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Y. A. W. de Kort, W. A. IJsselsteijn, I. M. L. C. Vogels,
M. P. J. Aarts, A. D. Tenner, & K. C. H. J. Smolders (Eds.)

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Volume Editors

Yvonne de Kort, PhD
Wijnand IJsselsteijn, PhD
Karin Smolders, MSc
Eindhoven University of Technology
IE&IS, Human-Technology Interaction
PO Box 513, 5600 MB Eindhoven, The Netherlands
E-mail: {y.a.w.d.kort, w.a.ijsselsteijn, k.c.h.j.smolders}@tue.nl

Ingrid Vogels, PhD
Visual Experiences Group
Philips Research
High Tech Campus 34, WB 3.029
5656 AE Eindhoven, The Netherlands
E-mail: ingrid.m.vogels@philips.com

Mariëlle Aarts, MSc
Eindhoven University of Technology
Department of Architecture Building and Planning
PO Box 513, VRT 6.34
5600 MB Eindhoven, The Netherlands
E-mail: M.P.J.Aarts@tue.nl

Ariadne Tenner, PhD
Independent consultant
Veldhoven, The Netherlands
E-mail: ariadne.tenner@onsmail.nl

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Reducing Light Intensity and Changing its Spectral Composition: Effects on Human's Sleep Characteristics and Melatonin Suppression Under "Natural Conditions"

Marina. C Giménez[1]✉, Pauline Bollen[1], Marijke C.M[1]. Gordijn, Matthijs L. van der Linden[2], Domien G.M. Beersma[1]

[1]Department of Chronobiology
Center for Life Sciences
University of Groningen, The Netherlands
m.c.gimenez@rug.nl

[2]Oculenti
University Medical Center
Groningen, The Netherlands

ABSTRACT

Light has a great impact in our everyday life for vision, but also for non-visual processes. The recent discovery of photosensitive retinal ganglion cells triggers new studies on the non-visual effects of light's spectral composition. In the present study via the use of soft orange contact lenses we investigated how, under natural conditions, a reduction in exposure to the short wavelengths (blue) light affects sleep and the suppression of melatonin concentrations to a standard light stimulus in healthy young subjects. The orange lenses were effective in reducing light input. If worn only during the light pulse melatonin suppression in response to a 2h 600 lux white light pulse was reduced from 29% in the control condition to 17.3% ($p<0.05$). No significant differences in melatonin suppression were observed between the control condition (29%) and after wearing the orange lenses for 16 days (34.1%). These results indicate that the non-visual response of melatonin suppression to light adapted. While wearing the orange lenses the amount of sleep was reduced, somewhat similar to the sleep changes that occur with ageing.

Keywords

Light intensity, Light spectral composition, Melatonin, Sleep, Humans.

INTRODUCTION

Due to the earth's daily rotation around its axis a temporal pressure is imposed on almost all organisms; a 24h day with light and dark cycles (day and night). In order to anticipate the temporal changes along the 24h day, organisms have evolved circadian clocks. The circadian clock generates cycles with an approximate period of 24h that needs to synchronize with the external environment. Light is the signal that sets the phase of our biological clock, which in turn synchronizes our physiological and psychological rhythms to the 24h rhythm of the environment [1, 2]. Furthermore, light has acute alerting and activating effects and acutely suppresses melatonin at night [3,4,5]. Synchronization of the biological clock depends on several aspects related to the light signal; its intensity and the time of exposure. The recent discovery of intrinsically photosensitive retinal ganglion cells (ipRGCs, maximal sensitive to short wavelengths) [6] has triggered new studies on the role of not only light intensity but also its spectral composition. Suppression of melatonin has been shown to be higher to light pulses of short wavelengths than to light pulses of other wavelengths [7,8,9]. Alertness was also shown to be more sensitive to short wavelengths [9]. These studies however, compared the effects of monochromatic light sources, which although informative to understand mechanisms is far from being a natural situation.

Considering the natural phenomenon of cataract (yellowish of the lens with ageing) [10], in the present study we investigate what the effects are of a reduction in (blue) light via the use of orange soft contact lenses. This situation resembles at least qualitatively what happens with ageing. We hypothesized therefore a disruption of sleep patterns and a reduction in the suppression of the nocturnal melatonin to nocturnal light exposure.

MATERIALS AND METHODS

Subjects

In total 50 subjects enrolled for the study. Only those subjects who were healthy, non-smoker, non-color blind, and with an intermediate chronotype [11, modified for Dutch population] were selected. Subjects who worked night shifts or travelled through more than 2 time zones during the 2 weeks prior the study were also excluded. Because subjects have to wear soft contact lenses during 2 consecutive weeks, 24h per day a check-up by a contact-lenses specialist was conducted at the University Medical Center of Groningen (UMCG) in order to assess subject's

eyes condition. After screening, 22 subjects were selected from whom 15 completed the study (7m:8f, mean age ± sem: 24.5 ± 4.6 years old). The study was conducted between December 2007 and September 2008. The Medical Ethical Committee of the UMCG, The Netherlands, approved the study protocol. All subjects signed a written informed consent form prior to their participation.

