Effects of Exogenous Melatonin on Sleep Quality in Healthy College Students

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This study investigated the effects of melatonin on the sleep quality of healthy college students with aerobic exercise as a covariate, using a single-factor, repeated measures design. Twenty-seven students (11 men and 16 women) were administered either 6 mg of melatonin or a physically identical placebo over a period of 6 nights. These participants, age 18–22, were prescreened for unstable sleeping patterns and excessive intake of sleep-altering substances. Each morning, participants rated the previous night's sleep and the previous day's exercise activities on a sleep and exercise questionnaire. Findings indicate that certain components of sleep quality, including the ease of falling asleep and the depth and continuity of sleep, significantly improved ($p < .05$) in the melatonin condition. However, subjective ratings of overall sleep quality and the psychological aspects of post-sleep experiences showed no significant improvement. This pattern implies that melatonin may have a limited effect among a healthy population that is not chronically sleep deprived.

MELATONIN IS A HORMONE THAT IS PRODUCED and secreted by the pineal gland. Light suppresses the production of melatonin; thus, the hormone is released primarily at night (Cagnacci, 1996). Research has established that melatonin is involved in the synchronization of circadian rhythms in humans (Armstrong, Cassone, Chesworth, Redman, & Short, 1986; Cassone, 1990; Lewy, Ahmed, Jackson, & Sack, 1992), and exogenous melatonin has been used to alleviate the symptoms of jet lag (Arendt et al., 1987; Arendt, Aldhous, & Marks, 1986). Melatonin is also believed to promote sleep onset (Anton-Tay, 1974; Anton-Tay, Diaz, & Fernandez-Guardiola, 1971; Cramer, Rudolph, Consbruch, & Kendel, 1974; Vollrath, Semm, & Gammel, 1981). Though it is not yet clear how melatonin physiologically mediates sleep (Cagnacci, 1996), earlier research indicated that an exogenous dosage accelerated sleep onset (Arendt, Borbely, Franey, & Wright, 1984; Dahlitz et al., 1991) and improved both sleep maintenance throughout the night and awakening qualities the following day (Waldhauser, Saletu, & Trinchard-Lugan, 1990). However, these results were found after healthy participants were exposed to a period of artificially induced insomnia. Such results need to be replicated with non–sleep-deprived individuals. The present study investigates whether or not an exogenous dosage of melatonin improves subjective ratings of sleep quality among young adults with healthy sleeping patterns.

Melatonin has been shown to significantly increase the subjective assessment of total sleep time and daytime alertness in individuals suffering from chronic insomnia (MacFarlane, Cleghorn, Brown, & Streiner, 1991). Insomniacs also report that their overall quality of sleep is improved under a regimen of melatonin ingestion (James, Sack, Rosenthal, & Mendelson, 1990). Likewise, there is evidence that melatonin enhanced sleep efficiency and decreased the time spent awake after sleep onset among elderly individuals suffering from insomnia (Garfinkel, Laudon, Nof, & Zisapel, 1995). These studies support

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the notion that exogenous melatonin plays a role in one's sleeping patterns, and that it may improve one's sleep experiences. Yet, in each case, participants were sleep deprived due to either chronic or artificially induced insomnia. Sleep deprivation may predispose individuals to experience a greater effect from an exogenous dosage of melatonin.

Other recent studies have examined melatonin's effects with non–sleep-deprived participants and found that it significantly increased actual sleep time and improved sleep efficiency in healthy, middle-aged individuals (Attenburrow, Cowen, & Sharpley, 1996). Analogous results were found when healthy, young adult men were administered melatonin. Melatonin reduced both the latency to sleep onset (Hughes & Badia, 1997; Zhdanova, Wurtman, Morabito, Piotrovska, & Lynch, 1996) and the time awake after sleep onset but increased the length of the total sleep period (Hughes & Badia, 1997). These results suggest that melatonin may be beneficial to individuals who are not chronically sleep deprived. However, the scarcity of such studies and the relatively small sample sizes used (between 8 and 15 participants) justify the need for further research among non–sleep-deprived individuals.

