Psychopharmacology (2017) 234:2971–2978
DOI 10.1007/s00213-017-4693-7

ORIGINAL INVESTIGATION

# Melatonin increases reactive aggression in humans

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Received: 9 March 2017 / Accepted: 3 July 2017 / Published online: 21 July 2017


**Abstract**
*Objective* 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.
*Methods* 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.
*Results* 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.
*Conclusion* This study provides novel and direct evidence for the involvement of melatonin in human social processes.

**Keywords** Melatonin · Reactive aggression · Taylor aggression paradigm · Antisocial behavior · Circadian rhythm

**Electronic supplementary material** The online version of this article (doi:10.1007/s00213-017-4693-7) contains supplementary material, which is available to authorized users.

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## Introduction

Melatonin, a hormone released by the pineal gland preferentially during the night (Lynch et al. 1975), affects circadian rhythms and aging processes (Brzezinski 1997). Melatonin supplements are among the most popular health products and are widely used to treat sleep disorders and to slow down the effects of aging. Melatonin receptor proteins are located in various brain regions involved in cognition, memory, emotion, and reward processing, including the prefrontal cortex, amygdala, hippocampus, caudate nucleus, and nucleus accumbens (Uz et al. 2005). As such, it is possible that, apart from the physiological processes involved in sleep and health, melatonin may also affect cognitive and social processes. Indeed, previous studies have shown that oral administration of melatonin impairs human performance in cognitive tasks, such as unpredictable tracking (Rogers et al. 1998) and logic reasoning (Slotten and Krekling 1996). It remains unknown to what extent melatonin may affect social interactions in humans. In the present study, we aimed to investigate the impact of melatonin treatment on human aggression, a harmful social interaction.

Aggression refers to goal-directed behaviors that have malicious intentions to harm or injure others who are motivated

to avoid such behaviors (Berkowitz 1993). Aggression may enable animals to gain access to limited resources and to increase the likelihood of gene transmission over generations (Buss and Shackelford 1997; Kravitz and Huber 2003). Much of the variance in animal aggressive behaviors can be attributed to the effects of hormonal modulators, among those are testosterone, adrenal steroids, and melatonin (for a review, see Soma et al. 2008). Both endogenous and exogenous melatonin increase aggression in seasonal breeders (Jasnow et al. 2000; Jasnow et al. 2002; Demas et al. 2004; Wang et al. 2012). Research on the photoperiodic changes has demonstrated that, in a resident-intruder test, hamsters maintained in short days (i.e., light/dark ratio is 8:16) displayed a greater number of attacks, longer duration of attacks, as well as shorter latency to initial attacks than those maintained in long days (light/dark ratio is 16:8) (Jasnow et al. 2000). Short days increase the duration of melatonin secretion (Goldman 2001), and short-day-like patterns of melatonin secretion (simulated with daily melatonin injections) increases resident-intruder aggression (Jasnow et al. 2002; Demas et al. 2004), i.e., attacks initiated by the experimental animal against unfamiliar intruders into its home cage (Koolhaas et al. 2013).

In human society, aggression is a socially undesirable behavior associated with negative consequences, including social rejection, low educational achievement, and unemployment (Kokko and Pulkkinen 2000). Human aggression comprises two subtypes: (1) proactive/controlled aggression, a premeditated action to achieve a profit-based goal and is associated with low emotional arousal; and (2) reactive/impulsive aggression, a reaction to perceived provocation/threat and is associated with high emotional arousal (Anderson and Bushman 2002). The second type of aggression in humans may be similar to the resident-intruder aggression in animals, as both of them are responses to provocation or threat and are associated with excessive emotional responses (Haller 2014). Notably, although melatonin-induced aggression was observed in nocturnal animals (Jasnow et al. 2002; Demas et al. 2004), and humans are not nocturnal, literature shows that most assaults occur late in the evening (Cohn and Rotton 1997) when people have high levels of melatonin (Lynch et al. 1975). It is possible that melatonin affects reactive aggression in humans as well, even though humans are not nocturnal animals or seasonal breeders. This hypothesis is in line with two clinical studies showing that melatonin treatment of six demented inpatients and melatonin receptor agonist treatment of a patient with sleep cycle disorder all led to changes in aggression, as measured by the Social Dysfunction and Aggression Scale (Haffmans et al. 2001) or by the Overt Aggression Scale (O'Neill et al. 2014), respectively. Consistent with the hypothesis, an observational study with a large sample ($N = 400$) found an association between melatonin use and increased aggression in children with autism spectrum disorders (Hill et al. 2014).

