The effects of daytime melatonin ingestion on arousal and vigilance vanish after sub-maximal exercise: a pilot study

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Abstract. – OBJECTIVE: Daytime melatonin ingestion is known to induce sleep at rest, which may affect arousal and vigilance. Physical exercise is known to produce an increase in core temperature and circulating cortisol which can enhance arousal and vigilance. The effect of submaximal exercise on vigilance and arousal following acute melatonin ingestion has not yet been studied.

The present study aimed at investigating the effect of submaximal exercise on vigilance and arousal following daytime melatonin ingestion.

PATIENTS AND METHODS: Eight physical education students undertook 45 min of submaximal exercise (at 60% of maximal aerobic speed) on a treadmill after melatonin-(6 mg) or placebo ingestion, in a randomized and counterbalanced order.

RESULTS: Heart rate (HR), rectal temperature (T_{re}), felt arousal scale (FAS), and thermal sensations (TS) were recorded at baseline (pre-exercise), immediately after exercise (post-exercise), and after 30 min of recovery (30 min post-exercise). Blood was sampled for lactate and cortisol. At 30 min post-exercise, the T_{re}, HR, blood pressure, lactate, FAS, and TS were measured. The participants performed vigilance tests pre-exercise, post-exercise and 30 min post-exercise. Daytime melatonin ingestion affected arousal and vigilance in the pre-exercise period ($p < 0.05$) but had no effect on T_{re}, HR, blood pressure, lactate, TS, arousal, and vigilance measured 30 min post-exercise ($p > 0.05$).

CONCLUSIONS: The negative effects of melatonin ingestion on vigilance and arousal vanished after a 45 min of submaximal exercise. The hypnotic effect of melatonin observed in the pre-exercise dissipated in the post-exercise period, possibly due to the significant elevation of T_{re}, HR, and cortisol at the end of submaximal exercise.

Key Words:
Anti-inflammatory, Antioxidants, Cognitive performance, Physical performance, Sleep.

Abbreviations

ANOVA: Analysis of variance; d: Effect size; FAS: Felt arousal scale; HR: Heart-rate; MAP: mean arterial pressure; MAS: maximal aerobic speed; T_{re}: rectal temperature; TS: Thermal sensation; VT: Vigilance test; η_p^2: partial eta-squared.

Introduction

Melatonin is a pineal gland hormone that has been associated with the control of the biological rhythms of mammals[1,2]. Since Alberti[3] discovered this hormone in bovines, the range of melatonin's actions has expanded. Melatonin is being studied for its potential to improve health outcomes in various clinical conditions[4-6]. It is now recognized that

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melatonin influences a wide range of physiological functions in humans[7-9]. Some authors[10,11] claim that exogenous ingestion of melatonin can help the intellectual and physical development of children, delay the aging process, and increase resistance to cancer and other diseases. Furthermore, a large number of research studies activity[6-8,12-15] have looked into the effects of melatonin on physical activity. Melatonin inhibits exercise-induced inflammation[8,16,17] and oxidative stress[7,8,17-19] when administered in both humans[19,20] and rats[13]. It also preserves glycogen content and stimulates fatty acid oxidation during exercise[21], while protecting the muscles from exercise-induced damage[22]. Melatonin ingestion may have several beneficial effects on health and athletic performance[23], however, it may also have some side effects, such as decreased cognitive performance[24,25].

It seems that melatonin ingestion has a stronger effect on the mental aspects than the physical ones of the short-term athletic performance[26]. Lieberman et al[27] (1984) reported that diurnal ingestion of a high dose of melatonin (e.g., 240 mg) slows reaction time throughout the day. Similar findings were later reported by Dollins et al[28] (1993), but with much lower doses of melatonin (e.g., 10 to 80 mg). While daytime melatonin' ingestion (5 mg) had no effect on short-term athletic performance[26], it did impact cardiovascular responses to exercise[14,26]. In fact, there have been a few reports[7,8,14,29-33] of negative effects of melatonin, one of them being the downregulation of nitric oxide synthase that can affect arousal and vigilance. Acute submaximal exercise-induced stress[7,14,15,17] may counteract the negative effect of melatonin on vigilance. To the best of the authors' knowledge, no previous study has looked at the acute effects of melatonin ingestion on arousal and vigilance after submaximal exercise.

