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Abstracts

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A1

Usage of Daylight in the Built Environment: Impact on Health

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Objectives: When entering a building, the characteristics of sunlight alters. How does this impact the users and what measures can be taken to overcome this?

Methods: Literature study.

Results: The sun is being acknowledged as the mother of all light sources; the source that enables life on earth as we know it. It therefore claims to have multiple health advantages. Some of these claims are associations, hypotheses or beliefs, while others have scientific evidence. The radiation emitted by the sun is filtered by the atmosphere, leaving a solar radiation at the Earth's surface mainly in the wavelength range from 200 to 4000 nm. The portion of this range to which the photosensitive sensors in the eye, related to vision (rods and cones) are sensitive – referred to as light – has a wavelength between 380 nm and 780 nm. Radiation with a wavelength between 100 nm and 400 nm is called ultraviolet (UV) radiation. Radiation with wavelength between 780 nm and 1 mm is called infrared (IR) and gives a thermal sensation on the skin.

Humans have evolved under the influence of daylight and the light–dark cycle. On the one hand, the human skin provides a layer of pigmentation to protect us from the highest radiation intensities when exposed to solar radiation. On the other hand, humans have developed a variety of physiological responses to the varied characteristics of daylight. Daylight was the main light source until electrical light became reliable and affordable. Since the introduction of electrical light, a large part of the Western society spends already 80–90% of their time inside buildings. It sometimes even appears as if daylight has only an architectural value, and all other daylight functions have been replaced by electrical lighting solutions.

We currently know that typical daylight exposure has an impact on human health via two biological systems:

1. Skin. When considering the health effects of sunlight via the skin, the shorter wavelengths of the solar radiation (UVB) seem to have the largest impact on health since it triggers the production of Vitamin D. Vitamin D deficiency can lead to rickets (children) and brittle bones in adults. Furthermore, lack of vitamin D also seem to impact certain types of internal cancer.

2. Eyes. Light activating the photosensitive sensors in the eyes allows people to perceive the environment. Next to the visual functions, light activates other, non-vision related effects, so called non-image forming (NIF) effects

Conclusions: Since the amount, the composition and the directionality of sunlight alters when entering a building it is to be expected that it also influences the well-being and health of people. A limited number of studies showed the impact of lack of daylight exposure in the built environment on health. What measures can be taken to overcome these issues.

Funding/Disclosures: None.

A2

A Single Night Light Exposure Acutely Alters Hormonal and Metabolic Responses in Healthy Participants

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Objectives: This study aims to investigate the impact of light at night and/or melatonin on plasma hormones and metabolites prior to and after a late evening meal in healthy young participants.

Methods: A favourable ethical opinion was obtained from the University Ethics Committee (EC/2013/93/FHMS). Seventeen healthy participants, 8 females [22.2 ± 2.59 years, body mass index (BMI) 23.62 ± 2.3 kg/m^2], 9 males [22.8 ± 3.5 years, BMI 23.8 ± 2.06 kg/m^2 (mean ± SD)] were enrolled. We randomized participants to dim light condition (<5 lx) and bright light condition (>500 lx), separated by at least seven days in a two way cross over design protocol. Each clinical session commenced at 18:00 h and finished at 06:00 h the next day. Participants consumed an isocaloric and non-carbonated evening meal (1066 Kcal, 38 g protein, 104 g CHO, 54 g fat, 7 g fibre). The meal times were individualised based on dim light melatonin onset (DLMO) estimated from participants' 48-h sequential urine collection. Preprandial and postprandial plasma samples were collected at specific time intervals to assess glucose, insulin, triacylglycerol (TAG) and non-esterified fatty acids (NEFAs) concentrations. Saliva samples were collected every 30 minutes (18:00–06:00 h) to assess melatonin levels. Statistical analysis was carried out using Statsoft STATISTICA with three factor repeated measures ANOVA (gender, time, treatment). The significance level was set at $p < 0.05$.

Results: Salivary melatonin levels were significantly higher in the dim light condition compared to bright light condition ($p = 0.005$). Plasma NEFAs responses were also significantly higher in dim light condition ($p < 0.01$), post hoc tests showed that the significant NEFA response was directly prior to the meal ($T = 0$). In contrast, plasma glucose and insulin levels were significantly greater in the bright light compared to dim light conditions ($p = 0.02$, $p = 0.001$) respectively. The post hoc test revealed the differences in glucose levels occurred at the 180 min and 210 min after the meal, while insulin response was significantly different at 180, 210 and 270 min after the meal. No significant difference was seen

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in plasma TAG. There were significant effects of time in all 5 measures, whereas no significant effects of gender were seen. TAUC and Student's t-test confirmed the significant differences obtained from ANOVA.

Conclusions: Melatonin suppression related to light intensity was expected. Melatonin has been reported to be involved in lipid metabolism and this could explain our finding of raised NEFA responses associated with melatonin release prior to the meal in the dim light condition (Rios-Lugo et al. 2010). Changes in insulin sensitivity could explain our finding of postprandial plasma glucose levels that were greater in bright light than in dim light despite the presence of higher insulin levels in the bright light condition. The significant reduction in insulin levels under the dim light condition may relate to the release of melatonin from dim light exposure (Coomans et al. 2013; McMullan et al. 2013).

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A3

Molecular Markers to Assess Circadian Phase

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Chronotyping an individual (i.e. assessing the phase of entrainment) is currently done either by questionnaires, such as the Munich Chronotype Questionnaire (MCTQ) or by determining physiological or behavioral parameters using many repeated measurements. Questionnaires are intrinsically not objective since they depend on an individual's own declarations. Furthermore, they do not assess an acute chronobiological state but rather ask for an overall preference or description of sleep habits. More objective alternatives such as determination of DLMO (dim light melatonin onset) are tedious and require special settings.

We present a new diagnostic approach to probe human internal time using a single blood sample. The principle of the method is based on the fact that about 10% of all genes are rhythmically transcribed in nearly all human cells with their phases being gene-dependent. The relative levels of oscillating transcripts are therefore unique at any given circadian phase. Details will be presented at the meeting.

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A4

Delayed Sleep Onset Latency, Poor Sleep Quality and Blunted Positive Affect in Evening Types: Experimental Findings and Implications for Treatment

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Objectives: Evening chronotypes have been repeatedly associated with depression but the mechanisms underlying this association remain unclear. Some research has shown that evening types suffer from poor sleep quality, but results have been inconsistent across studies. Also few studies in small samples have shown blunted positive affect levels in evening types. Biases in the emotion information processing of evening types have also been found. The aim of this study was to further investigate such underlying potential mechanisms of the eveningness-depression link by assessing differences in these known vulnerability factors of depression, namely low sleep quality, negative biases in emotional cognition, and low positive affect, in morning and evening chronotypes. This is the first study to investigate such a spectrum of vulnerability factors of depression in relation to chronotypes in a single design.

Methods: 69 participants (29 morning types and 40 evening types) participated in the study. Sleep quality was investigated during a 7 day period using actigraphy, a sleep diary, and self-report measures [Pittsburgh Sleep Quality Index (PSQI)]. Participants also completed an affective go/no-go task (which is a response inhibition task for positive and negative words) and the Positive and Negative Affect Schedule (PANAS) at two time points (morning and evening hours).

Results: Evening types showed significantly longer sleep onset latencies than morning types as shown through actigraphy. They also reported significantly worse sleep quality, as shown by a higher PSQI total score. Evening types also reported lower positive affect in the morning session compared to morning types. There were no differences between chronotypes on other sleep parameters and on the affective go/no-go task.

Conclusions: Compared to morning types, evening types showed difficulties falling asleep, reported worse sleep quality, and had blunted positive affect in the morning hours. All these factors could make (healthy) evening types more vulnerable to depression. Preventive strategies could entail the regulation of the sleep-wake rhythm to improve sleep quality in combination with behavioral interventions to improve mood early in the day.

Funding/Disclosures: None.

A5

Lunar Tidal Cycles in a Rapid Cycling Bipolar Patient

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Objectives: We examined the relationship between the spring-neap tidal cycle and 4 months of sleep log data of a rapid cycling bipolar patient. Wehr (Molecular Psychiatry 2017, Jan 24, Epub ahead of print) found that in 17 patients with rapid cycling bipolar disorder, time-series analyses detected synchronies between the mood cycles and lunar tidal cycles including the 14.8 day spring-neap cycle. In 2004, at age 34, this rapid cycling bipolar patient had been hospitalized with insomnia, suicidal ideation, and visual and auditory hallucinations. He had noted an episodic change in his sleep pattern while living in a very dark bedroom over the 1.5 years prior to admission. He had periods of increased sleep, up to 12 hours per day, alternating with short sleep periods, 0–3 hours per day. During the long sleep periods, he was very depressed, lethargic and slowed down. During the short sleep periods, he was usually not depressed, had rapid thoughts, was easily distracted and could not calm down. He was treated with a regular light-dark cycle with a 12-hour photoperiod. On follow-up in March, 2017, he reported that in January 2005 he had discontinued all his psychiatric medications, kept his light-dark cycle regular and had been free of both mood and sleep instability since then.

Methods: We plotted the sleep onsets, times of wake onsets, and sleep durations for that four-month period in relation to the lunar tidal cycle, the spring-neap cycle. A periodogram was performed on the times of awakenings.

Results: The plot of the sleep-wake data showed a clear periodic fluctuation of the duration of sleep, ranging between 0 and 12 hours of sleep per 24 hours with no clear change in the timing of the midpoint of sleep. The times of sleep-onset and wake-onset would alternately advance and delay their phase-positions repeatedly, and they did so in anti-phase to each other. The times of wake onset had a periodicity of 14.765 days, very similar to the periodicity of the lunar tidal spring-neap cycle. In addition, the times of the new moons and full moons were coincident with the times of the short sleep durations.

Conclusions: The lunar tidal spring-neap cycle appeared to have a significant impact on the sleep and mood of this bipolar patient. The morning and evening oscillators of his circadian system appeared split and in anti-phase. Questions remain concerning the mechanisms by which the lunar tidal cycles could influence sleep-wake cycles and what factors made this patient vulnerable to this effect. In light of previous research, the patient's mood changes could be explained as resulting from the changes in timing and duration of sleep that appear to have been caused by the lunar cycles.

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A6

Proceedings of the Bright Up Study: Light Therapy in Antepartum Depression

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Objectives: In this study, we will primarily study the effects of BLT on depression during pregnancy. Second, we will study whether this clinical improvement is accompanied by improved sleep quality and normalized melatonin and cortisol levels. Third, we will study the effects of BLT on gestational age, birth weight, infant behavior, infant cortisol stress response and long-term cortisol exposure of the infant. We will present the study protocol and preliminary results.

Methods: In this study, we aim to randomly allocate 150 pregnant women (12–18 weeks pregnant) with a DSM-V diagnosis of depressive disorder in a 1:1 ratio to one of the two treatment arms: treatment with BLT (9.000 lux) or treatment with dim red light therapy (100 lux). Both groups will be treated for 6 weeks at home on a daily basis for 30 minutes, within 30 minutes of habitual wake-up time. Follow-up will take place after 6 weeks of therapy, 3 and 10 weeks after end of therapy, at birth and 2, 6 and 18 months postpartum. Primary outcome will be the average change in depressive symptoms between the two groups, as measured by the Structured Interview Guide for the Hamilton Depression Scale – Seasonal Affective Disorder version and the Edinburgh Postnatal Depression Scale (EPDS). Changes in rating scale scores of these questionnaires over time will be analysed using generalized linear mixed models. Secondary outcomes will be the changes in maternal cortisol and melatonin levels, in maternal sleep quality and gestational age, birth weight and infant behaviour, cortisol exposure and cortisol stress response.

Results: We will present data on baseline characteristics, including comorbidity, chronotype, and symptom scores. After 5 months of recruitment, we have included 8 women. In April 2017, 28 women signed up for participation, of which 10 did not meet the inclusion criteria. Ten women refused participation or did not respond. Two women dropped out. Comorbidities in this study sample are PTSD (2), drug and alcohol abuse (2), panic disorder and social phobia (3). Five women experienced depression in the past. Three women used antidepressant medication. At inclusion, the following chronotypes were scored with the Munich Chronotype Questionnaire: moderate early, slight early (2), normal (2), slight late and extreme late (2). At inclusion, mean EPDS is 12.9 and mean 17-item Hamilton score is 11.8.

Conclusions: The Bright Up study is an ongoing study in The Netherlands, in which we study the effects of light therapy in antepartum depression. This study is the first to study these effects in a large study sample and to study these effects in the child.

Funding/Disclosures: The study is funded by The Netherlands Organization for Health Research and Development (ZonMw), in collaboration with Philips Lighting (grant number 058-14-003).

A7

Imaging and Genetic of Response

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Exciting new findings link exposure to light and dark, and the sleep-wake cycle, with core neurobiological processes of the brain which could provide a biological underpinning of the therapeutic effects of chronobiological techniques in psychiatry. Neurotransmitter switching is influenced by light, and regulates behavior. Cortico-limbic neural responses to emotional stimuli are influenced by the previous exposure to light. Clock gene variants influence brain function and structure. Sleep and sleep phase are associated with neurotransmitter function, synaptic remodeling, water homeostasis and the clearance of metabolic byproducts. At the behavioral level, the effects reveal as attitudes and cognitive styles which bias vulnerability to depression and to suicide.

Investigating the correlates of antidepressant response in patients treated with chronotherapeutic techniques allowed to identify changes in brain neurotransmitters and in brain function and structure which can be investigated with in vivo neuroimaging techniques and which are influenced by genetic variants. In recent years, remission after chronotherapeutics has been shown to be associated with effective connectivity in cortico-limbic circuitries during the processing of emotional stimuli, with changes in brain imaging markers of neurotransmitter function, with measures of cortical synaptic weights. These effects provide intermediate phenotypes associated with therapeutic effects of chronobiology, and new targets for treatments.

Funding/Disclosures: None.

A8

On the Integration of Non-Image-Forming (NIF) Effects of Light on Venetian Blinds and Electric Lighting Control

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Objectives: Lighting has an impact not only on our visual comfort and performance, but also on our behavior and physiology: it is shown that exposure to light can directly boost alertness, cognitive performance, and improve our mood. These non-visual effects of light are also called "Non-Image Forming" (NIF) effects. Considering NIF effects in lighting of indoor working environments can be very important to improve well-being and productivity of the users. So far, these effects have not been considered in building automation due to their unknown and complicated nature, as well as lack of proper technology. The objective of this study is to introduce and evaluate NIF effects of light on humans in control algorithms used for automatic regulation of venetian shadings and electric lighting in an office environment, always with an eye on energy saving. In other words, the existing scientific knowledge of NIF effects of light is introduced into the lighting engineering and automation domain.

Methods: A dynamic lighting protocol based on guidelines for biologically effective illumination and literature review is chosen as a set point for the integrated daylight and electric lighting system. An advanced control system based on room geometry, sun profile and fuzzy logic is designed to follow the protocol while ensuring the visual comfort of the user by regulating sun shadings and artificial lighting. Prioritizing the use of daylight rather than electric lighting pursues the objective of energy savings, thus the latter is activated only when natural lighting is not sufficient to reach the required work-plane illuminance. The assessment of the lighting conditions in the room is carried-out using a novel HDR vision sensor installed next to the user, which allows for an "on-the-fly" evaluation of the light flux received by the human eyes during daytime. The sensor continuously captures luminance maps and extracts the pupillary illuminance and the glare index "Daylight Glare Probability" (DGP). At the same time a second, identical sensor placed on the ceiling monitors the average luminance of part of the field of view to compute the horizontal work plane illuminance. Being integrated in the building control platform, both HDR vision sensors offer a personalized, refined control of the integrated electric lighting and sun shading system.

Results: A field study with human subjects will be carried out in the LESO solar experimental building in order to test the performance of the controller from an energy saving and occupant's visual/cognitive performance perspective. Different aspects like visual comfort and performance, neurobehavioral performance, alertness and mood are assessed by means of paper- and computer-based tests, as well as subjective surveys.

Conclusions: With respect to a reference case, the advanced control strategy is expected to bring significant energy savings as well as improved users' overall comfort, visual and cognitive performance.

Funding/Disclosures: None.

A9

Sand Rats See the Light: Use of Diurnal Rodents for the Study of Depression

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Objectives: Our general objective is using diurnal rodents for the study of the interactions between circadian rhythms and depression.

Methods: We maintained different diurnal species under short photoperiod conditions (SP; 5 hours light/ 19 hours dark) or neutral photoperiod conditions (NP; 12 hours light/ 12 hours dark) for 3 weeks. Species tested included fat sand rat (*Psammomis obesus*), Nile grass rat (*Arvicanthis Niloticus*), degu (*Octodon degus*) and golden spiny mouse (*Acomys russatus*). We also treated the animals with antidepressants (bupropion and imipramine), tested the effects of exercise and bright light treatment (white blue and red).

Results: Diurnal rodents maintained under SP developed depression- and anxiety-like phenotype which includes reduced activity in the forced swim test, reduced preference for sweet solution, reduced aggression and social interactions, and increased anxiety-like behavior in tests such as the elevated plus-maze and the open field. Bupropion and imipramine treatments, as well as physical exercise resulted in amelioration of the SP-induced behavioral changes in the sand rat. When we exposed the sand rats to 3 weeks of morning bright (white) light treatment it ameliorated the behavioral effects of SP, and morning exposure to bright light had a significantly stronger effect than evening exposure to bright light. Morning blue, but not red light treatment, resulted in similar effect. Although a direct comparison between the bright light experiments and the bupropion experiment is impossible (different experiments) we suggest that as in humans, bright light exposure is at least as effective as antidepressants in the model.

