Neuropsychobiology

Chronobiology

Society for Light Treatment and Biological Rhythms, 30th Annual Meeting, Groningen (The Netherlands), June 21–24, 2018

ABSTRACTS

Guest Editors
Mirjam Münch, Berlin
Anna Wirz-Justice, Basel

KARGER

Basel · Freiburg · Paris · London · New York · Chennai · New Delhi · Bangkok · Beijing · Shanghai · Tokyo · Kuala Lumpur · Singapore · Sydney

Neuropsychobiology

Abstracts

Neuropsychobiology 2017;76:1–46
DOI: 10.1159/000489584

Published online: May 18, 2018

A1

Circadian and Reward Measures Show Robust Bidirectional Relationships in Bipolar Spectrum Disorder in a 20-Day Naturalistic Ecological Momentary Assessment Study

Lauren B. Alloy[1], *Tommy H. Ng*[1], *Madison K. Titone*[1], *Laura E. Dennis*[2], *Namni Goel*[2]

[1]Department of Psychology, Temple University, Philadelphia, PA, USA; [2]Division of Sleep and Chronobiology, Department of Psychiatry, University of Pennsylvania Perelman School of Medicine, Philadelphia, PA, USA

Objectives: Adolescence/early adulthood is an "age of risk" for bipolar spectrum disorders (BSDs). BSDs have been linked to circadian rhythm and reward processing disruptions; such disruptions may serve as risk factors for BSD mood symptoms/episodes. However, the bidirectional relationships of the circadian and reward systems have not been systematically examined in BSD or at-risk individuals.

Methods: 150 adults (ages 18–27; mean age ± SD, 21.9 ± 2.1 y; 88 women), with high reward sensitivity and a BSD (n = 43), at-risk with high reward sensitivity but no BSD (n = 64), and low-risk individuals with moderate reward sensitivity and no BSD (n = 43) participated in a 20-day naturalistic ecological momentary assessment (EMA) study, involving 3 phases: 1. Baseline; 2. Goal striving and 3. Goal/reward outcome. Salivary dim light melatonin onset (DLMO) was assessed as a circadian phase marker in each phase and the Morningness-Eveningness Questionnaire (MEQ) assessed chronotype. The Willingly Assumed Set of Statistically Unlikely Pursuits (WASSUP) assessed ambitious goal striving, the UPPS Sensation-Seeking subscale determined sensation seeking, and the Card Arranging Reward Responsivity Objective Test (CARROT) and the SPSRQ Sensitivity to Reward subscale measured reward responsiveness and sensitivity, respectively. The Barratt Impulsiveness Scale evaluated impulsivity. Pearson's correlations were used for statistical analysis.

Results: Baseline DLMO positively correlated with goal striving ($r = 0.202$, $p < < 0.05$) and sensation seeking ($r = 0.543$, $p < 0.001$), and with reward sensitivity ratings and reward-relevant events (r's = 0.359–0.457, $p < 0.005$). MEQ negatively correlated with goal striving ($r = –0.135$, $p < 0.05$) and impulsivity ($r = –0.174$, $p < 0.005$). Notably, these relationships were maintained during the goal striving and reward outcome phases, indicating their stability across time.

Conclusions: Our results demonstrate for the first time that a number of validated circadian and reward measures have robust bidirectional relationships in BSD, whereby measures of greater eveningness/later phase (MEQ and DLMO) are related to greater reward sensitivity across various dimensions.

Funding/Disclosures: This work was supported by NIH R01 MH102310.

A2

The Effects of Exercise and Napping on Overnight Sleep

Karina Ando[1], *Hiroyuki Sagayama*[2], *Masaki Takahashi*[3], *Shigenobu Shibata*[3], *Masako Hoshikawa*[1], *Hideyuki Takahashi*[1]

[1]Japan Institute of Sports Sciences, Tokyo, Japan; [2]Japan Society for the Promotion of Science, Tokyo, Japan; [3]Waseda University, Tokyo, Japan

Objectives: To examine the effect of a 90-min daytime nap after high intensity intermittent exercise in the morning on overnight sleep efficiency.

Methods: Six young male athletes (mean ± SE, age: 23 ± 2 years VO2 max: 58 ± 3 mL/kg/min) participated in this study. They performed high-intensity intermittent exercise in the morning. The exercise session began at 10:30–11:00 am. The high intensity intermittent exercise consisted of 12 times × 1-min bout of cycling at 100% of VO2 max with 4-min at 60 rpm, and continuous cycling at 100% of VO2 max until exhaustion at last bout. After the exercise session, the participants ate lunch at 13:00 pm. Nap/no-nap trials were performed at 14:30–16:00 pm randomly for cross comparison and were separated by at least 1 week. Participants ate dinner at 19:30 pm. The bedtime and wake-up time were adapted to each participant and kept consistent between the nap/no-nap trials. The sleep efficiency of the daytime nap and overnight sleep was monitored by a sheet-shaped body vibrometer. As physiological indices, heart rate and respiration rate were measured overnight.

Results: All participants went to bed at 23:30–01:00 and woke up at 06:30–07:30. The length of time in bed did not differ between the nap and no-nap trials. Overnight sleep efficiency was not significantly different between the nap and no-nap trials (93.8 ± 2.0%; NAP, 93.1 ± 1.8%; No-NAP, $p > 0.05$). Heart rate and respiration rate during overnight sleeping were not significantly different between the nap and no-nap trials.

Conclusions: The present study suggested that a 90-min daytime nap after high intensity intermittent exercise in the morning does not interfere with overnight sleep efficiency in young athletes. Further research is required to investigate the effects of a 90-min daytime nap for recovery after morning exercise on afternoon performance in competing athletes.

Funding/Disclosures: None.

E-Mail karger@karger.com
www.karger.com/nps

A3

Synchrony between Bipolar Mood Cycles and Lunar Tidal Cycles Ended after Initiation of Light Treatment and Treatment of Hypothyroidism

David H. Avery[1], *Thomas A. Wehr*[2]

[1]Psychiatric Medicine Associates, Department of Psychiatry and Behavioral Sciences, University of Washington School of Medicine, Seattle, WA, USA; [2]Intramural Research Program, National Institute of Mental Health, Bethesda, MD, USA

Objectives: We examined the relationship between the biweekly lunar spring-neap cycle, which modulates the amplitude of the moon's twice daily tidal cycle, and the timing of mood switches in a 67-year old woman with rapid cycling bipolar II disorder who received maintenance treatment with lithium. Rapid cycling had begun when nortriptyline was prescribed, and it persisted after the drug was discontinued. After thyrotropin levels became elevated during lithium treatment, thyroxine was prescribed.

Methods: The clinical course was documented with calendar records of the switches between depression and hypomania/euthymia. The mood episodes were plotted in relation to the 14.8-day spring-neap cycle. Chi-square periodogram analyses were performed for the time series, and chi-square analysis was done on the distribution of the times of the mood switches in relation to three 5-day periods in the spring-neap cycle.

Results: During an initial 12-month period of observation, mood cycles exhibited a significant ($p < 0.05$) 29 to 30-day periodicity that approximated the lunar synodic month. Switches back and forth between depression and hypomania/euthymia were nonrandomly distributed ($p < 0.0001$), with 14 of 15 switches occurring within two days of full-moon or new-moon peaks of the spring-neap cycle. After light treatment was initiated and doses of thyroxine sufficient to treat lithium-induced hypothyroidism were administered, the mood cycles deviated from synchrony with the lunar cycle and then ceased to oscillate.

Conclusions: Findings in this patient are consistent with previous reports of associations between hypothyroidism and rapid cycling, antidepressant treatment and rapid cycling, and antidepressant treatment and lunar synchrony of mood cycles (Wehr, 2017). The cessation of this patient's rapid cycling during treatment with thyroxine appears to be consistent with earlier findings that hypermetabolic doses of thyroxine can suppress rapid mood cycling. The introduction of regularly scheduled exposures to light also may have contributed to the cessation of cycling by strengthening entrainment of the circadian pacemaker to the solar day. The possibility that lunar mood cycling might be contingent on factors such as antidepressant treatment, decreased thyroid function and exposure to certain types of light-dark cycles will be important in the interpretation of results of research on lunar tidal influences in the future.

Funding/Disclosures: DA has written topics for UpToDate.

A4

Effect of Chronotype and Time of Assessment on Cognitive Performance

Katarína Baranyaiová[1,2], *Kateřina Červená*[1], *Iveta Fajnerová*[1], *Tereza Nekovářová*[1,2]

[1]National Institute of Mental Health, Klecany, Czech Republic; [2]Faculty of Arts, Charles University, Prague, Czech Republic

Objectives: The study focuses on the performance of healthy individuals in cognitive tests that are a common part of the examination and are key to determining the cognitive deficit in neuropsychiatric disorders. As the patient might be tested at different times during the day, it is important to determine whether the time of the day when the test is performed and chronotype of the participant can affect performance to a clinically significant extent. The aim of this study is to determine 1) the extent of the effect of chronotype and time of assessment on cognitive performance, 2) whether cognitive performance depends on the day time of testing with respect to the subjectively preferred time, 3) identify a battery of tests suitable for monitoring the effects specific for extreme chronotypes and 4) find a battery of tests that are independent of the observed effects of time of testing.

Methods: The study was performed in 2 phases. Firstly, an online form of the Morningness Eveningness Questionnaire (MEQ) was used to identify individuals with extreme morning and extreme evening chronotype (MEQ scoring: morning (70–86) and evening (16–30)). During the ongoing second phase we monitor the performance of selected individuals in cognitive tests such as the Cognitive Performance Test (CPT), Trail Making Test (TMT), Stroop test, subtests of Wechsler Adult Intelligence Scale (WAIS-III, etc). Body temperature using iButton thermochrons and physical activity with wrist actigraphy was assessed in order to support chronotype determined by the MEQ questionnaire. Testing takes place in the morning (8:00) and in the evening (20:00) hours, on two separate days (during the weekend). The order of test methods and the time of the first examination are pseudorandomized among individuals.

Results: Until now, 22 healthy volunteers of extreme morning and evening chronotype have been tested. The results of the preliminary analysis have shown interaction between chronotype and the time of day mainly in tests aimed at working memory. A similar interaction was observed in the verbal learning test, both in terms of learning and delayed recall. Both chronotypes had also shown significantly better psychomotor speed during the TMT-A task at their preferred time – morning types in the morning, evening types in the evening testing.

Conclusions: Preliminary results are in line with the study hypothesis, as well as findings from previous studies that confirm the chronotype effect on performance in the working memory tests (Schmidt, 2015; Matchock and Mordkof, 2008). Regarding the limitation of the study – a small sample size, it can be assumed that increased number of participants may even enhance the observed effects.

Funding/Disclosures: The work was supported by grant GAUK no.138217 and project No. LO1611 with financial support of the Ministry of Education, Youth and Sports under the NPU I program.

A5

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

Marta Benedetti[1], *Jean-Louis Scartezzini*[1], *Mirjam Münch*[2], *Christian Cajochen*[3], *Ali Motamed*[1]

[1]École Polytechnique Fédérale de Lausanne (EPFL); [2]Charité Universitätsmedizin Berlin, Institute of Physiology, Berlin, Germany; [3]Psychiatric University Clinics Basel, Basel, Switzerland

Objectives: The objective of this study is to investigate the biological effects of a dynamic control of daylight and artificial lighting on humans. The Non-Image-Forming (NIF) effects of light are currently not sufficiently considered in lighting of indoor work environments, however taking these effects into account is important to improve the health and the productivity of users. We are going to evaluate the impact of different lighting conditions in offices on the circadian system and on visual comfort in healthy young subjects over several days. The aim is to show that an optimal dynamic lighting control integrating both natural and artificial light has beneficial effects on the human physiology and psychology, with respect to a conventional control system.