Considering the aforementioned points, the goal of this research was to explore the effect of melatonin ingestion on arousal and vigilance after exercise and 30 min post-exercise. Since submaximal exercise raises core temperature, cortisol, and circulating nitric oxide, which may have an effect on cognitive and physical performance[7,14,15,17,34,35], we hypothesized that submaximal exercise may suppress the hypnotic effect of melatonin.

Patients and Methods

Ethical Approval

The study protocol was performed in accordance with the Helsinki Declaration for conducting human experimentation and was approved by the Farhat HACHED Ethical Committee, Sousse, Tunisia (FH/1609021). All participants signed a written informed consent.

Participants

The study included eight physical education students [age: 21.8 ± 0.9 years; body mass index: 21.0 ± 0.8 kg/m^2] from the High Institute of Sport and Physical Education of Tunisia who did not have any neurological medical history. All participants had an intermediate chronotype profile. Participants were nonsmokers and abstained from exercising, consuming alcohol, and/or caffeine-containing beverages for at least 24 hours prior to the measurements. As previously described by Souissi et al[8] (2020), the Vameval test was used to determine the participants' maximum aerobic speed (MAS) during the first appointment. The second and third appointments were spent completing the protocol's two sessions (melatonin or placebo) in a randomized and counterbalanced order (Figure 1). All physical measurements were taken at a temperature of 23°C ±0.1°C. As a way to lessen the effects of diurnal variation in physical performance[36-38], all sessions were held at the same time of day (from 08:00 to 11:10).

Experimental Protocol

The participants were requested to insert a rectal thermistor (Universal YSI400, China) and wear a heart rate (HR) monitor (Polar RS800, Finland) and get ready for the test. Rectal temperature (T_{re}) and HR were measured in real-time. The participants were given either a melatonin or a placebo capsule with water at 09:00 and then rested for 40 min. They performed the vigilance test (VT) in a seated position. The treadmill (Finnlo by HAMMER, Germany) workout began at ~09:50 a.m. The participants ran for 45 min at a submaximal intensity set at 60% of their MAS. Blood samples were taken from the antecubital vein before (pre-exercise) and immediately after exercise (post-exercise). After recovering for approximately 30 min from the exercise, T_{re} and HR were recorded. Blood pressure was measured in the left upper arm using a Tensoval (Tensoval, Hartmann, Germany). As previously described by Souissi et al (2020)[36], lactate was measured at 30 min post-exercise using a Lactate Pro (Lactate Pro, Kyoto, Japan). All the physical tests were performed in the same order (Figure 1).

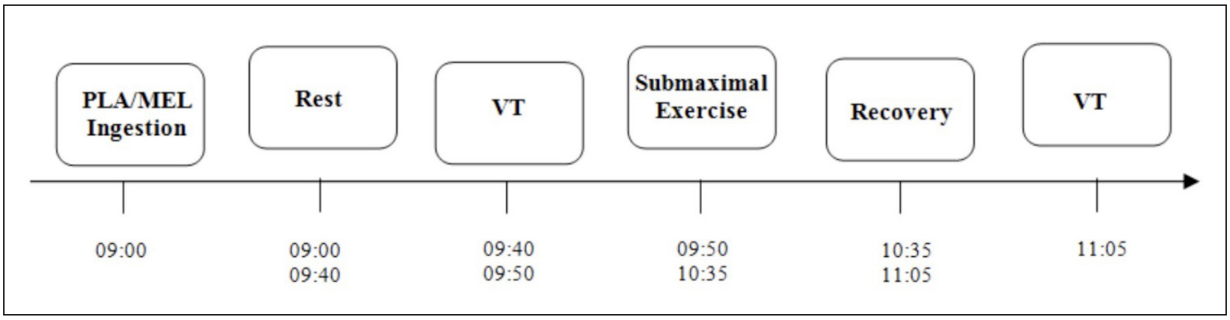

Figure 1. Study design. **MEL**: melatonin. **PLA**: placebo. **VT**: vigilance test.

Arousal Level and Perception of Heat

Thermal sensation (TS) was assessed after 30 min of sitting recovery using a modified ASHRAE 7-point scale that has been validated for use in physiological applications[39]. Each participant chose a verbal marker on the scale from "very cold" to "very hot" (i.e., 7 very cold, 6 cold, 5 slightly cold, 4 neutral, 3 slightly hot, 2 hot, 1 very hot).

