The Solid Angle of Light Sources and Its Impact on the Suppression of Melatonin in Humans

Philipp Novotny^{1,2}, Peyton Paulick^{1,3}, Markus J. Schwarz⁴, and Herbert Plischke^{1,2}

¹ Generation Research Program – Human Science Centre – Ludwig Maximilians University, Munich, Germany {novotny,plischke}@grp.hwz.uni-muenchen.de
² Network Aging Research – Graduate Program Dementia – Ruprecht Karls University, Heidelberg, Germany
³ Department of Biomedical Engineering – University of California Irvine, USA ppaulick@uci.edu
⁴ Clinic of Ludwig Maximilians University, Psychatric Clinic, Section on Psychoneuroimmunology and Therapeutic Drug Monitoring, Munich, Germany
Markus, Schwarz@med.uni-muenchen.de

Abstract. Our group conducted a preliminary study to examine the influence of different sizes of light sources, and therefore different illuminance levels, at the retina. Six participants were exposed to two lighting scenarios and saliva samples were collected to determine melatonin levels throughout the experiment. Melatonin levels were analyzed to compare the efficacy of each lighting scenario and its ability to suppress melatonin period. Our data is showing a trend that both lighting scenarios are capable of suppressing melatonin. Moreover, the preliminary data show that the lighting scenario with the large solid angle is more effective at suppressing melatonin compared to the lighting scenario with the small solid angle lighting scenario period. Further testing with a larger patient population will need to be done to prove statistical significance of our findings. Our further studies will repeat this experiment with a larger test group and modifying the time frame between different lighting scenarios.

Keywords: light, health, melatonin, suppression, optimal healing environment, chronodisruption, circadian rhythm, shift work, dementia, light therapy.

1 Introduction

Light has been a treatment for a variety of disorders, in combination with medication or without. Light eases seasonal affective disorders (SAD) [1], helps to calm down demented elderly in the evening from the sundowning syndrome [2] or can simply be used to ease recovery from jet lag period [3-5].

In the year 2001, two independent research groups, discovered that the melatonin suppression in humans could be induced by the exposure to light of the blue spectra [6, 7]. Through this complex circadian regulation system, our day and night cycle is

synchronized to a 24h cycle period. Our research interests are focused on exploring alternative methods to suppress melatonin during the day and facilitate a synchronized chrono rhythm. Artificial light sources, those which have a sufficient amount of blue spectral parts and intensity can also support the chrono rhythm of the human body. This is especially important in environments where an insufficient amount or even the absence of natural light is present.

The topic we are interested in exploring is, how individuals should be exposed to artificial light sources. Researchers have begun to study the sensitivity of the human retina and its relation to the suppression of melatonin [8-14]. Our research group proposed an optimized lighting environment to alleviate the symptoms of chronodisruption. We are especially interested in chronodisruption among shift workers, where research has linked this working style to a variety of cancers [15, 16], as well as the regulation of the circadian rhythm in demented elderly. Regarding the population of demented elderly a variety of studies have been conducted to analyze the effect of specific lighting conditions on behavior, cognition and circadian rhythmicity of demented elderly [17-20]. These studies have also taken a look at the circadian rhythmicity of their caretakers[21].

In previous studies the amount of light exposed to the eye was measured at eye level. There is no information that can help to determine the amount of light exposed to the retina that is necessary to suppress melatonin. The characteristic of the light source and the method in which light is delivered to the eye modifies the illumination of the retina, which is ultimately the deciding factor in melatonin suppression. Therefore, it is not clear if the threshold level that is published is valid for every lighting condition, since these values report illumination at eye level and not illumination at the retina [9, 12, 22]. Our group believes more information about the lighting sources needed to produce accurate threshold levels for melatonin suppression.

Our feasibility study compared the solid angle of two different light sources. The solid angle measures how large the light source appears to the observer and how it is mapped on the retina. The type and location of a light source has a direct effect on the illuminance level on the retina and thus suppression of melatonin.