Conclusions: Wealth of research results now establishes the validity of diurnal rodents as a model for studying the interactions between circadian rhythms and depression. Diurnal rodents respond to photoperiod manipulation in a similar way to humans, the behavioral outcome is directly related to the circadian system, and treatments that are effective in patients are also effective in the model, whereas less effective treatments in patients are also less effective in the model. We suggest that using diurnal animal models to study circadian rhythms related affective disorders such as depression will produce new insights which will eventually lead to the development of more effective treatments.

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A10

Melatonin Production in Essential Hypertension Under Common and Modified Light Schedules

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Objectives: According to numerous data, the pathogenesis of cardiovascular diseases is associated with desynchronization of biological rhythms. Nowadays many people are exposed to excessive light at night which results in the inhibition of melatonin secretion by the pineal gland. In this study we explored the biosynthesis of epiphyseal melatonin under extended light exposure in essential hypertension.

Methods: Experiments were carried out on male rats of SHR (hypertensive) and Wistar (normotensive) strains. Two different light-dark schedules were modeled: 12 hour light / 12 hour darkness with light on at 7.00 a.m. and off at 7 p.m. (12:12) and 16 hour light / 8 hour darkness with light on at 5.00 a.m. and off at 9.00 p.m. (16:8). Wistar rats were kept under 12:12 light-dark schedule, SHR rats were exposed to both 12:12 and 16:8 schedules. Melatonin production was assessed by measuring urinary concentrations of its stable metabolite – 6-Sulfatoxymelatonin (6-SMT). Urine collection was performed in metabolic cages twice for 24 hour period – during the daytime and nighttime. It is well known that urinary concentration of 6-SMT correlates with the total melatonin blood level [Griefahn et al., 2001; Rapoport S.I. et al., 2009]. Concentration of 6-SMT in animal urine was determined using ELISA kit for 6-Sulfatoxymelatonin (Buhlmann Laboratories AG, Switzerland).

Results: It was found that daytime urinary concentration of 6-SMT was significantly lower in comparison with the nighttime values in hypertensive rats exposed to both 12:12 and 16:8 light-dark schedules. Daytime 6-SMT concentration was 25.5 ± 1.49 ng/ml in normotensive Wistar rats and it was significantly decreased to 16.27 ± 1.23 and 14.55 ± 1.32 ng/ml in SHR hypertensive rats kept under 12:12 and 16:8 light-dark schedules respectively. There was also an increase in the difference between day and night 6-SOMT in hypertensive rats kept under both light-dark regimens compared with controls. Meanwhile no difference in daytime 6-SMT urine contents was seen under light regimen 12:12 in comparison with 16:8 between the two groups of SHR rats. As regards nighttime, the values of urinary 6-SMT in Wistar rats, SHR rats under 12:12 and 16:8 light-dark regimens were as follows: 32.74 ± 2.78, 30.37 ± 2.54 and 26.08 ± 2.35 ng/ml with no significant differences between animal groups.

Conclusions: The study results suggest the rate of daytime epiphyseal melatonin production is markedly lower under increased blood pressure. There was no significant effect of extending light exposure from 12 to 16 hours within the 24 hour period on melatonin biosynthesis by the pineal gland in essential hypertension.

Funding/Disclosures: None.

A11

Photoreception for Circadian, Neuroendocrine and Neurobehavioral Regulation

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Over the past twenty years, there have been fundamental advances in the understanding of photoreceptive input for physiological and behavioral regulation in humans and other mammals. Neural signals conveying information about environmental light are transmitted from the retina through the retinohypothalamic tract to the hypothalamic suprachiasmatic nuclei (SCN), master oscillators in the circadian system. In turn, the SCN transmit information about lighting and circadian time to diverse loci in the nervous system, including the pineal gland where the hormone melatonin is synthesized. In the early 2000's, analytical action spectra identified 446–477 nm as the most potent wavelength region for melatonin suppression in healthy humans. Those data indicated that a novel ocular photosensory system, distinct from the canonical visual rods and cones, is primarily responsible for regulating mela-

tonin in humans. Other analytical action spectra and studies that employed selected wavelength comparisons, further demonstrated that circadian phase-shifting, autonomic stimulation, the acute effects of light on alertness and performance are shifted towards the shorter wavelength, or blue-appearing, part of the spectrum (Lucas et al., TINS 2014).

Seminal discoveries have elucidated the fundamental anatomy and physiology of the photoneural system that supplies input for circadian, neuroendocrine and neurobehavioral regulation. It has been clearly demonstrated that a small population of widely dispersed retinal ganglion cells is directly responsive to light and projects to the SCN as well as other regulatory nuclei in the central nervous system. These intrinsically photosensitive retinal ganglion cells (ipRGCs) contain a vitamin A photopigment named melanopsin, that mediates phototransduction. Although melanopsin-containing ipRGCs are the primary mediators of light detection for circadian and neurophysiological responses, numerous studies clearly show that the visual rod and cone photoreceptors are anatomically and functionally interconnected with the ipRGCs. These synaptic inputs have been shown, in mice, to greatly expand the dynamic range and spectrum of the non-image-forming visual functions for which ipRGCs provide the principal retinal input (Weng et al., PLOS One 2013), contribute to brightness discrimination (Brown et al., Curr Biol 2012), and participate in discriminative spatial vision (Ecker et al., Neuron 2010). Thus, all photoreceptor classes contribute to the regulation of biological and behavioral responses to light with the relative importance of each photoreceptor being highly labile within and between response types. Additionally, the spectral sensitivity of this photoreceptive system is fundamentally context-dependent. Notably, in addition to regulating circadian, neuroendocrine and neurobehavioral responses, the rod, cone and melanopsin-ipRGC system also regulates elements of vision and image detection. Together, this emergent field of physiology opens the door to major changes in future lighting architectural strategies.

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A12

A Novel Brain Circuitry Modulates Depression Following Aberrant Light Exposure

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Objectives: Certain types of depression are linked to aberrant light exposure. For instance, Seasonal Affective Disorder (SAD) is a type of depression caused by reduced exposure to sunlight during the winter months in Nordic countries. Biological clocks have evolved, under strong selective pressure from sunlight, to anticipate predictable external and internal conditions and allocate physiological processes and behaviours to suitable portions of the day. 'Aberrant light' indicates the fact that the timing of light exposure cannot be predicted by the internal body clock. We suggest that a mismatch between the expected timing of light and dark, as set by the body's master clock and the actual presence or absence of light, activates the brain circuitry that encodes reward prediction error -the lateral habenula (LHb)- and modulates the dopaminergic and serotonergic systems. These neuromodulators in turn have a direct role in motivation, action initiation and attention; when chronically suppressed, they may lead to the appearance of the pathological signs of depression. We recently identified a poorly described anatomical brain region, which we have named 'peri-lateral habenula (pLHb)' and have genetically defined by *Sox14* expression, as a brain area that could process aberrant light to modulate mood and subsequently depression.

Methods: We induced depression-like symptoms in mice by exposing them to a non-24 hour light cycle, i.e. 2 weeks housing under 3.5 hours of light and 3.5 hours of dark (ultradian or T7 cycle). By using a *Sox14*cre mouse line combined to stereotaxic injections of cre-dependent adeno-associated virus expressing the diphtheria toxin subunit (AAV-Ef1α-DIO-DTA-mCherry), we selectively ablated the *Sox14*$^+$pLHb neurons and analyzed subsequent depressive-like behaviours throughout relevant behavioural paradigms such as sucrose preference, novelty-suppressed feeding (NSF) and forced swim tests (FST). Finally, using the retrograde mono-synaptic restricted rabies system (EnvA, ΔG-RV), we mapped the mono-synaptic afferences of *Sox14*$^+$pLHb neurons.

Results: Animals under depression-inducing T7 showed a strong decrease in sucrose preference (30% less) and in time spent feeding in the NSF task (60% less) as well as an increase in time spent immobile during the FST compared to animals maintained under T24, indicating a strong depressive phenotype. Strikingly, animals under T7 upon *Sox14*$^+$pLHb neuron ablation showed similar phenotype than T24 subjects in all three tests. Following rabies infection of *Sox14*$^+$pLHb neurons, we specifically mapped transsynaptically infected cells in the retina.

Conclusions: *Sox14*$^+$periLHb neurons are required for the appearance of depression-like symptoms after T7 treatment, i.e. following aberrant light exposure, indicating that this structure acts downstream of the retinal photoreceptors to trigger mood alterations and depression.

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A13

Bright-Study: Light Exposure, Circadian Rhythm and Sleep Problems in Elderly with Intellectual Disabilities

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Objectives: Sleep problems are prevalent in elderly with intellectual disabilities (Elderly-ID), possibly as a result of the unstable and fragmented circadian rhythm found in this population. Inadequate light exposure might contribute to the disrupted circadian rhythm and resulting health complaints. Due to mental and

physical comorbidities Elderly-ID are thought to be more prone to inadequate light exposure. In addition, previous studies showed poor illuminance levels in health care facilities for Elderly-ID. The current study focusses on the personal light exposure in elderly-ID and the association with circadian rhythm and sleep problems. Insight into the role of light exposure as cause of sleep problems in this population is a first step in the prevention of these problems.

Methods: Cross-sectional study design in 38 elderly-ID living in health care facilities in the Netherlands. Light exposure was measured using HOBO-data loggers. Circadian rhythm and sleep problems were measured using the Actiwatch 2.

Results: Preliminary results show that most of the participants do not reach the advised 50 minutes of daylight in the morning. Full results on the association of light exposure, circadian rhythm and sleep problems are expected in June 2017.

Conclusions: Given the increased risk for inadequate light exposure and forthcoming health risks in Elderly-ID, it is concluded that adequate lighting in the living areas of health care facilities for this population requires more attention. Sufficient illuminance levels at health care facilities might prevent the prevalent sleep problems in Elderly-ID.

Funding/Disclosures: None.

A14

Spatial Distribution of Lighting Scenes and Its Impact on Non-Visual Effects

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Objectives: Studies showed that the intrinsically photosensitive Retinal Ganglion Cells (ipRGCs) are not evenly distributed throughout the human retina, the density respectively the sensitivity of the ipRGCs is highest at the lower and nasal part of the retina. Thus, it can be questioned if the illuminance and the melanopic irradiance of the full visual field measured at the eye are the appropriate values to quantify non-visual effects. The aim of this study is to determine the range of the, spatially resolved, effective radiant flux stimulating the ipRGCs for different distribution of the incident light under a constant (full visual field) illuminance level at the eye.

Methods: A first estimation of spatial weighting, representing the retinal areas with higher ipRGC response will be derived from literature. This weighting will be used to determine the effective radiant flux for stimulating the ipRGCs of different spatial light distributions that result in the same illuminance at the eye. Measurements for this investigation are conducted in a complete backlit testing room, which allows setting specific luminance and correlated colour temperature for arbitrary fields of walls and ceiling. Therefore, it is possible to create different luminance and CCT distributions and to adjust them to the identical illuminance at the eye. The measurements are performed with a luminance and colour measuring video photometer (LMK) to derive the spatially resolved radiant flux (incident of light) for scenes, which in turn can be weighted with $V(\lambda)$, the spectral sensitivity response function for melanopsin as well as the spatial weighting for ipRGC position. The results from the backlit room will be compared to weighted measurements of lighting conditions from typical office scenes.

Results: Expected results in June 2017.

Conclusions: The study will show, that in case of studying ipRGC-based non-visual aspects, the full visual field measured illuminance and melanopic irradiance are not sufficient for the accurate comparison of lighting conditions. Thus, it is crucial to consider the spatial distribution of the incident light. Further research is needed and should, among other things, lead to more effective, and thus energy-efficient, lighting planning.

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A15

Light on Human Physiology and Behaviour

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The sharp delineation between day and night existing throughout most of our ancestral evolution has changed in industrialized society. Electric light has endowed us with a 24-h/7-day society, to the extent that more than 90% of individuals in the US and Europe experience light at night. It is not surprising that such around-the-clock exposure to light may foster multiple repercussions on human physiology and behaviour.

Artificial light striking the retina between dusk and dawn impacts on brain regions regulating sleep-wake cycles. Light inhibits sleep-promoting and activates arousal-promoting neurons along with a suppressed release of the soporific hormone melatonin at night. Importantly, these effects can outlast the duration of light exposure. Furthermore, there is a dose- and wavelength dependency with a strong 'blue-shift' for these effects most probably also involving the novel photoreceptor pigment melanopsin as a mediator of the non-image effects of light in humans. Recent evidence points to a potential dichotomy of a blue light-SCN-wake and green light-VLPO-sleep axis in a nocturnal species. This offers an interesting framework to be tested in clinical human sleep research settings.

Natural sunlight is most often absent in the late evening before going to sleep, during a time zone very sensitive to light according to the human phase response curve. Furthermore, our contemporary lifestyle in the evening has changed over the past decades. Energy efficient LEDs are now widely used in televisions and computer screens, laptops, tablets and hand-held devices between dusk and dawn. Checking messages etc. on their hand-held devices before going to sleep has become common practice in teenagers, but also in adults.

Thus, our research has mainly focused on repercussions of such lighting conditions in the evening on circadian physiology and sleep humans. We have recent evidence that, beyond melatonin suppression, blue-enriched light at 40 lx and light from LED-backlit computer screens elicit significant alerting responses as indexed by subjective and objective (i.e. EEG and EOG) correlates of sleepiness. Furthermore, well-being and cognitive perfor-

mance in attention, working memory and declarative learning tasks were enhanced during a 2-hour evening exposure to these light sources as compared to non-blue enriched light or non-LED computer screens. Blue-enriched light induced reduced frontal NREM slow-wave activity (2.5–4 Hz) during the first sleep cycle, as compared to non-blue enriched light. Interestingly, some of these responses showed individual trait effects that potentially modulate a differential response to light exposure, including sex and genetic trait polymorphism. Our recent results on dawn simulations based on LED technology and dynamic LED lighting solutions during 16-hours of scheduled wakefulness under normally entrained conditions, clearly point to beneficial effects on well-being, cognition and sleep when compared to conventional lighting conditions.

Collectively, our data indicate that the regulation of human alerting, neuroendocrine, and cognitive responses to light are far more complex and nuanced than initially thought. In a broader perspective, this should increase our awareness of the impact of both natural and artificial light for human health with socio-economic ramifications.

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A16

Chronotype Assessments of Three Monozygotic Child Twins

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Objectives: In this study, we aimed to find differences in circadian phenotype among young monozygotic twins living under the same conditions and in the same environment who are exposed to the same life situations.

Methods: Three pairs of monozygotic twins between 7 and 10 years old were involved in this study. For morningness-eveningness evaluation we used the Children's Chronotype Questionnaire (CCTQ). The chronotypes of mothers were assessed with the Horne and Östberg Morningness-Eveningness Questionnaire (MEQ). Salivary melatonin concentrations were evaluated in all pairs of children and their mothers using radioimmunoassay. Saliva samples were collected in June from Friday afternoon to Saturday at different time points: 14:00, 19:00, 21:00, 23:00, 01:00, 03:00, 06:00, and 09:00. The individual melatonin profiles were analysed by cosine analysis. The activity of the children was monitored by wrist actigraphy, with school-day and weekend records evaluated separately.

Results: The results suggest that young twins living in a shared environment may differ in chronotype, as scored by the CCTQ and verified by a phase shift in acrophase of melatonin rhythms and the level of weekend morning activity. Our results also show that even children with neither chronotype can get up for school with melatonin levels higher than 40% of the maximum and show significantly lower activity in the morning during weekends.

Conclusions: In a sample of three pairs of monozygotic twins aged 7–10 years who live together in a shared environment and have the same daily routine, we demonstrate that individual human chronotype may develop as early as before puberty. The data suggest that the environmental or epigenetic factors that contribute to the genetic propensities for certain chronotypes are rather subtle and may have an impact early in life.

Funding/Disclosures: None.

A17

A Double Blind, Placebo Controlled Randomized Trial of Light Therapy for Non-Seasonal Bipolar vs. Unipolar Depression

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Objectives: The aim of the study was to examine the efficacy and safety of morning bright light treatment (BLT) in treatment of patients with bipolar or unipolar affective disorder, depressive phase, without seasonal pattern. It was randomized, double-blind and placebo-controlled trial.

Methods: Adults, ages 18–70 years were randomized to treatment either with BLT or with a device called 'negative ion generator' (as a placebo control). Subjects were required to be on stable and therapeutic dose of psychotropic medication for at least 4 weeks prior to enrollment and the treatment was not sufficiently effective. Clinical state was monitored at the baseline and at the end of treatment. The HAMD-21, MADRS, BDI, CGI, PGI were used.

Results: Ninety-five patients were enrolled (50 with diagnosis of bipolar disorder and 45 with unipolar disorder). Fifty-two patients were randomized to treatment with BLT and 43 were in the placebo group. 83 subjects completed the study. There were 12 dropouts (5 in the light group and 7 in the placebo group). After 14 days of treatment a significant improvement was found in all groups ($p < 0.001$). Subjects treated with BLT demonstrated no significantly different improvement compared to patients treated with placebo ($p > 0.25$). There was no statistically significant difference between unipolar and bipolar disorders ($p > 0.3$).

Conclusion: The presented study did not confirm that light therapy is more effective than placebo in the treatment of non-seasonal depression. But it also has not been demonstrated that phototherapy does not work. Further research is needed to determine efficacy of BLT in this population.

Funding/Disclosures: None.

A18

Internal Synchrony and Mood: A Study of Circadian Misalignment in Bipolar Depression

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Objectives: The synchrony among circadian rhythms, body homeostasis and behavior plays a fundamental role for the well-being of an individual. The individual can experience fatigue, lack of motivation and impaired performance when this synchrony fails. In recent years, several new developments provide evidence which confirms the relationship between biological rhythms and mood. However, current knowledge does not allow a complete understanding of the biological and psychological correlates of the relationship between mood, the circadian timing system and depression. This is of concern especially for bipolar disorder, and even for the healthy population.

