TU Ilmenau FG Lichttechnik
Prof. Dr. sc. nat. Christoph Schierz
Dr.-Ing. Cornelia Vandahl

Biological effects of light – Literature overview

1 Introduction

It has been known for considerable time that light does not only serve for obtaining visual information but also has great influence on bodily functions. Many new aspects have been established in recent years.

The non-visual information is received via light that falls onto our eyes and is conveyed via a nerve connection (retinohypothalamic tract RHT) to the suprachiasmatic nucleus (SCN). The SCN is the central circadian Zeitgeber for the day-night rhythm, for the control of the body temperature and many other functions. Figure 1 shows the schematic coherence.

The non-visual system has its own receptors located in the retina. They are light sensitive ganglion cells containing the photo pigment melanopsin [10], [25). They are called "intrinsically photosensitive retinal ganglion cells“ (ipRGC). There number is about 1-3% of all retinal ganglion cells. They also function as ganglion cells of the visual system at the same time and therefore also receive signals from the rods and cones. In case of a failure of the visual system they can continue to function independently [40].

The effect of light on the biological rhythm depends on the intensity of light, the duration of exposure, the time regime, and the time of day, the spectral composition and the spatial distribution of light. Effects have been verified even for low illuminance levels. Rea [47] has demonstrated effects at 18 lx (blue LEDs). Zeitzer [61] has established effects at 106 lx with polychromatic light from fluorescent lamps (4000K) and Smith [56] at 200 lx.

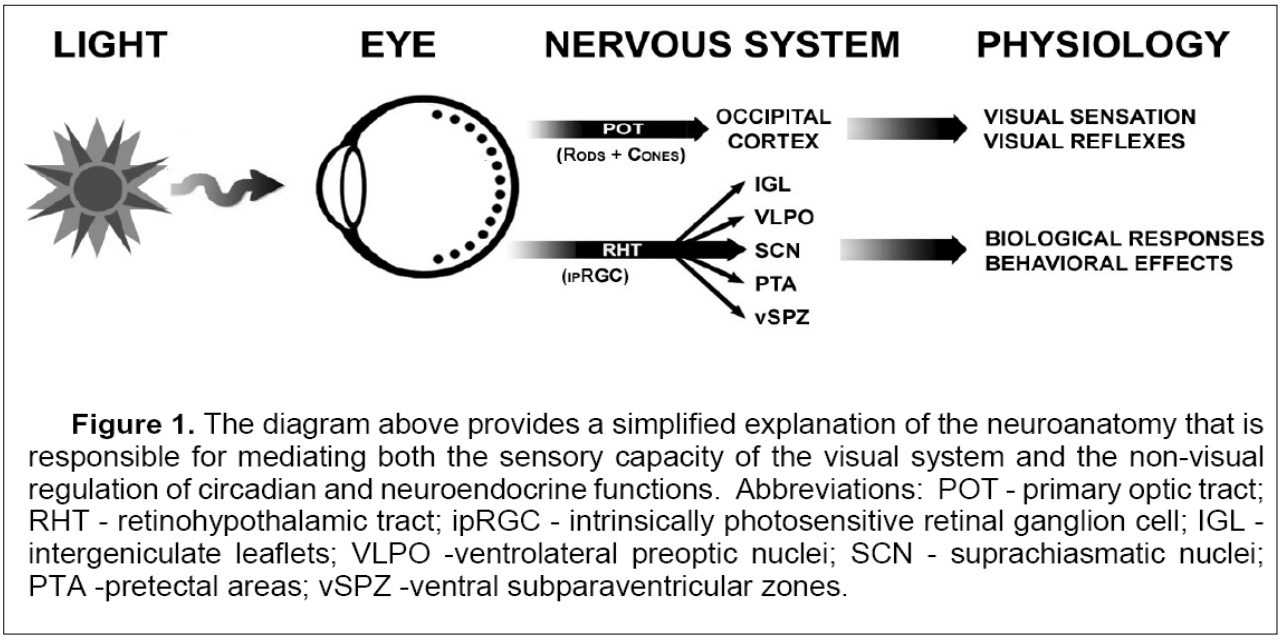

Figure 1. The diagram above provides a simplified explanation of the neuroanatomy that is responsible for mediating both the sensory capacity of the visual system and the non-visual regulation of circadian and neuroendocrine functions. Abbreviations: POT - primary optic tract; RHT - retinohypothalamic tract; ipRGC - intrinsically photosensitive retinal ganglion cell; IGL - intergeniculate leaflets; VLPO -ventrolateral preoptic nuclei; SCN - suprachiasmatic nuclei; PTA -pretectal areas; vSPZ -ventral subparaventricular zones.

Figure 1: Simplified schematic of visual and non-visual effects of light [10]

2 Effects of light on the circadian rhythm

The bodily functions of people are subject to a circadian (approximate day periodic) rhythmicity. This rhythmicity is generated by the SCN (Nucleus Suprachiasmaticus) and is about 24 hours [17]. The SCN acts as the inner clock controlling many physiological and psychological functions [18]. This rhythm manifests itself in changes of the body core temperature as well as the melatonin and cortisol levels. Furthermore it influences a multitude of other bodily functions (Figure 2).

The sleep-wake pattern of human can clearly be recognised. The minimum body core temperature is reached about 1 to 2 hours prior to awakening. The maximum of the melatonin synthesis is in the middle of the sleeping phase, about 2 to 3 hours before the minimum body core temperature (Figure 2) is reached. The beginning of the increase of melatonin levels, in other words, the maximum melatonin secretion or the minimum body core temperature are used for determining the individual phasing.

The phasing and the progression of the rhythmicity vary with the individuals. This results in the so called chrono-types. The morning chrono-types experience an earlier melatonin secretion compared to the evening chrono-types.

