

Bright-light exposure  
during daytime sleeping affects  
nocturnal melatonin secretion  
after simulated night work

模擬夜勤後の日中睡眠時の  
高照度光曝露は、その後の夜間の  
メラトニン分泌に影響を及ぼす

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**Abstract**

The guidelines for night and shift workers recommend that after night work, they should sleep in a dark environment during the daytime. However, staying in a dark environment during the daytime reduces nocturnal melatonin secretion and delays its onset. Daytime bright-light exposure after night work is important for melatonin synthesis the subsequent night and for maintaining the circadian rhythms. However, it is not clear whether daytime sleeping after night work should be in a dim- or a bright-light environment for maintaining melatonin secretion. The aim of this study, therefore, was to evaluate the effect of bright-light exposure during daytime sleeping on nocturnal melatonin secretion after simulated night work. Twelve healthy male subjects, aged  $24.8 \pm 4.6$  (mean  $\pm$  *SD*), participated in 3-day sessions under two experimental conditions, bright light or dim light, in a random order. On the first day, the subjects entered the experimental room at 16:00 and saliva samples were collected every hour between 18:00 and 00:00 under dim-light conditions. Between 00:00 and 08:00, they participated in tasks that simulated night work. At 10:00 the next morning, they slept for 6 hours under either a bright-light condition ( $>3000$  lx) or a dim-light condition ( $<50$  lx). In the evening, saliva samples were collected as on the first day. The saliva samples were analyzed for melatonin concentration. Activity and sleep times were recorded by a wrist device worn throughout the experiment. In the statistical analysis, the time courses of melatonin concentration were compared between the two conditions by three-way repeated

measurements ANOVA (light condition, day, and time of day). The change in dim light melatonin onset ( $\Delta$ DLMO) between the first and second days, and daytime and nocturnal sleep parameters after the simulated night work were compared between the light conditions using paired *t*-tests. The ANOVA results indicated a significant interaction (light condition and day) ( $p = .006$ ). Post hoc tests indicated that in the dim-light condition, the melatonin concentration was significantly lower on the second day than on the first day ( $p = .046$ ); however, in the bright-light condition, there was no significant difference in the melatonin concentration between the days ( $p = .560$ ). There was a significant difference in  $\Delta$ DLMO between the conditions ( $p = .015$ ): DLMO after sleeping was advanced by  $11.1 \pm 17.4$  min under bright-light conditions but delayed for  $7.2 \pm 13.6$  min after sleeping under dim-light conditions. No significant differences were found in any sleep parameter. Our study demonstrated that daytime sleeping under bright-light conditions after night work could not reduce late evening melatonin secretion until midnight or delay the phase of melatonin secretion without decreasing the quality of the daytime sleeping. Thus, these results suggested that, to enhance melatonin secretion and to maintain their conventional sleep–wake cycle, after night work, shift workers should sleep during the daytime under bright-light conditions rather than dim-light conditions.

## **Introduction**

Shift work is an essential part of the work-system in modern society, but it has been shown to be associated with higher incidences of various cancers (Davis et al., 2001; Schernhammer et al., 2001; Zhu et al., 2006) and of several diseases, including sleep disorders (Knutsson, 2003), cardiovascular disorders (Nabe-Nielsen et al., 2008; Suwazono et al., 2008), and gastrointestinal disorders (Angersbach et al., 1980; Saberi & Moravveji, 2010). In addition, the World Health Organization's International Agency for Research on Cancer (IARC) classified "shift work that involves circadian disruption" as probably carcinogenic to humans (including it in their Group 2A list), based on sufficient evidence from experimental studies but limited evidence from epidemiological studies (IARC Working Group on the Evaluation of Carcinogenic Risks to Humans, 2010). Several previous studies have suggested that the increased incidence of cancers may be related to the suppression of melatonin secretion at night (Stevens et al., 2014). The hormone melatonin, which is secreted from the pineal gland at night, is associated with the biological rhythm and sleep quality in humans. Its nocturnal secretion is suppressed by bright-light exposure during the night. Thus, for the health of shift and night workers, it is important to ensure a work environment that does not suppress nocturnal melatonin secretion.

Melatonin secretion is particularly impacted by short-wavelength light (approximately 460 nm, i.e., blue light). Higuchi et al. (2011) reported that wearing a cap with a red visor

during simulated night work was effective in preventing melatonin suppression, with no adverse effects on the performance of a vigilance test or on brightness and visibility in the work environment. They concluded that this cap was beneficial for shift workers exposed to artificial light in their workplace. Kozaki et al. (2008) showed that exposure during the night to light of a lower correlated color temperature (2300 K, 200 lx) had no effect on melatonin secretion in humans, just as with dim-light conditions (<10 lx); this light may therefore be appropriate in the workplace for night work. These studies suggested that light-induced melatonin suppression was preventable by reducing the exposure to short-wavelength light, which impacts the human circadian system. However, it can be difficult to adopt these countermeasures for night work in medical treatment and health facilities; for example, there could be a risk of patients receiving the wrong treatment because of a mistake due to an error of color recognition.

Several guidelines have been published around the world to reduce fatigue and the risk of diseases due to shift work (Health and Safety Executive, 2006; Horrocks et al., 2006; Rosa & Colligan, 1997). The Japanese Nursing Association (2013) has published its “Guidelines on Night Shift and Shift Work for Nursing,” which details practical measures for shift workers, such as napping during night work and the best times for meals on the day of the night shift. The guidelines also cover daytime sleeping. After night work, most shift work nurses in Japanese hospitals sleep during the daytime, which is important for recovery from

fatigue. The guidelines recommend that shift work nurses should sleep in a dark environment in daytime, because this is generally an effective way to recover from the fatigue. However, spending time under dark conditions during the day reduces melatonin hormone secretion at night (Takasu et al., 2006) and reduces the amplitude of the circadian rhythm of the core body temperature in humans (Wakamura & Tokura, 2000). Sleeping in a dark environment during the day may therefore not be the best approach for the health of shift and night workers.

Takasu et al. (2006) reported an experimental study which showed that melatonin secretion at night was increased by bright-light exposure during the day in humans. Furthermore, Hashimoto et al. (1997) reported that the onset time of melatonin secretion was advanced by daytime or morning bright-light exposure as compared with dim-light. Thus, bright-light exposure during the day helps with the adjustment of human biological rhythms and enhances the quality of subsequent nocturnal sleep. However, it is not clear whether bright-light exposure during daytime sleeping after night work has the same effect on melatonin secretion.

The aim of this study was to investigate whether bright-light exposure (>3000 lx) during daytime sleeping enhanced nocturnal melatonin secretion after night work, compared with dim-light exposure (<50 lx). After simulated night work, each subject slept during the daytime under bright or dim light, and we compared their profiles of nocturnal melatonin

secretion and the sleep parameters for daytime and nocturnal sleep between the two conditions.