Felt arousal scale (FAS)[40] was assessed at the start and end of the resting period (pre-exercise), at the end of exercise (post-exercise), and after 30 min of recovery (30 min post-exercise).

Vigilance Test (VT)

This test is used to assess the alertness[41]. It entailed identifying a specific three-digit number and circling as many instances as possible in a limited amount of time (1 min), working line by line, from left to right, while ignoring all other figures that were not three-digit numbers. There were 600 signs on the paper, divided into 36 lines. The total circling number was used to determine each participant's vigilance performance.

Statistical Analysis

The data were analyzed using repeated-measures analysis of variance (ANOVA). The Bonferroni test was used to determine significant differences. However, before conducting such analyses, the normality of distributions was tested with Shapiro-Wilk's test. The Shapiro-Wilk's test result was not significant ($p > 0.05$). Effect sizes were calculated as partial eta-squared (η_p^2) to assess the practical significance of our findings. All the statistical analyses were performed using Statistical Software Version 10.0 for Windows (StatSoft, Maisons-Alfort, France). The level of significance was predetermined to be $p < 0.05$ for all statistical analyses.

Results

Changes in HR, T_{re}, cortisol, lactate, FAS and TS variables observed with prolonged exercise are summarized in Figure 2. An important increase was observed immediately after submaximal exercise in both conditions, for HR, T_{re}, and cortisol, respectively ($p < 0.001$; $p < 0.001$; $p < 0.01$). HR was significantly higher at the end of exercise in the placebo condition ($p < 0.01$) (Figure 2).

A significant condition effect was obtained for FAS [$F_{(1,7)} = 16.20$, $p < 0.01$, $\eta_p^2 = 0.69$]. Analysis showed a significant exercise effect on FAS [$F_{(1,7)} = 84.00$, $p < 0.001$, $\eta_p^2 = 0.92$]. Melatonin reduced FAS by 25% (1.25; $p < 0.01$) during the resting phase, but the effect vanished immediately after the exercise phase ($p > 0.05$) (Figure 2).

Mean ± SD values for mean arterial pressure (MAP), HR, T_{re}, TS and lactate at 30 min post-exercise are presented in Table I. No significant condition effect was obtained for HR, T_{re}, MAP, TS and Lactate ($p > 0.05$).

Mean ± SD values for FAS and VT pre-exercise and 30 min post-exercise are presented in Figure 3. Analysis showed a significant condition effect on arousal [$F_{(1,7)} = 6.48$, $p = 0.03$, $\eta_p^2 = 0.48$]. A significant exercise effect was obtained for arousal [$F_{(1,7)} = 19.38$, $p < 0.01$, $\eta_p^2 = 0.73$]. Post-hoc revealed no significant melatonin effect on arousal at 30 min post-exercise ($p > 0.05$). Furthermore, analysis showed a significant (condition x exercise) interaction for vigilance [$F_{(1,7)} = 9.51$, $p = 0.01$, $\eta_p^2 = 0.57$]. Post-hoc revealed that melatonin reduces arousal by 25% and vigilance by 10% at rest ($p = 0.05$; $p = 0.01$, respectively),