Methods: We considered 13 patients affected by Bipolar Disorder (BP), major depressive episode without psychotic features and 13 healthy controls(HC), matched with patients for sex and age. All patients were evaluated using 21-item Hamilton Depression Rating Scale (HDSR). Severity of cognitive distortion was quantified by administering the Cognitions Questionnaire (CQ) (Fennell and Campbell, 1984) both in BP that in HC. Subjects were instructed to wear activity monitors on their non-dominant wrist. DLMO (dim light melatonin onset) was calculated with salivary sampling during the evening. PAD (phase angle difference between the DLMO and mid-sleep point) was calculated for each subject. Data were analyzed through correlations, homogeneity of slopes analysis and logistic linear regression.

Results: Measures of circadian rhythmicity were found to correlate with depressive cognitive distortions. PAD inversely correlated with the global CQ score ($r = –0.60$, $p = 0.005$), and with the subscales I-V: I = emotional impact ($r = –0.48$, $p = 0.031$); II = attribution of causality ($r = –0.56$, $p = 0.010$); III=generalization across time ($r = –0.48$, $p = 0.032$), and V = perceived uncontrollability ($r = –0.58$, $p = 0.007$). For the whole model the linear regression of PAD alone on CQ yielded an adjusted $R^2 = 0.316$ ($F = 10.234$, $p = 0.005$), with a significant effect ($\beta = 0.592$, $p = 0.005$) for PAD. An effect of diagnosis on PAD was demonstrated, as healthy controls showed a larger PAD than patients ($F = 5.24$; d.f. 1, 14; $p = 0.038$). The linear relationship between DLMO and midpoint of sleep was found only in healthy subjects but not in bipolar patients. Testing the homogeneity of slopes yielded significant effects of diagnosis ($W = 3.84$, $p = 0.049$), DLMO ($W = 4.74$, $p = 0.0295$), and of their interaction ($W = 4.294$, $p = 0.0382$), on the sleep midpoint. The GZLM (Generalized Linear Model) analysis of separate-slopes confirmed a significant interaction of diagnosis and DLMO (LR $\chi^2 = 8.831$, $p = 0.012$), indicating the relationship between DLMO and sleep midpoint did not follow parallel slopes in the two diagnostic groups.

Conclusions: The results pointed toward an optimal relationship between sleep timing and the DLMO as a marker of internal synchrony and consequent psychological wellness. Furthermore, our data suggest that internal timing could be a general mechanism in regulating mood and mood-congruent cognition, not limited to pathological conditions such as bipolar disorder, but also extended to the general, healthy population.

Funding/Disclosures: None.

A19

Metabolic Effects of Light

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Objectives: To review studies on the effects of light on body mass, appetite and metabolic rate in humans.

Methods: A literature search was done using our own database of publications and the PubMed library. Studies on either immediate or cumulative effects of light in healthy subjects were chosen. Analysed indices included: body mass (2 studies), appetite (1 study), oxygen consumption (3 studies). Other indices which characterise physiological systems determining metabolic rate (autonomic nervous system, hormonal system, thermoregulatory system) were also taken into consideration: sympathetic nerve activity, heart rate, alpha-amylase, noradrenaline, cortisol, thyroid hormones, body temperature.

Results: Light decreased body (fat) mass, decreased appetite, increased energy expenditure in some studies. Considering the acute effects of light, sympathetic nerve activity was found to be increased. Heart rate is usually slightly increased by light especially if the light is presented at night/early morning. An effect of light on α-amylase, which is considered to be a marker of sympathetic nervous system activity, has been negative. Noradrenaline levels (in blood or urine) were found to be increased following light treatment in some studies. Roughly half of previous studies measuring cortisol response (within the first 30–45 minutes) to light via open eyes – showed (temporal) increase, while the other half showed no change in the night/morning. Response of thyroid hormones is generally negative. The effects, however, may be different when light is used repeatedly. The factors which may influence the results, apart from time of day and number of light interventions, include also intensity and spectrum of light.

Conclusions: The available data indicate that light can increase energy expenditure and metabolism in humans. There is, however, no unequivocal physiological measurement that documents a robust effect. In addition, the pathways mediating metabolic effects of light are to be clarified.

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A20

6-Day Combined Partial Wake and Light Therapy for Depression

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Objectives: There are a dozen published studies on triple chronotherapy in depression (sleep deprivation [wake therapy] + light therapy + phase-advanced sleep stabilisation). Whereas its effectiveness has been shown for a total night wake therapy and for bipolar depression, less evidence exists for partial sleep deprivation (more feasible than a full-night awake) and non-bipolar depression. We tested a 6-day treatment protocol of partial sleep deprivation in combination with the most potent (based on the latest knowledge) blue-enhanced bright light (vs. blue-blocked [i.e. orange] light as control) in hospitalised patients with recurrent major depression or dysthymia.

Methods: The study was performed in Novosibirsk (55°N) from October 2016 to April 2017. Inclusion criteria for the patients were: age ≥18 yr; major depressive disorder (MDD), recurrent or dysthymia (according to DSM-5 criteria); current depressive episode; good and stable general health; stable dose of antidepressants (if taken) for the last 3 weeks. Exclusion criteria were: bipolar disorder; MDD with seasonal pattern, or with anxious distress, mixed or psychotic features; suicidal ideations. Partial wake therapy (sleep deprivation from 4 to 8 am) was performed in a light therapy room (blue-enhanced light [Philips LEDtube 6500 Kelvin] increased hourly 600→1300→2200→2800 lx) and the light treatment was repeated the next morning at 7–8 am. Time for sleep after the wake therapy night was 2 hours earlier, after the second night, 1 hour earlier. This 2-day cycle was repeated twice (3 cycles in total). Patients were randomised to wear no filtering (clear) or filtering blue light (orange) Chron-optic glasses during the treatments. The depression was scored blind using HDRS-21 (Hamilton Depression Rating Scale) before and after the 6-day treatment, and HDRS-6 was logged by the patient in a protocol every day at 2 pm. Compliance to the study was controlled by clinic personnel and actimetry.

Results: Twenty-two patients (13 males: 9 females, aged 27–68 y, 13 with MDD recurrent: 9 with dysthymia, 18 antidepressants-free) entered and completed the study. Preliminary analysis showed a significant decrease of depression score following the first night (37%) or the entire 6-day treatment (33%), with no difference between white and red lights. There were 8 responders (36%) to the first night therapy. No further improvement was observed in the responders group whereas in non-responders the depression levels continued to decrease ($p = 0.047$), yielding no significant difference between the two groups from intervention day 2 onwards. No eye-related adverse events were reported; all patients successfully resisted sleep during daytime; two patients were hyperthymic following the treatment.

Conclusions: Triple chronotherapy with partial wake + light therapy + phase-advanced sleep stabilisation is an effective and feasible-to-use therapy for non-seasonal depression. The degree to which light spectrum is important for the effect remains to be clarified.

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A21

Differences of the Pupil Response During Exposure to Light of Different Spectral Compositions and Intensities: Preliminary Findings

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Objectives: The pupil response to narrowband-width blue light stimuli after light offset has been shown to be a marker of intrinsic melanopsin activity (Gamlin et al., 2007; Park et al., 2011). This study aimed to investigate the pupil light response during daytime light exposures with two different polychromatic white light sources of similar color temperatures (CCT) but two different peaks in the blue light portion (i.e. at 435 nm vs. 480 nm), and with different light intensities.

Methods: In a mixed within-between-subject design we included 68 healthy participants (out of 72 to be tested; 46 female; 22 male; 24.4 ± 2.7 yrs; mean ± SD) with normal vision. Participants came to the laboratory one hour after habitual wake-up times for fours visits. They were exposed for three hours to one light condition per visit. Each light exposure was preceded by 30 min in dim light (DL; <5 lx). The light conditions differed in their spectral blue light portion but had similar CCT (= 3500 K; polychromatic white light with a peak at 435 nm or at 480 nm) and/or differed in illuminance (100 lx, 200 lx, 600 lx, 1200 lx). All participants also underwent a DL condition (randomized order of light conditions). During each session, the pupil response to two narrow-bandwidth bright blue light pulses of 1s duration was measured: once after 10 min of dark adaptation, and three times during experimental light exposures (i.e. light-adapted). The maximum contraction amplitude to blue light stimuli and the post-illumination response (=PIPR; defined as contraction amplitude 6 s after light offset) were analyzed, both relative to baseline (= 0.25 s before the onset of each blue light stimulus). In order to account for inter-individual differences, the outcome measures were also expressed relative to dark adaptation for each visit.

Results: The dark adapted baseline pupil sizes were similar within participants (i.e. across four visits). In response to 1 s blue light stimuli there was a significant main effect of light spectrum for maximum contraction amplitude ($F_{2,433} = 3.19$; $p = 0.04$) and PIPR ($F_{2,309} = 8.87$; $p < 0.001$), with smaller maximum contraction amplitude and smaller PIPR (= faster re-dilation) to polychromatic white light with the blue peak at 480 nm, when compared to 435 nm. Illuminance also showed a significant main effect for

maximum contraction amplitude ($F_{3,371}$ = 12.30; $p < 0.001$) and PIPR ($F_{3,259}$ = 3.05; $p = 0.03$), with smaller contraction amplitude and smaller PIPR at higher illuminance (600 lx, 1200 lx), when compared to lower illuminance (100 lx, 200 lx). There was no significant interaction between light spectrum and illuminance ($p > 0.76$).

Conclusions: Our preliminary results suggest that the PIPR is sensitive to different polychromatic white light conditions and could contribute to quantify light-dependent impacts of non-visual functions during daytime.

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A22

A Pilot Replication Study of Two PER3 Single Nucleotide Polymorphisms as Potential Genetic Markers for Morning and Evening Earliness-Lateness

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Objectives: To test two hypotheses that were formulated in accordance with the earlier reported positive findings on the association of single nucleotide polymorphisms (SNPs) with morning-evening preference. 1) The rare allele of rs2640909 might be linked to a higher score on morning earliness–lateness scale. 2) The rare allele of rs228729 might be linked to a higher score on both morning and evening earliness-lateness scales.

Methods: In total, 397 healthy volunteers participated in this study. The first hypothesis was tested on a Moscow group (N = 149), male professional bus drivers. The second hypothesis was tested on Novosibirsk and Stavropol groups (N = 248), general population. DNA was extracted from buccal epithelium swabs and corresponding SNPs were genotyped. A multi-dimensional 72-item questionnaire named 'Sleep-Wake Pattern Assessment Questionnaire' (SWPAQ) includes two 12-item scales for self-assessment of morning-evening preference. They were named 'morning and evening lateness' and abbreviated as M and E, respectively. Only these two scales were administered to the residents of Moscow, whereas the residents of two other cities completed the whole questionnaire.

Results: The allele frequencies of two potential markers of morningness-eveningness (rs2640909 and rs228697) were consistent with those reported for the Caucasian population. The one-way analysis of variance of the Moscow group representing three rs2640909 genotypes revealed a statistically significant main effect of genotype on morning earliness-lateness score, M [$F(2,146) = 5.591$, $p = 0.005$]. The carriers of two copies of rare alleles belonged to the evening type. However, we did not find an association of lateness in morning and evening behavior with the rare allele of rs228697.

Conclusions: Several PER3 polymorphisms have been studied so far as potential genetic markers of self-assessed morningness-eveningness (chronotype). We found that, in accordance with the hypothesis based on findings reported by Ojeda et al. (2013), homozygotes of the rare variant of rs2640909 had a significantly higher score in the morning lateness scale.

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A23

Chronotype as a Predictor of Future Status of Depressive and Anxiety Disorder Diagnosis

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Objectives: Depressive and anxiety disorder have a high prevalence in society. The role of chronotype, the individual preference of sleep/activity timing, in these disorders has been of interest. A cross sectional association was already identified between evening-type and a diagnosis of depressive and/or anxiety disorder. However, a predictive association has not been studied yet.

Methods: A sample of the cohort study Nederland Study of Depression and Anxiety (NESDA) was used. Diagnoses of depressive and anxiety disorder were DSM-IV based and determined at baseline, two-year follow-up (FU2) and four-year follow-up (FU4). Chronotype was assessed with the Munich Chronotype Questionnaire at baseline. With a multinomial logistic regression the cross-sectional association between chronotype and depressive and/or anxiety disorder status (N = 505) compared to healthy controls (N = 426) were analysed. With binomial logistic regression analyses the prospective association between chronotype and the status of diagnosis at FU2 and FU4 were analysed. The analyses were adjusted for relevant sociodemographic and somatic health factors.

Results: From the cross-sectional analysis an association between more evening-type and a current depressive and/or anxiety disorder was found [OR (95% CI) = 1.24 (1.05–1.46); $p = 0.01$].

From the prospective analyses, no association was found between more evening-type and status of diagnosis of depressive and/or anxiety disorder at FU2 [OR (95% CI) = 0.99 (0.83–1.19); p = 0.92] or at FU4 [OR (95% CI) = 0.94 (0.77–1.15); p = 0.57].

Conclusions: We confirmed the association between evening-type and a current depressive and/or anxiety disorder in cross-sectional analyses. At follow-up there was no association between chronotype and a depressive and/or anxiety disorder diagnosis, for patients with a diagnosis of depressive and/or anxiety disorder at baseline. These results are contrary to the hypothesis that evening-type is a trait, and results in a vulnerability for developing a disorder. It is likely that chronotype is a characteristic of the current state of the disorder, which can be a result of the symptoms involved. Chronotype could be more affected by lifestyle factors than what is thought, and therefore not be a trait-like but a more state-like factor.

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A24

The Effects of Light Exposure on Circadian Phase in Seasonal Affective Disorder

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Objectives: Light is recognized as the most prominent cue for entraining circadian rhythms. The effect of light on circadian phase depends on the intensity, wavelength, and timing of light exposure. While blue light is most effective for circadian photoreception, there are likely to be individual differences in the effects of light exposure on circadian rhythms. For example, reduced responsivity to light exposure may result in blunted or poorly timed circadian rhythms. Individuals with seasonal affective disorder (SAD) exhibit reduced responsivity to light, which may impair phase-shifting in response to light. However, it is not yet known how naturalistic blue light exposure impacts circadian phase in individuals with SAD compared to non-depressed controls. It was hypothesized that individuals with SAD would exhibit a weaker association between light exposure and circadian phase.

Methods: Individuals with SAD (n = 24), subsyndromal SAD (S-SAD; n = 5), and non-depressed controls (n = 37) were recruited in Pittsburgh (83% female; aged 18–65). Dim light melatonin onset (DLMO) was used as a marker for circadian phase. Participants wore an actigraphy watch with a photodiode for one week in winter prior to DLMO collection. Blue wavelengths of light (400–500 nm; photons/cm^2/s) were averaged across a minimum of four days. The mean timing of light above a given intensity (MLiT) was calculated for various intensities of light as well as the duration of light exposure (i.e., the standard deviation of MLiT). Age and gender were included as covariates and were entered into the model prior to light variables.

Results: Individuals with SAD and S-SAD were combined and separate linear regression models were conducted for SAD/S-SAD and controls. Non-depressed controls did not show a significant association between DLMO and the timing of light exposure (R^2 change = 0.05, β = –0.20, p = 0.144), or the duration of light exposure above threshold (R^2 change <0.01, β = –0.03, p = 0.807). However, in the SAD/S-SAD group, later light exposure was associated with later DLMO (R^2 change = 0.20, β = 0.38, p = 0.018). Furthermore, longer duration of light exposure above threshold (SD MLiT) was also associated with later DLMO (R^2 change = 0.21, β = 0.38, p = 0.017) in the SAD/S-SAD group. The association (β) between DLMO and light exposure duration was stronger in SAD/S-SAD compared to controls (p = 0.02). However, the association between DLMO and timing of light exposure was not stronger in SAD/S-SAD compared to controls (p = 0.06).

Conclusions: Contrary to the hypothesis, we found that the duration of blue light exposure is more strongly correlated with circadian phase in individuals with SAD or S-SAD compared to controls. Future studies will investigate whether the timing of diurnal peaks in retinal responsivity to light mediate the association between light exposure and circadian phase.

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A25

The "Life-ON" Project: Chronobiology, Sleep-Related Risk Factors and Light Therapy In Perinatal Depression

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Objectives: Perinatal depression (PND) has an overall estimated prevalence of roughly 12%. If left untreated, PND has significant negative consequences not only on the health of the mothers, but also on the physical, emotional and cognitive development of their children. No certain risk factors are known to predict PND and no completely safe drug treatments are available during pregnancy and breastfeeding. Sleep and depression are strongly related to each other because of a solid reciprocal causal relationship.

Bright light therapy (BLT) is a well-tested and safe treatment, effective in both depression and circadian/sleep disorders. The aims of the present project are: – to systematically and prospectively explore sleep-related parameters, as well as mood changes during the perinatal period, to identify potential early diagnostic markers of PND (Life-ON main study) – to explore the relationship between specific genetic polymorphisms and PND (substudy Life-ON 1) – to investigate the effectiveness of BLT in treating PND (substudy Life-ON 2) – to test whether a short-term trial of BLT during pregnancy can prevent PND (substudy Life-ON 3).

Methods: In a 3-year longitudinal, observational, multicenter study, about 500 women will be recruited and followed-up from early pregnancy (10th–15th week of gestation) until 12 months after delivery. Sleep will be assessed using wrist actigraphy, polysomnography and various sleep questionnaires. A blood-based analysis of potential biochemical, hormonal and genetic markers during the perinatal period will be performed. Women affected by PND, based on a psychiatric interview and an EPDS score >12, will be invited to participate in a randomized, placebo-controlled trial with morning bright light therapy (BLT) for 6 weeks. A subsample of 80 women without depression will also be randomized to participate in a 6-week open-label study with BLT during the third trimester of pregnancy.