To causally test the hypothesis, we applied a double-blind, randomized, placebo-controlled between-participant design to healthy male volunteers who completed a modified Taylor Aggression Paradigm (TAP; Taylor 1967; Krämer et al. 2007) after oral administration of melatonin or placebo. In each run, four male university students participated in the experiment and were separated into two two-member groups seated in separate rooms. Participants were instructed that they were playing a competitive reaction-time game against a randomly selected opponent from the other group and that whoever had the slower reaction time lost the current round of the game and would receive a high/low punishment (a combination of aversive noise and monetary loss) pre-selected by the opponent. The percentage of the high punishment selected for his opponent was taken as an index of aggression (Giancola and Parrott 2008). We predicted that the melatonin group would select high punishments more frequently than the placebo group. We introduced two opponents to increase the plausibility that participants were playing against two real opponents with different personalities. As provocation is a powerful elicitor of reactive aggression (Taylor 1967; Lotze et al. 2007), researchers suggested the inclusion of this variable in studies examining aggression (Giancola 2004; Krämer et al. 2007). The two opponents were therefore predetermined as a low-provoking one and a high-provoking one to examine whether the effect of melatonin on aggression would vary with provocation levels.

## Methods and materials

### Participants

A total of 64 healthy male Chinese university students participated in the experiment, with 32 (mean age ± SD, 21.3 ± 1.9 years) in the melatonin group and 32 (21.2 ± 1.9) in the placebo group. Exclusion criteria were color blindness/weakness, chronic diseases, mental disorders, sleep disorder, irregular sleep-wake cycle, medication, smoking, and drugs or alcohol abuse. Only males who usually wake up at 0700 h to 0800 h and go to sleep at 2300 h to 2400 h were included in the study. Participants abstained from food and drink (other than water) for 2 h before the experiment, and from exercise, caffeine, cigarette, and alcohol during the 24 h before the experiment. Additionally, no participants engaged in shift work or transmeridian travel for the 1 month preceding the test. 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. All participants gave written, informed consent and were paid for participation. Participants were asked to report strategies they used in the TAP and then were debriefed and thanked for their participation. No one reported that they

chose 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 sequence illustrated in Fig. 1. Upon arrival, participants completed a battery of questionnaires, including the Stanford Sleepiness Scale (SSS), Positive and Negative Affect Schedule (PANAS), Buss–Perry Aggression Questionnaire (BPAQ), Barratt Impulsiveness Scale (BIS-11), and Morningness-Eveningness Questionnaire (MEQ), which measured subjective sleepiness, emotional states, trait aggression, trait impulsiveness, and circadian preference, respectively (details of these questionnaires are presented in Supplementary Materials). At 1340 h, participants orally ingested either melatonin or placebo and then completed the threshold tests for the loudest bearable noise and the quietest audible noise (details are presented in Supplementary Materials). At 1505 h, they answered SSS and PANAS questionnaires for a second time. At 1510 h, participants first completed the Taylor Aggression Paradigm and then the Stroop Color-Word Task. Participants were seated in a dimly lit room after ingestion of melatonin or placebo and remained in this environment for the duration of the experiment.

