ORIGINAL INVESTIGATION

Melatonin increases reactive aggression in humans

Jinting Liu[1,2,3] · Ru Zhong[3] · Wei Xiong[3] · Haibo Liu[3] · Christoph Eisenegger[4] · Xiaolin Zhou[3,5,6]

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Abstract

Melatonin, a hormone released preferentially by the pineal gland during the night, affects circadian rhythms and aging processes. As animal studies have shown that melatonin increases resident-intruder aggression, this study aimed to investigate the impact of melatonin treatment on human aggression.

In a double-blind, randomized, placebo-controlled between-participant design, 63 healthy male volunteers completed the Taylor Aggression Paradigm (TAP) after oral administration of melatonin or placebo.

We found that when given the opportunity to administer high or low punishments to an opponent, participants who ingested melatonin selected the high punishment more often than those who ingested placebo. The increased reactive aggression under melatonin administration remained after controlling for inhibitory ability, trait aggression, trait impulsiveness, circadian preference, perceptual sensibility to noise, and changes in subjective sleepiness and emotional states.

This study provides novel and direct evidence for the involvement of melatonin in human social processes.

Keywords Melatonin · Reactive aggression · Taylor aggression paradigm ·

to avoid such behaviors (Berkowitz 1993). Aggression may enable animals to gain access to limited resources and to inchose the intensity of punishment because they believed that was the experimenter wanted them to do. One participant in the melatonin group reported suspicion of the TAP and was excluded from data analysis.

Procedures

Participants completed questionnaires, ingested melatonin/placebo, and completed the two tasks according to the secolor patches and were asked to respond to the printed color of a word or patch by pressing a corresponding key as quickly and as accurately as possible while ignoring the actual meaning of the word. The keys assigned to the four colors of the print were "D," "F," "J," and "K" on the keyboard, respectively. Participants were asked to use the middle and index fingers of the left and right hand to make the responses. A practice session was administrated to ensure the establishment of the key-finger correspondence. The Stroop task had three conditions: the congruent condition, in which the color of the print and the meaning of the word were the same (e.g., word RED printed in red); the incongruent condition, in which the color of the print and the meaning of the word were different (e.g., word RED printed in black); and the control condition, in which only a patch was presented (e.g., patch printed in red). Each condition was composed of 28 trials, with 7 trials for each color of the print. The order of the trials was randomized.

Results

The TAP task

The percentages of "high punishment" selections in different conditions were used as the dependent variable for the statistical purpose. A 2 (treatment: melatonin/placebo) × 2 (opponent: low-provoking vs. high-provoking) mixed ANOVA showed significant main effects of treatment and opponent. Participants in the melatonin group (57.3% ± 29.0%) selected more high punishments than those in the placebo group (41.5% ± 30.2%), (1,61) = 4.483, = 0.038, partial η^2 = 0.068. Participants also selected more high punishments against high-provoking opponents (60.8% ± 29.9%) than against low-provoking opponents (37.7% ± 35.2%), (1,61) = 59.557, < 0.001, partial η^2 = 0.494, demonstrating a fairness norm in aggressive interactions (Fig. 3). The interaction between treatment and opponent was not significant, (1,61) = 0.344, = 0.559, partial η^2 = 0.006, suggesting that the effect of melatonin administration was equally effective in eliciting aggression against high- and low-provoking opponents. That is, melatonin did not significantly affect the degree of adherence to the fairness norm in aggressive interactions.

The Stroop task

To examine whether the melatonin effect observed above was accompanied by the potential impact of melatonin administration on inhibitory ability, we conducted two 2 (treatment: placebo/melatonin) × 3 (congruency: congruent vs. incongruent vs. control) mixed ANOVAs on reaction times (RTs) and error rates in the Stroop task. Trials with incorrect responses or with no responses and trials with RT outliers (±3 SDs beyond the

mean RT for all the correct trials in each condition) were excluded from the analysis of RT. There were significant main effects of congruency on RTs, (2,60) = 46.484, < 0.001, partial η^2 = 0.608, and on error rates, (2,60) = 13.370, < 0.001, partial η^2 = 0.308. Participants were slower and less accurate in responding to the incongruent stimuli than to the congruent stimuli and the control stimuli, Bonferroni-adjusted , < 0.001 (Table 1). However, for both RTs and error rates, neither the main effect of treatment (= 0.237, 0.098, respectively), nor the interaction between treatment and congruency was statistically significant (= 0.728, 0.355, respectively), suggesting that the increased aggression under melatonin treatment could not be simply attributed to inhibitory ability.

This suggestion was further confirmed by a mediation analysis. The difference in RTs between congruent and incongruent trials was used as the Stroop interference score, with a lower score indicating a better inhibitory ability. To test whether the inhibitory ability mediated the relationship between treatment and reactive aggression, we bootstrapped

Discussion

This study investigated whether melatonin increased reactive aggression in humans. We found that when given the opportunity to administer high or low punishments to opponents in the Taylor Aggression Task, participants who ingested melatonin selected high punishments more frequently than those who ingested placebo. This finding is in line with animal studies showing that endogenous and exogenous melatonin increases resident-intruder aggression (Jasnow et al. 2000; Jasnow et al. 2002; Demas et al. 2004; Wang et al. 2012), and with clinical studies suggesting that elevating bioavailability of melatonin by medical interventions in human patients increases aggressiveness (Haffmans et al. 2001; Hill et al. 2014).

Psychological studies have shown that reactive/impulsive aggression is related to inhibition failure (Morgan and Lilienfeld 2000; Hoaken et al. 2003; Giancola 2004) or sleepiness (O'Brien et al. 2011). Thus, a possible explanation for the melatonin-induced aggression may be a failure in inhibitory ability or increases in sleepiness. However, in the Stroop Color-Word Task, we found no significant effect of melatonin on differences in RTs and error rates between the congruent and incongruent conditions. Moreover, the effect of melatonin on reactive aggression remained significant after controlling for covariates including participant inhibitory ability. In the current study, participants who ingested melatonin dem-

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Author contributions J. L. and R. Z. designed the experiment and analyzed the data, under the supervision of X. Z., J. L., R. Z., and W. X., and H. L. performed the experiment. J. L., C. E., and X. Z. wrote the manuscript.

Compliance with ethical standards The experiment was performed in accordance with the Declaration of Helsinki and was approved by the Ethics Committee of the Department of Psychology, Peking University.

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Conflict of interests The authors declared that they had no conflicts of interest.

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