Results: The study is ongoing since the middle of 2016. To date about 150 pregnant women have been recruited and about 20 of them participated in the preventive substudy Life-ON 3. A first interim analysis of the available data is planned for fall 2017. The final study results are expected in 2019.

Conclusions: The characterization of specific predictive and risk factors for PND may substantially contribute to improve preventive medical and social strategies for the affected women. The study results are expected to promote a better understanding of the relationship between sleep disorders and the development of PND and to confirm, in a large sample of women, the safety and efficacy of BLT both in prevention and treatment of PND.

Funding/Disclosures: This project is supported by the Swiss National Science Foundation (grant: 320030_160250/1) and the Italian Ministry of Health and Emilia-Romagna Region (grant: PE-2011-02348727). Lamps for BLT and actigraphy devices are provided for free by Philips Respironics, Italy.

A26

Depressed Inpatients in Southeast Facing Rooms Have Shorter Hospitalisation Than Those in Northwest Facing Rooms

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Objectives: Improvement for patients admitted to inpatient wards with severe depression is slow and patients are often discharged with residual symptoms setting them at risk for relapse. Therefore new treatments that can speed up recovery are highly desired. This naturalistic follow-up study investigated the impact of daylight, in a specialized affective disorders unit, on the length of hospital stay and improvement of depression.

Methods: For a period of one year, we collected data on sociodemographics, the length of stay, vitamin D, and depression severity, for patients in an inpatient affective disorders unit. The ward is located with one façade facing southeast (SE) and the opposite facade facing northwest (NW). The NW facing facade receives far less light and does not have any direct sunlight during wintertime.

Results: SE facing room received far more daylight that NW facing rooms. The length of stay was significantly lower in the SE rooms with 29.2 days (26.8) compared to 58.8 days (42.0) in the NW rooms ($p = 0.01$). There was a numerical but statistically insignificant greater reduction in depression severity for the patients staying in a SE facing room compared to a NW facing room.

Conclusions: Due to study design, the causality of the observed difference in length of stay cannot be given but the results strongly suggest that the lighting conditions had an impact on the length of stay.

Funding/Disclosures: None.

A27

A Multicenter Randomized Controlled Trial for Bright Light Therapy in Adults with Intellectual Disability and Depression: Study Protocol

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Objectives: The primary objective of this study is to investigate the effect of BLT on depressive symptoms in adults with intellectual disabilities (ID) in two different light therapy groups compared to regular care (control group). Secondary objectives of this study are investigating the difference in effect of BLT in the two different light therapy groups and if the effect of BLT is still visible 4 weeks after the end of the BLT (follow-up). Besides, we will study the effect of BLT on circadian sleep-wake rhythm and stress in both light therapy groups.

Methods: Participants with ID (IQ ≤70) and depressive symptoms are included in a multicenter randomized controlled trial (RCT) with three different study groups. Group I: 10,000 lux bright white light, group II: <499 lux bright white light (placebo) and group III: regular care (control group). BLT is used for a period of 14 days, 30 minutes a day, in the morning as soon as possible after wake-up. Circadian sleep-wake rhythm will be studied using Dim Light Melatonin Onset (DLMO) and actigraphy. Stress will be studied by measuring the level of cortisol in a hair sample.

Results: Inclusion of the participants started in May 2015 and is still ongoing. The primary outcome measures of this study are

depressive symptoms. The secondary outcome measures are circadian sleep-wake rhythm (DLMO and actigraphy) and stress (level of cortisol). Inclusion ends autumn 2017. Results of this study are expected in the first quarter of 2018.

Conclusions: This study is the first multicenter RCT evaluating the effect of BLT on depression in adults with ID. When the results reveal BLT is an effective intervention for adults with ID and depression, this intervention can become an (alternative or additional) option to decrease depressive symptoms in this population.

Funding/Disclosures: This study is funded by three care provider services (Amarant Group, Abrona and Ipse de Bruggen), the Dioraphte Foundation and the Foundation for support VCVGZ.

A28

Higher Light Color Temperature Positively Impacts Preschoolers' Cognitive Performance

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Objectives: While previous research has demonstrated that blue light exposure from a higher color temperature light source can lead to improvements in cognitive abilities for adults and older children, no research to date has looked at the presence of these effects in young children. The present study sought to explore whether preschool-aged children, who are just developing and fine-tuning their attention and executive function abilities, will experience the same cognitive benefits of exposure to higher color temperature light, as those recorded in adults and older children.

Methods: Thirty-eight children (21 female), aged 4.5 to 5.5 years, participated in this study. They first completed tasks of sustained attention (a go/no-go task) and cognitive flexibility (Hearts and Flowers task-switching task) under two color tunable LED fixtures set to 3500 K. The lights were then changed to a higher color temperature (5000 K) for the experimental group, while remaining the same for the control group. Illuminance was held constant across all lighting conditions. Following a 20-minute adaptation period, all participants completed each task a second time.

Results: Children in the experimental group showed significantly greater improvement in their accuracy when switching between tasks ($p = 0.04$). Participants in the control group showed an average improvement in percent correct of 6.7% across the two time points, whereas participants in the experimental group improved by an average of 15.2%. These results suggest the children exposed to higher color temperature light received a boost to their task-switching performance beyond that of just increased familiarity with the task and practice. For the go/no-go task, children in both lighting conditions showed only minor improvements, and there were no significant differences between the two groups in the magnitude of improvement.

Conclusions: This study adds to the growing literature indicating that the spectral composition of light can lead to improvements in cognitive performance, and shows that this relationship is present from an early age. Children at this age are just developing their executive function abilities, with cognitive flexibility having a particularly long progression over development. The present results suggest that preschoolers' cognitive flexibility can be enhanced following exposure to light set to a higher color temperature. These results can inform parents and teachers about the possibility of using light as a tool to aid in young children's learning.

Funding/Disclosures: None.

A29

The Combined Effects of Dawn Simulation and a Sleep State before Awakening on the Sleepiness Just after Awakening

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Objectives: Light plays an important role in alerting during day. Many studies have shown that dawn simulation in the morning improves subjective sleepiness, however little is known about what amount of light in dawn simulation is necessary. Furthermore, subjective sleepiness just after awakening is susceptible to sleep stages immediately before awakening. Thus, the purpose of this study is to investigate the combined effect of amount of light in dawn simulation and sleep stages just before awakening on subjective feelings of awakening.

Methods: A counterbalanced study was performed on totally two nights, one of which was control day (No DS: No Dawn Simulation), and another one was experimental day (DS: Dawn Simulation). Twenty healthy young men (22.4 ± 1.5), paid volunteers with the informed consent, took part in a laboratory protocol, and an approval of the institutional ethics committee in the university of Kyoto Institute of Technology was obtained. In the DS condition, the dawn simulated light which is located 50 cm above their faces, increases intensity up to approximately 250 lx during 30 min before awakening. PSG was recorded during nocturnal sleep. The amount of light before awakening was estimated by the sleeping position per second. Subjective sleepiness was examined by using OSA questionnaires just after awakening. Sleep stages were manually scored according to Rechtschaffen and Kales' standard manual.

Results: There is a significant reduction of subjective sleepiness in the DS condition compared to No DS condition in participants awaken from NREM sleep ($p < 0.05$), however there is no significant difference between two conditions in all participants. Furthermore, in participants awaken from NREM sleep with appropriate amount of dawn light exposure before awakening, subjective sleepiness also shows a significant decrease ($p < 0.01$) compared to No DsL condition. In participants awaken from phasic REM sleep, there is no significant difference in sleepiness between two conditions. Only in participants awaken from NREM sleep,

sleepiness score is significantly correlated with the amount of light exposure before awakening ($r = 0.56$, $p < 0.05$).

Conclusions: These results suggest that for the better awakening, not only appropriate amount of light exposure before awakening but also a sleep state immediately before awakening should be considered. Further research is needed to examine the new way of dawn simulation in response to the sleep state.

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A30

Luminaires with Non-Visual Characteristics – Photometric Measurements and Comparison of Five Electric Lighting Systems

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Objectives: This research project deals with the comparison of five different electric lighting systems, all of which aim to enhance non-visual responses (e.g. sleep-wake cycle). The non-visual light effects vary with daytime and quantity or rather quality of the light. In electric lighting, this is technically implemented by changing colour temperature and possibly illuminance during the course of the day. The project described herein focuses on the practical aspects in the application of such lighting systems. This includes the installation of luminaires with a non-visual impact in patient's rooms and as a key aspect, photometric measurements of the diurnal light variation. The measurements are accompanied by a survey of doctors, nurses and therapists about user satisfaction and the handling of the lighting. Practical long-term experience is derived from interviews with operators of retirement homes who have been using such a lighting system for some years. The paper focuses on the measurements.

Methods: The five lighting systems were installed from August 2015 until February 2016 in identical ward rooms (at the University Center for Geriatrics and Rehabilitation, Basle). During the full day photometric measurements in winter, parameters such as illuminance, luminance, correlated colour temperature, glare (UGR) and the non-visual effects were recorded hourly. The measurement positions reflect the perspectives of the patient and the nurse (vertical plane at the eye), respectively. The non-visual component of lighting is measured as a corneal spectral power distribution (380–780 nm). Two assessment methods of the biological effects are considered, here. The older method, the action factor for nocturnal suppression of melatonin $a_{ms,v}$ combines all non-visual effects into one single metric. The more current method takes the complex photoreceptive inputs to the non-visual responses into account by calculating the effective irradiance experienced by each of the rod, cone and melanopsin photoreceptors. The corresponding metric is $E_{e,\alpha}$, (with $E_{e,sc}$, $E_{e,mc}$, $E_{e,lc}$, $E_{e,z}$ and $E_{e,r}$). The metrics of the units $a_{ms,v}$ and $E_{e,\alpha}$ differ greatly from each other. Under the assumption that a progression similar to daylight is advisable, a qualitative comparison with a sunny day was made in the project.

Results: The two mentioned assessment methods cannot be compared to each other. This is particularly well demonstrated by the example of melatonin suppression, for which two differing spectral weighting functions are assumed. A comparison of electric lighting with daylight leads to different results: with $a_{ms,v}$, the diurnal progression of the luminaires "Vivaa" and "Vanera" appear reasonable. In regard to the α-opic irradiances, $E_{e,\alpha}$, the progression of "Mira LED" appears most similar to daylight.

Conclusions: The lighting systems functioned technically well. Of course, it would be desirable to be able to quantify which of the measured curve progressions would be most advantageous for the patient. However, it is not yet possible to draw conclusions about the effects of light on health and physiology based on the measurements.

Funding/Disclosures: Age-Stiftung, Kirchgasse 42, 8001 Zürich, Switzerland.

A31

Relationship Between Cytokines, Body Mass Index and Chronotype of People

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Objectives: The impact of diurnal preferences on health related behaviors is understudied. Our previous study demonstrated that the prevalence of evening-types among teenagers was only 3.2%. Evening-type teenagers were obese and had poor health (Hojageldiyev et al., 2016). It is known that cytokines affect nearly every biological process. Therefore we designed this study to investigate the association between diurnal preferences of people, body mass index (BMI) and concentration of cytokines in blood serum.

Methods: In this study 701 healthy undergraduate students and secondary school students (age range 13–21) participated. Horne-Östberg questionnaire used to assess chronotype of students. For blood cytokine analysis 16 evening-types with BMI ≥25 and 18 morning-types with BMI ≤21 were selected. Concentrations of serum IL-8, IL-18 and IFN-γ tested by using Vektor-Best (Russia) ELISA kit. Statistical calculations made by Student-t test.

Results: Test results showed that concentrations of IL-8, IL-18 and IFN-γ is higher in evening-types with BMI ≥25 (IL-8 mean = 10.04 ± 4.24 pg/mL; IL-18 mean = 213.0 ± 95.10 pg/mL; IFN-γ mean = 0.60 ± 0.0 pg/mL) than morning-types with BMI ≤21 (IL-8 mean = 6.02 ± 1.17 pg/mL; IL-18 mean = 119.93 ± 22.28 pg/mL; IFN-γ mean = 0.51 ± 0.10 pg/mL); $p < 0.05$.

Conclusions: This is the first study investigating variation of some cytokine concentrations according to diurnal preferences of healthy people. In evening-types higher concentrations of mostly inflammatory cytokines like IL-8, IL-18 and IFN-γ than morning-types may be reason of lower health condition and higher obesity tendency for evening-types. Also, recent studies showed that these cytokines play main role in oncological processes. Therefore, further more detailed cytokine related chronobiological studies will be rewarding.

Funding/Disclosures: None.

A32

Acute Non-Image Forming Effects of Diurnal Light Exposure: The Role of Prior Light Exposure

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Objectives: The literature on acute, diurnal non-image forming (NIF) effects of light exposure on subjective wellbeing and cognitive performance is growing. Yet, studies reveal considerable inconsistencies regarding the magnitude and direction of these effects. Previous in vitro studies have shown that light-induced response sensitivity of intrinsically photosensitive Retinal Ganglion Cells decreases when prior light exposure is relatively bright compared to dim. It may be that differences in prior light dose can partly explain the previous inconsistent findings. Therefore, the current study investigated whether prior light exposure influences the magnitude of diurnal NIF effects of bright light on alertness and cognitive performance. We hypothesized that participants who were exposed to relatively bright light in the hour prior to the experimental session would show reduced acute effects of bright vs. regular office lighting compared to those who received a relatively low light dosage beforehand.

Methods: Following a counterbalanced mixed design, participants (N = 34) came to the lab twice at the same time of day (morning or afternoon). They were first exposed to 18 minutes of 120 lx at the eyes (baseline), and then to one hour of 165 lx or 1700 lx at eye level. During this session, they continuously performed vigilance and working memory tasks. Subjective alertness and vitality were probed at the end of the light exposure. Prior light dose was measured using a wearable light sensor worn at chest height. The average illuminance level during the hour before the experimental session was calculated and a median split was performed to divide participants in a relatively bright and dim prior light exposure group. To examine the interaction of illuminance level and light history we performed multilevel analyses corrected for baseline values of the corresponding outcome variable.

Results: Experimental bright compared to regular light exposure significantly improved vigilance performance and subjective vitality and alertness in the morning, and decreased working memory performance in the afternoon. Although illuminance-induced effects on performance occurred irrespective of recent prior light exposure, acute effects on subjective indicators were significantly moderated by prior light exposure. Participants felt significantly sleepier and less vital after 165 lx compared to 1700 lx exposure when their prior light exposure was relatively bright. However, when prior light exposure was relatively dim, no significant differences between the two lighting conditions on these subjective indicators were found.

Conclusions: In contrast to our hypothesis, these findings do not suggest that relatively bright compared to dim prior light exposure reduces the magnitude of acute NIF effects of bright light, but rather that bright compared to dim prior light exposure increases sensitivity for subsequent *light shortages*.

Funding/Disclosures: None.

A33

Constructing a New Psychiatric Ward Using New Technology and Chronotherapeutic Principles

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Objective: We want to test if it is possible to integrate chronotherapeutic principles into the physical structure of an acute psychiatric ward, and to develop new methods of observation during the night.

Methods: *Setting*: A new acute psychiatric ward is being constructed at St. Olavs University Hospital, Trondheim, Norway. The ward will have 40 patient rooms in 4 sections and will receive about 1800 admissions each year. In half the ward, new light technology is installed that can be programmed to emit specific light frequencies at specific time intervals. In the other half of the ward, there will be ordinary light sources. A novel ultra-wide band radar technology is installed in all 40 patient rooms that can be used to improve clinical observation and for research purposes. The ward will open for admissions November 2017. *Chronotherapy*: Blue-depleted light at night: In half the ward, all light sources will be depleted of frequencies below 530 nm between 18:00 h and 08:00 h. There will also be filters that block these light frequencies in front of windows and electronic devices. Morning bright light: In the dining area of the same half of the ward, there will be bright light therapy lamps integrated into the walls. These allow selected patients to receive bright light therapy while having breakfast. This light will have daylight spectrum and approximately 8000 lx at the eye. *Observation at night*: The radar (Xehtru) is installed in the ceiling of patient rooms and bathrooms. The sensor can detect small movements associated with sleep and wakefulness, and can be used to detect respiration based on movement of the chest. This allows real-time contact-free assessment of sleep, wakefulness, movement, and respiration. Information about sleep/wakefulness will be sent to the staff-room and hand-held devices used by the hospital staff. Data can also be stored for monitoring patient sleep patterns throughout an admission.

Research Projects: We will conduct research projects related to both the light technology and studies to further test the accuracy of the assessments from the Xethru radar.

1. The impact and acceptability of the blue-depleted hospital environment will be tested in an eight-day randomized cross-over study of healthy individuals.

2. The effectiveness of the blue-depleted hospital environment on patient sleep, duration of admission, and medication use will be tested in randomized controlled treatment trials.

3. The accuracy of the radar to detect sleep, wakefulness, and respiration at night will be tested using concurrent assessment with polysomnography, actigraphy, sleep diaries, and the new radar.

Funding: The construction of the ward, including installation of light technology and installation of the radar technology, is funded by St. Olavs University Hospital. The radars are provided by Novelda AS.

A34

Circadian Rhythm Disturbances in Patients with Bipolar Disorder, Unaffected Siblings and Healthy Controls

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Objectives: Patients with bipolar disorder often suffer from circadian rhythm disturbances and it is suggested patients also suffer from these disturbances outside of the manic or depressive episode. These disturbances indicate the circadian timing system is an underlying pathophysiological mechanism behind the disorder. We aim to study these disturbances in the euthymic phase of the illness and to study whether these disturbances are also found in unaffected siblings using actigraphy.

Methods: Patients with bipolar disorder type 1, siblings and healthy controls are enrolled in a 14-day actigraphy protocol, a follow-up study on a large cohort study. From the actigraphy data non-parametric circadian variables are calculated and analyzed between the groups.