Methods: The study is carried out in two identical office rooms in the Laboratoire d' Energie Solaire (LESO) experimental building in the École Polytechnique Fédérale de Lausanne (EPFL). The rooms are south-oriented and occupied by a single user. An advanced controller for venetian blinds and electric lighting designed to follow the daylight course in terms of lighting conditions is implemented in the first office (*test room*). In the second office (*reference room*), a controller designed to keep static lighting conditions for only visual requirements is applied. The lighting parameters assessment is performed by High Dynamic Range vision sensors placed close to the workstation, which continuously record vertical illuminance and a glare index. Thirty-four subjects are going to take part in the experiment. Each subject will spend one week in the test room and one in the reference room, in a cross-over-within-subjects design. During the time spent in the offices – between 8h00 and 18h00 – subjects will carry out their normal work and regularly perform some cognitive tests, and complete questionnaires throughout the day to evaluate their cognitive performance, alertness, mood and visual comfort. Saliva samples will be taken regularly for the assessment of their cortisol concentrations. Moreover, their activity and sleep/wake patterns will be continuously monitored by means of actigraphy watches.

Results: A pilot study was performed in the two offices during 13 days in winter in order to assess the performance of the advanced controller for venetian blinds and electric lighting. The novel smart controller demonstrated its capabilities in terms of glare protection and daylight sufficiency, as both the glare index and vertical illuminance were kept in the desired ranges.

Conclusions: The study will allow to investigate the effects of a dynamic office lighting control on humans' circadian system and visual comfort. The advanced controller is expected to improve the alertness, cognitive performance and visual comfort of users. Preliminary tests of the controller showed its effectiveness in keeping target indoor luminous conditions.

Funding/Disclosures: The study is funded by the project "NEST SolAce Unit from EPFL Researchers" and by LESO solar experimental building at EPFL.

A6

Efficacy and Safety of Light Therapy for Bipolar Depression

Francesco Benedetti, Cristina Colombo

Psychiatry & Clinical Psychobiology Unit, Division of Neuroscience, San Raffaele Scientific Institute, Milano, Italy; University of Vita-Salute San Raffaele, Milano, Italy

The scientific approach to the treatment of depression with bright light started in the '80s. Soon at the beginning, in the first reported trials, antidepressant light therapy (LT) was administered to patients with bipolar depression (BD), and was given one to two hours before the usual time of awakening.

Since then, 45 scientific reports in peer-reviewed journals described the clinical outcomes of 890 bipolar depressed patients treated with antidepressant morning LT. A historical review of all this wide literature, yet unpublished, shows that both randomized controlled trials (RCTs) (n = 8) and open trials support the rapid antidepressant efficacy of LT, both when given alone, and when combined with other chronotherapeutic techniques, such as sleep deprivation and sleep phase advance; or when combined with antidepressant drugs and mood stabilizers.

No major side effects have been reported. In particular, the favourable safety profile of LT for BD is well evident when considering the risk of treatment-emergent mania: The switch process is a fundamental and defining characteristic of BD, and, based on available clinical trial data, the rate of switch into mania for patients with BD has been calculated at 4.2% during treatment with placebo, at 15–40% with antidepressant drugs, and below 3% with LT.

In general, meta-analyses and RCTs showed that the effect size of antidepressant LT, both for seasonal- and non-seasonal depression, is equivalent to those in most antidepressant pharmacotherapy trials. However, notwithstanding this story of success, the majority of devices for the administration of LT are registered as medical devices for the treatment of winter depression only, and some user manuals even reported the diagnosis of Bipolar Disorder as a contraindication to morning LT for the risk of triggering manic switches.

Bipolar depression is a difficult-to-treat condition, with extremely low success rates of antidepressant drugs, and with a 30% lifetime prevalence of completed suicide. Given the vast positive experience of many clinicians all over the world with morning LT in BD, we are concerned that this treatment will be limited by healthcare regulatory issues, causing problems in further clinical applications of light in our patients.

A7

The Circadian Rhythm of ADHD

Denise Bijlenga[1], *J.J. Sandra Kooij*[1,2]

[1]PsyQ Expertise Center Adult ADHD, The Hague, The Netherlands; [2]VU Medical Center, Department Psychiatry, Amsterdam, The Netherlands

Objectives: Attention-deficit/hyperactivity disorder (ADHD) is characterized by childhood-onset symptoms of inattention, impulsivity, and/or hyperactivity with a cross-national prevalence of 5.3% in children and 2.8% in adults, and has a major impact on well-being. Sleep is primarily impacted in ADHD, both in children and adults. The most common sleep problem in ADHD is a delayed circadian rhythm, with a prevalence of 78% in adults with ADHD. Sleep problems may be intrinsic features, causes, or effects of ADHD.

Methods: This presentation gives an overview of existing evidence of the link between ADHD and sleep problems, in particular the delayed circadian rhythm, throughout the lifespan. This evidence stems from genetic, sleep, therapy, lifestyle, and population studies.

Results: The strong relationship between ADHD and sleep problems is reflected by the functional and neuroanatomical overlap of brain regions involved in attention, arousal and sleep regulation. Some of the variations in clock genes that are responsible for a lengthening of tau have also been linked to ADHD. Also, there is a geographical correlation between higher solar intensity and a lower prevalence of ADHD, which may be explained by the clock-resetting effect of daylight. High daylight intensity is a stronger cue than low daylight intensity to synchronize delayed circadian rhythms, leading to less delayed rhythms and less ADHD symptoms.

Conclusions: Various sleep problems and symptoms of ADHD have shared etiology, genetic and environmental factors, that interact and influence each other. Those with a genetic disposition to a lengthening of the sleep cycle may profit from stronger synchronization cues such as high daylight intensity, leading to a better synchronized circadian rhythm, better sleep, and fewer ADHD symptoms.

Funding/Disclosures: None.

A8

Relationship between Diurnal Variation and Depression Severity in Patients with Unipolar Major Depression

Jonathan Jetsmark Bjerre, Signe Dunker Svendsen, Klaus Martiny

Psychiatric Center Copenhagen, New Interventions in Depression Group (NID), University of Copenhagen, Rigshospitalet, Copenhagen, Denmark

Objectives: The purpose of this study was to systematically examine diurnal mood changes and their interrelatedness to depression severity, chronotype, and melancholic features, in patients with a major depressive episode. If a clear relationship between depression severity and diurnal variation (evening best) is found, this can be used as a clinical tool for staff at inpatient wards to monitor patients' clinical state. Furthermore, we wanted to elucidate the old question regarding the division between melancholic and reactive depression by incorporating chronotype and newly developed symptoms profiles together with depression severity and diurnal mood changes. This is inspired by the work of Gordon Parker in Australia.

Methods: We included patients from an outpatient affective disorders ward and from a psychiatric specialist practice.

At baseline, sociodemographics were collected, and a diagnostic interview was performed. We assessed depression severity with the Hamilton scale, subjective depression severity with the Major Depression Inventory (MDI), sleep quality with the Pittsburgh Sleep Quality Index (PSQI), quality of life with the WHO-5, chronotype with the Morningness-Eveningness Questionaire (MEQ), and used a panel of questions designed to categorize melancholic and reactive depressions. In the following week patients evaluated depression severity every day at awakening, 9 AM, 12 Noon, 3 PM, 6 PM, 9 PM, and before sleeping, using the Preskorn scale (scored from 0 to 10 with 10 = worst depression). Furthermore, patients logged their sleep timing, using a sleep diary. Diurnal data were analysed by use of a mixed model with repeated measures, and relations between variables were analysed with a linear regression model.

Results: Preliminary results from the first 11 patients showed that all patients fulfilled the criteria for a major depressive episode. Mean age was 45.1 (SD = 10.9) years with a duration of current episode of 7.5 (SD = 5.6) month. Mean MDI score was 21.4 (SD = 11.2), and mean WHO-5 score was 34.0 (SD = 24.0) (normal values in Denmark are >70). The mean Hamilton score was 10.0 (SD = 4.2), ranging from 3 (no depression) to 25 (moderate-severe depression). Self-assessed mood ratings showed that nine patients had a positive diurnal variation (evening best) with a mean improvement in mood, during the day, of 1.4 (SD = 0.9). This was statistically significant in seven out of nine patients (77.8%), (all with $p < 0.05$). Two patients experienced worsening during the day. For the nine patients with a positive diurnal variation, we found a statistically significant relation between the degree of diurnal variation and corresponding Hamilton depression score ($p = 0.05$, R-square 0.45), and also between diurnal variation and corresponding WHO-5 score ($p = 0.05$, R-square 0.44).

Conclusions: There seems to be a clear relation between depression severity and the degree of diurnal variation and this might provide us with an important clinical tool for staff to access depression severity. The results regarding chronotype and melancholia are awaiting the results from a larger sample. The study is ongoing with a planned sample size of 50 patients. We will present the final data.

Funding/Disclosures: None.

A9

Prolonged Photoperiod Induces Changes in Sleep: The Impact of Blue-Enriched Light

Louise H. Bjerrum[1], Torhild T. Pedersen[1], Jelena Mrdalj[1], Jonathan P. Wisor[2], Andrea R. Marti[1], Michael Rempe[2,3], Tone E.G. Henriksen[1,4], Janne Grønli[1]

[1]University of Bergen, Bergen, Norway; [2]Washington State University, Spokane, WA, USA; [3]Whitworth University, Spokane, USA; [4]Valen Hospital, Helse Fonna, Norway

Objectives: Light exerts a direct effect on slow-wave sleep (SWS) and electroencephalogram (EEG) slow-wave activity (SWA; 0.5–4 Hz). It has been suggested that blue-enriched light promotes alertness in both humans and rodents through signaling via intrinsic photosensitive retinal ganglion cells (ipRGCs). Here we use a model of prolonged photoperiod (20 h light, 4 h dark; 20:4 LD) of two different light spectra (white and blue-enriched) to characterize the effects on sleep in rats.

Methods: Rats (n = 6/group) were housed in 12:12 LD cycle for 5 days, followed by 7 days of exposure to prolonged photoperiod 20:4 LD in either white or blue-enriched light, and 7 days recovery in 12:12 LD. Sleep (EEG and electromyogram) was recorded continuously by means of telemetry. We report data (% ± SEM change from 24 h baseline) and statistical analyses on total sleep time (TST), time in SWS, and SWA from day 7 of exposure to prolonged photoperiod (E7), and recovery day 1–7 (R1–R7).

Results: At E7, only white light increased TST (white: 8.9 ± 3.6%, p = 0.004 vs. blue: 3.6 ± 1.5%, p = 0.155) and time in SWS (white: 8.9 ± 3.7%, p = 0.014 vs. blue: 4.1 ± 1.7%, p = 0.193). SWA in SWS was not significantly changed at E7 compared to baseline. During recovery in the 12:12 LD condition, TST was increased at R2 (prolonged white: 8.3 ± 3.4%, p = 0.023), R3 (prolonged blue: 8.3 ± 3.4%, p = 0.030) and R4 (prolonged blue: 7.5 ± 3.1%, p = 0.042) compared to baseline. Time in SWS and SWA in SWS showed no significant differences at R1-R7 compared to baseline.

Conclusions: Prolonged photoperiod has short and long-term effects on sleep in the rat, and the effects are dependent upon light spectra. Prolonged exposure to white light increased total sleep time and time spent in slow-wave sleep, whereas prolonged exposure to blue-enriched light increased total sleep time in recovery only.

Funding/Disclosures: The work was funded by Helse Vest (ID HV911 893) and the Faculty of Psychology, University of Bergen (Småforsk, ID 173200-270452).

A10

The Effect of Bright Light on Blood Pressure and Heart Rate in Essential Hypertension

Mikhail L. Blagonravov, Anna A. Bryk, Evgenia V. Medvedeva, Vyacheslav A. Goryachev, Sergey M. Chibisov, Sergey P. Syatkin, Madina M. Azova, Tatyana Y. Zotova

Peoples' Friendship University of Russia (RUDN University), Moscow, Russia

Objectives: Bright light therapy (BLT) showed positive results with respect to seasonal affective disorders, non-seasonal depression, sleep disorders and so on. Meanwhile, there is still little data concerning the effects of light therapy on functional activity of the cardiovascular system and particularly in case of hypertension. We therefore studied the features of daytime and nighttime blood pressure (BP) and heart rate (HR) in genetically hypertensive and normotensive rats under the action of bright light (BL).

