HSD data for the interaction effect for the RNG variable showed that the creatine group demonstrated a significant linear improvement in performance throughout the test, while the placebo group exhibited no significant effect. Between-group data showed that a significant effect of creatine supplementation on RNG performance did not occur until the 36-h time period. This is different to the findings of McMorris et al. [3], who found that the creatine group were better at 24 h.

While the above results suggest a positive effect of creatine supplementation on random number generation, the results for the RED variable show no interaction effect and no effect of sleep deprivation but a significant main effect for group. Previous research has shown a significant effect for creatine supplementation without any intervening variables on cognition [35,36] and this may be shown here. However, given the results of McMorris et al. [3] and those for the RNG variable in this study, it is more likely that the differences in results for the two variables are due to their nature. The RNG variable is generally accepted as being the better measure of central executive functioning [27].

No significant effects of creatine supplementation were demonstrated for number recall. This is similar to the findings of McMorris et al. [3]. Given the fact that there was no effect of time on this task suggests that it is not sufficiently affected by sleep deprivation to stress ATP re-synthesis. There was no significant effect of creatine supplementation on choice reaction time. This is contrary to the findings of McMorris et al. [3]. It is difficult to see why there should be this difference in results between the two studies. The same reaction time test was used and the subjects were of similar backgrounds.

These results suggest that creatine supplementation has only a very limited effect on cognitive tasks during sleep deprivation with intermittent moderate-intensity exercise. Given the nature of random number generation, number recall and choice reaction time tasks it is possible that creatine supplementation only has a positive effect when the task is complex. Random number generation is a working memory central executive task [24]. Such tasks activate large areas of the prefrontal cortex [37] and the hippocampus [38]. Number recall is carried out by the phonological loop component of working memory [24], these tasks activate the lateral frontal and inferior parietal lobes [39]. Visual choice reaction time tasks activate, in particular, the visual cortex and basal ganglia [40]. It is generally thought that central executive tasks require more energy, are susceptible to stress [41] and probably require the re-synthesis of ATP more than the more simple tasks. It is distinctly possible that the simple tasks do not sufficiently stress creatine supplies, even under stress induced by sleep deprivation, for creatine supplementation to be useful or necessary.

While the above argument might explain why the central executive task was affected by creatine supplementation, it does not explain why the creatine group demonstrated a significant improvement in performance. One would have expected the placebo group to demonstrate a linear deterioration in performance and the creatine group to show no effect. However, research examining the effect of ≥36-h sleep deprivation on the performance of central executive tasks has shown equivocal results [11,20,42]. The performance outcome of the placebo group in this study was simply unaffected by 36-h sleep deprivation. Although it is tempting to claim that creatine supplementation resulted in a learning effect for the creatine group this is very unlikely. Random generation tasks do not show a learning effect unless feedback is given [28]. It is more likely that these results are related to increases in cognitive effort. Eysenck and Calvo [17] argued that, during high level of stress, increased effort results in a maintenance or even an improvement in performance. The effort results for this experiment show a main effect for effort. It is possible that the interaction between the availability of creatine and increased cognitive effort resulted in improved performance by the creatine group.

The results concerning balance also fail to support the hypothesis that creatine supplementation would have a positive effect on a psychomotor task and are different to those of McMorris et al. [3]. However, the test used in this experiment differs greatly from that used by McMorris et al. [3]. The subjects in that study carried out a static balance test, while those in the present study undertook a dynamic test. Although both stress the ability to integrate visual and proprioceptive information, and use this to control movement, there are sufficient differences to suggest that they may not be activating the same areas of the brain and/or musculature.

As with the number recall and choice reaction time tasks it may be that this task is such that it does not unduly stress ATP re-synthesis, even during and after 36-h sleep deprivation. This is supported by the fact that balance significantly improved linearly during the test. While increased effort may account for the results, another possible reason is the use of moderate-intensity exercise in this study, rather than the mild exercise used by McMorris et al. [3]. Moderate-intensity exercise has been shown to have a beneficial effect on psychomotor performance [43] and even cognitive performance [44]. The physiological and biochemical responses to exercise result in feedback to the brain, via the sympathetic nervous system, and