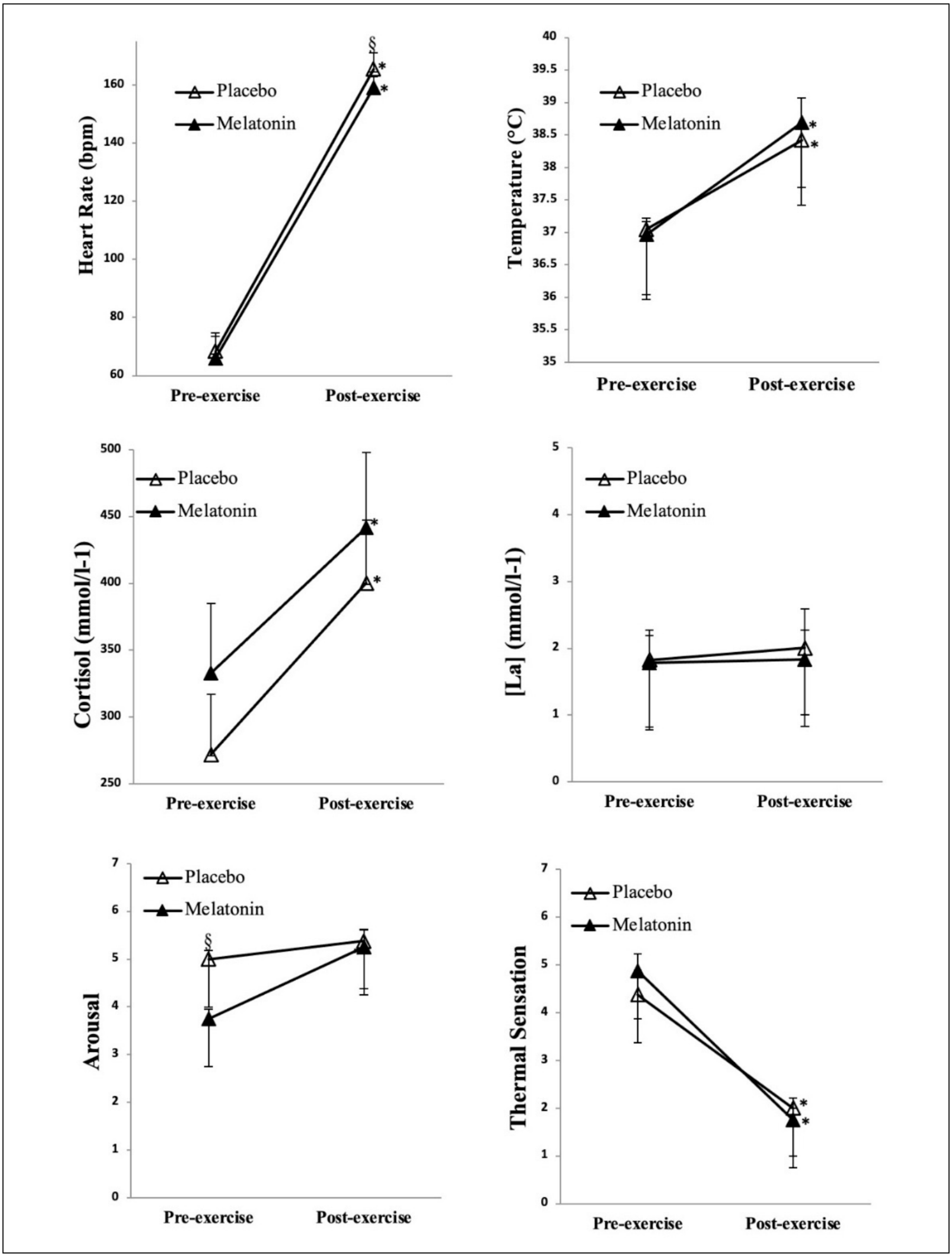

Figure 2. Physiological and psychological responses to prolonged exercise. *Significant difference between pre-exercise and post-exercise ($p < 0.05$). §Significant difference between melatonin and placebo ($p < 0.05$).

Table I. Physiological variables at ~ 30 min post-exercise for both conditions (n=8 healthy men).

	Placebo	Melatonin	Effect size	*p*
Heart-rate (bpm)	92 ± 9	90 ± 6	0.26	0.41
Rectal temperature (°C)	37.9 ± 0.35	38.05 ± 0.46	0.36	0.22
Mean arterial pressure (mmHg)	8.57 ± 0.31	8.43 ± 0.33	0.43	0.23
Lactate (mmol/l)	2.03 ± 0.29	1.73 ± 0.47	0.76	0.15
Thermal sensation	4.00 ± 0.00	3.87 ± 0.35	0.52	0.35

and this effect vanishes immediately after exercise ($p > 0.05$) (Figure 3).

Discussion

The main findings of the present study indicated for the first time that melatonin did not affect arousal or vigilance after running for 45 min at submaximal intensity. Performing submaximal exercise suppresses the hypnotic effect of melatonin as expected.

The results of the present study indicated no significant effect of melatonin on T_{re} and TS during exercise. This is consistent with recent studies[7,14,42,43] that found that melatonin had no effect on core temperature responses during a steady-state exercise. Contrary, at rest, previous research[44] reported that melatonin and its hypothermic effect at rest had a logarithmic dose-response relationship. Melatonin doses of 2-6 mg resulted in a significant reduction in core temperature (~0.2°C) at the resting period[14,44]. The current study's findings revealed that melatonin has no effect on MAP. It seems that an acute ingestion is not enough to significantly reduce blood pressure in healthy people as compared to chronic ingestion in people with high blood pressure ingestion[45,46]. The lack of melatonin effect on HR, MAP, and T_{re} during recovery in the present research could be attributed to a significant time lag between melatonin consumption and physiological testing (i.e., 125 min). Furthermore, we found no effect of melatonin on lactate levels after prolonged activity or at 30 minutes post-exercise. This might be because submaximal exercise did not significantly increase the blood lactate levels and/or the time lag between the end of the exercise and blood collection is around 1-3 min.