Results: 254 subjects were included in the study (142 women, 50 ± 13.4 years old), 110 patients, 74 siblings and 70 healthy controls. There were no differences in the non-parametric circadian variables between the groups (all 7 variables $p > 0.05$). Adding mood symptoms in the analysis yielded no different results. A sensitivity analysis neither showed that patients are having more circadian rhythm disturbances than the other groups.

Conclusions: From this large homogenous sample of bipolar disorder patients we can conclude euthymic patients do not suffer from more circadian rhythm disturbances compared to controls. This shows patients are able to maintain a stable rhythm when not confronted with mood problems. Circadian rhythm problems might be only state related, raising the question how the problems relate to mood problems.

Funding/Disclosures: None.

A35

Local Mid-Day Concentration of Carbon Monoxide in Arterial Blood in the Mammalian Head Area During Summer vs. Winter

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Objectives: We sought to determine relative mid-day concentrations of carbon monoxide in heart-proximal and brain-proximal arterial-vascular areas of the head during summer and winter.

Methods: At approximately 50ºN latitude, eight hybrids of wild boar and domestic pig about eight months of age were kept in natural light conditions for three days (N = 4 in summer outside, under a roof for shade, at 25ºC, daytime 4500 lx; N = 4 in winter inside a piggery, at 14ºC, daytime 50 lx). A day before the blood collection, anesthesia was induced following mild sedation. Two silastic catheters were inserted into one common carotid artery—one catheter heart-proximal towards the aorta and one catheter brain-proximal towards the internal carotid artery. The next day blood was collected every 30 minutes from 10:20 am to 1:20 pm. CO levels in the blood were analyzed by gas chromatography.

Results: In blood collected from the brain-proximal head area during the summer, the mid-day level of CO during summer and winter was significantly higher compared to blood collected from the heart-proximal common carotid artery (relative concentration 157.4 ± 20.40% vs. 100 ± 20.67%, $p < 0.05$). There was only a slight difference between the two in winter (relative concentration 115.4 ± 20.18% vs. 100 ± 21.97%, $p > 0.05$).

Conclusions: In naturalistic summer, a season of warmth and long, bright photoperiods, brain-proximal mid-day carotid blood levels of CO were approximately 60% greater than those of heart-proximal carotid blood. This difference was minimal in winter. These arterial results, in combination with prior CO blood data from the ophthalmic venous sinus, support the humoral phototransduction model suggesting that neuroactive gases such as CO, produced in the ophthalmic blood under bright summer light, can be delivered by counter-current transfer via the cavernous sinus to the internal carotid arteries and directly supply the brain.

Funding/Disclosures: The study was funded by the University of Rzeszów, Poland.

A36

Wake and Light Therapy for Moderate to Severe Depression

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Objectives: To examine the efficacy of using wake and light therapy as a supplement to standard treatment of hospitalized patients with depression. To describe the short-term effect of combined wake and light therapy and identify predictors in the short-term (first eight days) and the long-term phase (following eight weeks).

Methods: A randomized, controlled study, in which 64 patients with moderate to severe depression were allocated to standard treatment or to an experimental intervention, consisting of three wake therapy sessions in one week, and for the entire nine week study period 30 minutes daily light treatment and sleep time stabilization. Differences between groups were analyzed with repeated measures ANOVA (mixed model). Predictors of effect were identified in follow-up data from the 27 intervention-group patients using Fisher's exact test.

Results: Compared with the control group patients in the wake therapy group had a significant decrease of depressive symptoms in week one as measured by HAM-D17: 17.39 (CI 15.6–19.2) vs. 20.19 (CI 18.3–22.09) ($p = 0.04$), whereas no statistically significant differences were found between the groups in weeks two to nine. At week nine the wake therapy group had a significantly larger increase in general self-efficacy ($p = 0.001$), and waking up during the night was a significantly less frequent problem (1.9 times vs. 3.2) ($p = 0.0008$). In most weeks, significantly fewer patients in the wake therapy group slept during the daytime, and if they slept, their naps were shorter (week three: 66 min. vs. 117 min. $p = 0.02$). We found a significant negative correlation between the Morningness-eveningness (MEQ) score at baseline and HAM-D17 score, patients with lower MEQ scores (evening types) having a larger decrease in HAM-D17 scores ($p = 0.001$). Patients had a significant decrease of depressive symptoms during the first six days study-period measured by HAM-D6. (Baseline-score: 11.22 and score day six: 6.92), difference 4.39 ($p = 0.0001$). At day six, 40.7% of the patients responded to the treatment, and 18.5% fulfilled the criteria of remission. An increasing proportion of the patients experienced deterioration or had unchanged condition by days seven (25.9%) and eight (40.7%). In the short-term, a mild degree of treatment resistance compared to severe resistance was a predictor of remission ($p = 0.004$) and low educational level was a predictor of deterioration/unchanged condition ($p = 0.03$). Positive diurnal variation (evening best) was a predictor of both short-term and long-term response ($p = 0.02$).

Conclusions: Our results suggest that the combined chronotherapeutic intervention beyond the first week is less useful as a general antidepressant treatment for highly medicated treatment-resistant inpatients with moderate to severe depression. However, it seems beneficial for patients with positive diurnal variation and for evening types.

Funding/Disclosures: Novo Nordisk Foundation and Health Research Fund Central Denmark Region supported the project.

A37

Light at Night Darkness during the Day

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Most likely the circadian timing system in humans – CTS – is the evolutionary result of adaptation to our rotating planet. One of CTS's major functions is the coordination of biological processes within the 24 h-light-dark cycle in order to provide proper functioning including health and performance. Changes in the environmental light-dark cycle cause the necessity to concurrently adapt to e. g. seasonal changes. Over the last 20 years evidence has emerged, that the strongest Zeitgebers in humans are light and darkness. Changes in daylength are responsible for seasonal changes in the 24 hour variation of e.g. gene expression and behavior, well-timed application of e. g. light is able to phase-shift e. g. after transcontinental flight. Nevertheless, the magnitude of light during the day and darkness during the night necessary to provide optimal performance and health provided by clockwork machinery is unknown.

Over the last ten years evidence has emerged, that low and even very low illumination in the night, and 'regular' artificial lighting e.g. at workplace – though sufficient for vision – may have detrimental effects on performance and health. In this presentation I will summarize existing data on the effects of light at night and living in biological darkness during the day.

A38

Effects of Lighting Color Temperature on Effort Intensity for Cognitive and Listening Tasks

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Objectives: High color temperature white light with high proportion of short wavelength blue light induces a high alertness state, which should reduce the subjective demand of cognitive tasks and the associated effort investment. We predicted that effort-related cardiac response should decrease with increasing color temperature of light.

Methods: In two between-persons studies, we manipulated light color temperature across four levels (from 2800 K to 6500 K).

Effort was assessed as beta-adrenergic activity on the heart, indexed by cardiac pre-ejection period (PEP). In Study 1, after a baseline period, participants (N = 74) spent 15 min under one of the lighting conditions and then performed a modified Sternberg task (5 min). Procedure of Study 2 (N = 57) was identical except that the task was a listening task.

Results: Results of Study 1 confirmed our hypothesis: a single planned linear contrast was significant, $t(73) = 2.17$, $p = 0.03$, Cohen's $d = 0.51$, showing that cardiac reactivity during task performance decreased with increasing color temperature of light. This contrast was also significant for PEP reactivity during the light exposure, $t(73) = 2.36$, $p = 0.02$, Cohen's $d = 0.55$. For the Study 2, the linear contrast was significant for the mean PEP scores during the lighting exposure, $t(56) = 2.40$, $p = 0.02$, Cohen's $d = 0.64$. During the task, PEP reactivity scores did not follow the same linear pattern but PEP reactivity was stronger in the 5000 K condition than in other lighting conditions.

Conclusions: Our results provide the first evidence that lighting color temperature influences effort investment during mental and listening tasks.

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A40

Can Light Improve Alertness during the Daytime in a Dose-Dependent Manner?

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Objectives: Light is known to elicit both image- and non-image forming (NIF) responses, such as effects on alertness. Several studies have established the effects of light on alertness, but particularly during the nighttime when alertness is (relatively) low and melatonin concentrations are high. For the daytime, less information on a dose response curve of light intensity for alertness is available. If light modulates alertness during the day, this could have many important implications.

Methods: 50 healthy, non-sleep-deprived participants came to the Human Isolation facility of the University of Groningen the evening prior to the experiment. They went to bed at 11:30 P.M and were woken-up at 07:30 the next morning in dim light (DL) of <10 lx. After 1.5 hour, DL was alternated with 1 hour of experimental light (EL), emitted by a polychromatic white light source. Subsequently, DL was started again. In total, this sequence was repeated four times. Each subject was exposed to the same intensity of EL on all 4 occasions. In total, five intensities of EL were tested (24, 74, 222, 666 and 2000 lx). Alertness was assessed sixteen times, eight times during DL and eight times during EL spread over the day. Participants were asked to complete the KSS-questionnaire and perform an auditory version of the Go-NoGo reaction time task. Several blink-parameters were measured, as well as skin temperature, which was measured throughout the paradigm. Participants were provided with iso-caloric snacks adjusted for individual caloric need four times during DL. The experiment ended at 5:30 P.M.

Results: Linear mixed model analysis revealed a significant effect of time of day in all parameters of alertness, however there were no significant interactions between time of day and light intensity in none of the assessed parameters ($p > 0.05$). There were also no significant differences between DL and EL ($p > 0.05$) nor between different intensities of EL ($p > 0.05$).

Conclusions: Contrary to expectations, alertness did not improve by light exposure in a dose dependent manner. In fact, there were no effects of light on alertness whatsoever. Either light is not a strong enough cue to elicit a significant improvement in alertness during the daytime or there is a ceiling effect of alertness, making it impossible to improve beyond such limits. Possibly, melatonin plays a role in alerting effects of light, as a combination of low alertness and high melatonin concentrations have been proven to increase alertness in response to light in a dose dependent manner.

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A41

Hypothalamic Responses to Visual Features Other Than Irradiance

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We are used to thinking about light influences on the hypothalamus and the circadian clock largely in terms of responses to changes in ambient light (irradiance). The diurnal variation in irradiance provides a strong signal of time of day and there is abundant evidence that changes in irradiance can influence hypothalamic activity and elicit a wide array of behavioural and physiological responses. However, the diurnal change in irradiance always co-occurs with many other visual events – changes in irradiance over much shorter timescales caused by variations in shade, changes in the spectral composition (colour) of ambient light, and patterns of light caused by the reflection of objects within the visual scene. One might ask on the one hand whether these additional features impact the ability of the retina to encode the diurnal variation in irradiance and on the other hand whether they themselves provide a source of information about the environment to which the hypothalamus is responsive. We have been addressing this problem by working with laboratory mice, quantifying responses to different visual features in electrophysiological activity of the suprachiasmatic nucleus and surrounding hypothalamus and at the level of circadian entrainment and behaviour. We find that the retinal input to the hypothalamus multiplexes the simple irradiance code with multiple other representations of the visual scene. We find that some of these (the diurnal variation in colour)

have direct relevance for photoentrainment while others do not, but rather allow the possibility that a wider array of visual features could regulate hypothalamic control systems than previously considered.

A42

Social Jetlag and Dysfunctional Circadian Rhythm Entrainment Associate with ADHD Symptoms in Adults

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Objectives: We undertook this study to investigate whether indicators of a delayed circadian rhythm (sleep onset latency, later mid-sleep, delayed activity phase), circadian rhythm misalignment (social jetlag, intra-daily variability), and activity rhythm entrainment deficits (deviation from twenty-four hour period) were associated with measures of impulsivity and attention deficits in a non-clinical adult population.

Methods: A sample of 189 university students was used in this study. Subjects' self-reported chronotype, mid-point of sleep (MSF_{sc}) and subjective sleep quality were ascertained using the Munich Chronotype Questionnaire and Pittsburgh Sleep Quality Index respectively. Short performance tasks measuring inhibitory capacity and sustained attention (Conners Continuous Performance Task) and risky decision making (Iowa Gambling Task) were administered. Evaluation of ADHD symptoms (Adult ADHD Self-Report Scale), multidimensional trait impulsivity (Barrett's Impulsivity Scale), and executive function deficits (Cognitive Failures Questionnaire) were obtained. Estimates of sleep and rest-activity rhythms were ascertained by wrist-worn actigraphs (Actiwatch 2, Philips Respironics) which a sub-set of subjects (n = 54) wore for seven consecutive days.

Results: Tasks designed to probe impulsiveness found that recurring social jetlag (>1 h) was associated with faster pre-potent reaction time ($p = 0.005$) and that extreme cases of social jetlag (>3 h) produced greater commission error rates ($p = 0.029$) reflecting failures in response inhibition. Actigraphy estimates indicated later mid-sleep and sleep disruption were statistically significant predictors of ADHD symptoms ($R^2 = 0.249$, $p < 0.004$) and trait impulsivity ($R^2 = 0.237$, $p < 0.002$). Bivariate correlations conducted between all circadian rhythm parameters and symptom outcomes consistently revealed that the greater the difference of the circadian period from 24 h the greater ADHD symptom scores ($r = 0.443$, $p < 0.001$), impulsiveness ($r = 0.365$, $p = 0.008$), and executive function deficits ($r = 0.306$, $p = 0.029$).

Conclusions: The results show that sleep and circadian rhythm disturbances might be important factors which contribute to impulsive traits and executive function deficits associated with ADHD. Efforts to manage social jetlag through realigning social schedules and facilitate adequate circadian rhythm entrainment by controlling light exposure throughout the day might produce future clinical benefits for individuals diagnosed with ADHD.

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A43

A Bigger Bang for the Buck: Non-Image Forming Responses to Ultra-Short Light Flashes

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Objectives: Although socially imposed circadian misalignment results in significant consequences to a variety of systems (e.g. cardiovascular, neurocognitive, metabolic), the current countermeasure of bright light therapy protocols remain challenging. This is in part due to the incomplete understanding of the physiology of non-image forming (NIF) photoresponses in humans. Here we present a model of non-linear temporal integration of light by the NIF photoreceptive system, and show that distinct light flashes are integrated over time by the circadian system to prompt larger phase shifts than an equiluminous continuous light exposure.

Methods: Thirty-nine healthy adults (aged 19 to 36 years) were included in a 16-day protocol. Participants maintained a regular at-home sleep-wake schedule between days 1 and 14, and were exposed, in-lab, on day-15 to 60 minutes of either continuous light (n = 8) or sequences of 2-millisecond light flashes (n = 31) of various frequencies (interstimulus intervals [ISI] = 2.5 to 240 s). Continuous light and flashes were of equal illuminance (1,700 lux), and were timed to start 2 hours prior to each participant's average midpoint of sleep. Circadian phase shift was calculated as the difference in salivary dim light melatonin onset between day-15 and day-16. Melatonin suppression by light, along with changes in alertness and sleepiness, were also assessed.

Results: While continuous light elicited a circadian phase delay of -0.60 ± 0.34 hours, light flashes were integrated by the human circadian system in a ISI-dependent nonlinear fashion, with a linear rise to a peak phase delay of –1.85 hours (ISI = 7.6 ± 0.53 seconds) followed by a power function decrease as ISI increased. At peak ISI, on a photon-per-photon basis, flashes were more than 10,000-fold more effective than continuous light in phase delaying the circadian system. Furthermore, light flashes did not affect melatonin secretion, alertness, or sleepiness in an ISI-dependent manner.

Conclusions: Our findings add indispensable knowledge to the photoresponsive physiology of the human NIF system and demonstrate the phenomenal aptitude of the circadian system to integrate ultra-short light flashes in a non-linear manner. Whether retinal or subcortical, this integration process renders sequences of light flashes more effective than continuous light at eliciting circadian changes. As flashes did not systematically affect melatonin secretion, alertness, or sleepiness, they are potentially an ideal treatment for chronobiological disorders if delivered during the nighttime when the circadian system is most sensitive to light.

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A44

Bright Morning Light Exposure Reduces Daytime Cortisol Concentrations and Increases REM Sleep Duration

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Objectives: Bright light exposure in the early daytime has been shown to affect several physiological aspects, as demonstrated in a number of laboratory studies in strictly controlled environments (Dijk & Archer, 2009). Whether bright morning light exposure when implemented in every-day routine affects health aspects is not very well understood. One of the known physiological variables which is influenced by different lighting during daytime is the circadian variation of cortisol (Foret et al, 1993). The aim of the current study was to investigate whether three hours of early daytime lighting affect 24-h cortisol concentrations and sleep.

Methods: Twenty healthy young participants (mean age= 24.5 years ± 3.5; 10 female; 10 men) were exposed in a semi-naturalistic between-subject design to either polychromatic bright blue-enriched (=300 lx in a vertical direction at the eye) or warm-white lighting (=55 lx) from 8–11 am for three mornings in the laboratory. The light exposures took place every second day, and for three consecutive days at the end of the week. Urine and salivary samples were regularly collected for hormonal analyses of melatonin and cortisol. Polysomnography was recorded in the first night after an adaptation night at the beginning of the study and during the night at the end of the light intervention week. In between laboratory sessions, participants left the laboratory to follow their daily routines.

Results: For the time course of melatonin saliva secretion there were no significant differences or a change in circadian phase (as assessed in the evening dim light melatonin onset; DLMO) between the two lighting conditions. Urine and salivary cortisol were analyzed in 4 h and 1 h bins respectively, with a mixed linear regression model. For urine cortisol, there was a significant reduction in concentrations in the experimental group (main effect of 'group'; $p < 0.01$; $F_{1,28} = 9.48$). For salivary cortisol, there was a significant interaction between 'group x time course' ($p < 0.05$). Post-hoc analysis (Mann-Whitney test; corrected for multiple comparisons) revealed lower cortisol concentrations in the morning (8–12 h after DLMO) and in the afternoon (15–20 h after DLMO; $p < 0.05$) in the polychromatic bright-blue enriched when compared to the warm-white lighting group. From visually scored sleep stages we found no differences except that rapid-eye movement (REM) sleep latency became significantly shorter and REM sleep duration increased in the polychromatic bright-blue enriched compared to the warm-white lighting group ($p < 0.05$).