Methods: We performed our experiments on 32–34 weeks old male rats of SHR (hypertensive, n = 5) and Wistar-Kyoto (normotensive, n = 5) strains. Animals were kept in individual cages under 12:12 h light-dark schedule with light on at 7.00 am and off at 7.00 pm, daytime ~ 300 lux white light at eye level and nighttime absolute darkness. To estimate the effect of BL the animals were exposed to 1 hour action of ~ 10,000 lux white LED light from 10.00 am to 11.00 am. Systolic and diastolic blood pressure (SBP and DBP), heart rate (HR) were monitored continuously for 24 hours the day before (controls) and on the very day of BL exposure. BP and HR monitoring was carried out with the use of radio-telemetry system (DSI, USA) which consists of radio-transmitter (sensor) DSI HD-S11 implanted in the animal body, receiver, data exchange matrix and computer for storing data. BP was monitored in the lumen of the abdominal aorta. Thanks to the use of implantable sensors animals were totally freely moving the whole duration of the experiment. The data was processed with software Dataquest A.R.T. 4.33 (DSI, USA).

Results: It was found that SBP and DBP were significantly higher in the SHR rats compared to the normotensive rats for the whole 1 hour period of BL exposure in comparison with the same time interval (from 10.00 to 11.00 am) of the previous day when BL was not used. The average levels of daytime (10.00 am – 7.00 pm) SBP and DBP were significantly increased in the hypertensive rats compared with the control rats which might indicate that the effect of BL remains notable even after the end of its exposure. For HR only a clearly defined tendency to an increase was seen. For the nighttime period after the day of BL exposure all of the monitored parameters of the hypertensive rats had the same values as in the controls. In normotensive rats the action of BL induced no significant changes in BP or HR.

Conclusions: Our data shows that BL induces an increase in BP in hypertensive but not in normotensive rats both at the time of BL exposure and after it. This should be taken into account when using BLT in case of concomitant hypertension.

Funding/Disclosures: The publication was prepared with the support of the "RUDN University Program 5-100".

A11

Estimating Parameters in a Model of the Human Circadian Rhythm Using a Particle Filter

Jochem H. Bonarius[1], *Jean-Paul M.G. Linnartz*[1,2]

[1]Signal Processing Systems Section, Department of Electrical Engineering, Eindhoven University of Technology, Eindhoven, The Netherlands; [2]IoT Systems, Philips Lighting Research, Eindhoven, The Netherlands

Objectives: We address the challenge of tracking an individual's circadian phase and -amplitude in real-time using imperfect sensors. We extend existing mathematical models of the human circadian rhythm using Bayesian inference: as more observations of the response of an individual's circadian rhythm to light exposure become available, we can update the values of the models' function parameters to better fit the characteristics of that individual. As we ultimately want to improve human-centric lighting control, we do not aim for a clinically accurate estimate, but we need an estimate that is adequate for choosing between different options for light settings.

Methods: In our work we combine the Kronauer *et al.* model of the circadian pacemaker with the Phillips *et al.* model of the homeostatic sleep drive to form a model of sleep regulation. As these models were developed by fitting mathematical functions to the *average* of data collected in studies with human subjects, they will always give the same response to an input, which does not accurately represent the response of an individual. Instead, we consider that the function parameters in the models differ between individuals, as they reflect physiological characteristics, such as age, chronotype and light sensitivity. We show that the mathematical technique of a Particle Filter, a sequential Monte Carlo method, can estimate parameter values that best correspond with an individual's physiological characteristics by minimizing the error between model output and the real-life response of that individual, thereby reducing the modeling error.

Results: We illustrate our method by applying it to data from a field trial with 20 subjects. By processing light exposure- and actigraphy data recorded over several days with the proposed Particle Filter, we estimate every subject's intrinsic circadian period (tau). When correlating these to their Munich Chronotype Questionnaire midsleep time, a significant relationship was found: $r > 0.6$ and $p < 0.01$.

Conclusions: We have shown that it is possible to estimate the intrinsic circadian period of several human test subjects with reasonable accuracy using only light exposure- and actigraphy data as reference. This demonstrates how a Particle Filter can estimate parameter values in a model of sleep regulation, to be able to more accurately track an individual's circadian phase and amplitude.

Funding/Disclosures: Financial support was obtained from the NWO Domain Applied and Engineering Sciences under project Optilight. This project has been funded under a program co-financed by Philips Lighting Research. However, it was carried out and reported as an independent party by the Eindhoven University of Technology.

A12

From Space Flight Lighting Countermeasures to the Patient Bedside: Developing Light Therapy for Sleep and Mood Disruption in Brain Injury

George Brainard, Samer Jasser, Benjamin Warfield, Sreeramya Kanumilli, Leanna Panepinto, Fadee Disoke, Talia Glodjo, Kimberly Atkinson, Colette Glatts, Mijail Serruya, Lisa Bowman, Carissa Pineda, John Hanifin

Neurology Department and the Rothman Institute, Thomas Jefferson University, Philadelphia, PA, USA

Objectives: Sleep deficiency has been documented in astronauts during International Space Station (ISS) missions (Barger et al., Lancet Neurol., 2014). Light can be a powerful countermeasure for circadian misalignment and sleepiness. The ISS interior is being retrofitted with Solid-State Light Assemblies (SSLAs) that have three color temperature modes (NASA S684-13489, 2013). Ground-based and in-flight studies are being done to test the efficacy of SSLAs for supporting astronaut vision as well as effects on circadian, neuroendocrine, neurobehavioral and sleep physiology (Brainard et al., Acta Astronautica, 2013; COPM, 2016). The broad goal of the following project is to determine if this new space flight technology can be adapted for use in hospitals. A study on patients with traumatic brain injury showed the benefits of light therapy in alleviating fatigue and daytime sleepiness (Sinclair et al., Neurorehab. and Repair, 2014). The specific aim of the research reported here is to characterize sleep and mood disruption in patients with brain injury to determine if light therapy can improve such symptoms.

Methods: Two separate, two-week observational trials have been completed: 1) patients with concussion and age/sex matched control subjects ($N = 26$); and 2) stroke patients and age/sex matched control subjects ($N = 20$). A third, five-week lighting interventional study is in progress. The interventional study involves a randomized, controlled trial of daily 45 minute morning light therapy exposures. Light therapy was from solid-state devices. Placebo light units are accentuated light in the long wavelengths, hypothesized to be less active for stimulating the circadian system. Active light units are rich with light in short wavelengths, hypothesized to be more active for circadian stimulation. In all studies measurements include actigraphy and validated mood, fatigue, and sleep quality tests. Statistical analyses include ANOVA with post-hoc multiple range tests.

Results: Actigraphy provided objective measures of circadian and sleep stability. For example, in the completed studies, actigraphy demonstrated that concussion patients had statistically and clinically meaningful longer sleep latencies compared to control subjects ($p < 0.02$). Similar significant results were observed in the study with stroke patients ($p < 0.005$). Measurement of mood disturbance with the Beck Depression Inventory showed that concussion patients had significantly increased mood disturbance ($p < 0.001$) compared to control subjects. Stroke patients also showed significant increased mood disturbances ($p < 0.0001$) compared to their matched control subjects. The light therapy trial is ongoing.

Conclusions: The results are potentially important to the medical care of patients with brain injury. These studies will con-

tribute to the design of future, built-in smart lighting interventions for hospitals and home care environments to foster patient health and well-being.

Funding: NSF #EEC-0812056; PhotoPharmics, Inc.; TJU Dean's Transformational Science Award; The Institute for Integrative Health; and the Philadelphia Section of IESNA.

A13

Impact of Light's Origin on Acute Alertness

Kai Broszio, Martine Knoop, Stephan Völker

Lighting Technology, Technische Universität Berlin, Berlin, Germany

Objectives: Studies under nighttime conditions addressing melatonin suppression and phase shift as well as research into the human retina showed that the intrinsically photosensitive Retinal Ganglion Cells (ipRGCs) are not evenly distributed. Their density respectively their sensitivity is highest at the lower and at the nasal part of the retina. Beyond that, light illuminating both eyes is more efficacious in melatonin suppression if compared to illumination of only one retina. Our earlier analysis of lighting scenes confirmed that scenes with the same vertical illuminance can have very diverse luminance patterns within the visual field. This might influence the effective radiation for non-image forming (NIF) effects. Thus, illuminance at the eye is not the adequate measure to quantify the light's potential to induce NIF effects. The aim of this study is to investigate the impact of two very different luminance distributions with the same illuminance and the same melanopic-weighted irradiance at the eye on NIF effects, in this case acute alertness. Whereas the results might be used to validate the impact of light's origin on a nighttime NIF effect, they will also give insight into the importance of this design parameter on alertness during daytime.

Methods: In this study, subjects will be exposed to different lighting scenes in an office-like test room. The experiments will be conducted at day- and nighttime. Our previous analysis indicated what specific luminance distributions can be more effective in causing NIF effects, when a higher sensitivity or density of ipRGCs in specific retinal areas or a higher effectiveness of illumination of both retinas is assumed. From this, two very different luminance distributions in the visual field will be defined for this study. One lighting scene with assumed high and one lighting scene with assumed low NIF efficacy; both with the same illuminance, respectively melanopic-weighted irradiance, at the eye. These luminance distributions will be adjusted to three absolute levels: a dim, a medium and a bright light condition. The medium level will be the 'bright' nighttime and the 'dim' daytime level. The spectrum respectively the CCT of the light will not be modified. Acute alertness will be assessed in both the night- and daytime condition. A pilot study, preceding the main study, should address the following questions: Which method is adequate for measuring acute alertness in a setting investigating the light's origin impact? Which illuminance levels are suitable to induce and detect daytime and nighttime NIF effects?

Results: Results of the pilot study are expected by fall 2018 and preliminary results of the main study are expected in summer 2019.

Conclusions: This study will give insight into the impact of light's origin on acute alertness during day- and nighttime.

Funding/Disclosures: None.

A14

Effects of Light Therapy on Mood and Glucose Metabolism in Patients with Depression and Type 2 Diabetes

Annelies Brouwer[1], Daniel H. van Raalte[2], Femke Rutters[3], Peter M. van de Ven[3], Petra J.M. Elders[4], Eus J.W. van Someren[5], Frank J. Snoek[6], Aartjan T.F. Beekman[1], Marijke A. Bremmer[1]

[1]Department of Psychiatry, Amsterdam Public Health Research Institute (APH), VU University Medical Centre (VUmc) and GGZ inGeest, Amsterdam, The Netherlands; [2]Diabetes Center, VUmc, Amsterdam, The Netherlands; [3]Department of Epidemiology and Biostatistics, APH, VUmc, Amsterdam, The Netherlands; [4]Department of General Practice and Elderly Care Medicine, APH, Amsterdam, The Netherlands; [5]Department of Integrative Neurophysiology and Medical Psychology, Centre for Neurogenomics and Cognitive Research, Neuroscience Campus Amsterdam, VUmc, Amsterdam, The Netherlands; [6]Department of Medical Psychology, VUmc and Academic Medical Center, Amsterdam, The Netherlands

Objectives: Depression and type 2 diabetes often co-occur. Novel treatment strategies for depression in this patient population are warranted, as depression is associated with poor prognosis and treatment results. Light therapy has shown to be an effective antidepressant, possibly by entrainment of the circadian rhythm and improvement of sleep. The circadian system is also involved in the regulation of glucose metabolism, in particular by modulating peripheral insulin sensitivity. Hence, we aimed to evaluate the effects of light therapy on mood and glucose metabolism in patients with depression and type 2 diabetes.

Methods: We conducted a randomized, double-blind, parallel trial in which 83 patients with depression and type 2 diabetes were exposed to active light (10,000 lux, broad-spectrum white-yellowish) or placebo light (450 lux, monochromatic 545 nm green) half an hour every morning for 4 weeks at home. Numerous psychological, circadian and metabolic measures were obtained during the light therapy treatment period, and four weeks after completion of the treatment.

Results: Data collection has been concluded in November 2017 and data-analysis started in March 2018. At the SLTBR meeting June 2018 we will present the effects of light therapy on absolute and significant reduction in depressive symptoms, depression remission, and subjective and objective sleep measures. Additionally, we will present the effects of light therapy on HbA1c and insulin sensitivity, as measured with a hyperinsulinemic euglycaemic clamp procedure – the golden standard for measuring peripheral insulin sensitivity.