The present study showed that acute melatonin ingestion resulted in a significant decrease in arousal and vigilance at rest (pre-exercise). Likewise, previous investigations[26,47,48] showed

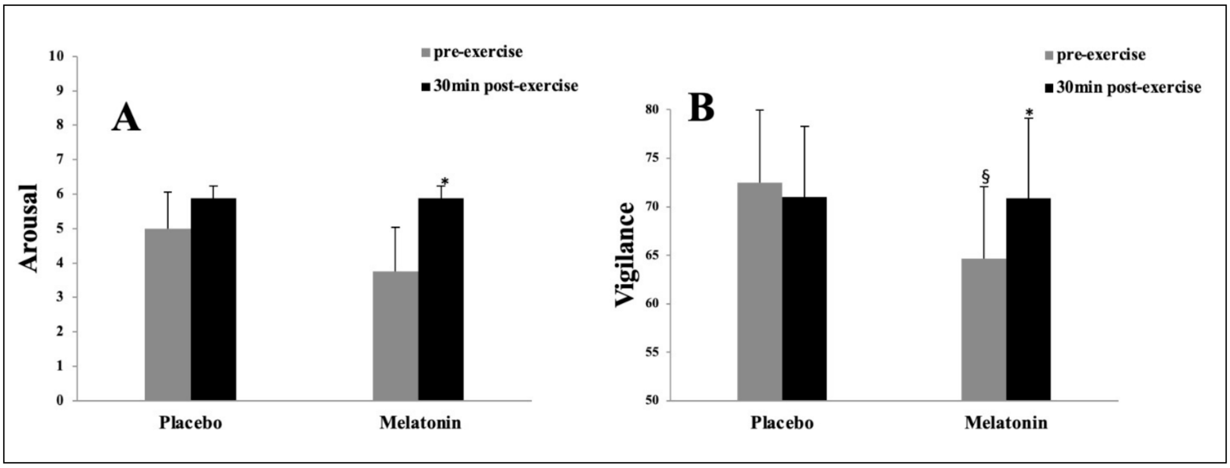

Figure 3. Effect of melatonin ingestion on arousal and vigilance in pre-exercise and recovery (n=8 men). **A**, Felt arousal scale after melatonin or placebo ingestion. **B**, Vigilance test after melatonin or placebo ingestion. Data in (**A** and **B**) were analyzed with ANOVA-test. The values are presented as the mean ± SD. *Significant difference between pre-exercise and 30 min post-exercise ($p < 0.05$). §Significant difference between melatonin and placebo ($p < 0.05$).

that melatonin ingestion affected vigilance, alertness, reaction time and short-term memory. The debilitative effects are more visible when the task is difficult[26] and vigilance is impaired for 5-6 h after 5 mg of melatonin ingestion[26,48]. Otherwise, melatonin ingestion at night (before sleeping) may have a positive influence on vigilance after waking in teenage athletes[49]. Indeed, many factors may be at the origin of the inconsistency between studies, such as melatonin dose, time of ingestion, latency between melatonin ingestion and exercise, type of exercise performed, and the level of motivation of the participants. Interestingly, in our study, we reported for the first time that the effect of melatonin on arousal and vigilance vanished after submaximal exercise. This finding can be explained by the increase in cortisol levels as a response to the exercise session[50].

We hypothesize that conducting submaximal exercise may mitigate melatonin's arousal and alertness-lowering effects. It would be interesting in the future to investigate the effects of exercise on patients suffering from sleepiness and a decreased capacity to perform mental work. The major limitation of the present study is that the sample size was small- and the-time latency between the end of the exercise and the blood collection was between 1-3 min.

Conclusions

Our study revealed that daytime melatonin consumption had an impact on arousal and vigilance. On the other hand, melatonin's effect on arousal and vigilance dissipated after 45 min of submaximal exercise. The hypnotic effect of melatonin found prior to exercise has dissipated after submaximal exercise, probably due to the metabolic and physiological changes induced by exercise.

Conflict of Interest

The authors declare that they have no competing interests.

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