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Orginal Article

Controlling light–dark exposure patterns rather than sleep schedules determines circadian phase

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ABSTRACT

Objective: To examine, in a field study circadian phase changes associated with two different light–dark exposures patterns, one that was congruent with a phase advanced sleep schedule and one that was incongruent with an advanced schedule.
Methods: Twenty-one adults (mean age ± standard deviation = 22.5 ± 3.9 years; 11 women) participated in the 12 day study. After a five-day baseline period, participants were all given individualized, fixed, 90-minute advanced sleep schedules for one week. Participants were randomly assigned to one of two groups, an advance group with a light–dark exposure prescription designed to advance circadian phase or a delay group with light–dark exposure prescription designed to delay circadian phase. The advance group received two morning hours of short-wavelength (blue) light ($\lambda_{max} \approx 476 \pm 1$ nm, full-width-half-maximum ≈ 20 nm) exposure and three evening hours of light restriction (orange-filtered light, $\lambda < 525$ nm = 0). The delay group received blue light for three hours in the evening and light restriction for two hours in the morning. Participants led their normal lives while wearing a calibrated wrist-worn light exposure and activity monitor.
Results: After seven days on the 90-minute advanced sleep schedule, circadian phase advanced 132 ± 19 minutes for the advance group and delayed 59 ± 7.5 minutes for the delay group.
Conclusions: Controlling the light–dark exposure pattern shifts circadian phase in the expected direction irrespective of the fixed advanced sleep schedule.

1. Introduction

The master clock in the suprachiasmatic nuclei orchestrates circadian rhythms at every level of physiology, from overt behavior to single cells. Retinal light exposures affect the phase relationship between the external clock time and the endogenous master clock time. Short-wavelength (blue) light is most effective for stimulating the master clock [1,2]. Empirically, the spectral sensitivity of human circadian system, as measured by nocturnal melatonin suppression and by phase shifting, peaks at approximately 460 nm [1–4]. The magnitude and the direction of phase adjustments in the suprachiasmatic nuclei resulting from retinal light exposure are characterized by the Phase Response Curve (PRC) [5–8]. The PRC can be characterized as a 24-hour cycle function with both a phase advance and a phase delay region. A well-defined PRC can be used to predict the best time of light delivery for the treatment of circadian misalignment such as advanced sleep phase disorder or delayed sleep phase disorder. In most humans, light applied during early evening and the first half of the night should delay the phase of the master clock, whereas light delivered during the late night and the early morning should advance its phase [7,9].

The effectiveness of light sources with increased short-wavelength radiation for treating different circadian sleep disorders in the field has been investigated. Two field studies exposing subjects to narrowband 470-nm peaking light in the morning were undertaken in attempt to phase advance circadian phase in adolescents [10] and in night owl young adults [11]. In the adolescent study, all participants in a between-subjects design had delayed bedtimes (one and a half hours) and wake times (three hours) on weekends relative to weekdays. All participants delayed circadian phase from Friday to Sunday, as measured by changes in the time of dim light melatonin onset (DLMO), by approximately the same amount irrespective of whether or not they were exposed to a 470-nm light for one hour upon awakening on weekends. The authors suggest that morning light treatment presented after delayed wake times during weekends had no benefit for advancing circadian phase in adolescents. However, light exposures at other times of the day were not monitored, so it is not known if for example, uncontrolled exposure to evening light canceled out or reduced the effect of the morning light treatment.

In the night owl study [11], there was no difference in circadian phase advance, as measured by a change in the time of DLMO

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between one group of participants who experienced only an advanced sleep schedule (one and a half to two hours daily for six consecutive days) and another group of participants who received one exposure to a 470-nm light on awakening in addition to an advanced sleep schedule. Unlike the adolescent study, light exposures during the light treatment and over the course of the waking period were continuously monitored in both groups. Although circadian light exposures in the first three hours after awakening were considerably greater in the group exposed to the morning blue light (verifying compliance to the experimental protocol), the total circadian light exposures while awake did not differ between groups. These data suggest that the entire daily light exposure profiles need to be considered when attempting to predict circadian phase and thereby to correct circadian sleep disorders in real-life applications.