Conclusions: If light therapy improves mood and has positive effects on glucose metabolism, it may be a valuable patient

friendly addition to the currently available treatment strategies for depression in patients with type 2 diabetes.

Funding/Disclosures: This study is supported by a European Foundation for the Study of Diabetes (EFSD)/Lilly Mental Health award. Aartjan T. F. Beekman has received unrestricted funding from Lundbeck (speakers bureau).

A15

Light Therapy: Is it Safe for the Eyes? A Systematic Review

Annelies Brouwer[1], Huang-Ton Nguyen[2], Frank J. Snoek[3], Daniel H. van Raalte[4], Aartjan T.F. Beekman[1], Annette C. Moll[2], Marijke A. Bremmer[1]

[1]Department of Psychiatry, Amsterdam Public Health Research Institute (APH), VU University Medical Centre (VUmc) and GGZ inGeest, Amsterdam, The Netherlands; [2]Department of Ophthalmology, VUmc, Amsterdam The Netherlands; [3]Department of Medical Psychology, VUmc and Academic Medical Center, Amsterdam, The Netherlands; [4]Diabetes Center, VUmc, Amsterdam, The Netherlands

Objectives: Light therapy has become an increasingly popular treatment for depression and a range of other neuropsychiatric conditions. Yet, concerns have been raised about the ocular safety of light therapy.

Methods: We conducted a systematic review into the ocular safety of light therapy. A PubMed search on January 4, 2017, identified 6708 articles, of which 161 were full-text reviewed. In total, 43 articles reporting on ocular complaints and ocular examinations were included in the analyses.

Results: Ocular complaints, including ocular discomfort and vision problems, were reported in about 0% to 45% of the participants of studies involving light therapy. Based on individual studies, no evident relationship between the occurrence of complaints and light therapy dose was found. There was no evidence for ocular damage due to light therapy, with the exception of one case report that documented the development of a maculopathy in a person treated with the photosensitizing antidepressant clomipramine.

Conclusions: Results suggest that light therapy is safe for the eyes in physically healthy, unmedicated persons. The ocular safety of light therapy in persons with preexisting ocular abnormalities or increased photosensitivity warrants further study. However, theoretical considerations do not substantiate stringent ocular safety-related contraindications for light therapy. The systematic review of the ocular safety of light therapy was complicated due to varying and often poor reporting of light therapy treatment characteristics in research articles. We believe that concise reporting of light therapy treatment characteristics may enhance the comparability of different light therapy treatments, particularly in the meta-analysis of clinical trials. We envision that a consensus statement on the topic, preferably supported by the Society for Light Treatment and Biological Rhythms (SLTBR), may contribute to better reporting in future.

Funding/Disclosures: This study is supported by a European Foundation for the Study of Diabetes (EFSD)/Lilly Mental Health award. Aartjan T. F. Beekman has received unrestricted funding from Lundbeck (speakers bureau).

A16

Impact of Light on Functional Brain Connectivity in Young and Older Individuals

Julie Carrier

Université de Montréal, Montréal, QC, Canada

Beyond being essential for vision, light has numerous non-visual effects, including stimulating cognitive functions and alertness. Non-visual effects of light could decrease with aging, and may contribute to cognitive complaints and sleepiness in older individuals. However, both the brain and the eye (lens yellowing, senile miosis) profoundly change in aging. Whether the effect of light on cognitive brain functions varies in aging and whether age-related ocular changes contribute to the variations are not established. We compared the impact of light on non-visual cognitive brain activity using functional magnetic brain imaging in younger and older individuals with their natural lenses or with intraocular lens replacement following cataract surgery. Brain responses to executive tasks and cerebral connectivity were analysed during either blue (480 nm) or orange (620 nm) monochromatic light exposures. Analyses reveal that light modulates executive brain responses in both young and older individuals. The effects of light were, however, stronger in young individuals including in the hippocampus and frontal and cingular cortices. Light effects did not significantly differ between older individuals with their natural lenses and older individual with intraocular replacement. Preliminary analyses also indicate that light wavelength modulate cerebral functional connectivity. These findings show that light can affect non-visual cognitive brain activity in aging but less than in young adults. The absence of differences between older individuals with clear or natural lenses supports that the aging brain adapts to progressive changes in light and show therefore plasticity in its non-visual light sensitivity.

A17

Differences in Energy Expenditure during Morning and Evening Maximal Ergospirometry in Extreme Chronotypes

Kateřina Červená[1,2], Roman Šolc[2], Katarína Baranyaiová[3], Zdeňka Bendová[1,2]

[1]Department of Sleep Medicine and Chronobiology, National Institute of Mental Health, Klecany, Czech Republic; [2]Faculty of Science, Charles University, Prague, Czech Republic; [3]Faculty of Arts, Charles University, Prague, Czech Republic

Objectives: The main objective of this project is to evaluate the effect of chronotype on cardiopulmonary and metabolic responses to exercise during early morning and late evening testing conducted during the long and short photoperiod using maximal exercise ergospirometry.

As a behavioral manifestation of the innate circadian period, chronotype can be influenced by many other factors. Our next goal is to distinguish the genetic basis of chronotype from other factors

by genotyping DNA samples from tested subjects, as well as from a larger population sample to determine polymorphic variants of selected clock genes involved in the genetic basis of chronotype formation.

Methods: 15 morning types and 18 evening types participated in the winter testing and 17 morning types and 15 evening types participated in the summer testing. Chronotype of the participants was determined using the Morningness – Eveningness Questionnaire (MEQ). Prior to the ergospirometry testing each participant performed a 10 min PEBL Perceptual Vigilance Task (PPVT) to assess reaction time, sleepiness and arousal. Cardiometabolic parameters were measured during maximal exercise ergospirometry. Heart rate, blood pressure, inhaled O2 and exhaled CO2 at rest and during all stages of the exercise protocol were obtained, including the time of Anaerobic Threshold (AT) and maximum rate of oxygen consumption (VO2 max), as well as post-exercise heart rate recovery rate.

Results: Preliminary results indicate more pronounced differences between morning and evening cardiopulmonary response to exercise performed in winter and relatively worse performance of evening types during morning exercise than morning types during evening exercise. Full results are expected in June 2018.

Conclusions: Our society largely favors extreme morning types in terms of work schedules. Given that extreme morning types comprise only few percent of the population and the resulting social jet-lag in many other individuals, actual data comparing early morning and late evening performance capacity are useful for the possible debate on potential work schedule adjustments based on individual chronotype.

Funding/Disclosures: None.

A18

Application of Mathematical Modeling for Faster Circadian Entrainment

Philip Cheng[1], *Olivia Walch*[2], *Christopher Drake*[1]

[1]Henry Ford Health System, Detroit, MI, USA; [2]University of Michigan, Ann Arbor, MI, USA

Objectives: In a fast-paced and globalizing economy, there is growing demand for non-traditional work schedules (e.g., night shift work) and flexible travel; however, these are often accompanied by the adverse consequences of circadian misalignment (e.g., shift work disorder, jet lag, etc.) Though phototherapy can have robust effects in shifting circadian phase, large phase shifts (e.g. 10–12 hours) often require repeated doses over approximately one week.

One solution is to use mathematical modeling to derive phototherapy schedules optimized for large phase shifts in minimal time. These schedules have been released through the mobile application, *Entrain*, since 2014, and have shown promise; however, their efficacy has never been tested in controlled laboratory conditions. This study aims to test the feasibility and efficacy of a mathematically optimized phototherapy schedule to create larger phase shifts than traditional phototherapy.

Methods: A total of 10 participants will be recruited and randomized into either the traditional phototherapy schedule or the mathematically optimized phototherapy schedule. In both conditions, participants will receive three large doses of bright light across three days in a laboratory environment controlled for ambient temperature and light. Participants in the traditional phototherapy condition will receive bright light in the phase delay portion of the phase response curve and darkness (<10 lux) in the phase advance portion. Light/dark exposure in the mathematically optimized schedule will be determined using the Kronauer model. Circadian phase will be assessed via dim light melatonin onset (DLMO) before and after the light interventions. Bright light (10,000 lux) will be delivered via light box for periods of 30 minutes that are alternated with 500 lux of ambient light. Darkness is operationalized as <10 lux during wakefulness, and complete darkness during sleep.

Results: Though data collection is still on-going, preliminary analyses indicate that the optimized phototherapy schedule will induce larger phase delays (10–12 hours) compared to the traditional phototherapy condition (4–6 hours).

Conclusions: This study takes the first steps in translating mathematically optimized phototherapy into real-world interventions.

Funding/Disclosures: This study is funded by the Henry Ford Health System Proposal Development Grant. Funding for PC is also provided through the National Institutes of Health (K23HL138166).

A19

Assessing the Impact of Light-at-Night on Sleep, Circadian Function and on Physical and Mental Well-Being

Michael Cleary-Gaffney, Andrew N. Coogan, Brian Espey

Maynooth University, Maynooth, Ireland

Objectives: The negative effects that both continuous light-at-night and dim light-at-night (LAN) exposure has on sleep and health has been well documented in experimental studies. However, it is unclear how an individual's routine nighttime lighting habits in their home environments impacts on their sleep and health. This study aims to gain a better understanding of the main sources of light-at-night in home settings and whether individuals perceive light-at-night as impacting on their sleep, cognitive function, physical and mental well-being. In addition, the study aims to understand whether our geographical location has an impact on light-at-night exposure.

Methods: In this ongoing cross-sectional study, participants, (n = 477, males = 148/females = 329, age (M = 37.97, SD 13.29) completed a developed questionnaire addressing the perception of the impact of LAN and perceived sources of LAN alongside validated measures of sleep quality (Pittsburgh Sleep Quality Index; PSQI), cognitive function (Cognitive Failures; CFQ) and physical and mental well-being (General Health Questionnaire). Astrophysical data was used to provide an objective measure of outdoor light exposure. This allows to cross-reference the individuals subjective perception of outdoor light against the objective measure of outdoor light.

Results: We found that individuals who subjectively perceive having outside light entering their bedroom report higher GHQ

scores (p = 0.017, Cohen's d = 0.21), have poorer sleep quality (p < 0.001, Cohen's d = 0.41), and higher cognitive failures (p = 0.017, Cohen's d = 0.359) compared to those who perceive low level outdoor light. However, when the GHQ is examined under its specific subscales the subjective perception of outdoor light is only having an effect on somatic symptoms (p = 0.008, Cohen's d = 0.24) and anxiety/insomnia (p = 0.001, Cohen's d = 0.30). Significant effects are not observed in the domains of social dysfunction and severe depression. When examining objective measures of outdoor light and the subjective perception of outdoor light, no relationship is found. Results also indicate that the perception of indoor light from outside the bedroom (e.g., light from bathroom) has no effect on psychological distress, sleep quality or cognitive failures. The perception that light emitting devices disrupt sleep has significant negative effects on total GHQ scores (p = 0.001, partial n^2 = 0.027), sleep quality scores (p = 0.001, partial n^2 = 0.066) and cognitive failure scores (p = 0.001, partial n^2 = 0.045).

Conclusions: The subjective perception of LAN exposure yielded mixed results with the perception of outdoor light having a negative effect on sleep quality and health. However, the same effects were not observed for indoor light outside the bedroom. There was a mismatch between the objective measures of outdoor light and the subjective perception of outdoor light. It may be that individuals who report having poor sleep and poor health have a heightened negative perception of light-at-night in the bedroom.

Funding/Disclosures: John & Pat Hume Doctoral Scholarship.

A20

Actimetric Day/Night Index as a Predictor of Treatment Response in Depression

Konstantin V. Danilenko[1,2], *Kristina A. Mazhara*[2], *Sergei V. Yarosh*[1], *Maria Y. Lebedinskaia*[1], *Evgenia V. Gadetskaia*[1], *Lyubomir I. Aftanas*[1,2]

[1]Institute of Physiology and Basic Medicine, Novosibirsk, Russia; [2]Novosibirsk State University, Novosibirsk, Russia

Objectives: Actimetry provides objective measures of rest-activity cycles. It yields indirect measures of certain sleep parameters, and when measured over several days, it may also approximate circadian measures, such as circadian phase (based on mid-sleep), circadian amplitude (based on the day/night activity index) and day-to-day sleep-wake cycle variability. We analysed actimetry-based circadian measures in depressed patients during xenon treatment.