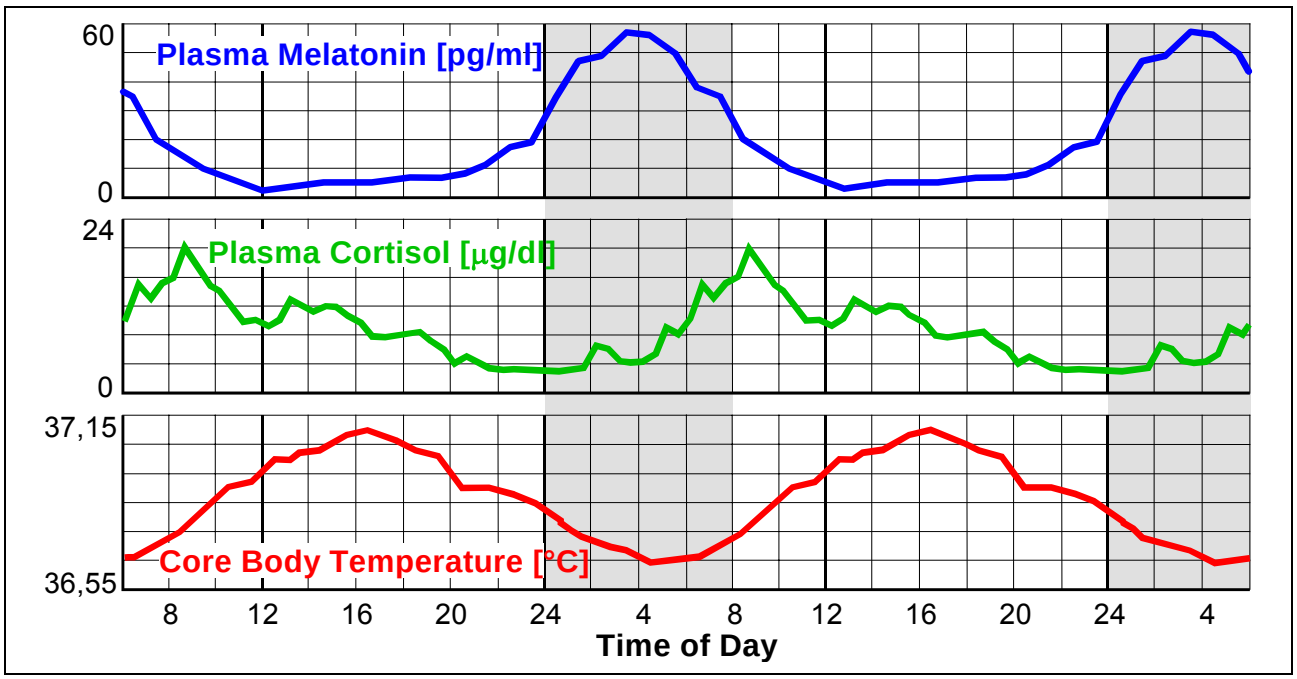

Figure 2: Circadian rhythmiticy of cortisol, melatonin and body core temperature (as per Hofstra [32]).

Sleep regulation depends on the circadian rhythm (circadian component, C) and the sleep homeostatic component, S. The homeostatic sleep propensity increases during the alertness phase and is reduced while sleeping.

The longer one is awake the greater it becomes. In the simplest case one can assume a linear progression [33]. Due to the increase of sleep propensity the homeostatic component of alertness rises during the day (Figure 3).

The circadian alertness component increases after awakening and decreases again after about 10 to 12 hours.

In a first approximation both components are additive. This assures that human can be awake during the whole day and subsequently enjoy a continuous sleep phase [8], [24],

[33], [36] (Figure 3). This cumulative curve of alertness must not be confused with the willingness to perform which varies with the time of day. More detailed models draw closer to the latter and take into account for instance the sleepiness after waking up [1] or the performance low experienced after noon [36].

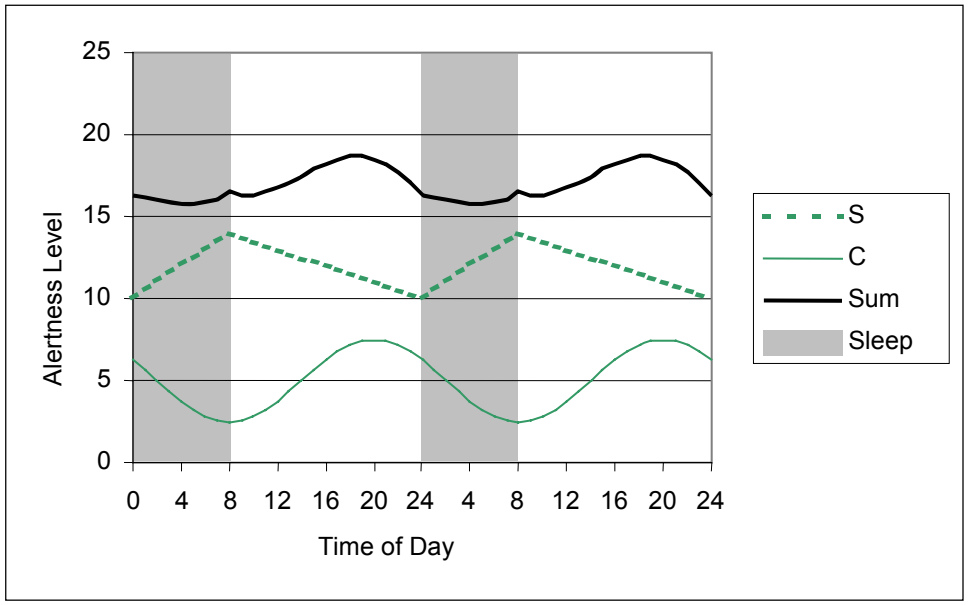

Figure 3: Homeostatic (S) and circadian (C) component of alertness level.

The total represents the alertness. It is lowest at night and thus facilitates a sleep phase lasting 8 hours (as per [8], [24], [33])

Since the duration of the circadian rhythm is not precisely 24 hours (in most cases it is somewhat longer than 24 hours) the inner clock must be synchronised by an external Zeitgeber. The decisive Zeitgeber is the bright-dark rhythm of daylight; other influencing factors are, amongst others, social surroundings, temperature changes during the course of the day and food intake.

The information regarding the availability of light is transported via special photo receptors in the eye to the inner, endogenous biological stimulator. This causes the suppression of melatonin secretion. Melatonin is transported via the blood circulation into all cells in the body and thus provides the information required for their synchronisation [18]. If the phasing of the inner clock does not coincide with the bright-dark phase of daylight (e. g: after intercontinental flights through several time zones) the synchronisation is also established via this mechanism.

For the synchronisation due to light the time of exposure is decisive. Light in the evening causes a phase delay and therefore delays the rhythm, since the body receives signals indicating it was still day. Accordingly light in the early morning causes a phase advance. Light at noon only has a very limited influence on phase-shifting. Furthermore the intensity, the spectral composition as well as the distribution of light in terms of time and space play a role.

3 Activation due to light

The alertness level can be increased with light. The subjective fatigue decreases respectively the subjective alertness increases with greater illuminance levels than 100 lx at the cornea. Such activating effects due to light have been established objectively on physiological parameters. The greatest effects can be achieved at 300 lx at the eye as per Cajochen [13].

Thus light has the potential to activate and to increase performance independently from the phasing of the inner clock. However, in studies it is quite difficult to separate potential effects of light from other variable factors of motivation. Laboratory studies permit the conclusion that high lighting levels do not only increase visual performance but generally improve work performance. This can be expressed by the reduced number of mistakes and an increased volume of work or better retentiveness. A comprehensive summary can be found at Cajochen [15].

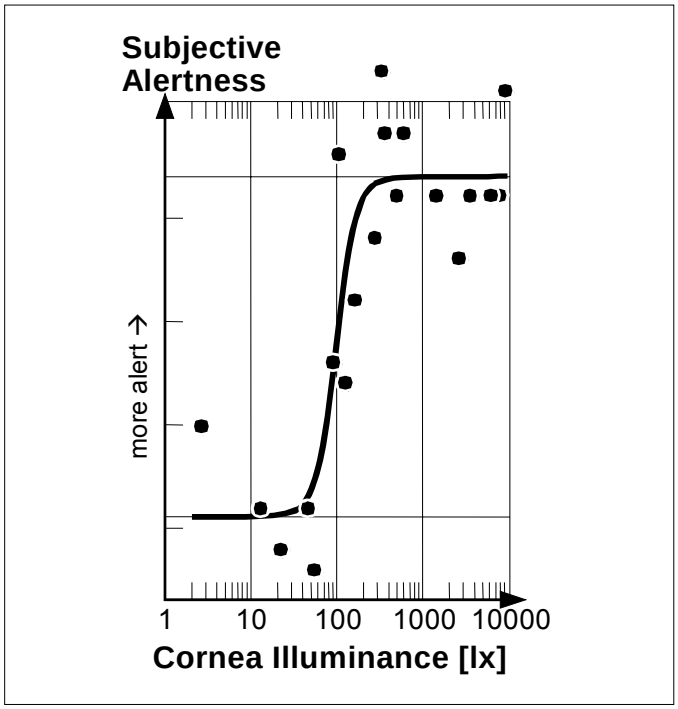

Figure 4:
Subjective alertness depending on cornea illuminance (Cajochen [13]).