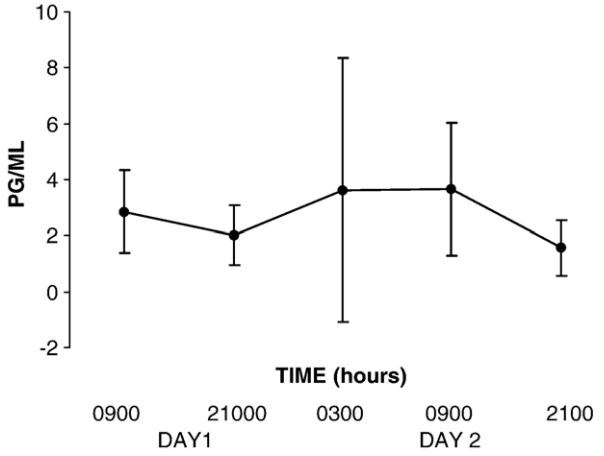

Fig. 4. The mean (S.D.) salivary concentrations of melatonin for each group at 0900 h Day 1, 2100 h Day 1, 0300 h Day 2, 0900 h Day 2 and 2100 h Day 2.

this is thought to induce the release of the neurotransmitters noradrenaline, dopamine and 5-hydroxytryptamine (5-HT) in the brain [45]. This results in increased arousal and improved cognitive and psychomotor performance [46]. This argument is based on research examining the effect of exercise without sleep deprivation. Although intuitively one would expect moderate exercise during sleep deprivation to induce physiological responses more akin to those found in heavy exercise in normal conditions, this has not been shown to be the case [47].

The results for effort, as measured by the effort sub-scale of the NASA-TLX, show a linear increase in effort until 24 h. This provides some support for the argument that improvements in performance during and following of sleep deprivation are due to increased effort. However, there were no significant changes in effort from 24 h to 36 h yet this is where the significant between-group effect for random number generation was shown. It is possible that creatine only demonstrated a between-group difference when effort had reached a peak. Overall we believe that these data suggest that effort may be a key factor in performance during sleep deprivation regardless of creatine supplementation.

Creatine supplementation produced no significant differences between mood states for the creatine and placebo groups. This is contradictory to McMorris et al. [3], who demonstrated a significant effect on mood after 24-h sleep deprivation. In the present study, the main effect for mood state demonstrated a significant linear deterioration up to 24 h. It would appear that 24 h acted as a cut-off point for any deterioration for mood. This is similar to previous research [12,13].

Creatine supplementation also had no between-group effects on cortisol concentrations. Although ATP is necessary for the synthesis of this hormone, it would appear that 36-h sleep deprivation does not decrease creatine concentrations sufficiently to result in a negative effect. Salivary cortisol concentrations on Day 2 were significantly lower than those on Day 1. These results are similar to those found by McMorris et al. [3] for plasma cortisol concentrations following 24-h sleep deprivation. These authors argued that the decreases in post-sleep deprivation concentrations of cortisol were due to decreases in stress following completion of the experiment. They stated that, at baseline, the subjects were anxious about undertaking the test and, therefore, had abnormally high cortisol concentrations. The relief of having completed the test resulted in lower Day 2 concentrations. The trend analysis showed that the cortisol diurnal cycle was similar to that found in normal conditions, this supports the findings of Goh et al. [8].

Although we were unable to examine the effect of creatine supplementation on melatonin concentrations, the data provide some interesting results. The contrast analysis suggests the possibility of a cubic trend as one would expect from normal diurnal changes. However, observation of Fig. 4 shows that the S.D. for the 0300 h concentrations is very high. This may represent the different ways in which individuals respond to sleep deprivation when in artificial light throughout. The diurnal cycle in melatonin is determined to a large extent by light/dark changes but synthesis is also stimulated by endogenous activity in the suprachiasmatic nuclei of the hypothalamus [48]. Observation of the raw data shows that the majority of subjects demonstrated concentrations lower than one would expect given the normal levels at 0300 h [8]. This suggests that sleep deprivation undertaken in artificial light resulted in an interaction between the light/dark cycle and endogenous secretion which differs between individuals.

The regression correlations show that Δ cortisol and Δ melatonin combined are moderate to good predictors of changes in performance on the balance and random number generation tasks, and of changes in mood state. McMorris et al. [3] found no significant correlations between Δ cortisol and any cognitive or mood variables. This may have been because they only measured concentrations twice, at baseline and after 24 h. As cortisol is related to perceptions of stress and melatonin with alertness, these correlations are not surprising. It is, in fact, more surprising that other correlations were not found.

To summarize, creatine supplementation had a positive effect on the performance of a complex central executive task, during sleep deprivation with intermittent moderate-intensity exercise, but there were no effects on more simple choice reaction time and number recall tests. There was no significant effect of creatine supplementation on performance of a balance test or mood state. Given that none of the tasks were negatively affected by sleep deprivation, while the creatine group demonstrated a significant improvement in performance of the central executive task, it was concluded that creatine supplementation during sleep deprivation with moderate-intensity exercise is only useful for tasks that activate large areas of the prefrontal cortex.

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