Methods: Actimeters MotionWatch 8 (CamnTech, England) were worn on the non-dominant arm in depressed patients with MDD or dysthymia (according to DSM-5 criteria) hospitalised for a randomised, double-blind, placebo-controlled xenon (Xe) therapy study. Xe (an antagonist of NMDA receptors) in combination with nitrogen/oxygen was inhaled in sub-anesthetic doses for 15 minutes daily for 10 days (excluding weekends). In the placebo group, only nitrogen/oxygen was used. Actimeters were usually worn during pre-treatment (2–5 days) and for the first half of the treatment session (4–5 days). The actimetric indices were calculated manually (mid-sleep) or using the MotionWare 1.1.20 tool (day/night activity index and sleep-wake cycle variability). Depression was scored using the Hamilton Depression Rating Scale (HDRS-17) before and at the end of treatment.

Results: Actimetric data were available from 30 patients, aged 19–66 y. The day/night activity index correlated significantly with the HDRS-17 score reduction (either for absolute or relative values, p < 0.04, Spearman test): a greater day/night index was associated with greater reduction. The result was mainly due to the active (Xe) group who improved more than the placebo treated patients. Circadian phase or circadian rhythm variability did not correlate significantly with the score reduction.

Conclusions: The result is in line with previous findings of an association between greater circadian day night amplitude in depression with better treatment outcome. Actimetry thus provides an easy-to-document predictive objective measure.

Funding/Disclosures: Budgetary fund.

A21

Caffeine or Light at Night; Effects on Sleep and Circadian Rhythms in Rodents

Tom Deboer

Laboratory for Neurophysiology, Department of Cell and Chemical Biology, Leiden University Medical Center, Leiden, The Netherlands

The presentation will summarize recent data regarding the influence of sleep deprivation, light and caffeine on circadian clock functioning. These can be single influences, but it has also been shown that they can interact.

Light is the most important zeitgeber for the circadian clock. Sleep deprivation was shown to reduce the phase shifting capacity of the circadian clock in reponse to light. Also neurons in the suprachiasmatic nucleus (SCN) were shown to respond less to light after sleep deprivation.

Caffeine has been used for many centuries and in different cultures to alleviate the effects of sleep deprivation and to increase alertness. We showed that the effect of sleep deprivation on the light-induced increase in SCN neuronal activity was also normalized after application of caffeine. More recently it was shown that caffeine not only decreases sleep pressure, but also slows down the circadian clock. Both in cell cultures and in intact mice and humans it was shown that the clock is delayed or circadian period is increased under influence of caffeine. The effects in vivo were particularly strong when combined with constant light exposure. Thinking of Aschoff's rule it may be that in intact mice caffeine slows down the clock by increasing the effect of light on the clock.

In addition, application of caffeine into the medium of cell cultures or chronically in the drinking water can increase day-night amplitude. We have new data, extending this research, which shows that the amplitude in the sleep-wake cycle is also increased under chronic caffeine consumption in mice. Most remarkably, the animals slept deeper in the first hours of the rest phase than animals consuming normal water.

Finally, constant light or dim-light at night disturbs sleep in humans and rodents and was shown to disturb circadian rhythms,

resulting in splitting of rhythms or in arrhythmia in rodents. We have now performed additional experiments in older mice and show that the effect of dim light at night is less strong in aged mice.

The data show that a clear difference between day and night in lighting conditions is important for a strong and healthy sleep-wake rhythm. The effects of chronic caffeine in rodents suggest that caffeine may have a supportive role for the central circadian pacemaker by increasing its amplitude, possibly by increasing the influence of light on the circadian clock.

A22

Polychromatic White Light Exposure Reduces Objective Sleepiness Depending on Melanopic Lux at Low Light Intensities During Daytime

Jan de Zeeuw[1,4], Alexandra Papakonstantinou[1,3], Claudia Nowozin[1,3], Sophia Wisniewski[1,3], Mandy Zaleska[4], Theresa Fox[4], Sven Hädel[1], Frederik Bes[1,3], Dieter Kunz[1,3,4], Mirjam Münch[1,2,3]

[1]Charité – Universitätsmedizin Berlin, Corporate Member of Freie Universität Berlin, Humboldt-Universität zu Berlin, and Berlin Institute of Health, Institute of Physiology, Sleep Research & Clinical Chronobiology, Berlin, Germany; [2]Institute of Medical Immunology; [3]Clinic for Sleep & Chronomedicine, St. Hedwig-Krankenhaus, Berlin, Germany; [4]Intellux GmbH, Berlin, Germany

Objectives: This study aimed to determine how subjective and objective sleepiness under well controlled conditions were affected by different light exposures during daytime. The polychromatic white light conditions differed in peak wavelength of the blue light spectrum and/or light intensity.

Methods: In a mixed within-between-subject design, 72 healthy participants (48 female; 24.4 ± 2.7 yrs; mean ± SD) visited the laboratory four times, arriving one hour after habitual wake-up times while wearing dark goggles. They were exposed for 3 h to a lighting condition, starting ~3 h after wake-up. The lighting conditions differed in peak wavelength of the blue portion of the light spectrum, while having similar CCT (=3500 K; blue light peak at 435 nm or at 480 nm), or they differed in illuminance (100 lx, 200 lx, 600 lx, 1200 lx), and included a dim light condition (DL; randomized order of conditions). Objective sleepiness, as assessed in the electroencephalogram (EEG) by the Karolinska drowsiness test (i.e. 5 min closed and 5 min open eyes) and subjective sleepiness by visual analogue scales were measured hourly and analyzed with mixed linear models.

Results: During three hours of light exposure, objective sleepiness (determined by the EEG alpha attenuation index) showed significant differences such that at 100 lx, it was most strongly reduced by light with a spectral peak at 480 nm when compared to 435 nm or DL ($F_{3,769} = 28.56$; $p < 0.001$). We also found a trend for a reduction of objective sleepiness by higher light intensities, which was greatest at 1200 lx ($F_{2,882} = 2.65$; $p = 0.071$). In addition, there were significant differences between the lighting conditions in the EEG delta, theta, sigma and beta ranges depending on the peak wavelength and light intensity ($p < 0.05$). Subjective sleepiness was significantly reduced in the first hour of light exposure, by light with a spectral peak at 480 nm compared to 435 nm or DL ($F_{1,81} = 4.14$; $p = 0.045$).

Conclusions: The impact of the different spectral compositions of light on the waking EEG (a marker for objective sleepiness) was most pronounced at low light intensities (100 photopic lux). Our results indicate that lighting conditions with higher melanopic lux (i.e. greater blue portion at 480 nm) had stronger alerting effects during daytime in well-rested participants. At higher light intensities the alerting effects are mixed and interact with spectral compositions, and thus are less obvious.

Funding: This study was funded by the German Federal Ministry of Education and Research (OLIVE project) and Intellux GmbH (Berlin), Germany.

Disclosures: None.

A23

Documentation of Mixed Lighting Conditions in Non-Image Forming Studies

Aicha K. Diakite, Nils Weber, Martine Knoop

Technische Universität Berlin, Berlin, Germany

Objectives: Non-image forming (NIF) effects of light are affected by a number of factors, such as light level, spectral power distribution of the light, duration, timing, light history, and spatial distribution of the light. Due to this complexity, proper documentation of experimental conditions and procedures to ensure future applicability and reproducibility seems to be of utmost importance. The poster will indicate that studies looking into NIF effects of light during daytime require an extended description of the considered lighting conditions. Until now, some of the relevant parameters are included in the description of the experimental procedure, such as the duration of light exposure and the timing of the experiment during the day. The lighting conditions are typically included in the description of the experimental set-up, reflected in vertical illuminances or melanopic-weighted irradiance and the correlated color temperature or spectral power distribution (SPD). When included, the origin of the light is described qualitatively with the position of the luminaires and the windows in the room. Even though the scientific basis is small, there is some indication that the incident angle of light could matter. Literature on melatonin suppression or phase shifts shows that inferior and nasal retinal light exposure is more effective than light falling on the superior or temporal side of the retina. In addition, binocular light exposure realizes a higher melatonin suppression than monocular light exposure. It is not clear yet, whether this is relevant for daytime NIF effects, but as daylight generally differs from the electric light sources in intensity, SPD and position of the light source, making a distinction between contributions from both light sources is required. Integral measurements, such as the vertical illuminance or melanopic-weighted irradiance are not suitable to describe the studied lighting conditions.

Methods and Results: To allow the subsequent incorporation of future spectral weighting functions for NIF responses and

relevant retinal areas, the TU Berlin has looked into an approach to conduct spatially and spectrally resolved measurements of lighting conditions. This is especially relevant in situations with various SPDs from light sources, possibly altered through reflection. Two novel colorimetric measurement devices for conditions with daylight and artificial lighting are currently being considered at the TU Berlin. A modified 'luminance' camera with filters adapted to the five photoreceptor types of the human retina, as well as a room scanner with a spectroradiometer. The poster will present the measuring approach, the devices, as well as examples of its application.

Conclusions and Outlook: Detailed documentation of lighting conditions is essential to allow future retrospective analysis of research results with adjustments to retinal areas of interests and their specific sensitivities. The proposed measurement devices will provide high-resolution data. The measurements will be used to look into the development of simplified sensors that can be applied at a larger scale.

Funding/Disclosures: The presented work is supported by TU Berlin and the Velux Stiftung [grant number 1087].

A24

Physical Activity, Sleep and Circadian Rhythm Patterns in Depressive and Anxiety Disorders: A 2-Week Ambulatory Assessment Study

Sonia Difrancesco[1], Femke Lamers[1], Harriëtte Riese[2], Kathleen R. Merikangas[3], Aartjan T.F. Beekman[1], Bert A.M. van Hemert[4], Robert A. Schoevers[2], Brenda W.J.H. Penninx[1]

[1]Department of Psychiatry, Amsterdam Public Health Research Institute, VU University Medical Center, Amsterdam, The Netherlands; [2]Department of Psychiatry, University Medical Center Groningen, Interdisciplinary Center for Psychopathology and Emotion Regulation, University of Groningen, Groningen, The Netherlands; [3]Genetic Epidemiology Branch, Intramural Research Program, National Institute of Mental Health, Bethesda, MD, USA; [4]Department of Psychiatry, Leiden University Medical Center, Leiden, The Netherlands

Objectives: Traditional assessment of physical activity (PA), sleep and circadian rhythms (CR) in depression/anxiety mostly relies on self-reported questionnaires, however, it may be biased by patient cognitive impairment and negative perception. Actigraphy may improve the assessment of PA, sleep and CR providing objective estimates. The objectives are: (1) study the relationship of actigraphy estimates of PA, sleep and CR with depression/anxiety; (2) study the association of objective estimates of PA, sleep and CR with clinical characteristics.

Methods: Data of 360 participants with current (n = 94), remitted (n = 176) and no (n = 90) depression/anxiety was obtained from the Netherlands Study of Depression and Anxiety. Depression/anxiety was diagnosed with the DMS-IV based Composite International Diagnostic Interview. Clinical characteristics included severity of depressive/anxiety symptoms, duration and number of psychiatric diagnoses, age of onset and, antidepressant use. Actigraphy estimates of PA, sleep and CR were Euclidean Norm Minus One (ENMO) and moderate-to-vigorous PA (MVPA), sleep duration (SD) and sleep efficiency and, relative amplitude between daytime and night-time activity level (RA) and sleep midpoint on free days (SMF), respectively.

Results: Compared to controls, persons with depression/anxiety had significantly reduced ENMO (median (IQR) = 28.83 (9.73) mg, $p = 0.022$), MVPA (median (IQR) = 35.32 (35.11) min/day, $p = 0.023$) and RA (median (IQR) = 0.82 (0.08), $p = 0.033$). Severity of depressive/anxiety symptoms and number of psychiatric diagnoses were associated with reduced ENMO and MVPA, longer SD and lower RA. A tendency in delayed SMF was found among those with more depressive symptoms.

