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Original Article

ORIGINAL ARTICLE

Melatonin suppression does not automatically alter sleepiness, vigilance, sensory processing, or sleep

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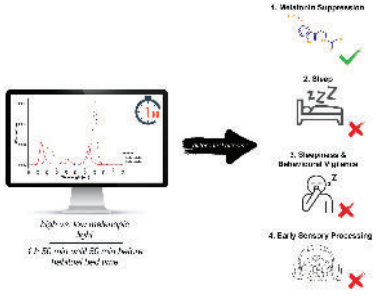
Abstract

Presleep exposure to short-wavelength light suppresses melatonin and decreases sleepiness with activating effects extending to sleep. This has mainly been attributed to melanopic effects, but mechanistic insights are missing. Thus, we investigated whether two light conditions only differing in the melanopic effects (123 vs. 59 lx melanopic EDI) differentially affect sleep besides melatonin. Additionally, we studied whether the light differentially modulates sensory processing during wakefulness and sleep. Twenty-nine healthy volunteers (18–30 years, 15 women) were exposed to two metameric light conditions (high- vs. low-melanopic, ≈60 photopic lx) for 1 h ending 50 min prior to habitual bed time. This was followed by an 8-h sleep opportunity with polysomnography. Objective sleep measurements were complemented by self-report. Salivary melatonin, subjective sleepiness, and behavioral vigilance were sampled at regular intervals. Sensory processing was evaluated during light exposure and sleep on the basis of neural responses related to violations of expectations in an oddball paradigm. We observed suppression of melatonin by ≈14% in the high- compared to the low-melanopic condition. However, conditions did not differentially affect sleep, sleep quality, sleepiness, or vigilance. A neural mismatch response was evident during all sleep stages, but not differentially modulated by light. Suppression of melatonin by light targeting the melanopic system does not automatically translate to acutely altered levels of vigilance or sleepiness or to changes in sleep, sleep quality, or basic sensory processing. Given contradicting earlier findings and the retinal anatomy, this may suggest that an interaction between melanopsin and cone-rod signals needs to be considered.

Clinical Trial Registry: German Clinical Trials Register, DRKS00023602, https://www.drks.de/drks_web/navigate.do?navigationId=trial.HTML&TRIAL_ID=DRKS00023602.

Graphical Abstract



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Statement of Significance

Metameric light allows to mechanistically investigate the contribution of one specific retinal receptor. Using this approach, we here investigated the effects of high- vs. low-melanopic light for 1 h in the evening at ecologically valid screen illuminance (≈60 photopic lx). Going beyond earlier research, we also investigated effects on sleep. We found that despite significant suppression of melatonin, other endpoints including sleep and sleep quality were not differentially affected. This underlines that melatonin suppression does not automatically translate to alterations of sleep, sleepiness, or vigilance. Furthermore, it suggests that melanopsin effects may need to be studied in the context of cone-rod signals. Future research should thus investigate the relevance of such an interaction, which may vary between endpoints.

Key words: artificial light; metameric light; melanopsin; melatonin; sleep; sensory processing; circadian timing system

Introduction

The effects of short-wavelength light on sleep and the circadian timing system are thought to be primarily mediated by specialized retinal ganglion cells that contain the photopigment melanopsin, wherefore they are intrinsically sensitive to light between 460 and 480 nm (intrinsically photosensitive retinal ganglion cells [ipRGCs]; [1–3]). Short-wavelength light exposure in the evening can acutely suppress melatonin secretion, although neuroendocrine sensitivity is characterized by considerable interindividual variability [3–5]. Moreover, evening light exposure has been shown to improve performance on tasks requiring sustained attention acutely [6, 7] and increase the available processing resources on a simple cognitive task as indicated by the amplitude of the P300 component of the human event-related potential (ERP; [8]) Furthermore, it can decrease sleepiness in the evening, prolong sleep onset latency and consequently increase sleepiness in the morning [9–12]. Moreover, evaluating sleep objectively with electroencephalography (EEG), Münch *et al.* [13] demonstrated that exposure to short-wavelength light compared to longer wavelengths leads to decreased slow-wave activity (SWA) during the first sleep cycle. The authors concluded this finding to reflect that the alerting effect of the light persisted into sleep, which is well in line with findings by Chellappa *et al.* [14], who reported a decrease in homeostatic sleep pressure following "blue" light exposure in the evening. Chang *et al.* [10] additionally found the use of light-emitting e-readers to decrease and delay REM sleep, but no change in total sleep time, sleep efficiency, or the duration of non-REM (NREM) sleep compared to reading a printed book.