### Stanford Sleepiness Scale

The Stanford Sleepiness Scale (Hoddes et al. 1973) was used to track changes of subjective sleepiness following melatonin/placebo administration. The SSS is a one-item seven-point scale with seven options (e.g., "1 = Feeling active, vital, alert, or wide awake," 7 = "No longer fighting sleep, sleep onset soon; having dream-like thoughts"), in which the respondents evaluate the degree of alertness they feel at the moment. A high score indicates a high amount of sleepiness.

### Melatonin/placebo administration

The drug sample consisted of 5 mg of melatonin and 200 mg of starch; the placebo sample consisted of 200 mg of starch. Previous studies have found that the peak effect of exogenous melatonin (0.1–10 mg, orally) on serum concentration is generated between 1 and 2 h after administration (Dollins et al. 1994; Rogers et al. 1998). We thus asked participants to complete the TAP and Stroop tasks 90 min after oral administration of the melatonin or placebo capsule. During the waiting period, participants watched irrelevant scientific videos.

### Taylor Aggression Paradigm

Aggression was elicited and assessed using a modified version of the Taylor aggression paradigm (TAP) (Taylor 1967; Krämer et al. 2007), in which the participant competed with his opponent and the winner could exert a high or low punishment against the loser of the current round of the game. Each participant was endowed with ¥20 before the initiation of the TAP task. A high punishment comprised the loudest bearable aversive noise (individually determined according to the threshold test) and a loss of ¥0.5, whereas a low punishment resulted in the quietest audible noise (individually determined) and a loss of ¥0.1. The duration of the noise punishment was 3.2 s. We set the punishment as a combination of aversive noise and monetary loss to ensure that the participant was motivated to avoid the punishment (Krämer et al. 2007).

The TAP task was divided into four sessions. Each session was composed of 10 rounds against a low-provoking opponent (opponent Q, who was anonymous but was labeled with letter "Q" in color on his silhouette) and 10 rounds against a high-provoking opponent (opponent W). The procedure of the TAP is depicted in Fig. 2. Note that the punishment selected by the opponent and the outcome of the game were predetermined by a computer program to ensure that, in each session, the probabilities of loss against the low-provoking and the high-provoking opponents were both 50%, and the percentages of high punishment selected by the low-provoking and high-provoking opponents were 20% and 80%, respectively. To "provoke" aggression from the participant, the first round of the first session was predetermined to ensure that the participant lost the game and received a high/low punishment from his opponent. For the remaining rounds, the opponent, the intensity of the punishment, and the outcome of the game were predetermined in a pseudo-randomized order, such that no more than three trials with the same opponent and the same outcome were presented consecutively. To track the extent of high punishment noise tolerance, participants were asked, at the end of each session, to rate to what extent he could tolerate this noise on a five-point Likert scale (1 = completely unbearable, 5 = completely bearable).

### The Stroop Color-Word Task

Previous studies have shown a negative relationship between aggression and inhibitory ability in antisocial groups (Morgan and Lilienfeld 2000) and provoked healthy groups (Hoaken et al. 2003; Giancola 2004). To rule out the possibility that the potential melatonin effect on aggression was somehow related to or determined by the potential melatonin effect on inhibitory ability, we tested the participants with the standard Stroop Color-Word Task (MacLeod 1991). Participants were shown words (RED, GREEN, BLUE, or BLACK, printed in color) or

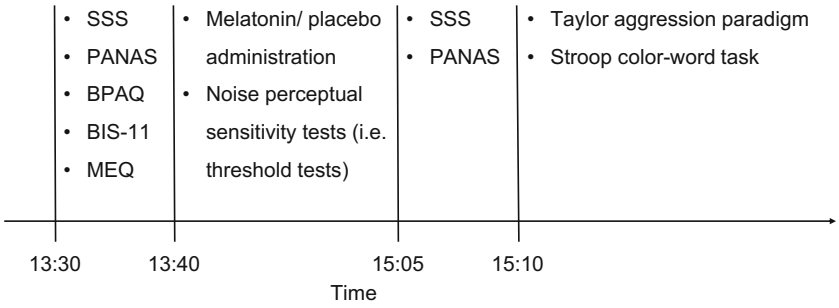


**Fig. 1** Sequence of events in the double-blind experiment with melatonin and placebo administration. *SSS* Stanford Sleepiness Scale, *PANAS* Positive and Negative Affect Schedule, *BPAQ* Buss–Perry Aggression Questionnaire, *BIS-11* Barratt Impulsiveness Scale, *MEQ* Morningness-Eveningness Questionnaire