4 Spectral effect of monochromatic light (overview as per Brainard [10])

Brainard names 8 action spectra in his publications [10] that were established in different research projects [3], [11], [27], [30], [31], [40]; [58], [61] on humans and animals using different methodologies. One example is the meanwhile well known curve as per Brainard [10] (Figure 5). All research was carried out using monochromatic light where the melatonin suppression was determined during the night. The results cannot be transferred to other times of the day or to polychromatic light by implication. However, they offer an excellent base for the development of a model for melatonin suppressing effects of light.

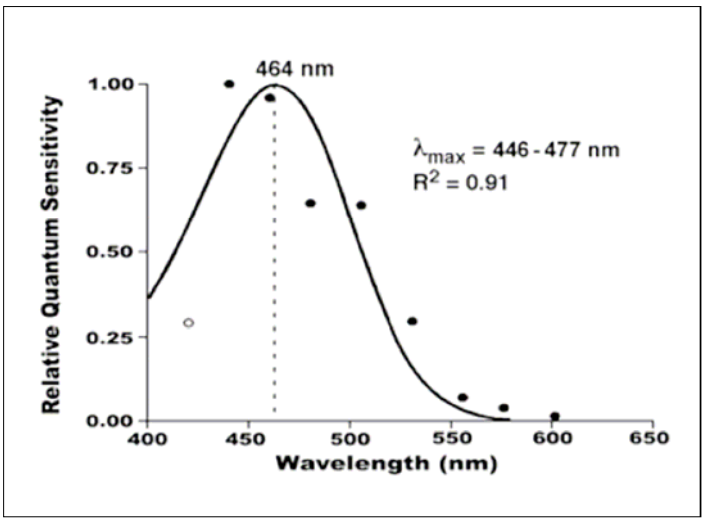

Figure 5:
Action spectrum for melatonin suppression in humans at night (Brainard [10])

5 Spectral effect as per DIN V 5031-100

Since 2009 the action spectrum $s_{ms}(\lambda)$ for nocturnal melatonin suppression is stipulated in DIN V 5031-100 [19] (Figure 6). This is based on the same measurements as the curve in Figure 5. However, in the short wave range it is based on the transmission curve of the human eye [26].

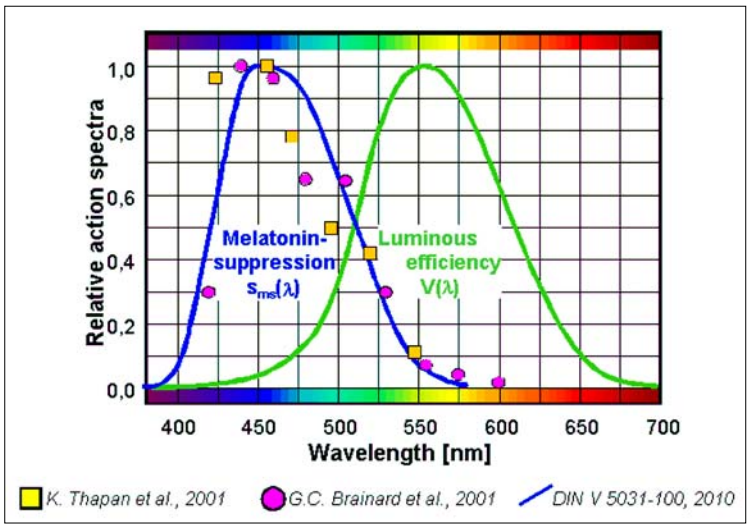

Figure 6:
Action spectrum for melatonin suppression in humans at night $s_{ms}(\lambda)$ (DIN [19]

In DIN V 5031-100 the following quantities for the evaluation of the biological effects of light are defined:

Biological evaluation:

$$X_{\text{biol}} = \int_{\lambda_1}^{\lambda_2} X_\lambda(\lambda) \cdot s_{\text{biol}}(\lambda) \cdot d\lambda$$

Biological action factor:

$$a_{\text{biol v}} = \frac{\int_{\lambda_2}^{\lambda_1} X_\lambda(\lambda) \cdot s_{\text{biol}}(\lambda) \cdot d\lambda}{\int_{380\,\text{nm}}^{780\,\text{nm}} X_\lambda(\lambda) \cdot V(\lambda) \cdot d\lambda}$$

X_{biol}	Quantity derived from radiant quantity X_e by evaluating the radiation according to its biological action
$a_{biol\ v}$	Biological action factor
$X_\lambda(\lambda)$	Spectral distribution of the radiation
$s_{biol}(\lambda)$	Action spectrum for biological effect, related to maximum $s_{biol,\max}(\lambda)=1$
$V(\lambda)$	Spectral luminous efficiency for photopic vision
λ_1, λ_2	Limiting wavelength

The defined spectral sensitivity $s_{ms}(\lambda)$ was used for the evaluation of the melatonin suppression:

$$X_{ms} = \int_{\lambda_1=380\,nm}^{\lambda_2=580\,nm} X_\lambda(\lambda)\cdot s_{ms}(\lambda)\cdot d\lambda$$

Besides the melatonin suppression light can also delay the circadian rhythm, can change the circadian amplitude and affect activation. Currently there are no exact findings regarding the action spectrum of these effects. There is, however, research [14], [38], that implies the action spectra are similar to those for the melatonin suppression. Therefore it is currently suggested to use this action spectrum for all effects mentioned.

Differing from this it is recommended to employ the V(λ) curve for the evaluation of effects of light in conjunction with the treatment of seasonally acquired depression (SAD). However, there is no scientific basis for this.

6 Spectral effect of polychromatic light

Figueiro [22], [23] and Rea [47] report of research where a comparison of the melatonin suppressing effects of two different types of radiation (LED and high pressure mercury vapour lamp) was carried out. The cornea illuminance generated by the LEDs was 18 lx that by the mercury vapour lamp was 450 lx. The effective radiation level (weighted as per the curve in Figure 5) was about twice as high for the mercury vapour lamp while the melatonin suppression was only half. According to Figueiro the yellow spectral components reduce the effectiveness of short wave light for the melatonin production at night; the circadian system does not work additively. Under certain circumstances the total effect may be less than the effect of the individual components. This effect is taken into account in a proposed effectiveness curve (Figure 7) which includes negative values that take into account the assumed compensatory effect of long wave radiation on the melatonin suppression.