Physical exercise has also been shown to have a beneficial effect on sleep. In a meta-analytic review of 38 studies, Youngstedt, O'Connor, and Dishman (1997) found that, throughout the research, exercise had a significant impact on participants' total sleep time. Similar results were also found in a review of 64 studies relating the effects of exercise to sleep (Kubitz, Landers, Petruzzello, & Han, 1996). Individuals exposed to both short- and long-term exercise generally experienced an increase in total sleep time and a decrease in sleep onset latency. Furthermore, those individuals who engaged in habitual exercise also exhibited a deeper sleep throughout the night (Kubitz et al., 1996). The influence of exercise on sleep is parallel to the purported effects of melatonin; both have been shown to have an impact on total sleep time, sleep onset latency, and time awake after sleep onset. If left unaccounted for, physical exercise may, at best, skew participants' responses and, at worst, serve as an alternate explanation for any ensuing results. Thus, the present research included the use of exercise as a covariate.

In this study, individuals, who were blind to the experimental condition, ingested either melatonin or a placebo 30 min before going to bed on each of 6 nights. Upon awakening each morning, they completed a sleep and exercise questionnaire (SEQ), which was based upon previous work by James et al. (1990). The SEQ recorded participants' sleeping patterns and assessed their sleep experiences throughout the night as well as their general mood upon awakening. In addition, participants recorded the duration and intensity of the previous day's aerobic activity (any activity which increases the heart rate continuously for at least 20 min). It was predicted that a 6-mg dosage of exogenous melatonin would significantly improve the sleep quality (as defined by the SEQ) of healthy, non–sleep-deprived college students, compared to a placebo, with exercise taken into account as a covariate.

Method

Participants

Fifty-eight potential participants were recruited from undergraduate classes at Santa Clara University. Twenty-seven individuals were excluded during a prescreening process due to unstable sleeping patterns, excessive intake of sleep-altering substances such as alcohol and caffeine, and/or preexisting medical conditions that posed a potential risk (e.g., diabetes, hypoglycemia, depression, leukemia, epilepsy, and any autoimmune disease). Four additional individuals were excluded after the experimental protocol began due to noncompliance.

Ultimately, 27 undergraduate students (11 men and 16 women) between the ages of 18 and 22 completed the study. Participants reported they slept between 5 and 8 hr per night ($M = 7.0$) and displayed stable sleeping patterns by regularly falling asleep and awakening within 1 hr of the same time each day. Participants did not demonstrate a tendency to take excessive naps throughout the average week ($M = 1.6$/week). In addition, participants did not exhibit trouble falling asleep, frequent nighttime awakenings, or early morning awakenings; they reported these occurrences an average of less than two times per weeknight ($M = 1.9$). These combined characteristics helped ensure that the sample was comprised of individuals with healthy sleeping patterns who have not demonstrated any symptoms of chronic sleep deprivation.

With regard to sleep-altering substances, the participants consumed an average of less than one cup of caffeinated coffee or tea ($M = 0.6$) and slightly more than one caffeinated soda ($M = 1.2$) per day. Participants reported consuming alcoholic beverages fewer than two weeknights ($M = 0.4$) per week. None of the participants were currently taking melatonin, nor did they regularly smoke.

Participation was voluntary for all individuals; those students enrolled in an introductory psychology class received research participation credit to satisfy course requirements. All participants received

educational information regarding melatonin and general principles that may promote quality sleep (e.g., to stabilize one's sleeping patterns or to refrain from eating a heavy meal within 3 hr of one's bedtime). Participants were treated in accordance with APA ethical guidelines, and all materials and procedures were approved by an internal human participants committee.