Soft orange contact lenses (OL)

The OL (CE: 0120, with UV protection) were supplied by Oculenti at the UMCG, The Netherlands from Ultravision International Ltd., UK. In the visible range of the spectrum (from 400-700 nm), the OL reduced transmitted light for 37% (calculated as the area under the curve) while in the short wavelengths (400-530 nm) the reduction was 56%. The reduction in light transmission through the OL can be seen in Figure 1.

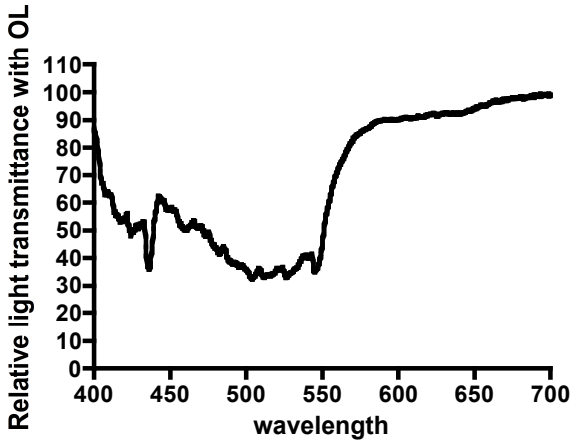

Figure1: Relative light transmittance through the OL from a halide light bulb (MDS 200.2, Philips).

Experimental design

A control condition (subjects wore their own contact lenses n=13, or no lenses n=2) and an experimental condition (subjects wore the OL) were assigned to each subject in a randomized order. The OL were worn 24h per day. Each condition lasted for 16 days, they were planned at least 2 weeks apart to avoid any potential carry-over effects, and they started on the same day of the week in order to have a similar pattern of behavior within each subject.

Measurements

During the 16 days that each condition lasted, subjects wore an actiwatch® (Cambridge Neurotechnologies, UK) to measure sleep-wake cycles and filled in sleep diaries. During the last two nights of each condition, subjects came to the lab in order to assess a dim light melatonin profile on the first night and melatonin suppression on the second one. During the first night, in order to assess melatonin profiles, light levels were dimmed (<10 lux) and saliva samples were taken using cotton swabs (Sarstedt BV, Etten-Leur, The Netherlands) hourly from 19:00 to 00:00 h, every half hour until 2:00 h, and 2-hourly from 3:00 until 9:00 h. On the second night the same protocol was followed until 00:00. From 00:00 until 2:00 h subjects were asked to sit in front of 2 light boxes with full spectrum white light (600 lux, Pharos Max, Osram Dulux-L tubes, ©Lumie) to investigate the suppression of melatonin. During these two hours subjects watched a movie on a TV situated in between both light boxes so that they could keep their level of gaze constant. Light intensity at eye level was regularly checked during the 2 hours light pulse and adjusted if necessary. On a separate night from each 16-days session, subjects came for an extra night at which the acute effect of the OL on suppressing melatonin was measured (S-OL). For this purpose, the protocol of the second night was repeated but in this session subjects put the OL in only 30 minutes before the light pulse (in contrast with 15 days of continuously wearing the OL; L-OL). Subjects were carefully instructed about the collection of saliva samples for melatonin assessment. Eating was restricted to the 15 minutes after each sample, chocolate, bananas, coffee or black tea were not allowed during the whole time. Samples were centrifuged immediately after its collection and stored at -20ºC until its analysis.

Analysis

Melatonin concentration measured in saliva was determined by means of radio-immunoassay (RK-DSM, Bühlmann laboratories AG, Siemens Medical Solutions Diagnostics, Breda, The Netherlands). The area under the curve was calculated from time point 00:00 until time point 2:00 for the control profile, and the control (CL), the L-OL and the S-OL suppression conditions to estimate the nocturnal melatonin suppression by light. A repeated measurements ANOVA was used to test the effects of these conditions.

Sleep parameters were assessed by means of actiwatches and sleep diaries. For this purpose only the first 14 days of each condition were used since sleep during the last two nights in our lab was disturbed by the sampling protocol. Actual sleep (the percentage of assumed sleep minus the time being awake), sleep efficiency (percentage of time spent asleep while in bed) and sleep fragmentation (the percentage of immobility phases of 1 minute as a proportion of the total number of immobility phases) were calculated. The effects of the OL were tested with Paired-T test.