## **Materials and Methods**

### ***Subjects***

This experiment was conducted in February and March, 2016. The subjects were male university students recruited voluntarily using a website and posters. In this study, we selected only males as subjects because the menstrual cycle affects melatonin secretion (Fernandez et al., 1990). None of the subjects had a history of night shift working, and none smoked tobacco, were taking medications, had a food allergy, or had traveled across time zones during the month prior to the experiment. Exclusion criteria were mental or physical disorders as determined by the Cornell Medical Index (Brodman et al., 1949; Kanehisa & Fukamachi, 1972), sleep disorders as determined by the Pittsburgh Sleep Quality Index (Buysse et al., 1989; Doi et al., 1998), or being extreme morning or evening types as determined by the Morningness–Eveningness Questionnaire (Horne & Östberg, 1976; Ishihara et al., 1984). Initially, 12 subjects (aged  $24.8 \pm 4.6$  years, range 20–37 years; body mass index,  $22.1 \pm 2.4$  kg/m<sup>2</sup>, range 18.7–26.9 kg/m<sup>2</sup>) completed the experimental protocol.

The subjects received an explanation from the chief investigator about the purpose of the research and the experimental protocol, and they all provided informed consent before

participating. The experimental protocol was conducted in accordance with the Declaration of Helsinki and was approved by the Ethics Committee of Kyoto University Graduate School and Faculty of Medicine. The study was registered in the University Hospital Medical Information Network database (registration number, UMIN000020642).

### ***Experimental protocol***

The subjects were asked to maintain a regular sleep–wake cycle (going to bed at 00:00 and waking up at 07:00) for the 3 days prior to the experiment; adherence to these requirements was confirmed by objective measurements of activity with an Actiwatch2 (Philips Respironics Inc., Bend, OR). The experimental protocol is illustrated in Figure 1. Each subject underwent this protocol twice (at least a week apart), once with bright light (>3000 lx) during the daytime sleeping and once with dim light (<50 lx), with the order of these decided randomly.

This experiment was carried out in a living facility that comprised several rooms; each subject stayed in one of these rooms throughout the experiment. Each room was equipped with a bed, table, toilet, and bathroom, and the room temperature was controlled within a narrow range ( $25^{\circ}\text{C} \pm 2^{\circ}\text{C}$ ). The subjects were asked to wear a short-sleeved T-shirt and long pants during the experiment. All light sources and windows in the experimental rooms were covered by black cellophane and black panels, respectively, to create the dim-light condition, with the curtains closed. In this condition, the intensity of the light was <50 lx measured vertically at eye level when the subject was standing. The light source on the ceiling was a white LED light,



and the relative spectral power distribution (SPD) of this light covered by black cellophane [illuminance: 46 lux, estimated irradiance: 15  $\mu\text{W}/\text{cm}^2$ ; the estimated irradiance was calculated using Irradiance Toolbox (Lucas et al., 2014)] is shown in Figure 2.

At 17:00 on the first day of the experiment, the subject entered the experimental room under the dim-light condition. He then took a short nap in the room in preparation for participating in simulated night work. From 18:00 to 00:00, salivary samples were collected every hour under the dim-light condition. At 00:00, following the collection of the last saliva sample, the subject moved to another experimental room with ordinary-light conditions (approximately 500 lx of light intensity was measured vertically at eye level) for simulated night work. The light source on the ceiling of this experimental room was a white fluorescent lamp (illuminance: 522 lux, estimated irradiance: 163  $\mu\text{W}/\text{cm}^2$ ); the relative SPD of this lamp is shown in Figure 2.

The simulated night work lasted for 8 h, from 00:00 to 08:00, during which the subjects completed a light exercise task and a computer-based task every 2 h. These tasks were designed to mimic the real tasks of night work nursing in hospitals. At 03:00, a 30-min meal break was taken. After the simulated night work, breakfast was served at 08:30 and the subjects then took a shower in their own rooms. At 10:00, they went to sleep for 6 h under the dim-light or the bright-light condition. In the bright-light condition, the window curtains were opened and the light coverings were removed. All windows faced south. However, the eyes of subjects stayed

>3 m away from the window during sleep, so they were not directly exposed to sunlight. In addition, two lighting devices (Bright Light Me, Solartone Ltd., Tokyo, Japan) were placed by the bed, one at each side. The light intensity measured horizontally at eye level with the subject in a lateral position on the bed was >3,000 lx. SPD of this light device (illuminance: 3036 lux, estimated irradiance: 996  $\mu\text{W}/\text{cm}^2$ ) is shown in Figure 2. During daytime sleeping, the subject was asked not to sleep in a prone position and not to pull the blanket over his head. Saliva sampling on the second day was the same as that on the first day. After the last saliva collection on the second day, at 00:00, the subject went to bed under the dark condition (0 lx). On the morning of the third day, the subject was free to leave the experiment.

The subjects were allowed to drink water freely, to read books, and to listen to music throughout the experiment. In addition, watching TV and using a mobile phone or a personal computer were permitted during the simulated night work. However, excessive physical exercise and naps were not permitted to control the participant's activity throughout the experiment. Evening meals were served at 19:00 on the first and second days. Participants had the same breakfast, supper, and night meals in both light conditions.

### ***Measurements***

Salivary melatonin concentration was measured as an indicator of the nocturnal secretion of melatonin by the brain. Saliva samples from the subjects were placed in collection tubes using a pure cotton swab (Sarstedt AG & Co., Nümbrecht, Germany), and immediately

centrifuged at 1500 g for 5 min and frozen to  $-20^{\circ}\text{C}$  until analysis. The samples were analyzed for melatonin using RIA kits (RK-DSM2 200 tests, Bühlmann Laboratories AG, Schönenbuch, Switzerland). The mean inter-assay and intra-assay coefficients of variation were 7.9% and 9.8%, respectively. The limit of detection was 0.2 pg/ml and the limit of quantification was 0.9 pg/ml.

The profiles of salivary melatonin concentrations were used to calculate the areas under the curve (AUC) and the dim light melatonin onset (DLMO). AUCs for the salivary melatonin concentrations on the first and second days were calculated using a trapezoidal method (Crowley et al., 2015). For each subject, the AUC for melatonin secretion on the second day was expressed as a percentage (%AUC) of the AUC for the first day. DLMO has often been used to assess the phase of biological rhythms (Pandi-Perumal et al., 2007). In this study, DMLO was defined as the time at which the salivary melatonin concentration increased and stayed above 3.0 pg/ml; this was determined by linear interpolation between the time points of the saliva collections before and after this threshold was passed (Benloucif et al., 2008; Chapdelaine et al., 2012).

An objective measurement of each subject's activity was obtained from an Actiwatch2 worn throughout the experiment. From this, we calculated the sleep parameters of daytime sleeping on the second day and nocturnal sleeping on the third day; these included total sleep time (TST), sleep onset latency (SOL), sleep efficiency (SE), wake after sleep onset (WASO),

and actual sleep time (AST).