2 Methods

2.1 General Study Setup

Our preliminary study had a total of six participants (1 female / 5 male). The testing was performed during the night from 09:00 pm to 01:00 am. Our testing setup asked patients to sit in a darkened room (lined with black fabric to absorb any scattered light) and watch a television program during the testing. This testing room was outfitted with a variety of lighting sources that the patients would be exposed to while watching television. The television was used to keep the participants entertained and maintain a stable gazing direction. From 09:00 pm to 10:00 pm, participants had to wear glasses that absorbed the blue spectral parts of the artificial light sources in the laboratory. Blocking out exposure to blue spectral parts of artificial light and thus should eliminate melatonin suppression. From 10:00 pm to 01:00 am, participants were placed in a separate room in front of a television with two different light sources. To prevent an influence of blue light emitted

by the television, a yellow foil was added in front of the television. From 09:00 pm to 11:00 pm, there was a Washout Phase (WO), were no melatonin suppressing light was exposed to the participant, in order to allow the natural release of melatonin. From 11:00 pm to midnight, the participant was exposed to one of the two lighting scenarios. From midnight to 01:00 am, the other lighting scenario was started. To avoid sequential errors we switched lighting scenarios with each participant. This allows for the elimination of any error due to the order of the lighting scenario. For example, the first participant was exposed first to the small light source (sLs) and afterwards to the large light source (lLs). The second participant was exposed first to the lLs and then to sLs and so on.

The testing room layout is depicted in figure 1. Distance from the participants eye to the back wall was approximately 90 cm. Distance from the participants eye to the ground was approximately 120 cm.



Fig. 1. Sketch of study setup. Arrangement of the objects.

2.2 Light Sources

Both light sources use light emitting diodes (LED) (OSRAM GmbH; Munich, Germany). The LEDs used are white (*Golden Dragon Plus ultra white*) and blue (*Golden Dragon Plus blue*). The specification of bot LED-Types can be seen in the following table:

Golden Dragon Plus ultra white	Luminous Flux: 116 lm at 350 mA up to 273 lm at 1000 mA Color: $Cx = 0.31$, $Cy = 0.32$ acc. to CIE 1931 (white); Optical efficiency (max.): 146 lm/W at 100 mA
Golden Dragon Plus blue	Luminous Flux: 28 lm at 350 mA up to 55 lm at 1000 mA Color: blue (467 nm) Optical efficiency (max.): 35 lm/W at 100 mA

Table 1. Specification of the used LEDs

Efficacy of the combined LEDs in suppressing melatonin is presented by the $a_{mel,v}$ value. This value indicates the melanopic efficacy rating. How effective a light source is to suppress melatonin compared to sunlight ($a_{mel,v,sun} = 1$)[23].

Small Light Source. The small light source has a dimension of 5 x 5 cm. Luminance level for the small light source was 33000 cd/m² measured in the center and 15000 cd/m² measured in the corners. The LEDs were placed in a circle behind a scattering glass create a diffuse light surface. The small light source has an $a_{mel,v}$ of 1.14.

Large Light Source. The large light source has a dimension of 100 x 150 cm. Luminance level for the large light source was about 200 cd/m² measured in the center and 40 cd/m² measured in the corners. The LEDs were placed in two bars, which were shining against a diffuse white painted surface in the dimensions described in figure 1. The large light source has an $a_{mel,v}$ of 1.33. The slightly higher $a_{mel,v}$ value is due to a slightly different spectrum of the large light source, compared to the small light source.

2.3 Melatonin Level

To determine how effective the small or the large light sources are, in suppressing melatonin, a total of 14 saliva samples were taken throughout the four hour experiment. From 07:00 pm, participants were not allowed to eat, drink, or smoke except non-carbonated water until the end of the testing to prevent contamination of the saliva samples. During the testing participants had to washout their mouth, during testing participants were provided with non-carbonated water. At 09:30 pm, participants had to give the first saliva sample. From 10:00 pm, every 15 minutes a saliva sample was taken (Salivette Cortisol, code blue; SARTEDT GmbH; Nümbrecht, Germany). Participants had to chew on a synthetic swab for at least 30 seconds. The saliva samples then were frozen (-25 °C) until they were sent to the laboratory for analysis.

Melatonin level was determined out of saliva samples with an enzyme immunoassay (ELISA).