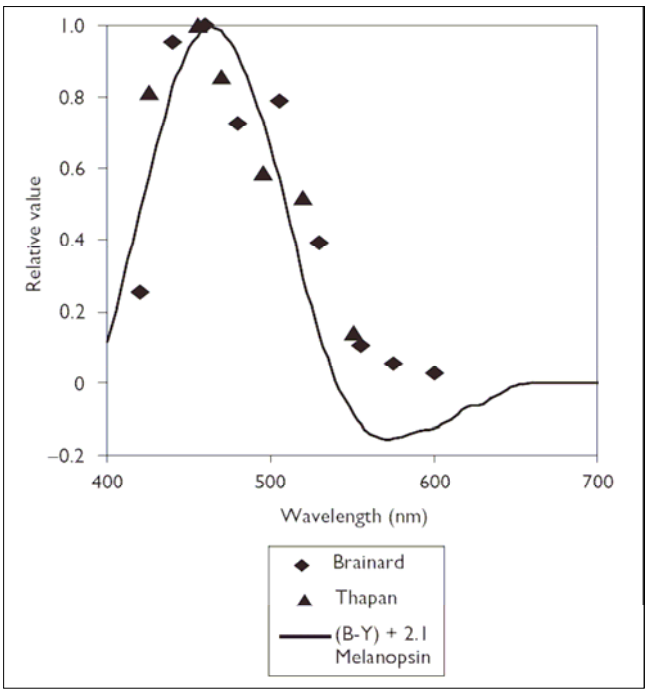

Figure 7:
Action spectrum for melatonin suppression in humans for polychromatic light (Figueiro [22])

In a further study by Rea [48] 4 white light sources (fluorescent lamps) with different correlated colour temperatures (CCT) were compared with each other. The suppressive effect on the concentration of melatonin in the blood was determined for two illuminance levels (300 lx and 600 lx) for each lamp type after one hour radiation at night. A higher level of melatonin suppression was found with all lamp types at the higher illuminance level. It was also determined that the CCT is not a reliable measure for describing the efficiency of the melatonin suppression. Lamps with lower CCT can facilitate the same or even higher melatonin suppression at night than lamps with a high correlated colour temperature at the same lighting level (Figure 8).

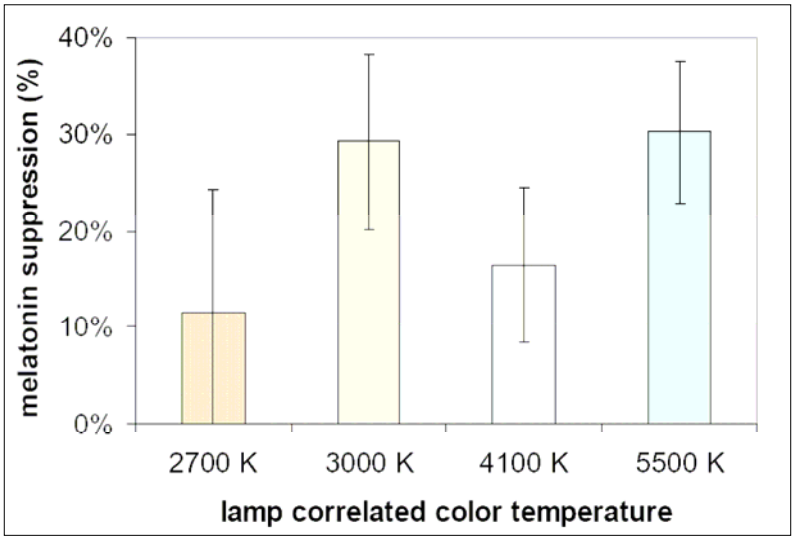

Figure 8:
Melatonin suppression for various colour temperatures (300 ... 600 lx) [48]

7 Dependency of the effect on the location of the illumination on the retina

More recent studies came to the conclusion that the different areas of the retina of the human eye respond with different sensitivity to light. From a research project [28] it can be deducted that light from above is more effective for the melatonin suppression than light from below (Figure 9). Lasko [37] also published similar results.

According to Rüger [52] lighting from the nose side is more effective than from the temples. This effect is less important since it is compensated for two-eye vision. Two eyes are more effective for the melatonin suppression than one on its own [59]...

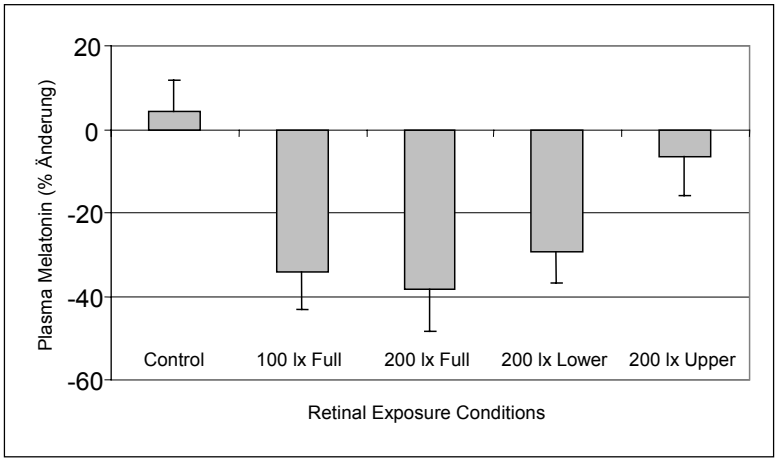

Figure 9:
Melatonin suppression subject to the size of the area [28]

Full: whole retina
Lower: lower retinal area
Upper: upper retinal area

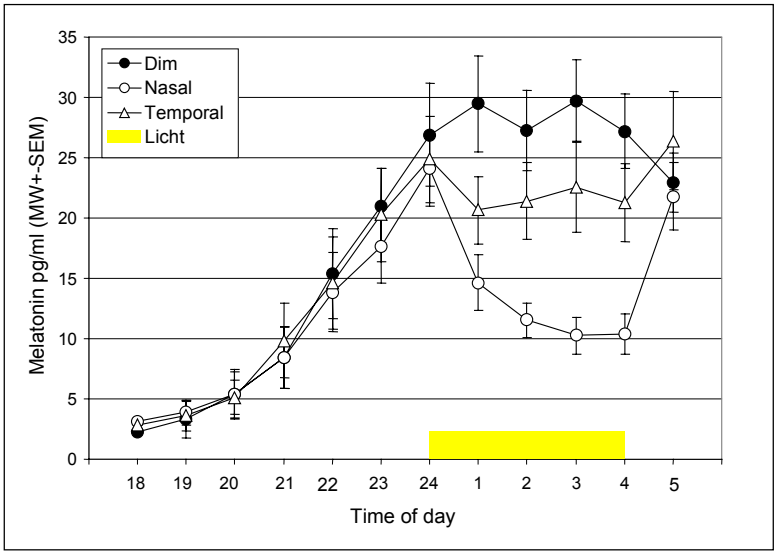

Figure 10:
Melatonin suppression subject to the retinal area [52]

Dim: no lighting
Nasal: lighting from the nose side
Temporal: lighting form the temples

8 Time dependency of the effect

Studies indicate that the sensitivity to light can vary over time. Figueiro describes a study [23] in which the melatonin suppression was compared for two light scenes (lighting with mercury vapour lamp at 450 lx and LED s at 18 lx) in two test periods of 1 hour each after midnight. It was established that the melatonin suppression was greater with both light sources during the second test compared to the first one (Figure 11).