### *Statistical analysis*

We compared the time courses of salivary melatonin concentration, %AUC, the change in DLMO ( $\Delta$ DLMO), and the sleep parameters between the two lighting conditions. The time courses of salivary melatonin concentration were analyzed by three-way repeated measures ANOVA with light condition (bright light vs. dim light), day (first day vs. second day) and time of day as the within-subject factors. In addition,  $\Delta$ DLMO, %AUC, and the sleep parameters were compared between the two light conditions using paired *t*-tests. For the ANOVAs, if the sphericity assumption was not met, the degrees of freedom were modified using the Greenhouse–Geisser method. When any main effects and interactions were significant, the Bonferroni method was used for multiple post hoc comparisons.

All data were described as the mean  $\pm$  standard error of the mean, and we calculated and described effect sizes. Cohen's *d<sub>Z</sub>* was used as the effect size for the paired *t*-tests and multiple comparisons with ANOVA, and partial  $\eta^2$  was also used in ANOVA. An appropriate sample size was calculated based on effect size  $d_Z = 1.2$  [from the result of  $\Delta$ DLMO in a previous study (Revell et al., 2005)], alpha error = .05, and beta error = .80 in a two-tailed test; this indicated that the sample size should be  $n = 8$ . The analyses were performed using SPSS ver. 24 (IBM, Tokyo, Japan) and a *p* value of  $<.05$  was considered statistically significant.

## Results

### *Time course of melatonin concentration*

Figure 3 shows the mean time courses of melatonin concentration for the first and second days under the bright- and dim-light conditions ( $n = 12$ ). In the three-way repeated measures ANOVA (light condition, day, and time of day), there was a significant main effect of time of day ( $F(1.22, 13.42) = 12.69, p = .002, \text{partial } \eta^2 = .563$ ) and a significant interaction between light condition and day ( $F(1, 11) = 11.50, p = .006, \text{partial } \eta^2 = .511$ ). Post hoc tests indicated that, in the dim-light condition, the melatonin concentration on the second day was significantly lower than that on the first day [simple main effect of day in the dim-light condition:  $p = .046$  ( $p = .011$  at 18:00,  $p = .019$  at 20:00, and  $p = .035$  at 24:00)]. However, in the bright-light condition, there was no significant difference in the melatonin concentrations between the first and second days ( $p = .560$ ).

### *Comparison of melatonin secretion*

Figure 4 shows the mean values of %AUC (the melatonin secretion on the second day as a percentage of that on the first day) for the bright- and dim-light conditions ( $n = 12$ ), which were  $109.6\% \pm 13.2\%$  and  $82.1\% \pm 8.9\%$ , respectively. The result of the paired  $t$ -test indicated that the value in dim-light condition was significantly lower than the value in the bright-light condition ( $p = .002, t = 3.90, d_Z = 1.13$ ).

### *Dim light melatonin onset times*

Figure 5 shows the mean DLMO times on the first and second days for the bright-light and dim-light conditions ( $n = 7$ ). DLMOs of five participants were excluded from analysis because their data could not be assessed, their melatonin levels did not rise above the threshold of 3.0 pg/ml during the sampling period (all the data of illuminance measured by Actiwatch2 were  $<10$  lux under dim-light condition).  $\Delta$ DLMO differed significantly between the conditions ( $p = .015$ ,  $t = 3.36$ ,  $d_z = 1.27$ ). DLMO time advanced by  $11.1 \pm 17.4$  min after daytime sleeping under the bright-light condition but delayed by  $7.2 \pm 13.6$  min after daytime sleeping under the dim-light condition.

### ***Sleep parameters***

The sleep parameters for the daytime and nocturnal sleep are shown in Tables 1 and 2, respectively. In the results for nocturnal sleep (Table 2), the data for TST, SE, WASO, and AST of two of the subjects were excluded from the analysis because of a failure of data collection. No significant differences between the two light conditions were found for any sleep parameter for the daytime or the nocturnal sleep.

### **Discussion**

This study is the first to demonstrate that the light environment during daytime sleeping after simulated night work was associated with subsequent nocturnal melatonin secretion. Our results indicated that nocturnal melatonin secretion until midnight was reduced

after daytime sleeping under dim-light conditions, but the secretion did not change after daytime sleeping in bright-light condition. These findings are consistent with those of several previous studies. Takasu et al. (2006) reported that the amplitude of nocturnal melatonin secretion was higher when subjects were exposed to daytime bright light (~5000 lx) for 7 days than when they were exposed to dim light (~10 lx) for the same duration. Other studies have also indicated that daytime bright-light exposure could enhance melatonin secretion at night (Fukushige et al., 2014; Kanikowska et al., 2001; Nagashima et al., 2017; Wakamura & Tokura, 2000). This result suggested that after night work, daytime sleeping under bright-light conditions is an effective way for shift workers to prevent reductions in their nocturnal melatonin secretion in the evening and at night. Therefore, the light conditions in which workers sleep after night work might play a key role in shift workers' health and lives.

AUC percentage under dim-light conditions was significantly lower than that under bright-light conditions, which agrees with the finding that melatonin secretion between 18:00 and 00:00 was significantly decreased by dim-light exposure during daytime sleeping.

However, the peak nocturnal melatonin concentration and its timing were uncertain under both conditions because salivary samples were not obtained from midnight for the simulated night work on day 2 and nocturnal sleeping on day 3. Thus, these significant differences might be caused by the phase shift of melatonin secretion. In the  $\Delta$ DLMO following daytime sleeping, there was a significant difference between bright- and dim-light conditions.

Hashimoto et al. (1997) reported that the onset phase of the plasma melatonin secretion was phase-advanced by midday bright-light exposure for three consecutive days. Our result also indicated that bright-light exposure during daytime sleeping advanced DLMO. However, phase-shift in both bright- and dim-light conditions was only approximately 10 min ( $11.1 \pm 17.4$  min and  $7.2 \pm 13.6$  min, respectively). This suggests that night shift working (00:00–08:00; after staying under dim-light condition) for only a single night may not have a large effect on the phase of DLMO in humans.

Animal studies have shown that peak nocturnal melatonin concentrations in male nude rats were 7-fold higher after daytime spectral transmittance of white fluorescent light through blue-tinted rodent cages (irradiance at  $421 \mu\text{W}/\text{cm}^2$  for 12 h) compared with clear cages (Dauchy et al., 2015). Moreover, Gabel et al. (2013) reported that morning exposure to blue monochromatic LEDs (100 lux at 470 nm for 20 min) can advance the onset of melatonin secretion in humans. The results of these previous studies suggest that the blue light irradiance of bright light during daytime impacts nocturnal melatonin secretion via intrinsically photosensitive melanopsin-containing retinal ganglion cells. In our study, the estimated value of effective melanopic irradiance for bright-light exposure on the eyelids was  $369 \mu\text{W}/\text{cm}^2$  [this value was also estimated using the Irradiance Toolbox (Lucas et al. 2014)]. A previous study (Bierman et al., 2011) indicated that the transmittance of the eyelids for blue light (at 480 nm) was approximately 0.28%; therefore, effective melanopic irradiance on



the retina was probably  $<1 \mu\text{W}/\text{cm}^2$ . Accordingly, bright-light exposure simulated with LEDs and blue monochromatic light during daytime, which has higher effective melanopic irradiance than fluorescent light, might have a greater effect on nocturnal melatonin secretion.