Materials

A prescreening questionnaire was completed by potential participants during an orientation session. The questionnaire was designed to exclude individuals with erratic sleeping patterns or excessive intake of alcohol, caffeine, and nicotine substances. Those individuals selected to participate were notified by the experimenters and scheduled to attend an instructional session. At this session, participants read and signed the informed consent document, which included basic information about melatonin (e.g., melatonin's role in the body and the relative safety of the dosage) and a brief summary of the experimental protocol. Exclusionary medical conditions were also listed to prevent at-risk individuals from participating. These conditions included a personal or family history of the aforementioned preexisting conditions. Pregnant and nursing women, as well as individuals with severe food allergies, were also excluded.

At the instructional session, participants received an individually coded packet of experimental materials and instructions for completing the study. The coding scheme identified the order of pill ingestion and the particular condition for any given day. The packet consisted of eight separate envelopes marked Day 1 through Day 8. Days 1 and 2 were provided as practice trials so that participants would become familiar with the experimental protocol; thus, those envelopes included only an SEQ. Days 3 through Day 8 included an SEQ and a dosage of either 6 mg (2 capsules containing 3 mg each) of melatonin or a rice-powder placebo. Past research has shown that 6 mg of melatonin is a safe yet potentially effective dosage (Hughes & Badia, 1997; Jan & O'Donnell, 1996; MacFarlane et al., 1991; Waldhauser et al., 1990). The melatonin capsules, obtained from Twinlab, each contained 3 mg of melatonin as well as a pharmaceutical filler. The placebo capsules were assembled under a laminar flow hood using heat-sterilized rice powder. These precautions were taken to ensure the sterility of ingested capsules. Special consideration was given to the size of the capsules and the texture and color of the chosen filler to ensure that both the melatonin and placebo pills would be physically similar.

The SEQ measured participants' subjective ratings of the previous night's sleep and required them to keep a record of their sleeping habits. This type of postsleep inventory, which focuses on comparative aspects of sleep quality, was deemed the most appropriate method to determine the efficacy of melatonin compared to a placebo (Buysse, Reynolds, Monk, Berman, & Kupfer, 1989). Previous research has found that subjective assessments of sleep quality correlate well with objective measures of sleep microstructure (Ferini-Strambi et al., 1993). The SEQ included questions pertaining to several subjective aspects of sleep that have appeared throughout the literature such as continuity of sleep, ease of falling asleep, ease of awakening, feelings and mood upon awakening, depth of sleep, and the overall quality of sleep[1] (Frankel, Buchbinder, & Snyder, 1973; James et al., 1990; Parrott & Hindmarch, 1978; Webb, Bonnet, & Blume, 1976). These and other related questions were scored on an 11-point scale with 1 representing the most negative response (*poor overall sleep, not deep sleep, or not continuous sleep*) and 11 being the most positive response (*good overall sleep, very easy to fall asleep, or feeling very rested upon awakening*).

Participants also recorded various objective aspects of their sleep experience in a sleep diary. These questions included the time of getting into bed, the estimated time of sleep onset, the number of awakenings throughout the night, the time spent awake during the night (between sleep onset and final awakening), the time of awakening, and the method of awakening. This information was used to determine the participants' total sleep times and to compare their objective continuity of sleep (the number of awakenings throughout the night). In addition, participants were asked to report the amount of alcohol and caffeine they consumed each day of the study. This information was included as a secondary screening measure to ensure that participants with excessive alcohol and caffeine consumption were not included in the final data analysis; however, no individuals were excluded due to these conditions.

The SEQ also contained questions about participants' involvement in aerobic exercise during the preceding day. Participants were asked to record the duration of their aerobic activities in minutes and to rate the intensity of those activities on an 11-point scale (1 = *low intensity* and 11 = *high intensity*). A numerical rating of exercise was determined by multiplying the duration of the activity by the subjectively rated intensity. This aerobic activity rating took

[1]Interested readers can obtain a copy of the entire SEQ by contacting the corresponding author.

into account the general principles of duration and intensity (Cooper, 1978). A higher score of exercise is correlated with a greater potential effect on sleep quality. This measure is consistent with the research which suggests that exercise positively influences sleep (Kubitz et al., 1996; Youngstedt et al., 1997).