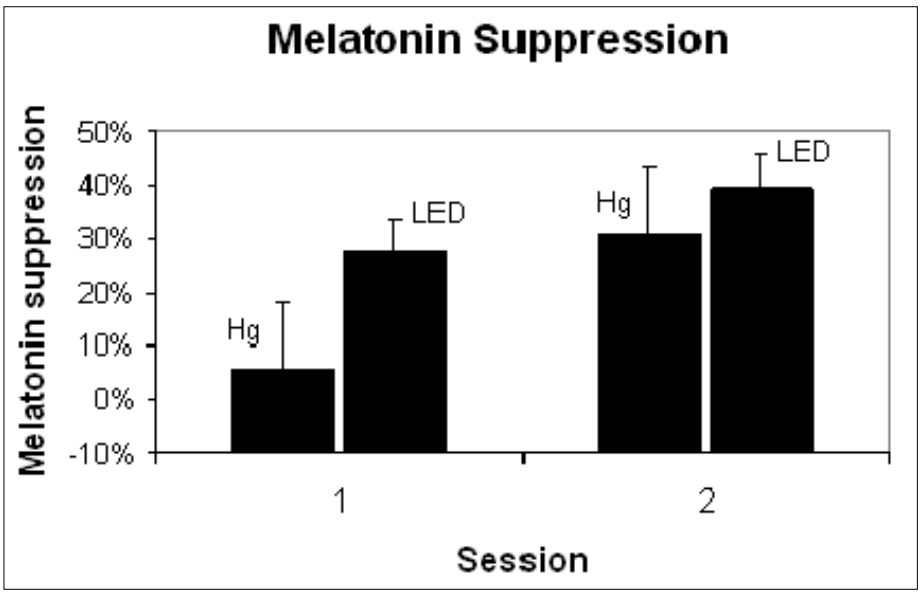

Figure 11:
Average melatonin suppression for two test periods of 1 hour each in the same night employing mercury vapour lamps and LEDs [23]

Another study by Smith [56] has also shown that the light scenes prior to the test have an influence on the effect of light. Figure 12 shows three different test periods of the light scenes. The cases B and C show exposure to 200 lx over 6.5 hours after midnight. The light scene prior to this test was significantly different (200 lx vs. 0.5 lx generated by fluorescent lamps with 4100 K in both cases). The influence of the progression over time on the melatonin content can be clearly seen. Similar or equal illuminance levels before and during the test (case A and B) show less impact than a considerable change of the lighting level.

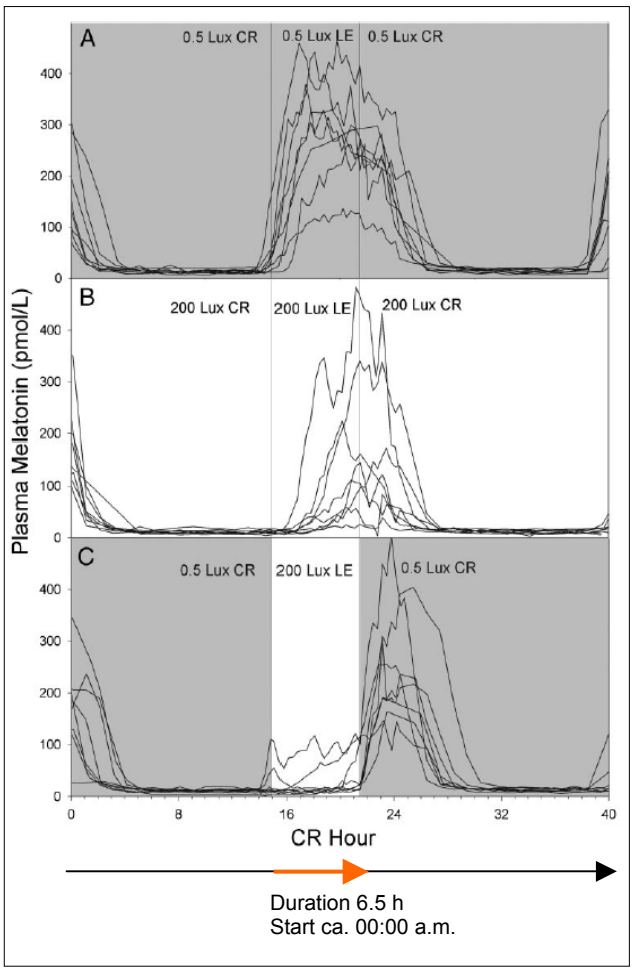

Figure 12:
Melatonin secretion for 3 different lihgting scenes over time, the graph shows the individual profiles for each of the 8 test persons [56]

Some studies [2], [7], [12], [29], [50] compare continuous lighting over time with a scenario of short times of exposure to very bright light. In all these studies high lighting levels were applied which allows the assumption that a saturation effect has already set in. 10 to 15 minutes bright light interrupted by 30 to 80 minutes of darkness practically have the same effect as continuous lighting with the same illuminance level (Figure 13). A summary and modelling can be found at Kronauer [35].

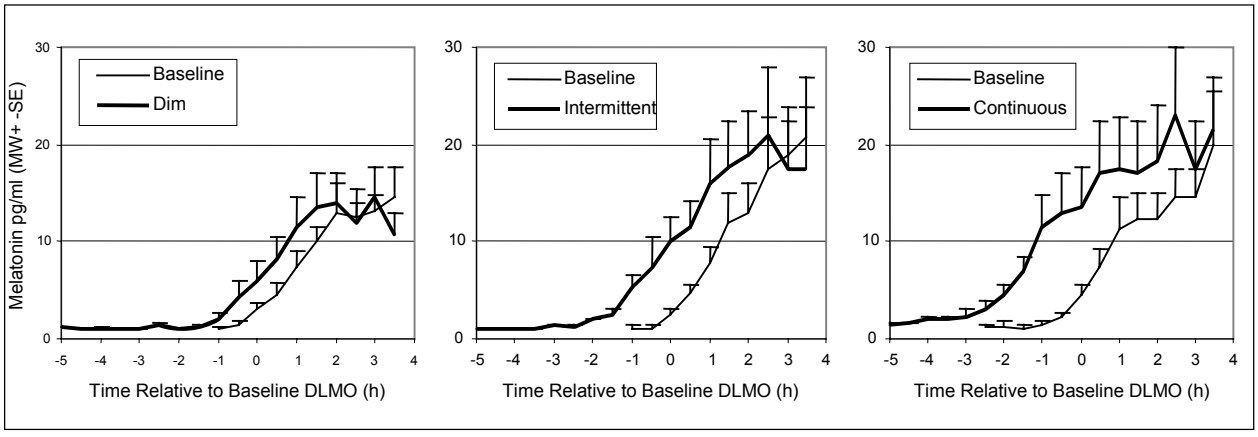

Figure 13:
Phase advance with 3.5 h light exposure each in the morning [12]; Dim: <60 lx, Intermittent: ca. 6000 lx / 60 lx alternately every 0.5 h, Continuous: ca. 6000 lx (with fluroescent lamps 4100 K), there is no significant variation betweeen intermittent and continuous illumination
(DLMO (Dark Light Melatonin Onset) Start of the melatonin secretion without lighting effect).

The intermittent lighting regime represents a good alternative for workplaces that cannot be illuminated continuously with sufficient lighting levels. For instance one could light the break room or cafeteria with such lighting and assure that workers get enough bright light by managing the schedule of coffee breaks.

9 Light and Dementia

A study by the TU Ilmenau [4], [5] researched the effect of light on people suffering from dementia. In a nursing home for the elderly a luminous ceiling was installed in the lounge area where lighting parameters such as illuminance level and colour temperature could be adjusted.

During a test series in February/March 2005 the light scenes were altered in phases in order to investigate the influence of the quality of light on the residents. During these tests the lighting level as well as the effective radiation intensity was increased considerably in phase II compared to phase I. The analysis has shown that in phase II with high lighting levels and high biological action spectra in the lounge area the test persons had less sleep phases during the day and enjoyed better sleep quality during the night. Furthermore it was established that even though there was no general improvement of the basic illness, a certain higher level of activity was noted which manifested itself by a better ability of orientation and higher emotional stability in phase II (Figure 14). Thus the quality of life of the people concerned can be improved due to increased initiative of the residents, better orientation and enhanced well-being.