Our field study was designed to more systematically examine the relationship between an advanced sleep schedule and prescribed light treatments. All participants were placed on a fixed, advanced sleep schedule in which both morning and evening light exposures were controlled. Half of the participants received a schedule-reinforcing advance regime of light and dark and the other half received a schedule-contradicting, delay regime of light and dark. It was hypothesized that the light–dark exposure patterns determine circadian phase and not the sleep schedule.

2. Methods

2.1. Participants

Twenty-one participants were recruited by word-of-mouth and email. Potential participants were asked to fill out the Munich Chronotype Questionnaire [12]. Those who normally woke up between 0630 and 0800, went to sleep between 2300 and 0130, and had regular sleep patterns were accepted into the study (bedtimes and wake times reported by participants during recruitment are shown in Table 1). All participants reported that they had no major health concerns and that they did not take pharmaceuticals, except for women taking birth control pills. Participants (11 women) ranged in age from 18 to 30 years old (mean age ± standard deviation, 22.5 ± 3.9). Each participant chosen for the study had to demonstrate an ability to use instant messaging and to respond quickly to prompts from the experimenter with his or her own personal mobile device. All participants were provided written informed consent approved by Rensselaer's Institute Review Board and were paid for their participation in the study.

2.2. Study overview

Every participant completed the 12-day mixed-design study, during which they were asked to wear a wrist-worn Daysimeter-D [13] at all times while awake and asleep except during showering and swimming. Participants kept their normal schedule during the first five days. At the end of this baseline period, participants reported to the laboratory for collection of evening saliva samples. Melatonin concentrations were used to assess circadian phase, as measured by the time of their DLMO. Participants were then randomly assigned to the advance group ($n = 10$) or the delay group ($n = 11$) for the next seven days. All participants were given an advanced sleep schedule; those in the advance group received a light prescription designed to advance their circadian phase in concert with the advanced sleep schedule. Those in the delay group received a light prescription designed to delay their circadian phase in opposition to the advanced sleep schedule. At the end of the intervention week, participants reported to the laboratory for a second evening saliva sample collection for a second circadian phase assessment.

2.3. Apparatus

2.3.1. Communication between participants and experimenter

Google Chat, an instant messaging system that maintains a message log, was used throughout the study to issue instructions to participants and to record their responses. The two-way Google Chat messaging was conducted with a mobile device (eg, cell phone, smartphone, tablet computer) that the participants carried with them at all times.

2.3.2. Light and activity measurements

Throughout the study participants wore a Daysimeter-D on their wrists at all times, including during sleep but not when showering or swimming. Participants were asked to avoid covering the devices with their coats and sleeves. The device continuously measures and records personal light exposure and activity levels [13]. It is calibrated by photopic illuminance (lux), circadian illuminance (CL_A), and circadian stimulus (CS). Values of CL_A are spectrally weighted illuminance values according to the model of phototransduction by Rea et al. [3,14] and scaled so that 1000 lux of CIE (International Commission on Illumination) Illuminant A (incandescent light source at 2856 K) is equivalent to 1000 units of CL_A. CS values are transformed CL_A values ranging from 0 to 0.7. CS values are proportional to levels of nocturnal melatonin suppression, from 0 at threshold to 70% at saturation during the midpoint of nocturnal melatonin production after one hour of light exposure for a 2.3-mm diameter pupil [15]. Because CS is defined by the circadian system's input–output relationship, it is considered a better measure of the effectiveness of light for stimulating the circadian system than either lux or CL_A. Activity using an Activity Index also was continuously recorded [16].

2.3.3. Eyewear

Participants in both groups wore two types of eyewear during prescribed time periods, orange-tinted glasses and blue-light goggles.

Table 1
Participant characteristics obtained during subject recruitment.

Participant characteristics	Advance group (n = 10)		Delay group (n = 11)	
	Women:	8	Women:	3
	Mean (SD)	Range	Mean (SD)	Range
Age (years)	22 (3)	18–30	23 (4)	18–32
MCTQ-reported weekday wake times (h)	0755 (0009)	0730–0800	0716 (0028)	0630–0800
MCTQ-reported weekday bedtimes (h)	2357 (0036)	2315–0130	2327 (0027)	2300–0030
MCTQ-reported weekend wake times (h)	0716 (0028)	0730–1130	0849 (0044)	0730–1000
MCTQ-reported weekend bedtimes (h)	2327 (0027)	2315–0200	0012 (0030)	2345–0130

MCTQ, Munich Chronotype Questionnaire; SD, standard deviation.