Design

The overall experimental design included one factor with two levels. Sleep quality among college students was measured under melatonin and placebo conditions. The levels were tested using a single-factor, repeated measures design. A within-subjects design was appropriate due to melatonin's relatively short biological half-life (Waldhauser et al., 1990). In low dosages (2.5 mg), plasma levels of melatonin have returned to the normal physiologic range within 7 hr after ingestion (MacFarlane et al., 1991). This finding indicates that melatonin received on one night would not continue to influence participants' sleep on the following night.

The possible orders in which participants could receive three melatonin and three placebo conditions were listed. We then eliminated orders in which melatonin or placebo occurred on three consecutive nights. Six of the remaining orders were chosen with a table of random numbers. Participants were assigned to orders in groups of six. This block randomization ensured that an equal number of individuals participated in each order.

Procedure

The first 2 nights (beginning on a Sunday) of the experiment provided participants with practice in completing the SEQ; they completed the SEQ upon awakening without ingesting a pill the preceding night. Data from these nights were not included in the analysis. The experiment continued for 6 additional nights on which pills were ingested, excluding the following Friday and Saturday nights to prevent the instability of sleep on weekend nights from interfering with data collection.

On each experimental night, participants were instructed to ingest the contents of the pill packet with a full glass of water 30 min prior to going to bed. This procedure was important because melatonin produces different sleep onset effects depending on the time of pill consumption (Tzischinsky & Lavie, 1994). Immediately upon awakening each morning, participants completed the SEQ. Participants were contacted by the experimenters during the study to ensure that they comprehended and adhered to the experimental protocol. After the protocol was completed, participants returned the experimental materials and were given general information concerning previous findings (Cassone, 1990) and the function of melatonin.

Results

For analysis purposes, the 15 questions from the SEQ were examined; 13 assessed sleep quality (see Table 1) and 2 were scored to determine aerobic activity. For each question pertaining to sleep, a mean rating was determined from the three individual scores in each condition—melatonin and placebo. A one-way, repeated measures analysis of covariance (ANCOVA) was used to analyze the data. The exercise scores for each condition were combined to obtain a mean exercise rating for the melatonin conditions and for the placebo conditions. The numerical rating of exercise, taking into account both intensity and duration, was factored into each analysis as a covariate.

Participants' mean ratings of the ease of falling asleep was greater for the melatonin condition (M = 8.73) than for the placebo condition (M = 7.86), $F(1, 25) = 10.01$, $p = .004$. Participants' mean ratings of the continuity of sleep was greater for the melatonin condition (M = 8.85) than for the placebo condition (M = 8.19), $F(1, 25) = 4.36$, $p = .047$. Participants' mean ratings of depth of sleep was greater for the melatonin condition (M = 8.67) than for the placebo condition (M = 8.10), $F(1, 25) = 5.61$, $p = .026$.

Significant results were not found ($p \geq .05$) for questions pertaining to postsleep psychological experiences, such as feelings of alertness and restfulness upon awakening. In addition, ratings of general sleep quality, including the number of nighttime awakenings and overall sleep quality, did not show a significant difference between the melatonin and placebo conditions. The significant results indicate that melatonin influences certain aspects of sleep quality, including participants' ease of falling asleep, continuity of sleep, and depth of sleep.