color 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%), $F(1,61) = 4.483$, $p = 0.038$, partial $\eta^2 = 0.068$. Participants also selected more high punishments against high-provoking opponents (60.8% ± 29.9%) than against low-provoking opponents (37.7% ± 35.2%), $F(1,61) = 59.557$, $p < 0.001$, partial $\eta^2 = 0.494$, demonstrating a fairness norm in aggressive interactions (Fig. 3). The interaction between treatment and opponent was not significant, $F(1,61) = 0.344$, $p = 0.559$, partial $\eta^2 = 0.006$, 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

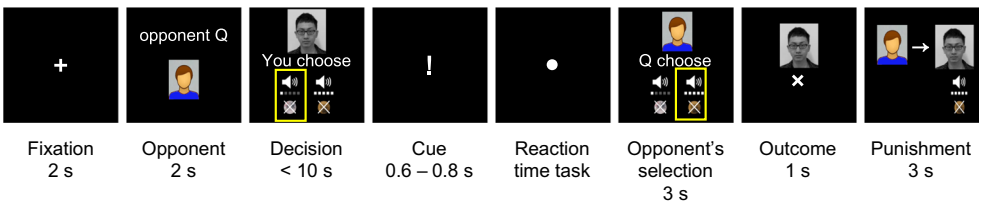


**Fig. 2** Task displays, timing, and design. In the TAP task, each round began by informing the participant that the program had randomly chosen one out of the two-member group as his opponent in the current round; the identities of the two opponents were represented by both a letter ("Q" or "W") and the color of the portrait (*red* or *blue*) (opponent screen). The colors of opponent Q and opponent W were counterbalanced across participants. The participant and his opponent had to choose the intensity of the punishment for each other within 10 s (decision screen). The positions of the low and high punishments were pseudo-randomly switched over rounds and fully balanced across opponents and outcomes of the game. During the reaction-time game screen, the participant and his opponent were asked to press the space bar as fast as possible to be the faster player, i.e., win the game. Before revealing the outcome of the competitive reaction-time game (outcome screen), they were shown the intensity of the punishment selected by their opponent (opponent's selection screen). After revealing the outcome of the game, the corresponding punishment was delivered to the loser of the game (punishment screen)

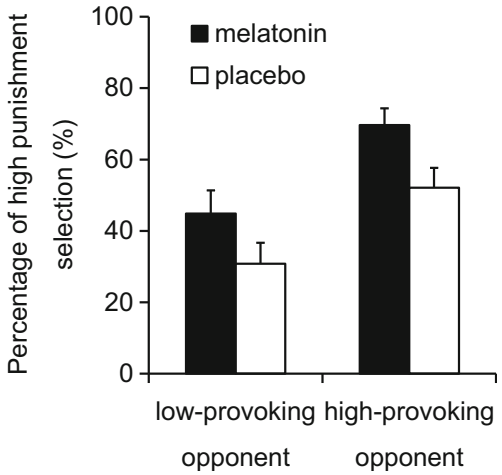


**Fig. 3** Effects of melatonin and provocation on reactive aggression assessed by the Taylor Aggression Paradigm. Participants in the melatonin group selected more high punishments than those in the placebo group. Participants selected more high punishments against high-provoking opponents than against low-provoking opponents. Interaction between melatonin treatment and provocation did not reach significance, $p = 0.559$