While many of the studies point to a special relevance of the short-wavelength-sensitive melanopic system in mediating the abovementioned effects, only recently so-called metameric light conditions have allowed to specifically target specific classes of retinal receptors in selected, isolated fashion while producing no responses in other classes [15–17]. Such studies yield strong mechanistic insights regarding the relevance of specific receptors and thus light characteristics. Contrasting two metameric light conditions (73.5 photopic lx), that is, high- vs. low-melanopic light with 77.7 and 24.7 melanopic lx, respectively, Allen *et al.* [18] demonstrated that 5-h exposure to high-melanopic light during the evening (18:00–23:00 h) resulted in stronger suppression of melatonin and a decrease of subjective sleepiness in a sample of 11 volunteers. Similarly, Souman *et al.* [19] found that 3-h high-melanopic (188.8 melanopic lx, 171 lx melanopic equivalent daylight illuminance [EDI]) exposure from 2 h before to 1 h after HBT suppressed melatonin compared with a low-melanopic (54.6 melanopic lx, 49 lx EDI; both low-/high-melanopic: 175 photopic lx) and a dim light condition, however without affecting alertness. Thus, while high-melanopic light is effective in suppressing melatonin secretion, the effects on cognition are less clear. Whether the effects of light on subsequent sleep that have been reported in other studies can largely be attributed to short-wavelength light acting on ipRGCs or rather result from an interaction with photopic or cone-mediated light characteristics is still unknown. Thus, this project aimed at investigating the effects of two metameric light conditions designed to only differ in their effects on ipRGCs but not cones on subjective and objective sleep parameters beyond melatonin suppression. We expected melatonin to be suppressed and SWA in the first sleep cycle to be decreased more effectively by high- compared to low-melanopic light. Besides this, we explored the effects on sleep, sleepiness, and behavioral vigilance using self-report scales and objective measurements, respectively.

Going beyond classic, sleep parameters (i.e. SWA, sleep architecture) that describe global brain states and reflect a *macroscopic* perspective, we were also interested in whether and how light exposure alters brain processes on the *microscopic* level. More specifically, we propose this could inform whether high-melanopic artificial light exposure leads to more "wake-like" processing during sleep that underlies the observed effects on "global brain states" and sleep quality. To this end, we investigated whether metameric light conditions would differentially alter basic sensory processing during wakefulness and subsequent sleep. Classically, basic sensory processing has been studied using so-called oddball paradigms, where rare deviating tones are included in a sequence of frequent standard tones. These deviating stimuli are well-known to give rise to a distinct component in the human event-related potential (ERP), the so-called mismatch negativity (MMN [20, 21], for a review see [22]). Although the MMN was often considered to reflect a low-level or "pre-attentive" prediction error [21], it is nowadays best explained by an active "top-down" predictive mechanism and only to a lesser extent by passive sensory adaptation and violations thereof [23]. Additionally, the MMN amplitude has been shown to be modulated by (selective) attention in some studies, although not requiring (waking) attention [24–26]. For instance, the MMN was found to be reduced by mental fatigue [27] and prolonged wakefulness [28]. Additionally, Vandewalle *et al.* [29] reported light (during daytime) to enhance brain responses in cortical areas that support attentional oddball effects. Okamoto and Nakagawa [8] furthermore found daytime exposure to short-wavelength light, to increase the amplitude of a later attention-modulated ERP, the P300 component. Thus, we here investigated whether 1-h pre-sleep exposure to two metameric light conditions would differentially alter attentional processes involved in early sensory processing as reflected by the mismatch response (i) during the light exposure and (ii) during a subsequent 8-h sleep opportunity (Figure 1). Specifically, we hypothesized that the light exposure would differentially affect the active prediction system during sleep