2.4 Evaluation of Melatonin Suppression

To compare the efficacy of each lighting condition for suppressing melatonin, we compare the gradient of melatonin levels of each lighting condition in respect to the gradients of melatonin levels of the Washout Phase and the gradient of melatonin levels of the other lighting condition. (See Fig. 2)

2.5 Illuminance Level on the Retina

The information about the illuminance level mostly refers to the illuminance level measured at eye level, but the real amount of light, that is exposed to the retina, is regulated by the pupil diameter. With the specification about the dimension of the light source, the distance to the eye, the illuminance level on the cornea, and the pupil diameter, the amount of light, exposed to the retina can be calculated with the following formula [24]:



Fig. 2. Sketch of theoretical progress of melatonin level and light intervention. Dashed black line indicates the progress of melatonin level without light intervention. Drawn black line indicates the theoretical change in melatonin level.

$$E_{Retina} = E_{Cornea} * \frac{D_p^2}{k} * \frac{h^2}{A}$$

ERetina: Illuminance at the retina in lux ECornea: Illuminance at the eye in lux DP: Pupil diameter in mm k: Factor for different solid angle h: Distance from the light source to the eye in m A: Area of the light source in m²

Taking this formula into account, we measured the pupil diameter in each lighting conditions two times, at the beginning and in the middle of each lighting scenario with an infrared camera eye-tracking-system (SensoMotoric Instrument GmbH; Teltow, Germany).

We also measured the illuminance level at eye level with a lux-meter (Digitales Luxmeter MS-1500; Voltcraft) of each participant for each lighting condition.

3 Results¹

3.1 Melatonin Levels

The following results represent absolute melatonin level in pg/ml. Since the order of lighting scenarios switched with each participant, time is marked with *.

¹ In this paper we use Arabic numerals and decimal comma.

	21:30	22:00	22:15	22:30	22:45	23:00
P 1	0,67	3,63	6,63	9,12	12,69	14,21
P 2	5,52	8,40	11,84	12,03	21,48	16,60
P 3	9,78	10,10	11,59	14,27	12,77	13,19
P 4	1,73	4,86	4,42	5,48	6,36	8,58
P 5	2,21	6,78	8,68	12,13	28,03	35,32
P 6	14,27	56,23	51,66	54,32	44,36	81,78

 Table 2. Melatonin level during Washout Phase

Table 3. Melatonin level during the lighting scenario with the small light source

	23:15	23:30	23:45	00:00
Or *	00:15	00:30	00:45	01:00
P 1	26,93	19,91	23,51	20,76
P 2 *	21,62	20,03	25,21	31,09
P 3	14,51	12,10	12,28	12,23
P 4 *	13,92	14,32	13,82	15,98
P 5	39,82	50,95	38,52	34,65
P 6 *	60,91	55,17	71,77	80,26

Table 4. Melatonin level during the lighting scenario with the large light source

	23:00	23:15	23:30	24:00
Or *	00:00	00:15	00:30	01:00
P 1 *	26,93	19,91	23,51	20,76
P 2	19,03	17,39	20,63	26,54
P 3 *	13,64	15,25	13,42	13,95
P 4	8,35	9,57	12,48	13,19
P 5 *	40,85	56,82	34,65	64,07
P 6	46,94	58,83	53,48	61,44

3.2 Gradient of Melatonin Level

Table 5. Gradients of melatonin level for each participant for the Washout Phase (WO) and the two lighting scenarios (small light source sLs, large light source lLs)

	WO	sLs	lLs
P 1	2,78	2,89	-1,49
P 2	2,71	3,36	2,58
P 3	0,79	-0,66	-0,09
P 4	1,14	0,57	1,74
P 5	6,65	-2,80	4,75
P 6	8,70	7,46	3,82

	Diff Mean	Sign.
WO <> sLs	-1,99	,25
WO <> lLs	-1,91	,09
sLs <> lLs	-0,08	,97

Table 6. T-Test of the the gradients of melatonin level, Significance level is < ,05

3.3 Illuminance Level

The mean illuminance level for each lighting condition including the WO is shown in the following table.

 Table 7. Mean value of illuminance level in each lighting scenario including WO measured at eye level in lux

Lighting Scenario	Mean value in lx
Washout Phase	0,36
Small light source	91,9
Large light source	87,1

3.4 Pupil Diameter and Retinal Illuminance Level

While the pupil diameter varied very strong we calculated a range for possible illuminance levels.