Also notable is the effect of evening light exposure until midnight. The participants in this study were exposed to dim light from 18:00 to 00:00 for measuring DLMO. This situation was unusual for shift workers, who are mostly exposed to electric light in the evening; therefore, their melatonin secretion during the evening may have been suppressed by this light exposure. However, Kozaki et al. (2015) reported that subjects exposed to bright light during daytime had significantly lower light-induced melatonin suppression compared with those exposed to dim light during daytime. Therefore, compared with dim-light exposure, bright-light exposure during sleeping at daytime might reduce melatonin suppression caused by evening electric light exposure. To examine the relationship between daytime and evening light exposure, measurements of evening melatonin secretion under ordinary room light conditions should be obtained in a future study.

The sleep parameters of daytime sleeping in our study, particularly SOL and WASO, did not differ significantly between the light conditions, although many previous studies have indicated that subjective sleepiness was reduced by bright-light exposure during daytime (Phipps-Nelson et al., 2003; Rüger et al., 2006). This may be due to increased homeostatic sleep pressure after simulated night work. Under the bright-light condition, the mean time of

SOL for the daytime sleeping was only  $3.5 \pm 1.5$  minutes. This result was very similar to that of a multiple sleep latency test ( $3.0 \pm 2.9$  minutes) following one night of total sleep deprivation (Franzen et al., 2008). Thus, with the greater homeostatic sleep pressure due to night work, bright-light exposure during daytime sleeping may have little impact on daytime sleeping after night work.

Santhi et al. (2005) have indicated that daytime sleeping in a dark environment was effective for shift workers adapting to night work. In their study, DLMO was delayed for 2 h by post-night-shift sleep (8 h, 08:00–16:00, in darkness) for 3 consecutive days. Delays in the circadian phase may be associated with sleep disorders. Human sleep–wake cycles are regulated by the interaction between sleep–wake homeostasis and the circadian timing system in the “two-process model of sleep regulation” (Borbély et al., 2016). Delays in the circadian phase increase alertness at night. Thus, if the circadian phase is delayed, people have difficulty in falling asleep at their habitual bedtimes. We therefore predicted that nocturnal sleep quality following the dim-light condition would be significantly worse than that after the bright-light condition. However, the sleep parameters for nocturnal sleep did not differ significantly between the conditions. This result may be due to the small sample size. The effect size of light environment on WASO was  $d_z = 0.39$ , which is considered to indicate a medium effect (Cohen, 1988). Thus, daytime sleeping under dim-light conditions after night work may result in a slight increase in WASO during the subsequent nocturnal sleep,

compared with bright-light condition. However, this effect may be small. Further studies using a larger sample size is needed to explain the association between sleeping under dim-light conditions and the nocturnal sleep quality.

According to the results of this study, after night work, shift workers should sleep during the daytime in a bright-light environment to enhance their nocturnal melatonin secretion and to maintain their habitual sleep–wake cycle. However, it was suggested that, before night work, daytime sleeping under dim-light conditions was effective for shift workers in increasing a subjective alertness during night work (Horowitz et al., 2001). It may therefore be important for shift workers to sleep during the day in an appropriate light environment, taking into consideration the type of the next shift (or free day); if the next shift is a night shift, they should sleep under dim-light conditions to help with adaptation.

Our study had some methodological limitations. First, this study included only males, and it is uncertain whether the same results would be obtained in females. Thus, further study is needed to examine the effect of bright-light exposure during daytime sleeping in females. Second, we did not observe the motion of the subjects during daytime sleeping and therefore, did not strictly control their amount of bright-light exposure. If the subject slept in a prone position or pulled the blanket over his head, the effects of bright-light exposure might have been underestimated. Future studies should include the use of light goggles for a strict examination of the effects of bright-light exposure during daytime sleeping. Furthermore, the

sleep parameters were calculated only from the Actiwatch2 readings, which could not assess the sleep stage. A previous polysomnography study indicated that sleeping with the light switched on resulted in shallow sleep and arousals (Cho et al., 2013). Thus, it is possible that sleep parameters assessed by polysomnography, such as non-REM sleep and REM sleep, may have differed between bright- and dim-light conditions. Further studies using polysomnography are needed to assess sleep stages. In addition, after sleeping, cognitive brain performance and subjective alertness should be measured to assess the consequence of different light conditions. Lastly, we could not conclude whether the significant difference in the time course of melatonin concentration was due to a decreased peak of melatonin concentration or a delayed phase shift of melatonin secretion in dim-light conditions, because we could not collect saliva samples after midnight. Thus, for concluding how the bright-light exposure affects nocturnal melatonin secretion, its concentrations from onset to offset need to be obtained.

In conclusion, the results of this study demonstrated that daytime sleeping under bright-light conditions after night work did not reduce the subsequent late evening melatonin secretion until midnight or delay the phase of melatonin secretion, without decreasing the sleep quality of the daytime sleeping. These results suggested that to enhance melatonin secretion and to maintain their conventional sleep–wake cycle, shift workers should sleep during the day under bright-light conditions after night work, rather than in dim light. After

night work, shift workers should sleep in an appropriate light environment, taking their next shift and their circadian rhythm into consideration. Further epidemiological studies are needed to examine whether daytime sleeping under appropriate light conditions after night work can improve the health of shift workers.

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### **Declaration of Interest Statement**

All the authors reported no conflict of interest.

### **Author Contribution**

S.N. conceptualized the study, researched the data, analyzed the data, wrote the manuscript, contributed to the discussion, reviewed/edited the manuscript and as the

guarantor of this study, had full access to the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. M.O. conceptualized the study, researched the data, analyzed the data and contributed to the discussion. H.M., W.O., A.A. researched the data, contributed to the discussion. T.W. conceptualized the study, contributed to the discussion, reviewed/edited the manuscript.