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, $F(2,60) = 46.484$, $p < 0.001$, partial $\eta^2 = 0.608$, and on error rates, $F(2,60) = 13.370$, $p < 0.001$, partial $\eta^2 = 0.308$. Participants were slower and less accurate in responding to the incongruent stimuli than to the congruent stimuli and the control stimuli, Bonferroni-adjusted $ps < 0.001$ (Table 1). However, for both RTs and error rates, neither the main effect of treatment ($p = 0.237$, 0.098, respectively), nor the interaction between treatment and congruency was statistically significant ($p = 0.728$, 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 the indirect effects 20,000 times using the SPSS version of INDIRECT macro (http://www.afhayes.com/) developed by Preacher and Hayes (2008). The indirect effect was not significant, indirect effect estimate = −0.0034, SE = 0.0080, 95% bias-corrected confidence interval was [−0.0507, 0.0104].

**Table 1** Means and standard deviations of reaction time and error rate in the Stroop Color-Word Test

| | Congruent | Incongruent | Control | Total |
|---|---|---|---|---|
| Reaction time (ms) | | | | |
| Melatonin group | 814 ± 177 | 954 ± 186 | 808 ± 125 | 857 ± 144 |
| Placebo group | 755 ± 157 | 917 ± 198 | 769 ± 137 | 812 ± 149 |
| Error rate (%) | | | | |
| Melatonin group | 4.3 ± 5.9 | 8.1 ± 6.0 | 3.7 ± 4.1 | 5.3 ± 3.4 |
| Placebo group | 4.6 ± 4.4 | 11.6 ± 8.8 | 4.8 ± 5.4 | 7.0 ± 4.3 |

## Sleepiness

To examine whether the increased aggression after melatonin administration could be attributed to changes in subjective sleepiness, we conducted a 2 (treatment: placebo/melatonin) × 2 (time: pre−/post-treatment) mixed ANOVA on subjective sleepiness. Results revealed significant main effects of treatment ($F(1,60) = 3.931$, $p = 0.052$, partial $\eta^2 = 0.061$) and time ($F(1,60) = 40.624$, $p < 0.001$, partial $\eta^2 = 0.404$), as well as a significant interaction between treatment and time, $F(1,60) = 4.399$, $p = 0.040$, partial $\eta^2 = 0.068$. Post hoc $t$ test revealed significantly greater post-treatment sleepiness in the melatonin group (3.83 ± 1.23) than in the placebo group (3.09 ± 1.12), $t(60) = 2.476$, $p = 0.016$, while there was no significant difference in pre-treatment sleepiness between the two groups (melatonin 2.58 ± 0.89 vs. placebo 2.44 ± 0.84), $t(61) = 0.658$, $p = 0.513$. The correlation between changes in subjective sleepiness and the Stroop interference score was not significant, $r = −0.195$, $p = 0.128$. To test whether changes in subjective sleepiness mediated the relationship between treatment and reactive aggression, we bootstrapped the indirect effects 20,000 times. The indirect effect was not significant, indirect effect estimate = 0.0027, SE = 0.0203, 95% bias-corrected confidence interval was [−0.0394, 0.0449].

## Controlling for potential contributing factors

To examine whether the melatonin-induced aggression could be accounted for by other potential contributing factors, we compared the differences in trait aggression, trait impulsiveness, circadian preference, perceptual sensibility to the noise, and changes in emotional states between the two groups. We found no significant differences in these measures between the two groups (Tables S1, S2), indicating that the increased aggression under melatonin treatment could not be attributed to these potential contributing factors. This suggestion was confirmed by the hierarchical regression analysis in which these potential contributing factors together with the Stroop interference and changes in subjective sleepiness were treated as covariates. Hierarchical regression analysis (step 1, entering covariates; step 2, entering both covariates and treatment) with the percentage of high punishment selection as the outcome variable showed that the effect of melatonin on reactive aggression remained significant after controlling for the covariates, $p = 0.039$ (Table S3).