Conclusions: Actigraphy may be a complementary tool to clinical interview and self-reported questionnaires in the assessment of PA, sleep and circadian rhythms in depression and anxiety. PA and CR interventions in depression and anxiety may especially focus on patients with higher severity of depressive/anxiety symptoms and with more psychiatric comorbidity.

Funding/Disclosures: This work was supported by Innovative Medicines Initiative 2 Joint undertaking under grant agreement No 115902.

A25

Novel Biomarkers for Circadian Rhythms and Sleep

Derk-Jan Dijk

Surrey Sleep Research Centre, Faculty of Health and Medical Sciences, University of Surrey, Guildford, UK

Insufficient and mistimed sleep as well as circadian misalignment are associated with various adverse health outcomes. Assessment of sleep and circadian rhythmicity has traditionally relied on subjective measures of sleep, sleepiness and circadian preference, polysomnography, long term assessment of rest-activity cycles, and time series of markers of circadian rhythmicity such as melatonin or core body temperature. These traditionally measures have their drawbacks because they are either subjective or too labour intensive or costly to implement on a large scale in real life situations. The human blood transcriptome is sensitive to both acute total sleep loss and chronic insufficient sleep as well as mistimed sleep and also contains information about the circadian phase of the SCN and maybe other organs. Recent progress in the discovery and validation of blood-based biomarkers derived from one or a few blood samples, for circadian phase and insufficient sleep will be presented.

A26

Actigraphy in Combined Chronotherapy to Determine Predictors of Response in the Treatment of Depressive Disorder

Stella J.M. Druiven[1], *Jeanine Kamphuis*[2], *Benno C.M. Haarman*[2], *Ybe Meesters*[3], *Robert A. Schoevers*[3], *Harriëtte Riese*[1]

[1]University of Groningen, University Medical Centre Groningen, Department of Psychiatry, Interdisciplinary Centre for Psychopathology and Emotion Regulation (ICPE), Groningen, The Netherlands; [2]University of Groningen, University Medical Centre Groningen, Department of Psychiatry, Research School of Behavioural and Cognitive Neurosciences (BCN), Groningen, The Netherlands; [3]University of Groningen, University Medical Centre Groningen, Department of Psychiatry, Groningen, The Netherlands

Objectives: Combined chronotherapy includes sleep deprivation and morning light therapy and has been successfully used to treat severe depressive episodes. However, it is still largely unknown when chronotherapy should be indicated in the treatment of a depressive patient and therefore not yet part of regular treatment protocols. Some predictors of response to chronotherapy have been identified, such as diurnal mood variability and higher levels of clinician-observed arousal. It is worthwhile to search for other predictors in order to improve the use of chronobiological interventions in treatment of depressive disorders. By using actigraphy, post-treatment changes in physical activity levels and variability have been documented for those who responded to chronotherapy. It is of great interest to measure activity-rest rhythms prior to chronotherapy as this may provide more answers. For example, it may be possible that individuals with high variability in their day-to-day activity rhythm may be particular susceptible to chronobiological influences. Therefore, the aim of this study is to examine whether possible predictors of response can be identified by assessing activity-rest rhythm in addition to mood patterns of patients suffering from a depressive disorder.

Methods: Fifty patients diagnosed with a depressive episode in the context of a major depressive disorder or a bipolar depressive disorder, as assessed with the Mini-International Neuropsychiatric Interview, will be included. The patients will be treated according to our chronotherapy protocol including three nights of total sleep deprivation, each followed by a recovery night, and daily morning light therapy for two weeks. The level of depressive symptoms will be assessed weekly using the Inventory of Depressive Symptoms – Self Report (IDS-SR). Additionally, mood variability is assessed with daily Ecological Momentary Assessment (EMA). Starting one week before the start of the chronotherapy, wrist actigraphy measurements will be recorded until the end of the therapy.

Discussion: Discussion about the protocol with SLTBR members may be helpful for improving the design.

Funding/Disclosures: None.

A27

Benefits of Evening versus Morning Training in the Acquisition and Consolidation of Motor Skill in Older Adults

Carmit Gal[1,2], *Avi Karni*[1,2], *Maria Korman*[1]

[1]The Edmond J. Safra Brain Research Center for the Study of Learning Disabilities, University of Haifa, Haifa, Israel; [2]Laboratory for Human Brain and Learning, Sagol Department of Neurobiology, University of Haifa, Haifa, Israel

Objectives: Using a training protocol that effectively induces skill memory in young and older adults, we examined whether training during evening hours compared to morning training would result in different time courses of skill learning (acquisition, consolidation and retention) in typical healthy elderly individuals.

Methods: We tested the effects of a single session training on motor finger tapping sequence learning (FTSL) task, scheduled to either morning or evening hours, in 29 healthy elderly participants (60–75 years). Contribution of three parameters to learning was assessed: (a) time of training (morning vs. evening) (b) sleep quality (actigraphy) and (c) chronotype.

Results: Our results showed that: (1) Older adults have the potential for effective procedural motor within-session and between-session (consolidation phase) learning and fully retain practice-dependent performance gains attained at the end of practice session a week after training; (2) The initial level of speed of motor performance and the course of learning of older adults are different from young adults – baseline of performance is lower and the practice-related gains are smaller. However, accuracy of performance is similar to that of the younger peers; (3) Participants trained in the evening expressed overnight consolidation phase gains, in addition to online within session gains in performance. In contrast, participants trained in the morning showed only maintenance of performance level attained at the end of training. (4) Benefits of evening training are surprising in the light of the fact that all study participants were moderately morning type (except for the two subjects exhibiting neither type). Evening group mean MEQ score was 63 ± 5.33, Morning group mean MEQ score was 59.7 ± 8.7); (5) All participants had sleep patterns typical of age, with average sleep efficiency of ~82%, and approximately 6 hours of sleep.

Conclusions: Our results suggest that procedural motor memory consolidation processes are preserved in healthy elderly individuals, but these processes are under-engaged if the practice session is scheduled to morning hours. Although all participants (irrespective of the time-of-training) were moderate morning types, suggesting that morning training should be optimal for these individuals, other factors precluded the evolution of the delayed off-line gains in performance. We conjecture that if practice session took place in the morning, post-training consolidation processes are disrupted by unspecific interference as a result of numerous task-irrelevant motor behavioral experiences during the long awake period prior to night sleep. Training in the evening hours can relax some of these constraints on overnight consolidation in older adults. The current results are in line with the notion that the control of what is to be retained in procedural memory is atypical or more stringent in the elderly.

A28

The Influence of Daytime Light on Nighttime Sleep

Moniek Geerdink[1,2]*, Tom Woelders*[1]*, Domien G.M. Beersma*[1]*, Marijke C.M. Gordijn*[1,2]

[1]Department of Chronobiology, GeLifes, University of Groningen, Groningen, The Netherlands; [2]Chrono@Work B.V., Groningen, The Netherlands

Objectives: Light is not only crucial for vision but also influences other aspects of physiology and behavior. One well studied aspect of light is its effect on our biological clock which is also linked to sleep timing. Yet, the effect of daytime light on nighttime sleep itself has hardly been studied in humans. In our within-subject design laboratory study we examined the influence of daytime light on the subsequent nighttime sleep. We measured effects on the biological clock as well as on sleep homeostasis.

Methods: Participants with mild sleep complaints were exposed to three conditions: Either to one day (9–17 h) with moderate intensity polychromatic 'office light', one day with high intensity polychromatic light 'bright light', or one day with extra blue LED light on top of the 'office light'. The influence of this daytime light on the biological clock was measured via analysis of the melatonin rhythm and on sleep quality/homeostasis via sleep-EEG measurements. Multilevel regression analyses were used to quantify the effects on the accumulation rate of slow wave activity.

Results: Compared to melatonin onset in the office light condition, the onset was earlier in the bright light condition (0.35 h, $p < 0.05$) and there was a trend for an earlier onset in the blue light condition (0.30 h, $p = 0.07$) compared to the office light condition. Sleep efficiency was higher (95.8% vs. 92.1%, $p < 0.05$) and the percentage of REM sleep was larger (23.3% vs. 19.7%, $p < 0.05$) in the bright light condition compared to the office light condition. The accumulation rate of slow wave activity during sleep, a measure of sleep pressure decay, was significantly higher in the bright- as well as in the blue light condition compared to the office light condition.

Conclusions: Light intensity during the day affects sleep via an effect on the clock and by influencing sleep homeostasis, with higher light intensities leading to more consolidated, deeper sleep.

Funding/Disclosures: This study was financially supported by an unrestricted research grant of Philips Consumer Lifestyle B.V. Drachten, The Netherlands, developed by the legal authorities of both parties.

A29

Circadian Measures Are Not Phase Delayed in Bipolar Spectrum Disorder in a 20-Day Naturalistic Ecological Momentary Assessment Study

Namni Goel[1]*, Madison K. Titone*[2]*, Tommy H. Ng*[2]*, Laura E. Dennis*[1]*, Lauren B. Alloy*[2]

[1]Division of Sleep and Chronobiology, Department of Psychiatry, University of Pennsylvania Perelman School of Medicine, Philadelphia, PA, USA; [2]Department of Psychology, Temple University, Philadelphia, PA, USA

Objectives: Prior work demonstrates circadian rhythm disruptions of sleep/wake, activity, hormones, and melatonin in individuals with bipolar spectrum disorder (BSDs). Such disruptions may be a key mechanism underlying neurobiological vulnerability to BSDs.

Methods: 150 adults (ages 18–27; mean age ± SD, 21.9 ± 2.1 y; 88 women), with high reward sensitivity and a BSD (n = 43), at-risk individuals with high reward sensitivity but no BSD (n = 64), and low-risk individuals with moderate reward sensitivity and no BSD (n = 43) participated in a 20-day naturalistic Ecological Momentary Assessment (EMA) study. The EMA study involved 3 phases: 1. Baseline; 2. Goal striving and 3. Goal/reward outcome; salivary dim light melatonin onset (DLMO) was assessed as a circadian phase marker in each phase. The Morningness-Eveningness Questionnaire (MEQ) assessed chronotype, iButtons measured skin temperature continuously, and wrist actiwatches measured sleep-wake cycles. Multilevel linear models and Pearson's correlations were used for statistical analysis.

Results: In our large sample, MEQ scores, DLMOs, skin temperature maximum acrophases and actigraphic sleep midpoints were not significantly different across the three groups at baseline (all Ps > 0.05). Notably, throughout the study, these variables showed the expected phase relationships, whereby MEQ was negatively correlated with DLMO ($r = –0.562$, $p < 0.05$) and DLMO-sleep onset phase angle was positively correlated with skin temperature maximum acrophase ($r = 0.577$, $p < 0.001$), thus validating our circadian measures in a naturalistic EMA design.

Conclusions: Our results show for the first time that BSD, individuals at-risk for BSD, and low-risk individuals did not differ across multiple objective circadian markers in a naturalistic EMA study. We contend that reported delays in circadian rhythms in BSD may emerge with greater bipolar severity (e.g., bipolar I disorder), after multiple episodes, and/or with increasing age, among other factors. Our results are relevant for the treatment of BSDs using chronotherapeutic modalities such as light and/or sleep deprivation.

Funding/Disclosures: This work was supported by NIH R01 MH102310.

A30

Light and Darkness; From Clinical Treatment to Healthy Lifestyle Approach

Marijke C.M. Gordijn

Chrono@Work B.V. Groningen, University of Groningen, Groningen, The Netherlands

Thirty years of SLTBR; thirty years in which scientists and clinicians met on an annual basis to discuss the role of light and biological rhythms for mood, sleep and wellbeing. During these years, the field of chronobiology rapidly evolved and the awareness of the importance of light increases. In some cases we were probably too optimistic: exactly 30 years ago I started as a PhD student and I studied the role of sleep and the biological clock in non-seasonal depressed patients. After many years, trying to improve mood by shifting sleep or shifting rhythms of the biological clock, I had to conclude that the role of the biological clock in mood regulations in these severely depressed patients was not that clear. Nevertheless the mood improving effect of light, especially for seasonal depression, was very clear and also the potential of light to shift the clock was undisputed.