## References

- Angersbach D, Knauth P, Loskant H, Karvonen MJ, Undeutsch K, Rutenfranz J. 1980. A retrospective cohort study comparing complaints and diseases in day and shift workers. *Int Arch Occup Environ Health*. 45:127-40. doi:10.1007/BF01274132.
- Benloucif S, Burgess HJ, Klerman EB, Lewy AJ, Middleton B, Murphy PJ, Parry BL, Revell VL. 2008. Measuring melatonin in humans. *J Clin Sleep Med*. 4:66-69.
- Bierman A, Figueiro MG, Rea MS. 2011. Measuring and predicting eyelid spectral transmittance. *J Biomed Optic*. 16:067011. doi.org/10.1117/1.3593151.
- Borbély AA, Daan S, Wirz-Justice A, Deboer T. 2016. The two-process model of sleep regulation: a reappraisal. *J Sleep Res*. 25:131-143. doi: 10.1111/jsr.12371.
- Brodman K, Erdmann AJ, Wolff HG. 1949 (Revised 1955). *Cornell medical index health questionnaire manual*. New York (NY): Cornell University Medical College.
- Buysse DJ, Reynolds CF, Monk TH, Berman SR, Kupfer DJ. 1989. *The Pittsburgh Sleep*

Quality Index: a new instrument for psychiatric practice and research. *Psychiatry Res.* 28:193-213. doi:10.1016/0165-1781(89)90047-4.

Chapdelaine S, Paquet J, Dumont M. 2012. Effects of partial circadian adjustments on sleep and vigilance quality during simulated night work. *J Sleep Res.* 21:380-389. doi:10.1111/j.1365-2869.2012.00998.x.

Cho JR, Joo EY, Koo DL, Hong SB. 2013. Let there be no light: the effect of bedside light on sleep quality and background electroencephalographic rhythms. *Sleep Med.* 14:1422-1425. doi:10.1016/j.sleep.2013.09.007.

Cohen J. 1988. *Statistical power analysis for the behavioral sciences.* 2nd ed. New York (NY): Psychology Press.

Crowley SJ, Cain SW, Burns AC, Acebo C, Carskadon MA. 2015. Increased sensitivity of the circadian system to light in early/mid-puberty. *J Clin Endocrinol Metab.* 100:4067-4073. doi:10.1210/jc.2015-2775.

Dauchy RT, Hoffman AE, Wren-Dail MA, Hanifin JP, Warfield B, Brainard GC, Xiang S, Yuan L, Hill SM, Belancio VP, Dauchy EM, Smith K, Blask DE. 2015. Daytime blue light enhances the nighttime circadian melatonin inhibition of human prostate cancer growth. *Comp Med.* 65:473-485.

Davis S, Mirick DK, Stevens RG. 2001. Night shift work, light at night, and risk of breast cancer. *J Natl Cancer Inst.* 93:1557-1562. doi.org/10.1093/jnci/93.20.1557.

- Doi Y, Minowa M, Uchiyama M, Okawa M. 1998. Development of the Japanese version of the Pittsburgh Sleep Quality Index. *Japanese Journal of Psychiatry Treatment*. 13:755-763.
- Fernandez B, Malde JL, Montero A, Acuna D. 1990. Relationship between adenohipophyseal and steroid hormones and variations in serum and urinary melatonin levels during the ovarian cycle, perimenopause and menopause in healthy women. *J Steroid Biochem*. 35:257-262. doi:10.1016/0022-4731(90)90282-W.
- Franzen PL, Siegle GJ, Buysse DJ. 2008. Relationships between affect, vigilance, and sleepiness following sleep deprivation. *J Sleep Res*. 17:34-41. doi:10.1111/j.1365-2869.2008.00635.x.
- Fukushige H, Fukuda Y, Tanaka M, Inami K, Wada K, Tsumura Y, Kondo M, Harada T, Wakamura T, Morita T. 2014. Effects of tryptophan-rich breakfast and light exposure during the daytime on melatonin secretion at night. *J Physiol Anthropol*. 33:33. doi:10.1186/1880-6805-33-33.
- Gabel V, Maire M, Reichert CF, Chellappa SL, Schmidt C, Hommes V, Viola AU, Cajochen C. 2013. Effects of artificial dawn and morning blue light on daytime cognitive performance, well-being, cortisol and melatonin levels. *Chronobiol Int*. 30:988-997. doi:10.3109/07420528.2013.793196.
- Hashimoto S, Kohsaka M, Nakamura K, Honma H, Honma S, Honma K. 1997. Midday



- exposure to bright light changes the circadian organization of plasma melatonin rhythm in humans. *Neurosci Lett.* 221:89-92. doi:10.1016/S0304-3940(96)13291-2.
- Health and Safety Executive. 2006. *Managing shiftwork: health and safety guidance.* London (UK): Health and Safety Executive.
- Higuchi S, Fukuda T, Kozaki T, Takahashi M, Miura N. 2011. Effectiveness of a red-visor cap for preventing light-induced melatonin suppression during simulated night work. *J Physiol Anthropol.* 30:251-258. doi:10.2114/jpa2.30.251.
- Horne JA, Östberg O. 1976. A self-assessment questionnaire to determine morningness-eveningness in human circadian rhythms. *Int J Chronobiol.* 4:97-110.
- Horowitz TS, Cade BE, Wolfe JM, Czeisler CA. 2001. Efficacy of bright light and sleep/darkness scheduling in alleviating circadian maladaptation to night work. *Am J Physiol Endocrinol Metabol.* 281:E384-91.
- Horrocks N, Pounder R. 2006. Working the night shift: preparation, survival and recovery-a guide for junior doctors. *Clin Med.* 6:61-7. doi:10.7861/clinmedicine.6-1-61.
- IARC Working Group on the Evaluation of Carcinogenic Risks to Humans. 2010. Painting, firefighting, and shiftwork. *IARC Monographs on the Evaluation of Carcinogenic Risks to Humans.* 98:9.
- Ishihara K, Saitoh T, Inoue Y, Mikita Y. 1984. Validity of the Japanese version of the morningness-eveningness questionnaire. *Percept Mot Skills.* 59:863-866.

doi:10.2466/pms.1984.59.3.863.

Japanese Nursing Association. 2013. Guidelines on night shift and shift work for nurses.

Tokyo (Japan): Medical Friend Co. Ltd.

Kanehisa T, Fukamachi T. 1972. CMI, Cornell Medical Index. Kyoto (Japan): Sankyobo.

Kanikowska D, Hirata Y, Hyun K, Tokura H. 2001. Acute phase proteins, body temperature and urinary melatonin under the influence of bright and dim light intensities during the daytime. *J Physiol Anthropol Appl Human Sci.* 20:333-338.

doi:10.2114/jpa.20.333.

Knutsson A. 2003. Health disorders of shift workers. *Occup Med (Lond).* 53:103-108.

doi:10.1093/occmed/kqg048.

Kozaki T, Koga S, Toda N, Noguchi H, Yasukouchi A. 2008. Effects of short wavelength control in polychromatic light sources on nocturnal melatonin secretion. *Neurosci Lett.* 439:256-259. doi:10.1016/j.neulet.2008.05.035.

Kozaki T, Kubokawa A, Taketomi R, Hatae K. 2015. Effect of day-time exposure to different light intensities on light-induced melatonin suppression at night. *J Physiol Anthropol.* 34:1-5. doi:<https://doi.org/10.1186/s40101-015-0067-1>.