Reports by other authors at the CIE convention 2006 in Ottawa [16] have shown similar results.

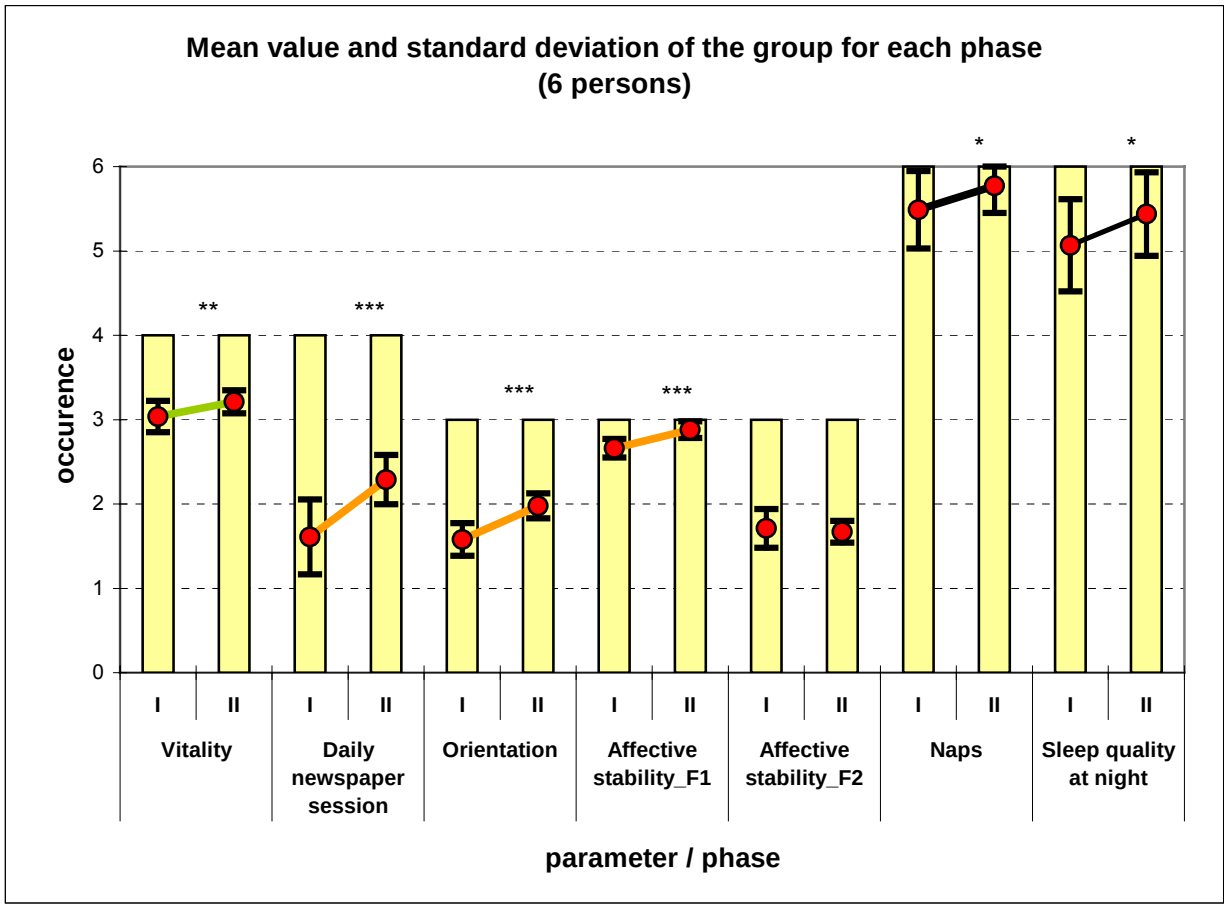

Figure 14: Change of behaviour of the test persons in phase II compared to phase I (significant changes are marked with *) [5]

10 Risk of cancer

There is a number of studies that indicate that exposure to light during the night can abet the development of cancer. However, there are also studies claiming the opposite.

About 30 global studies regarding the relationship between shift work and cancer have been evaluated at the Institute for Occupational Health, Social Medicine and Public Health at the University of Cologne [21]. One key result of these analyses is that in both researched groups of test persons – namely flight personnel and shift workers – a statistically significant increase of the risk of getting cancer was established. The risk increases with the number of years a person works shifts. An increased risk of about 40 – 70% compared to the non-shift working population is given.

Light could be one possible cause for this accumulation of cancer for shift workers. At night light prevents the production of the hormone melatonin which has been proven to initiate regeneration and repair processes. Melatonin also protects the cells from potential damage due to free radicals. Erren [20] provided an overview over these studies.

It is assumed that melatonin has an inhibiting effect against cancer [6], [55]. Research regarding shift work and sleeping behaviour of cancer patients also indicates an increased risk of cancer due to nightly exposure to light. Furthermore it is known that melatonin inhibits the production of estrogens. The estrogenic level increases if less melatonin is produced. Estrogens play an important role in the development of breast cancer. Here there is also an indication of a link to exposure to light at night.

In October 2007 the International Agency for Cancer Research (IARC), a facility of the World Health Organisation, has classified shift work at night as probably cancer-causing. In the explanatory statement is says: “Epidemiological studies have found that long-term night workers have a higher risk of breast cancer than women who do not work at night. … The studies are consistent with animal studies that demonstrate that constant light, dim light at night, or simulated chronic jet lag can substantially increase tumour development. Other experimental studies show that reducing melatonin levels at night increases the incidence or growth of tumours.“ [34].

A further summary can be found at Megdal [42], Pauley [45] and Stevens [57].

11 Summary

The following statements can be deducted from the given overview and in support of Boyce [9]:

1. It is known that light has an effect on the melatonin suppression but it does provide an explanation of the effects on the circadian processes. Anatomic studies have shown that the SCN is connected to many other parts of the brain such as the hypothalamus, the pituitary gland, the septum and the mesencephalon (midbrain). These parts regulate the production of a wide range of hormones which probably have an impact on many different physiological functions.
2. The spectral effect of polychromatic light (and thus for almost all relevant lighting applications) has only been researched in a small number of studies and thus is not yet securely defined.
3. The $s_{ms}(\lambda)$ curve only describes the melatonin suppressive effect of monochromatic light and thus only part of the biological effects of light.

4. There are research studies that show that other parameters also have an influence on the melatonin suppressing effect such as:
   - The local distribution on the retina
   - The point in time of exposure to light
   - The lighting scenarios of the previous hours and days (regarding lighting level, spectrum and time duration)

   All these parameters must be implemented into the action spectrum in order to be able to predict the effect.
5. It is also important to look for the negative effects of light on the circadian rhythm. The fact that there may well be negative effects is indicated by the relationship between light therapy and in case of SAD ailments and the accelerated growth of tumours in case of exposure to light during the night. These findings should serve as a warning against the hasty application of light as a measure for improving one's health.
6. The current level of knowledge is not sufficient for the deduction and development of control concepts for the lighting of work places. There are still many questions to be answered if light is to be used for stimulating the circadian system. Currently the spectral sensitivity, the relative spectral sensitivity of different retina zones, the question if adaptation processes exist as in the visual system, how the exposure to light over time can be integrated and the influence of the control over time of the exposure to light are of primary importance.