RESULTS

The suppression of melatonin during light exposure measured as the area under the curve relative to the control profile condition (= 0 level in figure 2) can be seen in figure 2. The repeated measurement ANOVA revealed a significant effect of condition ($F(4,9) = 5.694$, $p < 0.05$). Post hoc comparisons showed no significant differences between suppression after wearing the OL for 16 days (L-OL) with the control suppression (CL) ($F(1,13) = 0.26$ $p = 0.62$). However, when compared to the control suppression

the acute suppression achieved in the S-OL condition was significantly different ($F(1,12) = 10.427$, $p < 0.01$).

Wearing the lenses for 16 days lead to a small but significant reduction in the actual sleep percentage ($t = 3.41$, $p < 0.01$), no significant differences were found however in the sleep efficiency nor in the fragmentation index (table 1).

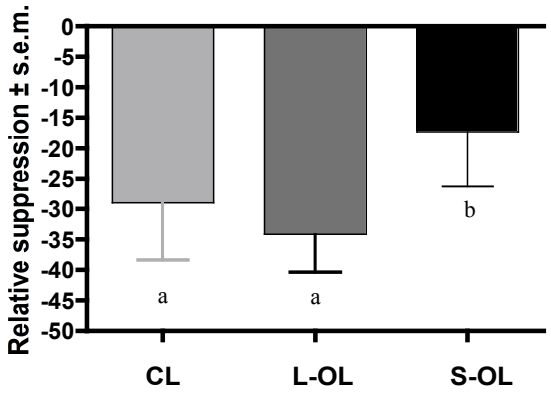

Figure 2: Melatonin suppression (calculated as area under the curve) ± s.e.m. relative to the control profile (0 level). No significant differences in suppression were found between the control (light grey bar) and the OL (dark grey bar) condition (denoted by a), while the acute suppression of the OL (black bar) was significantly different from the control condition (denoted by b).

	Control	L-OL	p-value
Actual sleep %	85.05 ± 1.49	83.64 ± 1.44	< 0.01
Sleep efficiency	80.77 ± 2.05	80.10 ±1.68	ns
Fragmentation Index	27.54 ± 3.13	28.71 ± 3.00	ns

Table 1: Mean ± s.e.m. and p values of the sleep parameters measured in this study for both conditions.

DISCUSSION

The aim of this study was to investigate the effects of diminishing the light input, in particular in the short wavelengths range of the visible spectra. In order to do this and trying to simulate a natural situation [10], subjects wore soft orange contact lenses (OL) for 16 consecutive days, 24h per day.

Melatonin suppression by light is a way to estimate the effects of light input to the biological clock [12]; the smaller the suppression to the same stimulus the less sensitive the system is. In the present study we clearly showed that wearing the OL only during the light pulse (S-OL) reduced the light input to the system; the suppression of melatonin to a white light stimulus was less then without the lenses (CL). When the OL were worn for 16 days (L-OL) the suppression of the nocturnal melatonin was not different from the suppression without the OL (CL). It can be concluded that the system has become more sensitive after 16 days of reduced (short wavelengths) light input by wearing the OL. It has already been shown that exposure to dim light during one week by staying inside and using dark goggles (2% light transmission) increased the suppression of the nocturnal melatonin due to a higher sensitivity of the system [13]. Our study represents a more realistic situation in terms of both the reduction in light intensity as well as the "bright light exposure" condition. In Hébert *et al.*[13], subjects exposed themselves to bright light boxes in the bright light week condition while in the present study they exposed themselves to natural and artificial light in accordance to their personal behaviour. The mechanisms by which adaptation occurs and at which level in the circadian system it happens is not know. At the retinal level several possibilities could be hypothesized. Photostasis, gradual changes in the retina to keep a constant number of photons absorbed per day, has been already shown in rats [14], although there is still no proof of such processes happening in the human retina. A shift to the responsive form of the bistable melanopsin molecule due to a reduction in exposure to short wavelengths and a relative increase in exposure to long wavelengths while wearing the OL is another possibility [15].

Regarding sleep parameters a reduction in the actual percentage of time that subjects spent sleeping was found as a result of wearing the OL. Although also sleep efficiency and fragmentation index showed minor changes in the direction of a more disturbed sleep pattern while wearing the OL these differences were not significant. Obviously the reduction of light exposure due to the OL was not big enough to induce sleep disturbances in these young people, or the adaptation process was fast enough to normalize the overall sleep pattern over the 16-days period.

The present study does not support the idea that the changes seen in the circadian system with ageing can be explained by the development of cataract in the elderly. However, the present study has been conducted in young healthy subjects and probably extrapolating these data to the elderly might not be possible. With ageing the circadian input system might become less flexible and looses its capability of adapting to the different situation.

In conclusion short wavelengths do play an important role in the suppression of melatonin [7,8,9, and the present study], but exposure to changes in the spectral composition of "natural light" on the long-term lead to adaptation of the non-visual responses to light in young subjects. These results are important both for understanding individual differences in non-visual responses to light, and for artificial indoors lighting developments.

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