Lucas RJ, Peirson SN, Berson DM, Brown TM, Cooper HM, Czeisler CA, Figueiro MG,

Gamlin PD, Lockley SW, O'Hagan JB, Price LLA, Provencio I, Skene DJ, Brainard

GC. 2014. Measuring and using light in the melanopsin age. *Trends Neurosci.* 37:1-9.

doi.org/10.1016/j.tins.2013.10.004.

Nabe-Nielsen K, Garde AH, Tüchsen F, Hogh A, Diderichsen F. 2008. Cardiovascular risk factors and primary selection into shift work. *Scand J Work Environ Health*. 34:206-212. doi:10.5271/sjweh.1230

Nagashima S, Yamashita M, Tojo C, Kondo M, Morita T, Wakamura T. 2017. Can tryptophan supplement intake at breakfast enhance melatonin secretion at night? *J Physiol Anthropol*. 36:20. doi:10.1186/s40101-017-0135-9.

Pandi-Perumal SR, Smits M, Spence W, Srinivasan V, Cardinali DP, Lowe AD, Kayumov L. 2007. Dim light melatonin onset (DLMO): a tool for the analysis of circadian phase in human sleep and chronobiological disorders. *Prog Neuropsychopharmacol Biol Psychiatry*. 31:1-11. doi:10.1016/j.pnpbp.2006.06.020.

Phipps-Nelson J, Redman JR, Dijk DJ, Rajaratnam SM. 2003. Daytime exposure to bright light, as compared to dim light, decreases sleepiness and improves psychomotor vigilance performance. *Sleep* 26:695-700. doi:10.1093/sleep/26.6.695.

Revell VL, Kim H, Tseng CY, Crowley SJ, Eastman CI. 2005. Circadian phase determined from melatonin profiles is reproducible after 1 wk in subjects who sleep later on weekends. *J Pineal Res*. 39:195-200. doi:10.1111/j.1600-079X.2005.00236.x

Rosa RR, Colligan MJ. 1997. Plain language about shiftwork. Cincinnati (OH): US Dept of Health and Human Services, DHHS (NIOHS) publication 97-145.

- Rüger M, Gordijn MC, Beersma DG, de Vries B, Daan S. 2006. Time-of-day-dependent effects of bright light exposure on human psychophysiology: comparison of daytime and nighttime exposure. *Am J Physiol Regul Integr Comp Physiol*. 290:R1413-20. doi:10.1152/ajpregu.00121.2005.
- Saberi HR, Moravveji AR. 2010. Gastrointestinal complaints in shift-working and day-working nurses in Iran. *J Circadian Rhythms*. 8:9. doi:10.1186/1740-3391-8-9.
- Santhi N, Duffy JF, Horowitz TS, Czeisler CA. 2005. Scheduling of sleep/darkness affects the circadian phase of night shift workers. *Neurosci Lett*. 384:316-320. doi:10.1016/j.neulet.2005.04.094.
- Schernhammer ES, Laden F, Speizer FE, Willett WC, Hunter DJ, Kawachi I, Colditz GA. 2001. Rotating night shifts and risk of breast cancer in women participating in the nurses' health study. *J Natl Cancer Inst*. 93:1563-1568. doi:10.1093/jnci/93.20.1563.
- Stevens RG, Brainard GC, Blask DE, Lockley SW, Motta ME. 2014. Breast cancer and circadian disruption from electric lighting in the modern world. *CA Cancer J Clin*. 64:207-218. doi:10.3322/caac.21218.
- Suwazono Y, Dochi M, Sakata K, Okubo Y, Oishi M, Tanaka K, Kobayashi E, Nogawa K. 2008. Shift work is a risk factor for increased blood pressure in Japanese men: a 14-year historical cohort study. *Hypertension* 52:581-586. doi:10.1161/HYPERTENSIONAHA.108.114553.

Takasu NN, Hashimoto S, Yamanaka Y, Tanahashi Y, Yamazaki A, Honma S, Honma K.

2006. Repeated exposures to daytime bright light increase nocturnal melatonin rise and maintain circadian phase in young subjects under fixed sleep schedule. *Am J Physiol Regul Integr Comp Physiol.* 291:R1799-807.

doi:10.1152/ajpregu.00211.2006.

Wakamura T, Tokura H. 2000. The influence of bright light during the daytime upon

circadian rhythm of core temperature and its implications for nocturnal sleep. *Nurs Health Sci.* 2:9. doi:10.1046/j.1442-2018.2000.00037.x.

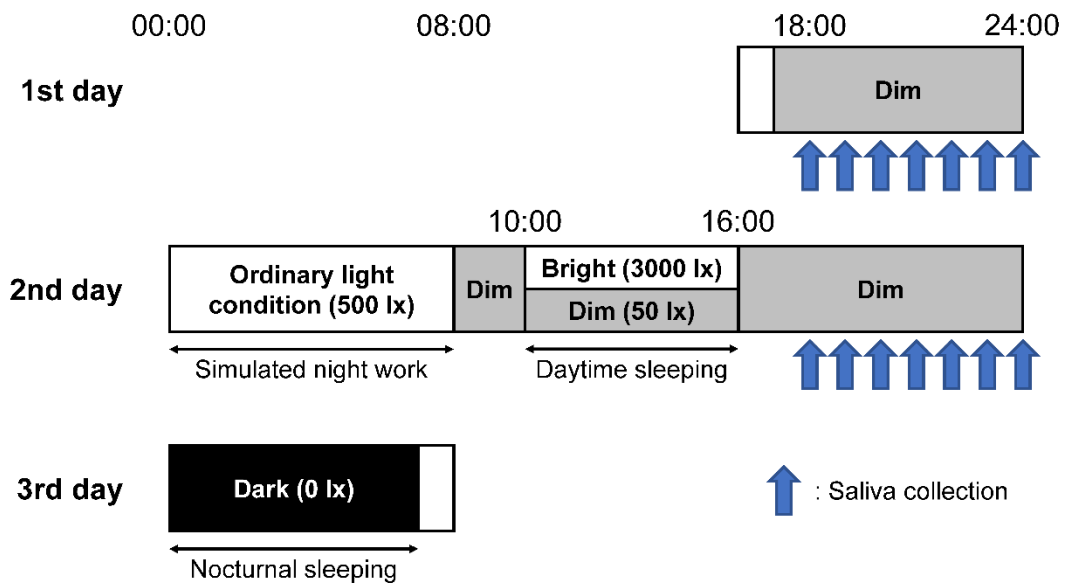
Zhu Y, Zheng T, Stevens RG, Zhang Y, Boyle P. 2006. Does “clock” matter in prostate

cancer? *Cancer Epidemiol Biomarkers Prev.* 15:3-5. doi:10.1158/1055-9965.EPI-05-0631.