Conclusions: Our results suggest that regular bright and blue-enriched polychromatic light exposure in the morning lowers daytime and early evening cortisol levels, which might reduce negative consequences associated with chronically increased cortisol levels such as in patients with depression. These results together with shortened REM sleep latency and longer REM sleep duration suggest a beneficial effect of regular light exposure in the morning on sleep, health and well-being.

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A45

Bright Light Effects on Blood

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Objectives: This session will describe the physical and biological principles underlying some known effects of bright light upon blood and their potential relationship to the treatment of winter seasonal depression (SAD) and possibly to light treatment of in non-seasonal depression.

Methods: A synthetic review of concepts and data concerning the objectives.

Results: Melanopsin, and rod and cone photoreceptors all are critical to detecting the presence of clock-regulating external light. Yet these cells are not the only known biological clock-regulating photoreceptors, at least in the retina. They remain to be proven to be the photoreceptors that mediate light's antidepressant effects. The capacity of bright light to dissociate carbon monoxide (CO) from hemoglobin was reported more than 120 years ago. The dogma that CO was physiologically inert, however, led scientists and physicians to discount the physiological implications of this finding for the first century following its publication. The later discoveries that bright light activates the production of CO and other physiological 'gasotransmitters' encourages consideration of a model of 'humoral phototransduction' via the ophthalmic venous drainage to the cavernous sinus and diffusion into brain-directed arterial blood. Since this model was first proposed by this author, the existence of a cavernous sinus-internal carotid artery countercurrent transport system has been established in porcine models by Krzymowski and colleagues for several other molecules such as gonadotropin releasing hormone, oxytocin, beta-endorphin, dopamine, and progesterone. Koziorowski and colleagues subsequently established the presence of presumably bright-light driven seasonal and diurnal changes in ophthalmic venous CO levels in an animal model. In work presented earlier at this meeting in collaboration with the author, Koziorowski and colleagues have shared data supporting this finding in arterial blood supply to the brain. Our same group obtained preliminary data published earlier this year indicating that bright light administered acutely to male pigs at 1100 a.m. increased levels of CO measured in ophthalmic venous blood.

Conclusions: Data from animals and humans repeatedly establish that light is capable of releasing CO and other 'gasotransmitters' into blood and of causing the production of these physiologically important gases that may diffuse from eye to brain. While the findings to date do not yet prove that the interaction of light with gaseous neurotransmitters is central to either the physiology or treatment of depression, the mediation of light's effects on mammalian blood by the analogs of chromophores that mediate light's effects on the chronobiology and photobiology of plants invite further exploration of this aspect of animal biology.

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A46

The Role of Melanopsin in the Regulation of Sleep and Arousal

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Light plays a critical role in the regulation of numerous aspects of physiology and behaviour, including the entrainment of circadian rhythms and the regulation of sleep. These responses involve melanopsin (OPN4)-expressing photosensitive retinal ganglion cells (pRGCs) in addition to rods/cones. Nocturnal light exposure in rodents has been shown to result in rapid sleep induction, in which melanopsin plays a key role. However, studies have also shown that light exposure can result in elevated corticosterone, a response that is not compatible with sleep. To investigate these contradictory findings and to dissect the relative contribution of pRGCs and rods/cones, we assessed the effects of light of different wavelengths on behaviourally defined-sleep. Here we show that blue light (470 nm) causes behavioural arousal, elevating corticosterone and delaying sleep onset. By contrast, green light (530 nm) produces rapid sleep induction. Compared to wildtype mice, these responses are altered in melanopsin-deficient mice (Opn4-/-), resulting in enhanced sleep in response to blue light, but delayed sleep induction in response to green or white light. We go on to show that blue light evokes higher Fos induction in the SCN compared to the sleep-promoting ventrolateral preoptic area (VLPO), whereas green light produced greater responses in the VLPO. Collectively, our data demonstrates that nocturnal light exposure can have either an arousal- or sleep-promoting effect, and that these responses are melanopsin-mediated via different neural pathways with different spectral sensitivities. These findings raise important questions relating to how artificial light may alter behaviour in both the work and domestic setting.

A47

Evening Light Exposure Relationship between Morning-Evening Preference and Sleep Timing

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Objectives: The timing of sleep and wakefulness varies among individuals. Some individuals referred to as 'owls' or 'evening chronotypes' are usually sleepier in the morning than in the beginning of the night and tend to have late bedtime and late rising time. In contrast, individuals referred to as 'larks' or 'morning chronotypes' tend to wake up early in the morning and they feel sleepy earlier in the night. There are two different methodologies for self-assessment of these differences. One of them provides a measure of trait-like rather than state-like difference because it focuses on questionnaire self-assessments of morning-evening preferences and predispositions. Another estimates early-late chronotype from self-reported habitual sleep times and, therefore, it focuses on state-like rather than trait-like differences. Although, as expected, a questionnaire score usually correlates with an estimate of sleep timing, there are some real life situations when such a correlation might be weakened or even reversed. One can speculate that, in the modern day societies, sleep timing of a typical 'lark' might be dramatically changed by evening light exposure and the estimate of this timing might not be any more regarded a 'true' measure of natural preferences and predispositions of such an individual. The aim of the present report was to test this speculation experimentally.

Methods: The participants were 13 unselected first grade students of Sechenov First Moscow State Medical University (2 males, age either 17 or 18 years). Their chronotype was self-assessed with the Sleep-Wake Pattern Assessment Questionnaire (SWPAQ) on 12-item Morning and Evening Lateness scales, M and E (scores vary from –12 and +12, and M+E score varies from –24 to +24). The middle of their sleep (midsleep) was estimated for four consecutive nights from actigraphic records obtained with SOMNOwatch (SOMNOmedics, Germany). At 22:00 of the 3rd and 4th days they were exposed for 30 minutes to blue light (470 nm) emitted by Apollo Health GoLite M2 (Apollo Inc., USA).

Results: Paired t-test indicated significant difference between estimates of midsleep for the 2nd and 4th nights (3.45 vs. 4.28, $t = -2.520$, $p = 0.027$) ($p < 0.05$), and the sign of correlation of midsleep with E score and M+E score changed from positive to negative. After two-day 30-min exposure to blue light, midsleep didn't change much in late chronotypes, whereas midsleep in early chronotypes delayed to typical for late chronotypes times.

Conclusions: It seems that a delaying effect got stronger in early chronotypes due to stimulation of the phase-delay portion of their phase response curve whereas this portion was not stimulated in late chronotypes due to its relatively late timing in these types. In general, our speculation seems to be supported by the findings of this study.

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A48

Influence of Monochromatic Light on Melatonin Suppression and EEG Data in Patients with Bipolar I Disorder in Comparison to Healthy Subjects

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Objectives: This study aimed to investigate the effects of narrow bandwidth red and blue light on patients with bipolar affective disorder (19 women, 14 men, mean age 44 years) in comparison to healthy participants (36 women, 21 men, mean age 39 years). The research hypothesis was that melatonin suppression and alertness (as determined by EEG alpha/theta ratio) was stronger during the blue light condition in patients with bipolar affective disorder compared to healthy subjects.

Methods: The study was conducted during winter 2015/16. Participants were randomized to one of three conditions, darkness, red or blue light exposure and underwent a standardized protocol with light exposure from 23.00 to 23.30 o'clock. The EEG recording was initialized at 18.00 o'clock (C3, O1, F3, A2, Cz and GND electrodes) with a sampling rate of 256 Hz. Lights were switched off at 20.00. At 21.00 o'clock participants pupils were dilated and eyepatches were applied to create complete darkness. Blood samples for the measurement of melatonin were taken at 21.00, 22.00, 23.00, 23:30 and 00:00 o'clock. The number of photons during light exposure was $1.6*10^{13}$ per second and cm². LEDs with peak wave-length of 475 nm (blue) und 624 nm (red) were used; full width at half maximum was 25 nm (red) and 18 nm (blue). This created light levels of 8 lx for blue and 9.2 lx for red at eye level of the participant. In the study around 1200 hours of EEG data was collected and subjected to spectral analysis (theta and alpha power). Karolinska Sleepiness Scale (KSS) values were asked at the time of blood sampling.

Results: Theta Power during light administration (C3/A2) in bipolar patients was significantly higher compared to healthy subjects ($p = 0.002$). KSS Values are significantly ($p = 0.04$) lower during blue light administration in healthy participants. The results on melatonin suppression will be presented but were not available at the time of submission.

Conclusions: Contrary to the initial hypothesis bipolar patients appear to be significant more sleepy during blue light exposure according to Theta Power and KSS Score.

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A49

Melanopsin Driven Pupillary Reflexes in Seasonal Affective Disorder

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Objectives: With shorter, darker winter days at temperate latitudes, up to 2% of the population develops seasonal affective disorder (SAD). A pre-existing retinal sub-sensitivity to light may trigger SAD in vulnerable individuals under low wintertime light conditions. The main aim of this study was to assess the responses of melanopsin-containing retinal ganglion cells in SAD and controls, in summer and winter.

Methods: Participants (N = 55) in the SAD group were diagnosed with unipolar SAD, while Controls had no history of depression. Participants were invited to attend both a summer and winter visit, although some individuals only attended one visit. Retinal responses to light were measured using the post-illumination pupil response (PIPR) to assess cellular responses of melanopsin-containing retinal ganglion cells in the non-visual light input pathway.

Results: A significant group x season interaction ($p = 0.033$) showed that SAD participants had an attenuated PIPR relative to Controls in winter testing ($p = 0.003$), but not during summer ($p = 0.194$). This finding was independent of gender, wake time and testing time on the day of testing, and the attenuation of light incident on the retina by age and pupil diameter. The PIPR of SAD participants was lower compared to controls, but only in the winter and not in the summer.

Conclusions: Our data suggest that melanopsin-containing retinal ganglion cells are less responsive during the shorter day length in the winter months, and this retinal sub-sensitivity may be related to the pathophysiology of SAD. Specifically, retinal sub-sensitivity combined with low winter light levels may result in insufficient light input to the brain for euthymic functioning.

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A50

Increase of Alertness Due to Spectral Power Distribution and Illuminance at Eye Level in a Lecture Hall

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Objectives: Even though a large number of studies are conducted, non-visual effects of light are still not fully understood. These studies are often difficult to compare, because various aspects are studied under different circumstances. Lighting conditions are sometimes not well enough documented, even though the spectral power distribution and the lighting conditions at eye level are crucial for non-visual effectiveness. The project "NiviL" (non-visual effects of light) looks into various non-visual effects like alertness, well-being, melatonin suppression, sleep quality and cortisol concentration simultaneously in different applications and age groups. Lighting conditions and experimental designs are controlled and comparable. Aim of the project is to create a large representative data set, to be used to build a model which describes non-visual effects of light.

Methods: As part of this project, the impact of spectral power distribution and increased illuminance at eye level on alertness was studied in a lecture hall during normal use. 86 students (18–30 years, 12 female) participated in the experiment throughout the winter semester. The impact on alertness was studied by means of a d2R-test and the subjects' response with respect to well-being and lighting with a questionnaire, both before and after a 90 min lecture. The lecture was given two times a week: one in the morning and one in the afternoon, so the influence of the time of day can be investigated. During both lectures of one week one of four lighting setting was shown: standard light (E_{mel} = 130 melanopic lux, CCT = 4.000 K, E_{eye} = 200 lx), warm light (E_{mel} = 70 melanopic lux, CCT = 2.300 K, E_{eye} = 200 lx), cool light (E_{mel} = 230 melanopic lux, CCT = 8.000 K, E_{eye} = 200 lx) and bright light (E_{mel} = 260 melanopic lux, CCT = 4000 K, E_{eye} = 400 lx).

Results: The study was conducted between October 2016 and February 2017 and data analysis will be concluded until June 2017.

Conclusions: The results of this study will give valuable information on the impact of spectral power distribution und illuminance at eye level on alertness in a realistic setting.

Funding: The project "Nicht-visuelle Lichtwirkungen" (NiviL) is funded by the German Federal Ministry of Education and Research.

A51

Light Exposure via Head-Mounted Devices Suppresses Melatonin and Improves Vigilant Attention Without Affecting Cortisol and Subjective Comfort

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Objectives: We aimed at assessing whether a new generation of head-mounted light therapy devices, enriched in blue wavelengths, was able to suppress melatonin secretion and to improve vigilant attention in the late evening hours. We also assessed whether using such light device is associated with visual discomfort and physiological stress.

Methods: Seventeen healthy young participants (8 females; 22.8 ± 1.8 years) without sleep complaints followed a regular sleep-wake schedule, verified by actigraphy, the week preceding each of two in-lab experimental conditions. At each visit, participants entered the laboratory 7 h before usual bedtime. They were kept under dim light conditions (<5 lx) for 5 h before being exposed in a counterbalanced within subjects design for 2 h to a blue-enriched light (1500 lx corneal level) or to a 'placebo-like' red light (150 lx at corneal level). Light was delivered using a LED head-mounted portable device which includes a patented holographic surface reflecting light toward the lower retina such that sight is not hindered (Luminettes® – Lucimed). Participants were kept under dim light (<5 lx) for 1.5 h following light exposure prior to leaving the lab. Saliva samples were collected at hourly intervals up to light administration and at half hour intervals thereafter to assay melatonin and cortisol levels. Subjective sleepiness scores were collected regularly, together with vigilant attention assessments via a 5-min visual psychomotor vigilance task. Mixed model analyses of variance, including the factor light condition and session were applied by using the statistical package SAS®.

Results: A significant light condition*session interaction [$F(11,364) = 3.28$; $p = 0.0003$] indicated that while not differing between conditions before light exposure, melatonin levels were significantly reduced during the blue-enriched light, compared to the placebo exposure. For vigilant attention, a significant light condition*session interaction [$F(9,302) = 2.3$; $p = 0.017$] revealed that attentional lapses (RTs >500 ms) were reduced at the end of the blue-, compared to the red-light exposure and subjects tended to feel less sleepy concomitantly ($p = 0.056$). Neither cortisol levels nor subjective comfort significantly differed between the two light conditions (all $p_s > 0.05$).

Conclusions: While the efficacy of head-mounted light therapy devices for treating seasonal affective disorder has been debated, these results demonstrate that, compared to a placebo-like red light, blue-enriched light delivered by a new generation head-mounted device elicits typical non-visual responses to light. These effects were observed in the absence of detectable subjective discomfort and physiological stress assessed through salivary cortisol levels.

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A52

Overview of Clinical Applications of Light Therapy

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Objectives: The purpose is to provide an overview of the clinical applications of light therapy. The emphasis is on light therapy for mood disorders.

Methods: The aims are to review the clinical indications and contraindications; light treatment protocols to optimize response, highlighting the proper dosing (level of illumination, number of minutes), timing (morning, midday, evening), anticipated time to response and remission, and duration of light therapy; side effects; strategies to reduce or mitigate treatment-emergent symptoms; assessment tools; and how to select the appropriate light box for your patient.

Results: Light therapy is effective for seasonal affective disorder (SAD), non-seasonal major depression, and bipolar depression. Phase-delayed sleep and neurovegetative features including hypersomnia, hyperphagia, and lethargy are common symptoms of depression and highly responsive to exposure to bright light therapy. Implementation of the appropriate protocol, utilizing strategies to monitor response and reduce adverse effects, and selection of the proper light box can optimize the response to bright light therapy.

Conclusions: Given the efficacy, ease of use and tolerability, light therapy is ideally suited for the treatment of depression. Bright light therapy may gain widened acceptance with improved practitioner awareness.

Funding/Disclosures: None.

A53

Determining Retinal Exposure – The Importance of Field-of-View

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Objectives: To explore the impact of field-of-view (FOV) in quantifying the spectral variations and retinal irradiance of light stimuli during laboratory and clinical studies. The aim of these studies was to improve measures of retinal light exposure dose in varied environments. Although the photometric quantity of illuminance (lux) or the radiometric quantity of irradiance (W/cm^2 and W/m^2) have been successfully used to describe exposures from a single light source of a patient undergoing phototherapy, the more applicable measurement quantities are luminance (brightness) and radiance, which consider the extent of illumination (i.e., source size or reflected scene area). Retinal illumination is directly proportional to the luminance and radiance of a viewed light source or scene. In evaluating potential retinal hazards of bright light, the limits are set in radiance along with spectral weighting (e.g., for blue-light hazards). In this regard the radiance or luminance must be averaged over appropriate FOVs. For the same corneal illuminance/irradiance, the retinal irradiance from a relatively small source will be far greater than from a much larger light source. Since the photosensitive retinal ganglion cells, cones and rods are not at all evenly distributed across the retina, the impact of localized retinal exposure variations could be significant.

Methods: Since visual FOVs vary with illumination levels (e.g., indoors and outdoors), previously measured FOVs were applied to light measurements in different settings. Since the upper limiting angle of the FOV for human retinal exposure varies depending upon ambient scene luminance, measures were taken to block overhead light that does not enter the eye. A review of the known distribution of photosensitive retinal ganglion cells (pRGCs) across the retina further demonstrates the importance of FOV to the "non-visual" stimulus imparted to the retina. In brightest outdoor environments, upper lids block light above 15º elevation angle.

Results: The spectral distribution of several representative indoor office and domestic settings revealed that the short-wavelength reflected light (e.g. 430 nm–500 nm) from work surfaces, carpets, tiles, etc. were frequently low compared to long-wavelength reflectance. Natural foliage and ground surfaces in outdoor settings were also "blue-deficient." Measuring vertical spectral irradiance in both indoor and outdoor settings without limiting the instrument FOV included overhead light (outdoor skylight; luminaires indoors) that cannot directly reach the reach the retina and provided conflicting results.