## 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 demonstrated greater increases in sleepiness than participants who ingested placebo, which is consistent with previous studies (Lieberman et al. 1984; Dollins et al. 1994); however, this increased sleepiness did not significantly mediate the impact of melatonin on reactive aggression, and the melatonin effect remained significant even after controlling for covariates such as changes in sleepiness. Notably, the relatively small sample size of the current study may be underpowered to detect small effects. It is plausible that the indirect effects from melatonin to reactive aggression through sleepiness, inhibitory ability, or emotional responses could be detectable in a large sample.

Dual-process theories propose that human behaviors, including aggression, are governed by two different processes, the automatic ("hot," emotional) process and the controlled ("cold," cognitive) process (Bluemke and Teige-Mocigemba 2015). Our findings have shown that the melatonin-induced aggression cannot be attributed to changes in cognitive resources, which were measured with subjective sleepiness and cognitive inhibitory abilities. This suggests that melatonin may increase aggression more through its impact on the automatic process than on the control process. This suggestion is consistent with the observation that reactive aggression occurs when strong emotions of anger are elicited (Wilkowski and Robinson 2008), and is further supported by the finding that exogenous melatonin increases aggression as well as cortisol levels (which have been conceived as a physiological index of emotional arousal; Abercrombie et al. 2005) in animals (Demas et al. 2004). Based on these findings, we assume that melatonin might elevate reactive aggression in humans by intensifying the emotional response following provocation. As this study measured emotional states before (not after) provocation (see Supplementary Materials), this assumption should be examined directly by measuring emotional states following provocation in future melatonin administration research.

A growing number of studies have demonstrated that individuals during the afternoon/evening or non-optimal time are more likely to engage in cheating and lying behaviors (Kouchaki and Smith 2014; Gunia et al. 2014), show greater stereotypic bias in probability judgments of guilt (Bodenhausen 1990) and in the Implicit Association Test (Zadra and Proffitt 2014), and perform worse in facial emotion recognition (Paradee et al. 2008) than individuals during the morning or optimal time (the time during which physiological and cognitive functions are at the highest point). Given the role of melatonin in the regulation of the human circadian rhythm (Brzezinski 1997; Cajochen et al. 2003), our study, together with studies on circadian variations in social behaviors, might suggest that, apart from aggression, melatonin plays a role in a variety of anti- and pro-social behaviors in humans and may serve as one of the biological causes underlying the circadian variations of human social behaviors. Clearly, these hypotheses are in need of future studies.

Limitations of this study deserve consideration. First, as a laboratory aggression paradigm, the modified version of the TAP suffers from demand characteristics (Ritter and Eslea 2005). The permissive cues of aggressive responding and the lack of a non-aggressive way to interact with the opponents might encourage non-aggressive individuals to behave aggressively. This problem is a challenge for future research that attempts to simulate real-world aggression in the laboratory. Second, the effect of melatonin on aggression was observed here in provoking situations and was accompanied by a large effect of provocation. This leaves an open question regarding whether the effect of melatonin on aggression could extend to aggression without provocation, such as proactive aggression.

To conclude, by treating individuals with melatonin or placebo and measuring these participants' aggression with the Taylor Aggression Paradigm, we provide novel and direct evidence that melatonin increases reactive aggression in humans. Our study suggests that melatonin might serve as a biological explanation for the circadian variations in human social behaviors, such as unethical behaviors and stereotypic judgments. The adverse effect of melatonin on human social functions is worth noting given the wide use of melatonin in clinical practice.

**Acknowledgments** We thank Professor Drew Dawson and Dr. Xuan Zhou from the University of South Australia for their suggestions on melatonin administration and Dr. Philip Blue for the preparation of the manuscript.

**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.

**Funding** This study was supported by grants from the National Basic Research Program of China (973 Program: 2015CB856400) and National Natural Science Foundation of China (31630034) to Xiaolin Zhou and the National Natural Science Foundation of China (31600928) to Jinting Liu.

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

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