12 Literature overview

[1] Achermann, P., Borbély, A.A. (1994): Simulation of daytime vigilance by the additive interaction of a homeostatic and a circadian process. Biol. Cybern. Vol. 71, Nr. 2, S. 115-121.

[2] Baehr, E.K., Fogg, L.F., Eastman, C.I. (1999): Intermittent bright light and exercise to entrain human circadian rhythms to night work. American Journal of Physiology-Regulatory Integrative and Comparative Physiology, Vol. 277 Nr. 6 S. R1598-R1604

[3] Berson, D. M.; Dunn, F. A.; Takao, M.: Phototransduction by retinal ganglion cells that set the circadian clock, Science 295, pp. 1070-1073, 2002

[4] Bieske, K:; Dierbach, O.: Evaluation des Einsatzes von tageslichtähnlichem Kunstlicht in der gerontopsychiatrischen Pflege und Betreuung Hochbetagter, Tagung Licht und Gesundheit Berlin 2006

[5] Bieske, K.; Gall, D.; Vandahl, C.; Dierbach, O.: Influence of artifical light on gerontopsychiatric care of elderly people, Proc. Symp. „Lighting & Health" CIE x032:2006, pp.106-109

[6] Blask, D. E.; Brainard, G. C.; Dauchy, R. T.; Hanifin, J. P.; Davidson, L. K.; Krause, J. A.; Lynch, D. T.; Sauer, L. A., Jasser, S. A.: Melatonin Suppression by Ocular Light Exposure During Darkness: Impact on Cancer Growth and Implications for Cancer Risk in Humans, Proc. Symp. 2004 „Light & Health" CIE x027: 2004, pp. 42-45, 2004

[7] Boivin, D.B., James, F.O. (2005): Light treatment and circadian adaptation to shift work. Industrial Health, Vol. 43 Nr. 1 S. 34-48

[8] Borbely, A. A., Acherman, P., Trachsel, L. and Tobler, I. (1989): Sleep initiation and initial sleep intensity: interaction of homeostatic and circadian mechanisms. J. Biol. Rhythms Vol. 4 Nr. 2 S. 149-160.

[9] Boyce, P.: Implications for Lighting – What do we know? CIE Proc. Symp. „Lighting & Health“ Ottawa CIE x032:2006, pp. 27-31

[10] Brainard, G. C.; Hanifin, J. P.: The Effects of Llight on Human Health and Hehavior: Relevance to Architectural Lighting, Proc. Symp. 2004 „Light & Health“ CIE x027: 2004, pp. 2-16, 2004

[11] 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, pp. 6405-6412, 2001

[12] Burgess, H. J.; Crowley, S. J.; Gazda, C. J.; Fogg, L. F.; Eastman, C. I.: Preflight Adjustment to Eastward Travel: 3 Days of Advancing Sleep with and without Morning Bright Light, Journal of Biological Rhythms Vol. 18 No. 4, August 2003, pp. 318-328

[13] Cajochen, C., Zeitzer, J. M., Czeisler, C. A., & Dijk, D.-J. (2000). Dose-response relationship for light intensity and ocular and electroencephalographic correlates of human alertness. Behavioural Brain Research 115 (1), S. 75-83

[14] Cajochen, C., Münch, M., Kobialka, S., Kräuchi, K., Steiner, R., Oelhafen, P., Orgül, S., Wirz-Justice, A. (2005): High Sensitivity of Human Melatonin, Alertness, Thermoregulation, and Heart Rate to Short Wavelength Light. J of Clinical Endocrinology & Metabolism Vol. 90, No. 3 S. 1311-1316

[15] Cajochen, C. (2007): Alerting effects of light. Sleep Medicine Reviews, Vol. 11 Nr. 6 S. 453-464

[16] CIE Proc. Symp. „Lighting & Health“ Ottawa CIE x032: 2006

[17] Czeisler, C.A., Duffy, J.F., Shanahan, T.L., Brown, E.N., Mitchell, J.F., Rimmer, D.W., Ronda, J.M., Silva, E.J., Allan, J.S., Emens, J.S., Dijk, D.J., Kronauer, R.E. (1999): Stability, precision, and near 24-hour period of the human circadian pacemaker. Science Vol 284 S. 2177-2181.

[18] Dijk, D.J., Czeisler, C.A. (1995b): Contribution of the circadian pacemaker and the Sleep Homeostat to Sleep Propensity, Sleep Structure, Electroencephalographic Slow Waves, and Sleep Spindle Activity in Humans. The Journal of Neuroscience, Vol. 15 Nr. 5 S. 3526-3538

[19] DIN V 5031-100: Strahlungsphysik im optischen Bereich und Lichttechnik – Teil 100 : Über das Auge vermittelt, nichtvisuelle Wirkung des Lichts auf den Menschen – Größen, Formelzeichen und Wirkungsspektren

[20] Erren, T.C., Reiter, R.J., Piekarski, C. (2003): Light, timing of biological rhythms, and chronodisruption in man. Naturwissenschaften, Vol. 90 Nr. 11 S. 485-494.

[21] Erren, T.C., Reiter, R.J., Piekarski, C. (2008): Chronodisruption and melatonin: the need for sensible exposure metrics in epidemiological studies. Journal of Pineal Research, Vol. 45 Nr. 3 S. 335-336.

[22] Figueiro, M. G.; Bullough, J. D.; Parsons, R. H.; Rea, M.S.: Preliminary evidence for spectral opponency in the suppression of melatonin by light in humans, Neuroreport 5, pp. 313-316, 2004

[23] Figueiro, M. G.; Bullough, J. D.; Parsons, R. H.; Rea, M.S.: Preliminary evidence for a change in spectral sensitivity of the circadian system at night, Journal of circadian Rhythms 2005, 3:14

[24] Folkard, S., Akerstedt, T., Macdonald, I., Tucker, P., Spencer, M.B. (1999): Beyond the three-process model of alertness: Estimating phase, time on shift, and successive night effects. Journal of Biological Rhythms, Vol. 14 Nr. 6 S. 577-587.

[25] Foster, R. G.: Bright Blue Times. Nature 433, pp. 698-699, 2005

[26] Gall, Dietrich (2002): Circadiane Lichtgrößen und deren messtechnische Ermittlung Licht 54 (2002) 11/12, S. 1292–1297

[27] Gamlin, P. D.; Smith, V. C.; Dacey, D. M.; Pokorny, J.; McDougal, D. H.: Melanopsin-containing retinal ganglion cells drive the pupillary light reflex in the primate, Invest. Ophthalmol. Vis. Sci. 45, pp. ARVO E-Abstract 2262, 2004

[28] 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, Journal of Biological Rhythms, Vol. 18 No. 1, pp 71-79, 2003

[29] Gronfier, C., Wright, K.P., Kronauer, R. E., Jewett, M.E., Czeisler, C.A. (2004): Efficacy of a single sequence of intermittent bright light pulses for delaying circadian phase in humans. American Journal of Physiology-Endocrinology and Metabolism, Vol. 287 Nr. 1 S. E174-E181

[30] Hankins, M. W.; Lucas, R. J.: The primary visual pathway in humans is regulated according to long-term light exposure through the action of a nonclassical photopigment, Current Biology 12, pp. 191-198, 2002

[31] Hattar, S., Lucas, R. J.; Mrosovsky, N.;, Thompson, S.; Douglas, R. H.; Hankins, M. W.; Lem, J.; Biel, M.; Hofmann, F.; Foster, R. G.; Yau, K.-W.: Melanopsin and rod-cone photoreceptive systems account for all major accessory visual functions in mice, Nature 424, pp. 76-81, 2003

[32] Hofstra., W.A., de Weerd, Al W. (2008): How to assess circadian rhythm in humans: A review of literature. Epilepsy & Behavior Vol. 13 Nr. 3 S. 438–444.

