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Circadian effectiveness of two polychromatic lights in suppressing human nocturnal melatonin

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Abstract

Forty subjects participated in a study to test the accuracy of a recent model of human circadian phototransduction for predicting the relative effectiveness of two polychromatic light sources at suppressing nocturnal melatonin. Brief exposures to four different light levels (30, 100, 300 and 1000 photopic lux at the cornea) and two different "white" lamp spectra (4100 and 8000 K) were used. Results suggest that the model can properly order the relative magnitudes of the two circadian stimuli, but that nocturnal melatonin suppression follows a rate-limited response to light that cannot be predicted from the magnitude of the suppressing light stimulus alone. Some practical implications of these results are discussed.

Keywords: Melatonin suppression; Photoreceptors; Melanopsin; Circadian phototransduction; Polychromatic light

Light reaching the retina provides the stimulus for vision as well as for circadian regulation of biological functions in most species on earth. Although the stimuli for both systems must be registered on the retina in mammals, the physical characteristics of retinal illumination important for each system are remarkably different [26]. In humans, the circadian system has a much higher threshold for activation than the visual system [26] and has a peak spectral sensitivity at shorter wavelengths [4,5,12,17,19,20,24,25,34,37,38]. The visual system is served by optical refraction and a fovea that are primarily concerned with fine spatial resolution, and by the peripheral retina that largely mediates detection, but not recognition of objects. The circadian system is largely indifferent to spatial distribution, although the inferior retina appears to be more sensitive to light than the superior retina [14]. Most significantly perhaps, the visual system responds in a fraction of a second whereas the circadian system takes several minutes for activation [2]. Finally, the circadian system is differentially sensitive to light depending upon the time of day [10,15], whereas the visual system is capable of processing suprathreshold stimuli with little regard to the time of day.

Given these fundamental differences, it is logical to determine how conventional light sources designed for the visual system affect the circadian system. Recently, Rea et al. [27] developed a model for human circadian phototransduction that can be used for predicting the relative effectiveness of different light sources for stimulating the human circadian system. Consistent with recently published evidence from neurophysiology and neuroanatomy, the model incorporates the newly discovered intrinsically photosensitive retinal ganglion cells (ipRGCs), as well as rods and cones. It also takes into account the high sensitivity of the human circadian system to short-wavelength light, and, importantly, it considers evidence for a phenomenon known as spectral opponency that underlies human color vision [8,9]. Moreover, because the model was based on several sets of psychophysical data where nocturnal melatonin suppression was measured after brief (30–90 min) light exposures [4,9,18,24,25,34], it can also support quantitative predictions of nocturnal melatonin suppression after exposures to different light levels and for different light source spectra.

A number of studies have compared the relative effectiveness of monochromatic lights for stimulating the circadian system [4,5,12,17,19,34,37,38], but few studies have directly compared the relative effectiveness of different polychromatic, white light sources. Certainly none have generated *a priori* predictions of circadian effectiveness. The ability to make quantitative predictions of the effectiveness of different white light sources for stimulating the human circadian system is important because indoor

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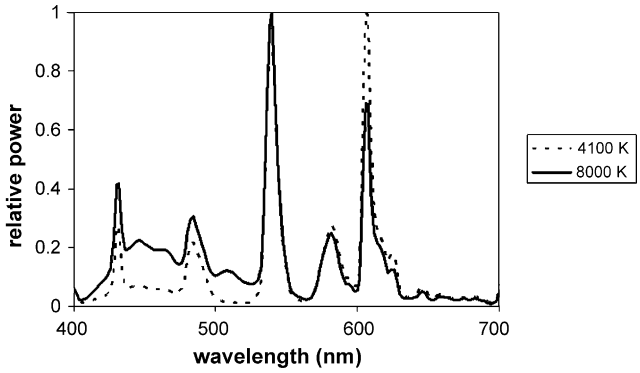
environments are exclusively illuminated with these sources. Rea et al. [24,25] measured melatonin suppression to different combinations of high and low correlated color temperature (CCT) fluorescent illumination, but since these data were incorporated in the model by Rea et al. [27], they do not provide an independent test of the model. CCT is a measure of the color appearance of an illuminant along a "warm-cool" dimension [23]; a lamp with a high CCT will have more energy in the short-wavelength region of the visible spectrum than one with a low CCT and will appear more bluish-white [23]. Morita and Tokura [20] investigated the ability of 3000 and 6500 K lamps to inhibit the rise of nocturnal melatonin, but because only one light level was used for both sources, it is impossible to assess equivalent amounts of light from different spectral power distributions (SPDs) for stimulating the human circadian system. The present study was designed to test the accuracy of the model [27] in predicting nocturnal melatonin suppression after brief exposures to four different light levels and two different "white" lamp spectra.