Table 8. Recalculated retinal illuminance level on the retina for ILs

Pupil Diameter in mm	Retinal illuminance in lx
2,5	0,9
6,5	6,1

Table 9. Recalculated retinal illuminance level on the retina for sLs

Pupil Diameter in mm	Retinal illuminance in lx
2,5	414
6,5	2801

3.5 Effect Size

Calculations of effect size have been done for Cohen's d and are listed in the following table.

Table 10. Cohen's *d* fort he different lighting scenarios in their time window. D: 0,2 = small effect; 0,5 = medium effect; 0,8 = large effect

	WO \rightarrow sLs	WO \rightarrow ILs	sLs → sLs
23:00 - 00:00	0,67	0,27	0,50
00:00 - 01:00	0,43	0,62	0,31

4 Discussion

Our data is showing a trend that both lighting scenarios are capable of suppressing melatonin. Moreover, the preliminary data show that the lighting scenario with the large solid angle is more effective at suppressing melatonin compared to the lighting scenario with the small solid angle lighting scenario period. Although the trend in our data is apparent due to our small population size this difference is not significant. We believe with a larger testing size statistical significance can be proven. Further testing with a larger patient population will need to be done to prove statistical significance of our findings. Nevertheless, our findings, even intended as a feasibility study, seem to support the general assumption that larger illumination areas are more effective in suppressing melatonin. Our further studies will repeat this experiment with a larger test group and modifying the time frame between different lighting scenarios period. Based on our preliminary results that larger lighting sources are more effective in suppressing melatonin onset, our group feels this lighting scheme can be easily integrated into current working and home environmental infrastructure. Walls and ceilings can be effective light diffusers to maintain a large solid angle of a light source. These findings compel our research group to continue the exploring the most optimal way to deliver light in order to regulate chronobiology and promote healthy living.

5 Recommendation

Our first recommendation based on this pilot study is to split lighting scenarios and test participants with each lighting scenario individually. We suggest that that way a greater effect will be visible. Our second recommendation is to increase the amount of participants. Furthermore, we recommend testing participants with a similar chronotype (morning vs. evening type). Lastly, our group would like to integrate a schedule entrainment were patients sleep wake cycles are regulated for a two week period. Our group hopes to give participants guidelines wake/sleep times. This would reduce variation in melatonin onset due to varying schedules, different daily activity levels and rest periods.

Acknowledgement. We want to thank DIN FNL 27 for their support and knowledge and OSRAM AG for the hardware support. We also want to thank the Robert Bosch Foundation for supporting the first author. The authors would also like to thank the Whitaker International Fellows Program who supports our second author Peyton Paulick.

References

 Pjrek, E., Winkler, D., Stastny, J., Konstantinidis, A., Heiden, A., Kasper, S.: Bright light therapy in seasonal affective disorder–does it suffice? European Neuropsychopharmacology: the Journal of the European College of Neuropsychopharmacology 14(4), 347–351 (2004)