Conclusions: Although a great deal of attention has been paid to the spectral characteristics of light exposures, there has been insufficient recognition of the spatial distribution of light reaching the retina. Measuring only horizontal or vertical illuminance or a spectrally weighted vertical irradiance without significantly limiting the FOV ignores the potentially widely varying impact of the spatial distribution of environmental light upon the melanopic or "circadian" stimulus. The use of horizontal irradiance or illuminance that equally treats the upper and lower quadraspheres will typically result in serious errors – including a completely opposite picture of the true retinal exposure. These results may also be helpful in interior lighting design.

Funding/Disclosures: None.

A54

Turn Down the Light at Night? Investigating the Effect of Blocking Blue Light Exposure in the Evening on Sleepiness and Sleep

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Objectives: The aim of the current project was to 1) quantify light exposure patterns in the late evening and at night among students in real life, and 2) test the effect of using blue-blocking glasses on students' feelings of sleepiness in the evening and sleep in real-life situations.

Methods: Blue light exposure in the evening (from 6 pm until sleep onset) was manipulated by means of orange (blue-blocking) vs. transparent glasses in a crossover design. Students (N = 32) participated for four days in each condition, with three days in between conditions and the order of conditions counterbalanced across participants. Wearable sensors (light sensors, activity trackers) combined with an experience sampling method and sleep diaries were used to monitor participants' light exposure patterns, sleep, and their feelings of sleepiness before going to sleep. The experience sampling questionnaire probed self-reported sleepiness on an hourly basis from 6 pm until participants' sleep onset. Multilevel analyses were performed for the data analyses.

Results: Results revealed that participants were exposed to relatively low intensity levels, with an average of about 50 lx (assessed close to the eyes). There was no significant difference between participants' light intensities during the two conditions (measured without correction for the filter), suggesting that participants experienced similar ambient light intensities during both conditions. Exposure to blue light was – as expected – substantially reduced when correcting the light measurements for wearing the orange filter. Multilevel analyses investigating the effect of pair of glasses revealed a significant on subjective sleepiness in the evening, with higher sleepiness scores during the sampling days on which participants wore the orange glasses ($p < 0.05$). This effect particularly occurred towards the end of the evening. In contrast, no significant effects of using blue-blocking glasses in the evening on sleep timing sleep duration or sleep quality were found (all p's > 0.10).

Conclusions: The current findings suggest that even though participants felt sleepier in the evening when exposure to blue light was blocked, their sleep timing and quality remained unaffected. Given the fact that the current literature is inconsistent on the effects of reducing blue light exposure in the evening on sleepiness and sleep, more large scale field studies are required in order to establish whether – and under which conditions – blocking the amount of blue light in the evening can act as an effective coun-

termeasure for reduced sleepiness, sleep duration and/or sleep quality in real life.

Funding/Disclosures: None.

A55

Modelling Inter-Individual Variations in Daily Rhythms in Students' Sleepiness and Self-Control as a Function of Chronotype

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Objectives: We aimed to model the effect of time of day and chronotype on students' state sleepiness and self-control during a lecture week. Moreover, we explored the impact of students' chronotype on the amplitude and phase angle of the daily patterns in sleepiness and self-control as function of local clock time in real life.

Methods: One large-scale field study (N = 120) employing an experience sampling methods combined with a sleep diary was performed among first-year college students. During one sampling week, students received eight notifications to complete short questionnaires probing their affective state. Notifications were randomly scheduled during participants' waking episode on weekdays and during the weekend (with at least 30 minutes in between two notifications). Multilevel cosinor analyses were performed to model the amplitude and phase angle of the variables' diurnal patterns for weekdays and during the weekend separately. Subsequent correlation analyses were performed to determine the correlational strength between chronotype and participants' estimated amplitude and phase angle in relation to local clock time. Moreover, multilevel analyses were performed to investigate the effect of chronotype on sleepiness and self-control at a between-subject level, controlling for structural variations as functions of local clock time.

Results: Cosinor analyses revealed significant time-of-day dependent variations in self-reported sleepiness and self-control during students' daily routine. The amplitude and phase angle of these daily rhythms were not significantly influenced by students' chronotype. Chronotype had a significant main effect on participants' state self-control ($B = -0.15$; $p = 0.01$), even when controlling for effects of local clock time. These results showed that relatively late chronotypes reported, on average, lower state self-control during their waking episodes. In contrast, chronotype had no significant effect on individuals' average levels of sleepiness.

Conclusions: The current study suggested that sleepiness and state self-control showed structural variations with local clock time during students' daily routine. Yet, chronotype had no significant effect on the amplitude or phase of these temporal patterns on weekdays or during the weekend. Moreover, students with a relatively late chronotype experienced less self-control throughout the day. This finding is in line with prior studies reporting a relationship between chronotype and trait self-control.

Funding/Disclosures: None.

A56

Towards Human-Centric Lighting for Office Buildings: Pilot Study on the Interactions of Visual, Perceptual and Non-Visual Effects of Workplace (Day) Lighting

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Objectives: Although knowledge about the impact of light on individuals beyond vision is becoming substantial and less and less controversial, there is still a gap on how to properly address what type of *lighting quality* one should seek in an indoor space. What constitutes *good lighting* conditions from a truly holistic, human-centered perspective, i.e. encompassing both visual and non-visual aspects? Very few models are currently available to embed non-visual lighting in a design decision-making process beyond the ability to compare how effective different sources are expected to be in generating non-visual effects. One model has been proposed that attempts to address non-visual lighting in a design context, called the non-visual Direct Response model (nvR_D), developed alongside another novel model for visual interest of daylight composition, named modified Spatial Contrast model (mSC). The aim of this study is to make a first attempt to test whether the non-visual system may constitute a dominant driver for determining the quality of lighting conditions in a working context and how it seems to interact with visual factors.

Methods: A cross-sequential study was conducted in 31 single and double-occupied offices within a research building at EPFL, Switzerland. Occupants from East and West facades were recruited on a volunteer basis. According to baseline questionnaires that were initially distributed, only healthy participants-without psychological or sleep disorders-were selected for a 9-day monitored study. Two reference rooms-empty offices-on each facade were in parallel equipped with cameras, spectrophotometers and luxmeters to monitor variations in daylight patterns simultaneously, while limiting intrusions within the researchers' work environment. Daily point-in-time surveys were distributed among participants, twice a day, to measure subjective responses for alertness, discomfort glare, workplane illuminance and perceptual interest, together with a tick-box table to observe their behaviour regarding shading and lighting control within their offices. Objective data were computed according to existing metrics for visual lighting, such as Daylight Glare Probability, to analyse visual performance and visual comfort, while the two novel approaches cited above were explored: the modified Spatial Contrast model mSC, to assess visual interest, and the non-visual Direct Response model nvR_D, to assess alertness.

Results: Initial findings show that the temporal variations of these different metrics are correlated to specific characteristics of the objective lighting data gathered for the different offices over the days, and are noticeably influenced by orientation, time of day and weather. Future steps of development will include correlational analyses to estimate the association between objective and subjective measures, and multivariate regression analyses to determine the relative weight of each (instantaneous) visual factor compared to the (cumulated) non-visual component, depending on the lighting conditions simultaneously measured inside the offices.

Conclusions: This pilot study allows to reveal relationships between lighting performance metrics that have until now only been addressed separately, if at all, and to confront objective lighting monitoring with subjective self-evaluation and novel models for perceptual aspects of light, both visual and non-visual, in office buildings.

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A57

Nocturnal Exposure to White Light Without Melatonin Suppression: Using Spectral Tuning to Turn Light into Biological Darkness

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Objectives: In modern society, humans are commonly exposed to too much light in the evening and at night. This has been shown to have acute suppressive effects on melatonin levels in the human body, as well as phase-delaying effects on the circadian rhythms underlying sleep. Previous studies have shown that melatonin suppression by light exposure can be reduced by selectively filtering out the short wavelengths. However, these studies confounded the spectral manipulation with decreases in illumination level and/or correlated color temperature. Moreover, the light they used mostly had a very orange appearance and poor color rendering properties. Here, we show for the first time that even under typical indoor white light conditions melatonin suppression can be drastically reduced, or enhanced, by tuning the spectral composition of the light.

Methods: We created two white light spectra with the same illuminance at the eye (175 lx) and the same correlated color temperature (2700 K), but with different power in the range 450–530 nm. In one spectrum, short wavelength power was boosted, predicting high melanopic stimulation. In the other, reduced power in the 450–530 nm range was combined with an extra peak around 420 nm, to maintain the same color temperature. Sixteen participants were exposed to the spectra during 3 h, on different evenings. Salivary melatonin measurements and alertness measurements (KSS, PVT) were compared to those from a dim (<5 lx) light baseline evening.

Results: Strong melatonin suppression was observed for the spectrum with high power in 450–530 nm. At the same time, melatonin levels were not significantly different from the dim light baseline for the other spectrum, with low power in 450–530 nm. No differences in alertness were found.

Conclusions: These results open up new opportunities for light at night or in the evening, allowing for good visual performance with minimal non-visual impact of light exposure, thereby reducing the potential negative health consequences associated with the use of conventional lighting.

Funding/Disclosures: JS, TB, LS and ML are employed by Philips Lighting. IG did her M.Sc. graduation project at Philips Lighting. BV was employed by Philips Research until February 28th, 2017.

A58

Two Hours of 10 Lux Light Exposure Induced Suppression in Melatonin of Humans

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Objectives: Melatonin, the hormone of the pineal gland is released during the dark part of the day and provides an internal biological signal about external photoperiod. Exposure to bright light during the night inhibits melatonin synthesis. However, there are very rare data about the impact of low illuminance on melatonin production. Therefore, the aim of our study was to test, if two hours of exposure to low illuminance (10 lx) and different light quality (warm vs. cold light) will affect melatonin production in young healthy volunteers.

Methods: Young (20–38 years old) volunteers (n = 15) participated in the study. They signed the informed consent prior initiation of the study. The study was performed during the winter and consisted of two trials with two months between them. In the first trial participants were exposed to 2 hours of light pulse from 24.00 to 02.00. Participants were randomly divided to 2 experimental facilities with the same illuminance of 10 lx at the eye level, but different light quality. Ceiling LED lighting had color temperature 3000 K or 5900 K, respectively. The illuminance reaching the eye was measured with Light Watcher Personal Data Recorder on the headband next to the participant's eye. Participants return from 02.00 to 03.00 to darkness again. In the second trial the same participants took part and they stayed from 22.00 to 03.00 in completely darkness. During whole experimental sections participants provided saliva samples to salivette with synthetic swab in 20 min intervals. Saliva melatonin was measured with RIA.

Results: The average melatonin concentrations in saliva between midnight and 02.00 in darkness were 30.0 ± 3.5 pg/ml. There were individual differences among participants. The lowest average melatonin concentration was 13 pg/ml in 2 participants and the highest 55 pg/ml in other 2 participants. During light exposure we observed the significant decrease in saliva melatonin in both lighting conditions (ANOVA for repeated measurements). The average decrease of melatonin concentration after 2 hours light exposure was 27.0% ± 5.3% (SEM) under 5900 K light and 35.0% ± 5.6% (SEM) under 3000 K light compared to control values. There were no significant differences in melatonin from 22.00 to midnight in both the control trial and the light pulse trial.

Conclusions: We found the significant decrease in melatonin concentration after two hours of exposure to 10 lx LED in both 3000 K and 5900 K experimental groups. Results suggest that even low intensity of ambient light during the nighttime can significantly suppress melatonin production in young healthy people with potentially negative consequences on well-being and health.

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A59

A Pilot Metabonomic Study of Major Depressive Disorder with Winter-Type Seasonal Pattern

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Objectives: In Ontario, major depressive disorder with winter-type seasonal pattern (MDD-s) accounts for 11% of MDD and 18% of recurrent MDD with a prevalence of 2.9%. Susceptibility to shifts in neurotransmitter metabolism has been implicated in the pathophysiology of MDD-s, but the range of metabolic changes remains unexplored.

Methods: In summer, 2014, we recruited medication-free euthymic subjects with a history of MDD-s, and recent winter episodes, and followed them up in winter. At both times, we conducted a structured clinical interview for DSM-V depression criteria. We screened 225 serum metabolites using 3 bioanalytical platforms (DI-MS, NMR and LC-MRM/MS). We compared metabolites between visits using Wilcoxon signed-rank tests partial least squares discriminant analysis (PLS-DA) with receiver operating characteristic curve analysis.

Results: Twelve subjects completed a baseline interview (August-October, 2014), and returned in the winter (December, 2014–February, 2015) at which time 9 met depression criteria (ages 24–62, 5/9 female, 2–5 previous episodes). In univariate analyses, 64/225 metabolites differed between visits, including catecholamine precursors tyrosine and tryptophan ($p < 0.05$). In a PLS-DA model ($p = 0.018$), a signature of 5 increased metabolites (hypoxanthine, acetone, propylene glycol, 3-hydroxyisovalerylcarnitine, and sphingomyelin C24:0) and 1 decreased metabolite (adenosine monophosphate [AMP]) discriminated winter from summer visits with 91% accuracy (67% sensitivity, 78% specificity). Waist circumference increased 3.3 ± 3.6 cm from summer to winter (paired $t = 2.6$, $p = 0.034$), and hypoxanthine correlated with body mass ($p = –0.755$, $p = 0.031$).

Conclusions: Among many serum metabolite changes, preliminary results implicate a bioenergetic shift related to adenosine metabolism in those with winter depression, which might be consistent with a phylogenetically conserved circannual metabolic biorhythm. Further study is needed to confirm the findings and to distinguish markers of depression from seasonal markers.

Funding/Disclosures: None.

A60

Correlated Colour Temperature Effects of Morning Light Expsoure on Alertness and Body Temperatures

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Objectives: Light exposure acutely affects alertness and performance. However, the influence of the correlated colour temperature (CCT) in these responses is only partially understood. In this study we apply morning light of two different CCT's under 3 different ambient temperatures to investigate how this affects alertness, reaction times, body temperatures and comfort.

Methods: Sixteen healthy females (age 18–30, BMI 18–25 kg/m^2) participated in two laboratory sessions with different morning light exposures. Each session started with a 45 min, thermoneutral, baseline (5 lx, 4000 K). After that, the light changed to 50 lx of either 2700 K or 6500 K while 3 temperature conditions of 75 min each were offered: 26°C (cool), 29°C (neutral) and 32°C (warm). Light sessions and temperature conditions were randomized among subjects. The order of the temperature conditions remained the same in both sessions of a participant. Core body temperature (CBT) and skin temperatures were measured on a 1-min interval. Questionnaires were completed every 15 min. After 55 min of each temperature condition, participants performed a 10-minute auditory psychomotor vigilance task (PVT). This was followed by blood sampling for cortisol analyses.

Results: The PVT reaction time (RT) was faster during the 2700 K session ($p < 0.05$) for all temperature conditions. Subjective sleepiness (KSS) was not significantly affected by the light exposure. During the cool condition participants tended to be less sleepy during the 6500 K light exposure ($p = 0.08$). The baseline melatonin levels were not different. Also, the decline in cortisol levels was similar for both light sessions. CBT was higher during the 6500 K light exposure ($p < 0.05$). During the cool condition, proximal skin temperature was higher under 6500 K light ($p < 0.05$). The change in CBT did not correlate with the change in RT between the two light sessions. Participants rated the 2700 K as being the most comfortable light condition.

Conclusions: The CCT of morning light affects reaction time and CBT independent of the ambient temperature. Reaction times and CBT were lower under 2700 K light as compared to 6500 K light. Subjective sleepiness was not different between the light sessions. The change in RT between the two light sessions was not correlated with the observed change in CBT. The higher visual comfort during the 2700 K light exposure can have contributed to the improved PVT performance.

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A61

Chronotherapy in the Netherlands

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Objectives: In the last 5 years there is a renewed and growing interest in the application of chronotherapy in the Netherlands. We already know from research in the early '70–80s' that treatment methods like sleep deprivation and light therapy can influence mood and circadian rhythms with positive effects in affective and sleeping disorders.

In 2013, the Dutch Network for Chronotherapeutics (Chronotherapie Netwerk Nederland – CNN) was set up as a multidisciplinary platform to support the dissemination of chronobiological and chronotherapeutical knowledge among scientists and therapists. In 2014 the first yearly symposium was organized. One of the goals of CNN is to bring colleagues together who translate research results into clinical practice. Since the founding of CNN more attention is given to chronotherapy and some promising developments have been achieved since then. We give an overview of these developments to demonstrate how a network for Chronotherapeutics can help the field to attract more attention to the usefulness of chronotherapeutics in healthcare.

See: http://www.chronotherapienetwerk.nl

Funding/Disclosures: None.

A62

Room-Light: Dynamic LED-Light as Treatment for Depressed Inpatients – A Randomized Clinical Trial

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Objectives: Despite developments in pharmacotherapy and psychotherapy a substantial part of patients with depression only recover incompletely during hospitalization. LED-lighting, rich in the blue short-waved spectral range, is an acknowledged antidepressant agent, which can play an important role in effective treatment of depression. This study develops and tests a new solution for inpatient wards, *an architectural light therapy concept*. Through an architectural lighting design, the light is dosed 24 hours a day from low intensity warm white light (2.000 K) in the evening, to bright light (6.500 K) in the morning and early daytime. Opposed to normal light therapy, it provides light therapy during the whole hospitalization. The built-in light therapy concept is based on an observational study performed in 2015, suggesting that there is a large potential of improving the light at north-west-facing wards, compared to south-east-facing wards. Inspired by the architectural planning of the original Nightingale Wards, with facades facing south-east and south, in order to make the most of the sunlight, the trial implements "A Sunny South East Side" to the darker north-west and north facing wards. The objective of the randomized trial is to investigate whether this sunlight therapy solution, based on LED-light, has an antidepressant effect on depressed inpatients when compared to conventional LED-lighting.