Four light boxes, 81(wide) × 81(deep) × 102(high) cm, were used. Every light box was made of white foam board (made of extruded polystyrene core laminated on both sides with matte finish clay coated paper) and built so that when a subject was performing a printed visual task, his/her head was inside the box; this helped maintain the prescribed illuminance at the cornea. Two lamp spectra were selected, a 61 cm fluorescent lamp having a nominal CCT of 4100 K (F17T8/TL741, Philips), which is commonly found in commercial applications, and a novel, high-CCT 61 cm fluorescent lamp (FO17/SkyWhite/ECO, OSRAM Sylvania) having a nominal CCT of 8000 K, both operated on electronic ballasts (T8-2 Lamp, Motorola). Light generated by these two sets of fluorescent lamps was emitted into the box from a 43 cm × 28 cm aperture cut into its roof and diffused by its all-white interior and by a white acrylic sheet placed below the lamps. Mechanical filters placed just above the diffuser were used to adjust the light levels without affecting the light source SPDs. A 7.6 cm diameter hole in the back of each box accommodated infrared pupilometry with a video camera.

Fig. 1 shows the relative SPD, CCT, color rendering index (CRI) and chromaticity (x, y) values measured inside the boxes. The CCTs are somewhat below the nominal values due to slight spectral selectivity of the foam board. Four photopic light levels at the cornea (30, 100, 300, 1000 lx) were measured before each experimental session using an illuminance meter (P30SC0, LMT) placed at the subjects' eye position and angle of gaze while performing the printed reading task. When subjects were seated at the box, some light was absorbed by their clothing, resulting in as much as 20% lower light levels than those measured prior to testing. Pupil measurements for every subject were taken right after subjects arrived at the laboratory prior to testing. Retinal illuminance levels were estimated from the measured pupil areas and estimated lens transmissions [35].

Forty subjects, 22 males (age range = 18 to 54, median = 21 years) and 18 females (age range = 18 to 35, median = 23 years) participated in the study. Subjects were screened for sleep habits and selected according to their responses on the Munich ChronoType Questionnaire [29]. Only



	4100 K lamp	8000 K lamp
CCT	3572 K	6593 K
CRI	82	87
(x,y)	(0.41,0.41)	(0.31,0.34)

Fig. 1. Relative SPDs, CCT, CRI, and chromaticity (x, y) of the light seen by the subjects in the experimental boxes generated by the 4100 and 8000 K fluorescent lamps.

those who normally were asleep between 22:00 and 00:00 were selected for the study. Subjects were asked to avoid napping or sleeping, as well as to refrain from caffeine intake starting 15 h before the first blood collection, which took place at 01:00. Color vision and acuity measurements were also obtained from every subject; none of the subjects were dichromats [30] and all had acuity of 20/35 or better.

The experimental protocol was approved by Rensselaer Polytechnic Institute's Institute Review Board. Subjects were recruited using an Internet newsletter provided to university students and employees. The study ran from 23:30 to 04:30 on 10 nights (four subjects per night) during July through September 2005.

Every subject saw both light spectra at the same light level during two sessions on one night. In other words, those subjects that were exposed to the 8000 K lamp during the first session were exposed to the 4100 K lamp at the same photopic illuminance during the second session, and vice versa. Two of the four light levels were presented each night.

After subjects signed the consent form, a registered nurse inserted an in-dwelling angio-catheter into one of the subject's arms for blood withdrawal during the experiment. Room lights were turned off at 00:30 except for several red light emitting diode (LED) traffic lights ($\lambda_{max} = 630$ nm) that provided dim illuminance throughout the laboratory, enabling subjects to see and, if necessary, move safely about the laboratory without inducing light-dependent nocturnal melatonin suppression.

Subjects sat quietly in the dimly illuminated laboratory until 02:00. The first experimental session of the night lasted from 02:00 to 02:40. Subjects were moved from the dimly illuminated environment to their assigned light box at 02:00; the blood sampling times from the four subjects were slightly staggered to facilitate collection by the nurse. At 02:40, subjects returned to the dimly illuminated laboratory environment. The second, and