Discussion

The results were consistent with the initial prediction that melatonin would have a significant effect on some aspects of the sleep quality of healthy college students. Significant improvements were reported for the melatonin versus placebo conditions with respect to several components of sleep (ease of falling asleep, depth of sleep, and continuity of sleep). These findings are consistent with previous research which concluded that melatonin decreases sleep onset latency (Arendt et al., 1984; Dahlitz et al., 1991; Ferini-Strambi et al., 1993; Garfinkel et al., 1995; Hughes & Badia, 1997; Waldhauser et al., 1990;

TABLE 1

Summary of the Mean Ratings for the Melatonin and Placebo Conditions by Question

Question	Melatonin	Placebo
Number of awakenings	0.93	1.15
Ease of falling asleep	8.73	7.86[a]
Feelings of grogginess or tiredness	7.88	7.53
Ease of awakening	5.83	5.91
Ease of getting out of bed	5.89	5.85
Continuity of sleep	8.85	8.20[b]
Feelings of restfulness	6.62	6.98
Feelings of alertness	6.62	6.73
Energetic feelings	6.38	6.52
Feelings of refreshment	6.35	6.47
General mood upon awakening	6.74	6.75
Depth of sleep	8.67	8.10[b]
Overall quality of sleep	8.03	7.86

[a]Comparison significant at $p < .01$.
[b]Comparison significant at $p < .05$.

Zhdanova et al., 1996) and improves sleep maintenance throughout the night (Attenburrow et al., 1996; Hughes & Badia, 1997; Waldhauser et al., 1990) among populations of both healthy individuals and those suffering from chronic insomnia. These results reaffirm the notion that melatonin does indeed have a sleep-promoting effect on humans (Anton-Tay, 1974; Anton-Tay et al., 1971; Cramer et al., 1974; Vollrath et al., 1981).

These results are not consistent with past research that found melatonin to significantly improve participants' awakening qualities subsequent to ingestion (Arendt et al., 1987; MacFarlane et al., 1991). Although participants reported a decrease in sleep onset latency and improved sleep maintenance throughout the night in the melatonin condition, they failed to indicate any differences in their subjective evaluations of overall sleep quality, mood, or alertness. One might expect that these factors would contribute to improved postsleep experiences. Yet, the findings of the present study fail to support this hypothesis. Melatonin has been found to augment subjective assessments of daytime alertness (MacFarlane et al., 1991) and overall sleep quality (James et al., 1990) among chronic insomniacs. It may be that this preexisting condition increases the potential for melatonin to exert a greater effect on such a population. For such people, just 1 night with improved sleep continuity and depth would likely result in a subsequent improvement in their postsleep psychological assessments. This condition may explain why such postsleep benefits failed to be found in studies examining the effects of melatonin in healthy individuals (Zhdanova et al., 1996).

These findings, in conjunction with the results of other studies examining both healthy and sleep-deprived individuals, suggest that melatonin may benefit those in need of a temporary sleeping aid as well as those suffering from more chronic difficulties. However, this study is limited because it includes only subjective measures of sleep quality. Although many of the effects of sleep can be measured subjectively, there is a need to reinforce these measures with physiological data that can add to the discussion of how melatonin impacts sleep. Questions such as the ease of falling asleep and the continuity of sleep can be readily supported by polysomnographic ratings of the length of sleep onset latency and the number of awakenings throughout the night. Yet, physiological ratings are also limited in that they cannot measure how a person feels subsequent to an experience. Thus, there is a need to incorporate both physiological and subjective measures when investigating sleep quality.

Although evidence concerning melatonin's long-term effects is lacking, the findings do not indicate that there are negative consequences (e.g., feeling less alert or more tired the day after ingestion) associated with short-term usage of a 6-mg dose. Questions remain concerning how melatonin diversely affects various populations. Perhaps future research may sample an older population to examine melatonin's impact on those who generally have more difficulties sleeping and who produce less endogenous melatonin than younger college students (Garfinkel et al., 1995). In addition, a younger sample may provide a more complete comparison across the ages. Another useful comparison could be made with college students who display irregular sleeping patterns and who may ultimately derive more benefits from melatonin. Future research may also wish to investigate whether or not subject variables such as sex or weight significantly influence melatonin's impact. The present results indicate that an exogenous dosage of melatonin may accelerate sleep onset and increase sleep efficiency throughout the night, properties that can benefit healthy and troubled sleepers alike.

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