[33] Horowitz, T.S., Tanigawa, T. (2002): Circadian-based new technologies for night workers. Industrial Health, Vol. 40 Nr. 3 S. 223-236.

[34] IARC (2007): IARC Monographs: http://www.iarc.fr/en/Media-Centre/IARC-Press-Releases/Communiques-recents/IARC-Monographs-Programme-finds-cancer-hazards-associated-with-shiftwork-painting-and-firefighting

[35] Kronauer; R.E., Forger, D.B., Jewett, M.E. (1999): Quantifying Human Circadian Pacemaker Response to Brief, Extended, and Repeated Light Stimuli over the Phototopic Range. Journal of Biological Rhythms, Vol. 14 No. 6, S. 501-515

[36] Kunz, D. (2006): Melatonin und Schlaf-Wach-Regulation. Habilitationsschrift Medizinische Fakultät der Charité Berlin

[37] Lasko T.A., Kripke D.F., Elliot J.A. (1999): Melatonin suppression by illumination of upper and lower visual fields. J. Biol. Rhythms Vol. 14 Nr. 2 S. 122-125

[38] Lockley, S. W.; Brainard, G. C.; Czeisler, C. A. (2003): High Sensitivity of the Human Circadian Melatonin Rhythm to Resetting by Short Wavelength Light. The Journal of Clinical Endocrinology & Metabolism 88(9): 4502-4505

[39] Lockley, S. W.: Light and Human Circadian Regulation, Proc. Symp. 2004 „Light & Health“ CIE x027: 2004, pp. 35-38, 2004

[40] Lucas, R. J.; Douglas, R. H.; Foster, R. G.: Characterization of an ocular photopigment capable of driving pupillary constriction in mice, Nature Neurosci. 4, pp. 621-626, 2001

[41] Lucas, R. J.; Foster, R. G., Hankins, M. W.; Barnard, A. R.: Melanopsin, Photosensitive Retinal Ganglion Cells and Non-Image Forming response to Light, Proc. Symp. 2004 „Light & Health“ CIE x027: 2004, pp. 21-26, 2004

[42] Megdal, S.P., Kroenke, C.H., Laden, F., Pukkala, E., Schernhammer, E.S. (2005): Night work and breast cancer risk: A systematic review and meta-analysis. European Journal of Cancer, Vol. 41 Nr. 13 S. 2023-2032.

[43] Melyan, Z.; Tarttelin, E. E.; Bellingham, J.; Lucas, R. J.; Hankins, M. W.: Addition of human melanopsin renders mammalian cells photoresponsive, Nature 433, pp. 741-745, 2005

[44] Panda, S.; Nayak, S. K.; Cambo, B.; Walker, J. R.; Hogenesch, J. B.; Jegla, T.: Illumination of melatonin signaling pathway, Science 307, pp. 600-604, 2005

[45] Pauley, S.M. (2004): Lighting for the human circadian clock: recent research indicates that lighting has become a public health issue. Medical Hypotheses, Vol. 63 Nr. 4 S.588-596.

[46] Qiu, X.; Kumbalasiri, T.; Carlson, S. M.; Wong, K. Y.; Krishna, V.: Provencio, I.; Berson, D.: Induction of photosensitivity by heterologous expression of melatonin, Nature 433, pp. 745-749, 2005

[47] Rea, M. S.; Bullough, J. D.; Figueiro, M. G.; Bierman, A.: Spectral Opponency in Human Circadian Phototransduction: Implications for Lighting Practice, Proc. Symp. 2004 „Light & Health“ CIE x027: 2004, pp. 111-115, 2004

[48] Rea, M. S.; Bullough, J. D.; Bierman, A,; Figueiro, M. G.: Implications for White Light Sources of Different Correlated Color Temperatures. CIE Proc. Symp. „Lighting & Health“ Ottawa CIE x032: 2006, pp. 33-38

[49] Revell, V. L; Burgess, H. L.; Gazda, C. J.;Smith, M. R.; Fogg, L. F.; Eastman, C. I.: Advancing Human Circadian Rhythms with Afternoon Melatonin and Morning Intermittent Bright Light, J Clin Endocrinol Metab, January 2006, 91(1):54–59 55

[50] Rimmer, D.W., Boivin, D.B., Shanahan, T.L., Kronauer, R.E., Duffy, J.F., Czeisler, C.A. (2000): Dynamic resetting of the human circadian pacemaker by intermittent bright light. American Journal of Physiology-Regulatory Integrative and Comparative Physiology, Vol. 279 Nr. 5 S. R1574-R1579

[51] Rüger, M. (2005): Lighting up the human circadian clock. Dissertation Universität Groningen

[52] Rüger, M.; Gordijn, M.C.M.; Beersma, D.G.M.; Vries, B.; Daan, S. (2005): Nasal versus temporal illumination of the human retina: effects on core body temperature, melatonin, and circadian phase. J of Biological Rhythms, Vol. 20 Nr. 1 S. 60-70

[53] Rüger, M., Gordijn, M.C.M., Beersma, D.G.M., de Vries, B., Daan, S. (2006): Time-of-day-dependent effects of bright light exposure on human psychophysiology: comparison of daytime and nighttime exposure. Am J Physiol Regul Integr Comp Physiol Vol. 290 S. R1413-20

[54] Sato, M.; Hiroki, N.; Takeshi, M.: The Effect of the Light with Different Spectral Ditribution During the Night Time on Melatonin Secretion and Psychological Factors in Humans, Proc. Symp. 2004 „Light & Health“ CIE x027: 2004, pp. 206-208, 2004

[55] Schernhammer, E.; Schulmeister, K.: Epidemiology of Night Work and Cancer Risk, Proc. Symp. 2004 „Light & Health“ CIE x027: 2004, pp. 46-49, 2004

[56] Smith, K. A.; Schoen, M. W.; Czeisler, C. A.: Adaptation of Human Pineal Melatonin Suppression by Recent Photic History, J Clin Endocrinol Metab, July 2004, 89(7):3610–3614

[57] Stevens, R.G. (2006): Artificial lighting in the industrialized world: Circadian disruption and breast cancer. Cancer Causes & Control, Vol. 17 Nr. 4 S. 501-507.

[58] 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, pp. 261-267, 2001

[59] Wang J.Y., Hanifin J.P., Rollag M.D., Brainard G.C. (1999): Ocular regulation of the human pineal gland: The significance of total retinal exposure for melatonin suppression. Biologic Effects of Light 1998, Kluwer Boston, S. 367-373.

[60] Yoshimura, T.; Ebihara, S.: Spectral sensitivity of photoreceptors mediating phase-shifts of circadian rhythms in retinally degenerate CBA/J (rd/rd) and normal CBA/N (+/+) mice, J. Comp. Physiol. [A] 178, pp. 797-802, 1996

[61] Zeitzer, J. M.; Dijk, D. J.; Kronauer, R. E.; Brown, E. N.; Czeisler, C.A.: Sensitivity of the human circadian pacemaker to nocturnal light: melatonin phase resetting and suppression, Journal of Physiology 526.3, pp. 695-702, 2000