Methods: 120 inpatients diagnosed with depression will be included in this randomized parallel group design including an experimental LED-light group and standard LED-light group. The lighting design includes three elements, all developed for this trial: 1) Two ceiling mounted light fixtures 2) One light fixture next to the bed 3) One light panel mounted in the windowsill, mimicking sunlight in a south-east-facing window. In the experimental intervention, the light panel is activated. The light fixtures in the ceiling and next to the bed have dynamic LED-light, varying in both light intensity and spectral light composition through the day and year. In the control intervention, the light fixtures in the ceiling and next to the bed have a constant light intensity and spectral light composition, and the light panel is deactivated. The primary outcome is severity of depression after 4 weeks treatment assessed with Hamilton Depression Scale by a blinded rater.

Results: The trial is ongoing and is expected to be finished ultimo 2019.

Conclusions: Awaiting results.

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A63

The Daylight Academy

Lukas von Orelli

Velux Stiftung, Switzerland

The science funding foundation 'Velux Stiftung' has initiated the Daylight Academy to provide a novel and stimulating setting to the quest for scientific discoveries. The purpose of the Daylight Academy is to be a catalyst for innovative ideas and connect researchers and other professionals working in daylight research, regardless if they are approaching the topic with the eye of a chemist, architect or psychologist. Daylight affects human life and nature in many ways, is an inexhaustible source of energy – and it is for free. Due to the variety of its effects, it taps into many different areas of research.

Nowadays society is facing complex challenges which can only be addressed involving all necessary disciplines. Yet scientific disciplines are getting ever more specialized. Daylight can act as a bridge bringing them together.

The Daylight Academy is led by a panel of international scientists and currently consists of 65 founding members. The inauguration of the Daylight Academy in November 2016 marked the beginning of this novel platform for exchange that promotes international and interdisciplinary cooperation. The Academy organizes annual activities and meetings to foster networking, collaboration and transdisciplinary knowledge exchange. The Daylight Academy can be found on the web: www.daylight.academy.

Funding/Disclosures: None.

A64

The Effect of Naturalistic Light on Depressive Mood, Fatigue, Subjective Sleep Quality and Melatonin and Cortisol Blood Levels in Stroke Patients Admitted for Rehabilitation

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Objectives: The circadian rhythm is mainly controlled by natural daylight, especially because of the significant content of blue spectrum light in daytime. Patients admitted for rehabilitation often lack sufficient naturalistic light spectrum in daytime due to long indoor admission and is often exposed to artificial blue light spectrum in the evening and at night. Hypothesis: Naturalistic Light during the admission will improve the circadian rhythm in post stroke patients admitted for rehabilitation resulting in reduced depressive mood and fatigue, improved subjective sleep quality and stabilization of melatonin and cortisol circadian blood levels.

Methods: The study was a prospective parallel longitudinal randomized controlled study. Stroke patients were randomized to either the intervention (IU) (naturalistic lighting, Chromaviso, Denmark) or the control rehabilitation unit (CU) (standard lighting). The naturalistic light was installed in the entire IU. Examinations were done at inclusion and at discharge after at least 2 weeks of admission. Changes in depressive mood were assessed by the Hamilton Rating Scale for Depression ($HAM\text{-}D_6$) and The Major Depression Inventory scale (MDI). Subjective sleep quality was measured by the Pittsburgh Sleep Quality Index (PSQI), while Fatigue was measured by Epworth Sleepiness Scale (ESS), Multidimensional Fatigue Inventory questionnaire (MFI-20), a Rested Statement and Visual Analog Scale for fatigue (fVAS). Melatonin and cortisol blood levels were measured for a 24-hour period every 4 hours and mean levels were assessed and Cosinor analysis was performed.

Results: During one year 90 patients were included. At discharge patients from the IU scored significantly less depressive mood symptoms and fatigue compared with the CU patients (ANCOVA, SAS). Depressive mood: $HAM\text{-}D_6$, $p = 0.018$; MDI, $p = 0.009$. Fatigue and sleep: Rested Statement, $p = 0.041$; MFI-20 General, $p = 0.029$. The ESS showed decreased fatigue during the admission in the IU and no change in the CU group (paired t-test). No differences were observed in fVAS and sleep quality (PSQI). The melatonin levels showed no significant circadian rhythm at admission and discharge in either of the patient groups. During the admission period, the melatonin levels increased significantly in patients in the IU ($p = 0.030$) and were unchanged in the CU ($p = 0.418$). In both patient groups, the cortisol levels showed significant circadian rhythm.

Conclusions: Naturalistic light has a positive impact on depressive mood, fatigue and the circadian parameters melatonin and cortisol levels in stroke patients hospitalized for at least 2 weeks.

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A65

A History of Light Therapy

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Sun worship is the most ancient religion, growing out of that immense source of energy, warmth, spiritual and emotional sustenance. In the 19th century it was recognised that sunshine, and then electric light in various parts of the spectrum, could have therapeutic effects on rickets, psoriasis, lupus, fungal infections, eczema, sleep disorders, etc.- and not just emotional well-being.

The new era of light therapy (non-UV) was based on key insights in circadian biology in the 60's and 70's (Aschoff and Pittendrigh), followed by two crucial methodological advances: being able to measure circulating pineal melatonin by RIA (Arendt) or GCMS, and the discovery of its suppression by bright light (Lewy). This permitted study of light effects on circadian phase and amplitude, and melatonin developed into the marker for the human circadian clock. And bright light became a treatment: initially by Kripke for nonseasonal depression (these insights took decades to be followed up by randomised trials), and then by Wehr and Rosenthal for the newly rediscovered Seasonal Affective Disorder (SAD). In the 80's and 90's an enthusiastic wave of research world-wide (particularly in the higher latitudes of Scandinavia and Canada) investigated photoperiodic, phase shifting, and parametric effects of light on SAD. Light boxes with broad spectrum white light (~4000 K) and intensities from 5–10'000 lx became standard, and were tested in many clinical trials, with imaginative searches for an adequate placebo, from dim red light to inactivated negative ionisers. Remarkably rapidly, the diagnostic criteria for SAD entered both DSM-IV and ICD-10. Light therapy became accepted by academic medicine as the treatment of choice for SAD. Terman and Wirz-Justice founded SLTBR in 1988, followed by the nonprofit website www.cet.org to provide accesible, research-based information about light therapy to professionals and the public.

In parallel, Wever in the Andechs bunker showed that bright light affected human circadian rhythms (increasing the range of entrainment), and the Honmas, followed by Minors and Waterhouse, published the first phase response curves to single light pulses, completed a decade later by Khalsa et al. A second wave of light research began in 2002 with the discovery of blue-sensitive

photoreceptors (ipRGCs) – that rapidly (perhaps too rapidly) led to a wave of blue wavelength therapy devices on the market that were not adequately tested. Even low intensity blue light may, under certain circumstances, impose ophthalmological risks (blue light hazard).

The initial epoch of light therapy research has now expanded into treatment of many other disturbed sleep patterns in psychiatry and medicine. It has enhanced awareness of the importance of daylight (https://daylight.academy/), changed lighting regulations to include the nonvisual input, and is becoming a factor in "healthy" architecture and urban planning.

More information and video interviews with pioneers on https://srbr.org/resources/chronohistory/ and www.clocktool.org/clock-modules/chronohistory.html; Overy C, Tansey E M. (eds) (2014) The Recent History of Seasonal Affective Disorder (SAD). http://histmodbiomed.org/article/wellcome-witnesses-volumes.

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Daily Light Exposure Patterns Reveal Phase and Period of the Human Circadian Clock

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Objectives: In the field of human circadian modelling, much emphasis has recently been on predicting circadian phase (Dim-light melatonin onset; DLMO) from ambulatory data (e.g. activity, light exposure). One important aspect of the circadian pacemaker has been largely neglected in this regard: intrinsic period under free-running conditions (tau). As phase of entrainment is the result of an interplay between (artificial) light exposure patterns and tau, we strongly believe that an accurate low-cost and time-efficient estimation of tau is crucial to obtain a better understanding of fundamental properties of circadian entrainment in humans. Therefore, the main objective of this study was to explore whether intrinsic period can be estimated by analyzing ambulatory collected light exposure data.

Methods: Ambulatory light-exposure data (9 days; 1-minute sampling rate) was collected for 20 participants, with a DLMO assessment scheduled on the last day. The individual light exposure data was then used as an input for Kronauer's limit cycle oscillator model of the human pacemaker. By iteratively tuning the parameter describing tau for each individual until the measured DLMO overlapped with the model-predicted DLMO, an estimation of tau was obtained for each individual separately. Regression analyses were then performed to explain phase of entrainment from estimated intrinsic period and average daily light exposure level.

Results: Later estimated intrinsic period was related to later phase of entrainment, whereas higher light intensities were related to an earlier phase of entrainment. For (DLMO – sleep offset), an increase of 1 hour in intrinsic period was estimated to delay phase of entrainment by 4.6 ± 0.77 (± SE) hours, whereas an increase in average light intensity by 1 log (lx) was estimated to advance phase of entrainment by 2.84 ± 0.65 (± SE) hours. In total, the regression model explained 72% of the variance in phase of entrainment.

Conclusions: Our results show that low-cost estimations of intrinsic period may be possible by analyzing ambulatory collected light and activity data followed by one DLMO assessment in the lab. Such advances are not only useful from a scientific point of view, but may prove to be of crucial importance when optimizing individual light treatment for shift work and jetlag applications and designing individualized chronotherapy treatment schedules.

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Light Exposure, Circadian Entrainment, and Metabolism

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Objectives: Disturbed circadian rhythms and disturbed sleep are thought to contribute to the development and exacerbation of metabolic diseases such as obesity and diabetes. The circadian timing of sleep and wakefulness are altered in modern society, due in part to light exposure patterns, chronic short sleep schedules, and shift work schedules. Findings from studies that examined the influence of modern light exposure patterns on circadian entrainment, circadian misalignment, and of daytime bright indoor light alone and combined with intermittent blue-enriched white light on energy and glucose metabolism will be discussed.

Methods: Field and laboratory based studies in healthy adults with assessments of light exposure, sleep, circadian phase, energy expenditure and glucose metabolism.

Results and Conclusions: Modern light exposure patterns result in exposure to light at night and less exposure to bright light during the daytime, as well as changes in the phase angle of entrainment and phase relationships between internal circadian timing and sleep-wakefulness. Morning circadian misalignment during short sleep schedules (<5 h per night) and circadian misalignment during night shift work schedules are associated with alterations in energy and glucose metabolism that may increase the risk of metabolic diseases. Compared to typical indoor room light (2,700 K, ~100 lx angle of gaze), a day of exposure to continuous brighter white light (2,700 K, ~750 lx) or to brighter white light alternating every hour with blue-enriched white light (17,000 K, ~750 lx) had no significant influence on energy and glucose metabolism in healthy adults maintaining ~8 h sleep schedules. Enhancing daytime indoor light exposure in healthy adults maintaining recommended sleep opportunities appears to have little impact on metabolism.

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Daylight in Living Environments and Its Influence on Health

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Objectives: (1) the construction of an all-glass 'Photon Cabin' using entirely new glass processing with adjustable light transmission properties, (2) the evaluation of the impact of this building environment on perception of light, alertness, emotional well-being and its effects on sleep, rest-activity patterns and circadian alignment of melatonin.

Methods: A transparent all-glass building with a comfortable indoor climate to live-in across all seasons has been constructed on the Island of Bornholm, Denmark. This 'Photon cabin' is 35 m^2 in size and enables natural light to penetrate from the roof and from all sides down to floor level. The study employs a randomised, cross-over design with participants spending three days (18:00 to 10:00) in the glass house and the other three days in an ordinary villa in close proximity. External and indoor climate (light, humidity, temperature) is constantly monitored over prolonged periods and seasons with four sets of sensors two for the glass house and two for the villa. Subjective alertness, colour perception, visual comfort and emotional well-being is recorded several times during the day, while activity-rest patterns and light exposure are actigraphically monitored throughout. After each living condition, the participants undergo 19 hours of an adapted constant routine under dim (<3 lx) light, in which alertness and melatonin concentration is assessed in hourly intervals with napping permitted between sampling to minimise sleep deprivation. A 48-hour wash-out period is scheduled between conditions.

Results: Preliminary data from this ongoing study include 15 participants. Participants went to sleep at around 22:30 under both conditions, while they woke up 27 min earlier on average in the Photon cabin (07:23) than in the villa (07:50). Across conditions, subjective rating of sleep quality derived from PSQI indicates good sleep (villa: 3.18 vs. Photon: 2.80) and alertness during daytime using the Karolinska Sleepiness Scale ranged from very alert to sleepy (scores 2–7) with more alertness in the morning regardless of condition. Subjective wellbeing derived from the Warwick-Edinburgh Mental Wellbeing scale ranges between 41 and 68, which is within and above average of positive states of thinking, behaving and feeling. Under dim light conditions, however, there is a trend for more alertness in the afternoon and in the morning hours, if participants had been in the Photon cabin beforehand compared to having been in the villa beforehand.

Conclusions: A unique dataset is being accumulated from a chronobiologically exceptional opportunity of assessing real daylight influence from living in an all-glass house. With all confounding factors, such as indoor temperature, food intake, social interaction and outdoor activity levels being removed, current data are suggestive of a greater alertness and an earlier start of the wake period under natural daylight exposure.

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Effectiveness of Visual vs. Auditory Closed-Loop Stimulation on Delta Sleep Brain Oscillations in Humans

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Objectives: The aim of the study was to investigate whether visual stimuli have the same potency to increase delta sleep power density in humans as auditory stimuli do.

Methods: Healthy subjects underwent two polysomnographic trials – adaptation and experimental. EEG electrodes were positioned at Fz-Cz (bipolar derivation). Auditory (pink noise) and visual (LED red light) paired 50 ms signals were automatically presented via headphones/eye mask. The stimuli onset was anchored to the moment when the program detected a decline of EEG waves below an amplitude threshold, with the elapsed time 0.5 s to fall at peak to increase amplitude of brain electrical oscillations (closed-loop in-phase stimulation as per Ngo et al., 2013). The amplitude threshold and stimuli intensity (that should not cause movements or awakenings) were chosen individually during the adaptation night. The 30-sec epochs with stimuli of a certain modality (light, sound, or light-and-sound simultaneously) were preceded and followed by 30 s epochs without stimulation, and these 1.5-min cycles, in turn, were presented alternately in the sequence 'light' – 'sound' – 'light & sound' cycles throughout the night. Sleep stages were scored in 30 s steps. EEG power density in these 30 s epochs was calculated for every 0.5-Hz band in the frequency range 0.5–30 Hz and log-transformed. Artefact-free cycles of sleep N3 stage were analysed. The number of cycles taken in the analysis was such that the cycles with stimuli of different modalities were matched by number of stimuli presented.

Results: Ten subjects completed the study, nine of them (2 males, 7 females; age 21–46 yrs) provided sufficient data for the analysis. The amplitude threshold for the stimuli presentation varied inter-individually from 50 to 70 mV, stimuli intensity – from 1 to 1.4 lx (for light) and from 43 to 46 dB (for sound). The number of paired stimuli per EEG cycle ranged from 3 to 8; the number of cycles of each modality selected for the analysis – from 4 to 21 (median = 11). Light stimuli did not influence EEG power density

($p > 0.01$ compared to the pre-exposure epochs). Acoustic stimuli caused an increase ($p < 0.01$) of EEG power density in the frequency band 0.5–3.0 Hz (delta waves) and a decrease at 11.5–14 Hz (alpha-beta range); the values reverted to baseline at post-stimuli epochs. Simultaneous light & acoustic stimuli effects did not differ from the acoustic stimuli effects. Sleep N2 stage analysis showed results similar to sleep N3 stage.

Conclusions: In contrast to the acoustic stimuli of the same duration and frequency dim red light presented in a closed-loop in-phase fashion, did not influence EEG power density during night sleep, and there was no synergistic effect of these two stimuli on the EEG.

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Dim-Light-Melatonin Onset – The Influences of Season and Weekly Structure

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Objectives: Like other organisms, humans adapt their physiology to the regular 24-hour changes in the environment with the help of a circadian clock. It actively synchronises (entrains) to cyclic environmental signals, thereby establishing a stable phase relationship to these zeitgebers. Light is the most important zeitgeber for the timing of human behaviour. Although entrainment has been extensively investigated in laboratories, only few studies have probed entrainment in real life conditions, by considering individual differences in phase of entrainment (chronotype), and under varying light environments. Here, we report results of investigating the influence of season (summer vs. winter) and weekly schedule (workdays vs. work-free days) on phase of entrainment (assessed via dim-light melatonin onset; DLMO).

Methods: We collected data about sleep and activity in 33 participants for 10 days at approximately the 21st of June (longest photoperiod) and the 21st of December (shortest photoperiod). In addition, we assessed DLMO on a workday and on a work-free day, both in summer and in winter.

Results: While all parameters varied according to the weekly schedule, none showed associations with season. Sleep and activity were later on work-free days. A chronotype-dependent influence of daily activities or schedule on DLMO was found, with the latest chronotypes showing a later DLMO on work-free days. Morning light (between 6:00 h and 12:00 h) was the strongest predictor for the variation in DLMO, with increased exposure to morning light associated with an earlier DLMO. Late chronotypes were exposed to less and later morning light on work-free days relative to workdays in comparison with early chronotypes, possibly explaining the difference in DLMO between workdays and work-free days.

Conclusions: Our results show that the habitual weekly schedule of late chronotypes is able to phase-shift their phase of entrainment (assessed via DLMO) between workdays and work-free days. To counteract this delay in DLMO over the weekend, late chronotypes should increase their morning light exposure on work-free days.

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