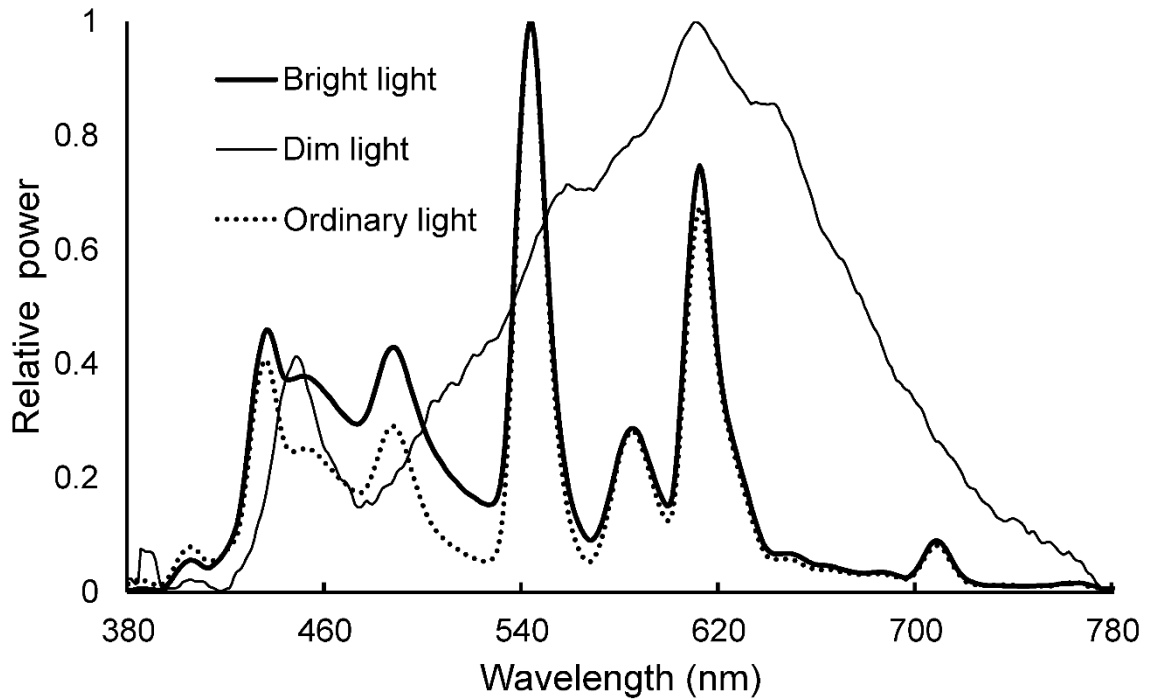
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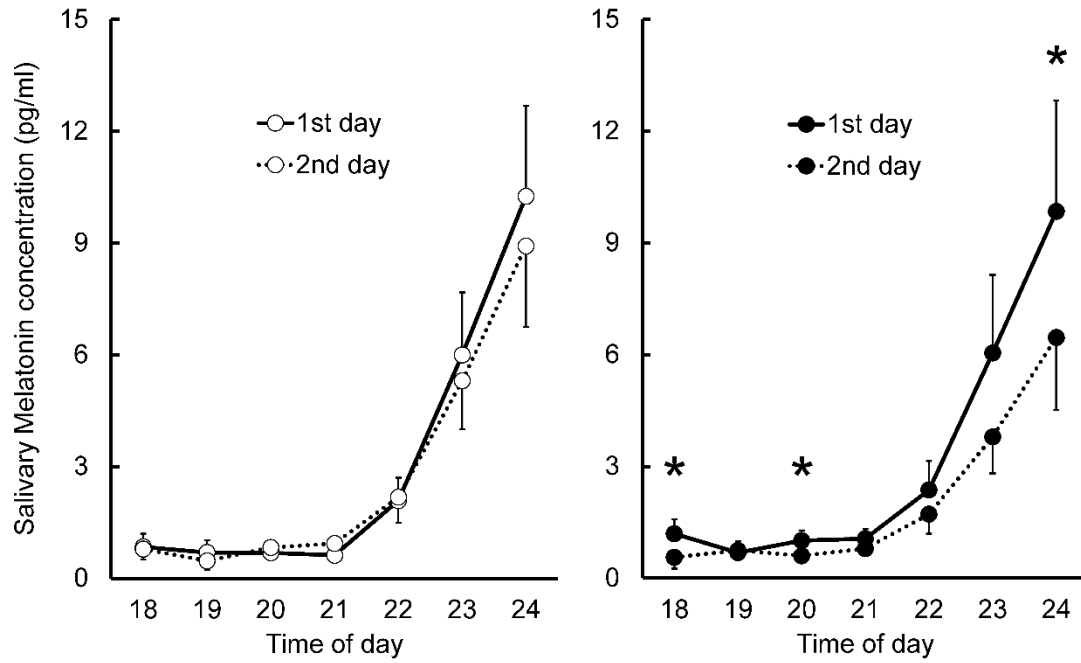
[www.tandfonline.com/doi/full/10.1080/07420528.2017.1394321](http://www.tandfonline.com/doi/full/10.1080/07420528.2017.1394321)



**Figure 1.** The experimental protocol. The shading of the horizontal bars indicates the experimental light conditions: gray, dim (<50 lx); black, dark (0 lx); and white, bright (>3000 lx). The arrows indicate the times of saliva sample collections.