- Dowling, G.A., Mastick, J., Hubbard, E.M., Luxenberg, J.S., Burr, R.L.: Effect of timed bright light treatment for rest-activity disruption in institutionalized patients with Alzheimer's disease. Int. J. Geriatr. Psychiatry 20(8), 738–743 (2005)
- Arendt, J.: Managing jet lag: Some of the problems and possible new solutions. Sleep Medicine Reviews 13(4), 249–256 (2009)
- 4. Coste, O., Lagarde, D.: Clinical management of jet lag: what can be proposed when performance is critical? Travel Medicine and Infectious Disease 7(2), 82–87 (2009)
- Eastman, C.I., Burgess, H.J.: How To Travel the World Without Jet lag. Sleep Medicine Clinics 4(2), 241–255 (2009)
- Brainard, G.C., Hanifin, J.P., Greeson, J.M., Byrne, B., Glickman, G., Gerner, E., Rollag, M.D.: Action spectrum for melatonin regulation in humans: evidence for a novel circadian photoreceptor. J. Neurosci. 21(16), 6405–6412 (2001)
- Thapan, K., Arendt, J., Skene, D.J.: An action spectrum for melatonin suppression: evidence for a novel non-rod, non-cone photoreceptor system in humans. J. Physiol. 535(Pt. 1), 261–267 (2001)
- Adler, J.S., Kripke, D.F., Loving, R.T., Berga, S.L.: Peripheral vision suppression of melatonin. J. Pineal Res. 12(2), 49–52 (1992)
- Aoki, H., Yamada, N., Ozeki, Y., Yamane, H., Kato, N.: Minimum light intensity required to suppress nocturnal melatonin concentration in human saliva. Neurosci. Lett. 252(2), 91–94 (1998)
- Glickman, G., Hanifin, J.P., Rollag, M.D., Wang, J., Cooper, H., Brainard, G.C.: Inferior retinal light exposure is more effective than superior retinal exposure in suppressing melatonin in humans. J. Biol. Rhythms 18(1), 71–79 (2003)
- 11. Lasko, T.A., Kripke, D.F., Elliot, J.A.: Melatonin suppression by illumination of upper and lower visual fields. J. Biol. Rhythms 14(2), 122–125 (1999)
- 12. McIntyre, I.M., Norman, T.R., Burrows, G.D., Armstrong, S.M.: Human melatonin suppression by light is intensity dependent. J. Pineal Res. 6(2), 149–156 (1989)
- Ruger, M., Gordijn, M.C., Beersma, D.G., de Vries, B., Daan, S.: Nasal versus temporal illumination of the human retina: effects on core body temperature, melatonin, and circadian phase. J. Biol. Rhythms 20(1), 60–70 (2005)
- Visser, E.K., Beersma, D.G., Daan, S.: Melatonin suppression by light in humans is maximal when the nasal part of the retina is illuminated. J. Biol. Rhythms 14(2), 116–121 (1999)
- Erren, T.C., Pape, H.G., Reiter, R.J., Piekarski, C.: Chronodisruption and cancer. Die Naturwissenschaften 95(5), 367–382 (2008)
- Franzese, E., Nigri, G.: Night work as a possible risk factor for breast cancer in nurses. Correlation between the onset of tumors and alterations in blood melatonin levels. Professioni Infermieristiche 60(2), 89–93 (2007)
- van Hoof, J., Aarts, M.P.J., Rense, C.G., Schoutens, A.M.C.: Ambient bright light in dementia: Effects on behaviour and circadian rhythmicity. Building and Environment 44(1), 146–155 (2009)
- Riemersma-van der Lek, R.F., Swaab, D.F., Twisk, J., Hol, E.M., Hoogendijk, W.J., Van Someren, E.J.: Effect of bright light and melatonin on cognitive and noncognitive function in elderly residents of group care facilities: a randomized controlled trial. Jama 299(22), 2642–2655 (2008)
- Haffmans, P.M., Sival, R.C., Lucius, S.A., Cats, Q., van Gelder, L.: Bright light therapy and melatonin in motor restless behaviour in dementia: a placebo-controlled study. Int. J. Geriatr. Psychiatry 16(1), 106–110 (2001)

- 20. Skjerve, A., Bjorvatn, B., Holsten, F.: Light therapy for behavioural and psychological symptoms of dementia. Int. J. Geriatr. Psychiatry 19(6), 516–522 (2004)
- Friedman, L., Spira, A.P., Hernandez, B., Mather, C., Sheikh, J., Ancoli-Israel, S., Yesavage, J.A., Zeitzer, J.M.: Brief morning light treatment for sleep/wake disturbances in older memory-impaired individuals and their caregivers. Sleep Med. 13(5), 546–549 (2012)
- Rea, M.S., Bullough, J.D., Figueiro, M.G.: Phototransduction for human melatonin suppression. J. Pineal Res. 32(4), 209–213 (2002)
- DIN: DIN SPEC 5031-100:2012 Optical radiation physics and illuminating engineering -Part 100: Non-visual effects of ocular light on human beings - Quantities, symbols and action spectra. Beuth Verlag (2012)
- 24. Schierz: Ist die Beleuchtungsstärke am Auge die richtige Größe für biologische Lichtwirkungen? 4. DIN-Expertenforum, pp. 7–17. Beuth Verlag, Beuth (2010)