New data from animal research show that there are direct pathways of light from the retina to brain areas involved in mood- and sleep regulation, not necessarily through the biological clock. This supports the idea that light has direct effects on mood and sleep and it is not only important to keep sleep-wake rhythms in synch with the environmental light-dark cycle, and so be an effective treatment for circadian rhythm sleep-wake disorders. Recent evidence shows indeed that light during the day is related to more consolidated, deeper sleep at night and the clear therapeutic effects of light in mood disorders is not necessarily explained by shifting circadian rhythms. After the discovery of the extra type of photoreceptor in the retina responsible for the effects on mood and circadian rhythms, recent data show the complex interactions between these cells and the classical photoreceptors. More studies investigating these fundamental properties are still needed.

The growing dataset showing the benefits of light also increases the knowledge about the downside of light at the wrong time; e.g. light at night. In the Netherlands the 'theme' of the Light Challenge 2018, a contest for students developing innovative solutions in society related to light, is "feel the night". Translating our scientific knowledge to prevent disturbances in society should be an important part of educational programs in the future. Recently we made a first step and developed educational material for Dutch teenagers, to be used at high schools: Charge Your Brainzzz. It contains information about sleep regulation and the role of light-dark exposure for healthy sleep. The interest in the package was huge and the material was downloaded by more than 150 schools (~25%) in the first 6 months since release, again showing the still growing interest in sleep and light in society.

Funding/Disclosures: Marijke Gordijn works as a consultant for Philips Consumer Lifestyle and was sponsored by the Brain Foundation to develop the educational package Charge Your Brainzzz.

A31

Characterisation of Non-Visual Responses in Humans, Accounting for Response Dynamics, Spectral and Spatial Characteristics of Light Exposure

Abhishek S. Prayag[1], Sophie Jost[2], Pascale Avouac[2], Howard M. Cooper[1], Dominique Dumortier[2], Claude Gronfier[1]

[1]Univ Lyon, Université Claude Bernard Lyon 1, Inserm, Stem Cell and Brain Research Institute U1208, Bron, France; [2]Univ Lyon, ENTPE, LGCB, Vaulx-en-Velin, France

The eye drives non-visual (NV) responses to light including circadian resetting, pupillary reflex and alerting effects. Initially thought to depend on melanopsin-expressing photosensitive retinal ganglion cells (ipRGCs), classical photopigments can also play a modulatory role in these responses. As most studies have been conducted for a limited number of NV functions, generally under conditions of relatively high light levels and long duration, it is unknown whether NV functions share similar spectral/irradiance sensitivities and response dynamics during light exposure. We addressed this issue using light exposure paradigms spectrally and spatially tuned to target either cones or ipRGCs, and by measuring simultaneously and longitudinally several NV responses in humans. Here we demonstrate that the response dynamics of several NV functions are faster than previously thought. We find that the brain and the heart are activated within 1–2 minutes of light exposure. Further, we show that NV functions do not share the same threshold sensitivities. While cognitive responses appear to be saturated around 500 melanopic lux after 20 minutes of light exposure and pupillary reflex after 5 minutes, the brain and the cardiovascular system are increasingly activated after 40 minutes. The effectiveness and response dynamics of light in driving non-visual responses can have important real-life implications.

A32

The Metabolic Cost of Daily Entrainment Under High Fat Diet in Mice

Roee Gutman, Anat Neuman

Laboratory of Integrative Physiology, MIGAL – Galilee Research Institute, and Departments of Animal Sciences and Nutritional Sciences, Tel-Hai College, Kiryat Shmona, Israel

Objectives: Disruption of circadian homeostasis is accompanied by elevated high-fat-diet (HFD) induced obesity (DIO). Endogenous circadian rhythms show a period length (*tau*) that usually deviates from 24-h. By descriptive studies, deviation of *tau* from the environmental photic cycle (T-cycle) of 24-h is related positively with DIO in mice. These studies support the hypothesis that misalignment between *tau* and T-cycle results in a constant need to entrain increasing susceptibility to DIO. However, this hypothesis was never tested in a controlled setup. Hence, our goal

was to conduct controlled animal experiments examining the role of the misalignment between *tau* and the T-cycle in propensity to DIO.

Methods: Three-week old B6 female mice were fed regular chow and hold under one of four symmetrical (half-dark half-light hours) T-cycles: 1. 24-h T-cycle; 2. constant darkness, enabling the measurement of the age appropriate *tau*, that was used to set up the third T-cycle (*tau*); and 4. T-cycle with a period length faster than *tau* by the deviation of *tau* from 24-h (*Δ tau*). Two weeks following experiment initiation, half of the mice from each regime were fed on HFD or low-fat-diet (LFD). T-cycle of *tau* and *Δtau* was adjusted biweekly acording *tau* of LFD-fed mice. Body weight and total 24-h energy intake were measured weekly, while cage locomotor activity was continual. T-cycle didn't affect energy homeostasis of LFD-fed mice.

Results: Under the regular 24-h T-cycle, HFD-fed mice develop the expected DIO, compared to LFD-fed mice. However, when raised under the *tau*-resmbling and faster-than-*tau* T-cycle, HFD-fed mice exhibit delayed onset of DIO and reduced HFD-induced weight gain, compared to the slower-than-*tau* T-cycle of 24-h. This attenuated weight gain did not result from lower energy intake, hence seem to result from higher energy expenditure, as supported by locomotor activity data.

Conclusions: These results provide additional evidence for the interconection between circadian homeostasis and energy homeostasis. More specifically, they show that entrainment-related mechanisms interfere with energy homeostasis under HFD affecting susceptibility to DIO. As such, these results support further exploration of the interconnection between entrainment-related mechanisms and energy homeostasis that may provide novel insights on etiology and prevention of DIO.

Funding/Disclosures: German-Israeli Foundation for Scientific Research and Development.

A33

Bright Light Therapy in Rheumatoid Arthritis to Improve Symptoms of Fatigue and Other Disease Outcomes: A Randomized Controlled Pilot Trial

G. Esther A. Habers[1], D.S. Veldhuijzen[1], C.F. Allaart[2], A.H.M. van der Helm[2], E. Vreugdenhil[3], T.W.J. Huizinga[2], A.W.M. Evers[1]

[1]Health, Medical and Neuropsychology Unit, Faculty of Social Sciences, Leiden University, Leiden, The Netherlands; [2]Department of Rheumatology, Leiden University Medical Center, Leiden, The Netherlands; [3]Department of Molecular Cell Biology, Leiden University Medical Center, Leiden, The Netherlands

Objectives: Rheumatoid arthritis (RA) is often associated with symptoms, including fatigue, which reduce quality of life negatively. Unfortunately, treatments for these symptoms are not adequate for all patients. A disturbed circadian rhythm has been found in patients with RA and may be an important underlying mechanism for those symptoms. In the current study, the efficacy of a 4-week Bright Light Therapy (BLT) program is examined for the first time in patients with RA. This study is a randomized, double blind, parallel-arm, placebo controlled pilot study that could serve as preparation for a future larger full-scale randomized controlled trial (RCT). The primary study objective is to explore the difference between an intervention group that receives active BLT and a control group that receives sham BLT in fatigue while taking into account baseline fatigue levels. As a secondary objectives, we explore a) secondary efficacy outcomes, b) the potential of the therapy in delaying the circadian entrainment, c) the 4-week follow-up effects, and 4) (barriers to) therapy adherence, therapy acceptability as well as study feasibility and acceptability.

Methods: Forty-eight adult patients with RA from the Department of Rheumatology of the LUMC are being recruited for this study. Eligible patients have elevated feelings of fatigue (CIS-8 $\geq$27) and low disease activity or are in remission. In both therapy arms, light therapy glasses are worn in the home of the participant every day for 30 minutes in the evening (between 20:00–21:00 h) during four consecutive weeks. The arms differ in the wavelength of light that is emitted by the glasses. The primary outcome is assessed by the Checklist Individual Strength – Subscale Fatigue (CIS-8). Secondary outcomes are: pain and morning joint stiffness (IRGL; subscale Pain), sleep (diary and ISI), emotional well-being and general health status (RAND-36), depression (HADS), and disease activity (DAS). Circadian entrainment is assessed by the melatonin onset in saliva (as tested with Dim Light Melatonin Onset) and a sleep diary.

Results: Data collection is expected to be just finished in June '18. At the conference we will discuss the background of the study, the used methods, and the experiences we have gained.

Conclusions: This study evaluates in RA preliminary efficacy, feasibility, and acceptability of BLT in RA, which directs at the disturbed circadian rhythmicity observed in this population.

Funding/Disclosures: The study is funded by the Dutch Arthritis Association.

A34

A Multicenter Randomised Controlled Trial with Bright Light Therapy to Decrease Depressive Symptoms in Adults with Intellectual Disabilities: Preliminary Results

Pauline C.M. Hamers[1,2], Dederieke A.M, Festen[1], Heidi Hermans[1,2]

[1]Intellectual Disability Medicine, Department of General Practice, Erasmus University Medical Center, Rotterdam, The Netherlands; [2]Amarant Group, Healthcare Organization for People with Intellectual Disabilities, Tilburg, The Netherlands.

Objectives: Treatment options to decrease depressive symptoms in adults with intellectual disabilities (ID) are scarce, especially in the severe/profound ID population. The primary objective of this study is to examine the effect of Bright Light Therapy (BLT) on depressive symptoms in adults with ID in two different light therapy groups compared to care as usual (control group). The secondary objectives are investigating the difference in effect of

BLT in the two different intervention groups and examine if the effect of BLT is still visible four weeks after the end of the BLT (follow-up).

Methods: Participants with ID (IQ ≤70) and depressive symptoms (ADAMS Depression subscale score ≥14) were included in a multicenter randomized controlled trial (RCT) with three different study groups. Participants in Group I received two weeks of BLT (10,000 lux, 30 minutes a day) in the morning, additional to their regular care. Participants in Group II received BLT (app. 300 lux, 30 minutes a day), additional to their regular care. Participants in Group III did not receive BLT but only their regular care (control group). The main outcome measures of this study are depressive symptoms measured with the ADAMS Depression subscale at baseline, within one week after BLT and four weeks after the end of BLT.

Results: In total, 41 participants (>18 years, 21 females) were included. 12 participants were included in Group I, 15 participants were included in Group II and 14 participants were included in Group III. The outcomes of the preliminary analyses showed more decrease in depressive symptoms in Group I compared to the other groups. More results are expected in May 2018.

Conclusions: It is difficult and challenging to perform an RCT to investigate the effect of BLT in adults with ID and depressive symptoms. As far as we know, this study is the first multicenter RCT investigating the effect of BLT in adults with ID and depressive symptoms.

Funding/Disclosures: This study is funded by three care provider services (the HA-ID consort: Amarant Group, Abrona and Ipse de Bruggen), the Dioraphte Foundation and the Foundation for support VCVGZ. We thank all participants, their legal guardians and professional care givers for their collaboration.

A35

Additive and Opponent Spectral Effects on Melatonin Regulation in Healthy Humans

John Hanifin[1], Michael Jablonski[1], Robert Levin[1], Benjamin Warfield[1], Kate Cecil[1], Kat West[1], Joel Pokorny[3], George Brainard[1]

[1]Department of Neurology, Thomas Jefferson University, Philadelphia, PA, USA; [2]Osram Sylvania, Boston, MA, USA; [3]University of Chicago, Chicago, IL, USA

Objectives: Different models of interaction between the melanopsin ganglion cells and classical rod and cone visual photoreceptors have been proposed, including the ideas that these photoreceptors are additive, opponent, complementary or dynamic over time and intensity. The goal of this study was to test whether specific combinations of wavelengths indicate an opponent cone contribution to the suppression of nighttime synthesis of the pineal hormone, melatonin, in healthy human subjects. Specifically, we tested the hypothesis that acute suppression of melatonin by short-wavelength light at 460 nm and 500 nm could be reduced by simultaneous exposure of long-wavelength light at 570 nm.