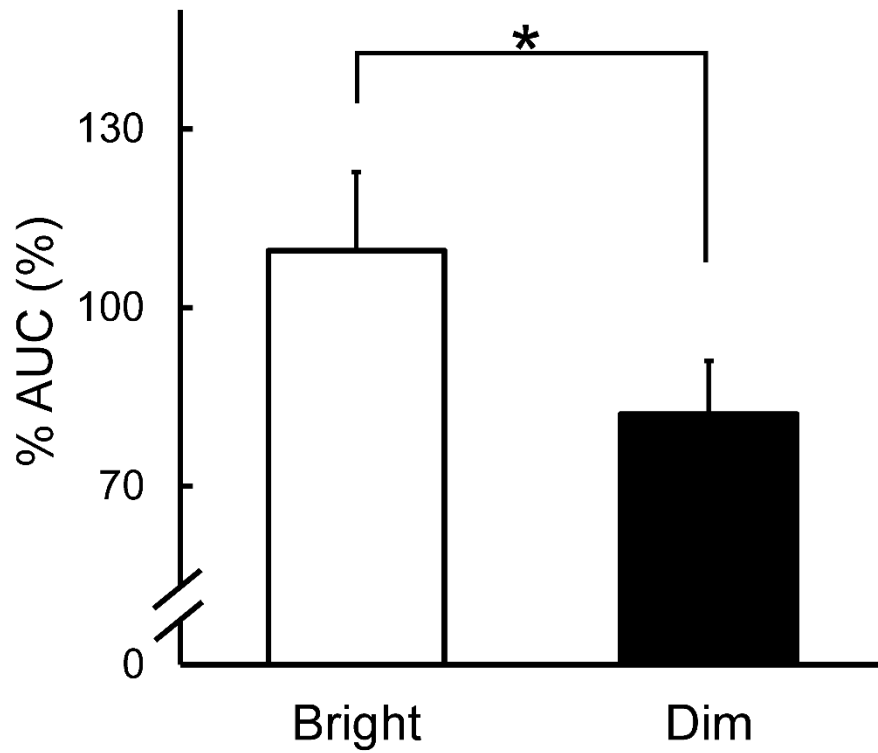


**Figure 2.** Relative spectral power distribution of experimental light sources. Relative spectral power distributions of bright light (Fluorecent lamp; Illuminance, 3036 lux and estimated irradiance, 996  $\mu\text{W}/\text{cm}^2$ ), dim light (LED lamp; Illuminance, 46 lux and estimated irradiance, 15  $\mu\text{W}/\text{cm}^2$ ), and ordinary room light (Fluorecent lamp; Illuminance, 522 lux and estimated irradiance, 163  $\mu\text{W}/\text{cm}^2$ ). The intensity of the light was horizontally measured at eye level with the subject in a lateral position on the bed; the intensities of dim light and ordinary room light were vertically measured at eye level. All estimated irradiances were calculated using Irradiance Toolbox (Lucas et al. 2014).

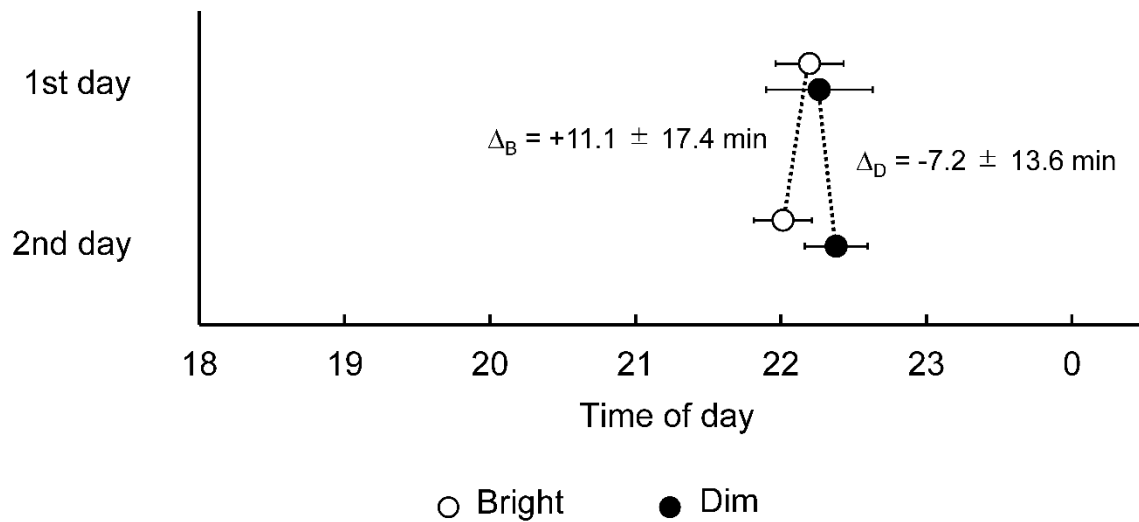


**Figure 3.** The time courses of salivary melatonin concentration. Left: The results for the bright-light condition (○). Right: The results for the dim-light condition (●). The solid and dotted lines indicate the results for the first and second days, respectively. Error bars indicate standard errors of the mean. \*  $p < .05$ , post hoc test between 1st and 2nd day ( $n = 12$ ).





**Figure 4.** Comparison of the change in melatonin secretion after daytime sleeping in bright- or dim-light conditions. %AUC: The area under the melatonin secretion curve on the second day (after the daytime sleeping) as a percentage of that on the first day. The error bars indicate standard error of the mean. \*  $p < .05$ ,  $t$ -test ( $n = 12$ ).



**Figure 5.** Dim light melatonin onset (DLMO) changes for the two light conditions. The opened and closed circles indicate the results on the first and second days for the bright- and dim-light conditions, respectively. The error bars indicate standard errors of the mean ( $n = 7$ ).  $\Delta_B$  and  $\Delta_D$ : The changes in DLMO between the first and second days for the bright- and dim-light conditions, respectively; a positive value indicates that DLMO was advanced.

**Table 1.** Sleep parameters for the daytime sleeping on the second day, comparing the bright and dim light conditions.

	<b>Bright</b>	<b>Dim</b>	<b>Difference</b>	<b>Correlation coefficient</b>	<b>t-value</b>	<b>p-value</b>	<b>dz-value</b>
Time in bed (min)	361.0 ± 1.1	360.7 ± 0.9	0.3 ± 1.5	-.172	0.22	.831	0.06
Total sleep time (min)	328.5 ± 15.3	343.9 ± 5.1	15.4 ± 14.6	.329	1.06	.313	0.31
Sleep onset latency (min)	3.5 ± 1.5	4.7 ± 1.5	1.2 ± 1.9	.157	0.60	.559	0.17
Sleep efficiency (%)	81.8 ± 4.1	85.4 ± 1.9	3.6 ± 3.5	.496	1.01	.332	0.29
Wake after sleep onset (min)	33.3 ± 5.7	36.0 ± 5.2	2.8 ± 3.1	.836	0.87	.401	0.25
Actual sleep time (min)	295.3 ± 14.7	307.9 ± 7.0	12.7 ± 12.8	.498	0.99	.342	0.29

The data are presented as mean ± standard error of the mean.

**Table 2.** Sleep parameters for nocturnal sleeping on the third day, comparing the bright and dim light conditions.

	<b>Bright</b>	<b>Dim</b>	<b>Difference</b>	<b>Correlation coefficient</b>	<b>t-value</b>	<b>p-value</b>	<b>dz-value</b>
Time in bed (min)	418.0 ± 1.8	418.5 ± 1.4	0.5 ± 2.5	.170	0.20	.843	0.06
Total sleep time <sup>a</sup> (min)	377.9 ± 15.2	380.1 ± 9.1	2.2 ± 13.2	.506	0.17	.871	0.05
Sleep onset latency (min)	34.0 ± 11.8	27.1 ± 8.0	6.9 ± 12.5	.242	0.55	.592	0.16
Sleep efficiency <sup>a</sup> (%)	80.6 ± 3.7	78.8 ± 4.1	1.8 ± 2.7	.763	0.67	.521	0.21
Wake after sleep onset <sup>1</sup> (min)	41.0 ± 5.8	51.2 ± 9.0	10.2 ± 8.3	.443	1.23	.250	0.39
Actual sleep time <sup>a</sup> (min)	336.9 ± 16.1	328.9 ± 17.3	8.0 ± 11.8	.750	0.68	.516	0.21

The data are presented as mean ± standard error of the mean.

<sup>a</sup> Data from 10 participants. The data for two participants were excluded from these analyses because of a failure of data collection.