Methods: A 1000 W Xenon compact arc lamp source with a grating monochromator was fitted with an optical mask system capable of providing two variable narrow spectral bands simultaneously. A total of 8 participants (4 females) with a mean age (± SEM) of 24.0 ± 1.0 years were included. Light exposure (90 min, 02:00–03:30 h) conditions were given in a ganzfeld dome included: 1) no light exposure, 2) narrow bandwidth light with a peak of 460 nm at 12.1 $\mu W/cm^2$, 3) narrow bandwidth light with a peak of 500 nm at 8.9 $\mu W/cm^2$, 4) narrow bandwidth light with a peak of 570 nm at 18.5 $\mu W/cm^2$, 5) 460 nm & 500 nm combined at 31.0 $\mu W/cm^2$, and 6) 500 nm & 570 nm combined at 26.7 $\mu W/cm^2$. Participant's had their eyes dilated and were randomly exposed. Plasma melatonin concentrations were assayed by radioimmunoassay.

Results: A comparison of the pre-light exposure values across all light conditions showed no statistically significant variation in plasma melatonin ($p = 0.85$). Compared to the control night, both the 460 nm and 500 + 570 nm light groups exhibited significantly suppressed melatonin percent change scores ($p < 0.001$ and $p < 0.05$, respectively). However, the combined 460 nm + 570 nm stimulus did not significantly suppress melatonin compared to control values. Control adjusted plasma melatonin percent change scores revealed no significant differences between the light exposure conditions ($p = 0.08$).

Conclusions: This result indicates opponency in that the addition of the 570 nm wavelength blunted the strong response to 460 nm. The results show that melatonin suppression data from monochromatic light exposures cannot always predict the effects of polychromatic light on melatonin suppression.

Funding Support: Osram Sylvania provided primary funding support. Secondary support provided by the Philadelphia section of the Illuminating Engineering Society and Lighting Enabled Systems and Applications (NSF #EEC-0812056).

A36

How Light through Retina-Brain Circuits Influences Circadian Rhythms, Mood and Learning

Samer Hattar

National Institute of Mental Health, Bethesda, MD, USA

Perhaps one of the most surprising discoveries in the retina have been the identification of a novel set of photoreceptors that are distinct from the classical rod/cone photoreceptors. These non-rod/non-cone photoreceptors are located in the ganglion cell layer of the retina, the layer of which axons from retinal ganglion cells (RGCs) form the optic nerve, which connects the retina to the brain. A subset of these RGCs are intrinsically photosensitive (ipRGCs) because they express the photopigment melanopsin, which is similar to rhodopsin and cone opsins found in rods and cones, respectively. Initially, the ipRGCs were thought to contribute only to circadian light functions, however, recent research shows that these photoreceptors influence a staggering number of behaviors, which include sleep, alertness, pupil constriction, mood and even learning. In my lecture, I will provide detailed retinal neural circuits that delineate how this population of photoreceptors influences such diverse behaviors. I will also provide practical recommendations for how this research can help in enhancing human

health. Finally, I will provide the major gaps that are still lacking in this area for us to utilize light to its full potential for work/home designs.

A37

Blue Blocking Treatment for Bipolar Mania

Tone E.G. Henriksen[1,2], Silje Skrede[1,4], Ole Bernt Fasmer[1,3] Helle Schøyen[1,5], Leva Leskauskaite[3], Jeanette Bjørke-Bertheussen[5], Jörg Assmus[1], Børge Hamre[1], Janne Grønli[1], Anders Lund[1,3]

[1]University of Bergen, Bergen, Norway; [2]Valen Hospital, Helse Fonna, Norway; [3]Haukeland University Hospital, Bergen, Norway; [4]Bergen Clinics Foundation, Bergen, Norway; [5]Stavanger University Hospital, Stavanger, Norway

Objectives: Blocking blue light by means of orange-tinted glasses is a way to inhibit daylight signal to the brain. The method is applied basic science and a consequence of the recent discovery of the blue light-sensitive retinal photoreceptors. Blue-blocking (BB) glasses are a potential treatment option for bipolar mania, and builds on promising results from previous case reports and a pilot study of dark therapy; use of complete darkness for 14 hours in the evening/night. We examined the effectiveness and feasibility of BB glasses in hospitalized bipolar patients in a manic state.

Methods: In a single-blinded, randomized, placebo-controlled trial (RCT), eligible patients (bipolar mania, age 18–70 years) were recruited from five clinics in Norway. Patients were assigned to BB glasses or placebo (clear glasses) from 6 p.m. to 8 a.m. for seven days, in addition to treatment as usual. Symptoms were assessed daily by use of the Young Mania Rating Scale (YMRS). Motor activity was assessed by actigraphy, and compared to data from a healthy control group. Wearing glasses for one evening/night qualified for inclusion in the intention-to-treat analysis. The feasibility of the method was assessed by means of self-report form on subjective experiences with the intervention, and monitoring of side-effects.

Results: From Feb 2012 to Feb 2015, 32 patients were enrolled. Eight patients dropped out and one was excluded, resulting in 12 patients in the BB group and 11 patients in the placebo group. Mean decline in the YMRS score was 14.1 (95% CI: 9.7, 18.5) in the BB group, and 1.7 (95% CI: –4.0, 7.4) in the placebo group, yielding an effect size of 1.86 (Cohen's *d*). The use of BB glasses fitted well with many patients own understanding of light as a trigger of episodes and themselves being particularly sensitive to light stimuli. In the BB group, one patient reported headache and two patients experienced easily reversible depressive symptoms.

Conclusions: This RCT showed that BB glasses were effective and feasible as add-on treatment for bipolar mania. The high effect size and rapid uniform decrease in manic symptoms in the BB-group generates a hypothesis that blue light exposure in evening/night is involved in the maintenance of manic episodes.

The results were published in Bipolar Disorders, May 2016.

Funding/Disclosures: Tone E. G. Henriksen is shareholder in Chrono Chrome AS.

A38

Promoting Healthy Light Exposure Regimes to Improve Sleep Timing and Quality Among Adolescents

Laura M. Huiberts, Karin C.H.J. Smolders, Ariane V.J.M. Rombouts, Yvonne A.W. de Kort

Eindhoven University of Technology, Eindhoven, The Netherlands

Objectives: For many adolescents it is a challenge to get up early in the morning, stay alert at school and get enough sleep, while also engaging in social activities. Previous research has shown that bright or blue-enhanced light exposure during the day and reduced short-wavelength light in the evening and at night can improve sleep timing and quality, and in turn, circadian alignment with environmental demands. Light exposure regimes can be improved by relatively easy, yet quite diverse strategies, i.e., increasing outdoor activities, and using light-reducing apps for displays in the evening. However, changing these behaviours in adolescents may be challenging. Therefore, developing attractive methods to encourage healthy light exposure regimes in this target group would be of great value. The aim of the current study was to 1) explore current behaviors that may improve or impede their sleep timing and quality, and discuss possibilities and challenges for an interactive coaching app to promote healthy light exposure and sleep timing and quality; 2) monitor and quantify inter- and intra-individual variations in current sleep-wake and light exposure patterns; and 3) provide recommendations for the development of an interactive coaching app to promote healthy light and sleep hygiene in this target group.

Methods: Focus groups with high school students (age 15–18; +/–5 persons per group) will be conducted to discuss challenges with respect to keeping a regular sleep-wake rhythm and behaviors they already engage in that may improve their sleep timing and quality. Moreover, we will discuss the idea to introduce an interactive coaching app to improve light exposure and sleep regimes and discuss what kind of features the target group would prefer and find useful in such a coaching app. Secondly, a field study will be conducted in which we will monitor adolescents' light exposure and sleep-wake patterns during school days and days off. To this end, wearable devices (light sensors and actiwatches) will be used. This data will be complemented with subjective data on sleep timing and quality based on a sleep diary, and an experience sampling protocol to assess potential structural fluctuations in daytime alertness and vitality.

Results: Data collection will take place in April and the first half of May. Results will be presented in detail at the conference, as all data is expected to be analyzed in May/June. Thematic analyses will be used to analyze the qualitative data. For the data gathered in the field study, multilevel analyses will be performed to explore inter- and intra-individual variations in light exposure and sleep-wake patterns, as well as potential relationships between these two.

Conclusions: The findings from the focus groups and the field study will serve as input for the coaching app in order to make it attractive for and tailored to this specific target group. Based on these findings, recommendations for the development of such an app will be discussed.

Funding/Disclosures: Funded by Stichting Onderzoek Licht en Gezondheid (SOLG).

A39

ADHD-Related Symptoms in Neuro-Typical Adults Are Correlated with Increased Day-Time Sleepiness, Reduced Arousal Levels and Evening Chronotype

Maria Korman[1], Ishay Levy[1,2], Adi Eshed[3], Avi Karni[1,2]

[1]The Edmond J. Safra Brain Research Center for the Study of Learning Disabilities, University of Haifa, Haifa, Israel; [2]Laboratory for Human Brain and Learning, Sagol Department of Neurobiology, University of Haifa, Haifa, Israel; [3]Department of Occupational Therapy, Faculty of Social Welfare & Health Sciences, University of Haifa, Haifa, Israel

Objectives: To test whether the Adult Self-Report Scale for ADHD, six-items version (ASRS-6) reflects circadian parameters of morningness-eveningness, arousal and day-time sleepiness.

Methods: The ASRS-6 was completed by 40 university students who affirmed that they were not suggested to have or were never diagnosed as having ADHD/ADD during their childhood or adulthood. Circadian preferences (MEQ) were prescreened to ensure a range of chronotypes to be represented; 20 participants with evening and 20 with morning/neither chronotype were included. Day-time sleepiness (Stanford Sleepiness Scale) and objective sleep evaluation using a week-long actigraphy were performed. Arousal levels (low-high) on Visual Analogue Scales (VAS) were tested at 8:00 AM and re-tested at 9:00 AM under two conditions presented on two different days: i. after 45 minutes of exposure to ambient office light (200 lux). ii. After 45 minutes of exposure to outdoors natural morning sun-light (>10,000 lux).

Results: Our results show that: (i) ASRS-6 score (ranging from 0 to 6) correlated with higher day-time sleepiness, morningness-eveningness continuous score and lower subjective alertness at 8:00 AM; (ii) All participants showed significant improvement in subjective alertness VAS scores at 9:00 AM after 45 min exposure to natural outdoor light, while exposure of the same participants to office light (on a different day) did not present substantial improvements in subjective alertness; (iii) After exposure to bright daylight, at 9:00 AM re-test, no correlation between ASRS-6 and subjective alertness VAS scores was observed.

Conclusions: First, current findings suggest that, in typical university students, the ASRS-6 measures not only the current symptoms of inattentiveness/hyperactivity, but also an additional correlated construct – the individual circadian characteristic of morningness-eveningness. Higher ASRS-6 scores administered in morning hours correlate also with typical eveningness-related symptoms – higher day-time sleepiness and lower subjective alertness. Second, we propose that a 45 min morning dose of daylight can upregulate subjective arousal during morning hours in all chronotypes and that such light treatment eliminates the correlation between the ASRS-6 scores and the subjective alertness. Altogether, we conclude that eveningness, day-time sleepiness and low arousal levels are related to ADHD symptoms in typical young adults without ADHD diagnosis.

Funding: E.J. Safra Brain Research Center for the Study of Learning Disabilities.

A40

Novel Chronotherapeutic Strategies in a Day Treatment Program for Complex Mood Disorders

Robert D. Levitan, Ryan Klein, Jeff Daskalakis

Centre for Addiction and Mental Health and Department of Psychiatry, University of Toronto, Toronto, ON, Canada

Objectives: Individuals with Major Depressive Disorder who attend the Integrated Day Treatment (IDT) program at CAMH, Toronto, Canada come to either the morning stream or the afternoon stream but not both. As it currently stands, patients choose which IDT stream they want to attend after an orientation session. We predicted *a priori* that individuals with higher MEQ scores (greater alertness and energy in the morning) would be more likely to choose the morning stream, and have better clinical outcomes in the morning stream, whereas later chronotypes would show the corresponding pattern in the afternoon stream.

Methods: Standard parametric statistics were used to compare MEQ scores in the morning and afternoon streams. Multiple regression was used to predict treatment outcome based on MEQ scores at baseline, treatment stream (morning or afternoon), and their interaction.

Results: As predicted, an analysis of the first 209 MDD patients found a higher mean MEQ score at baseline in the morning stream than in the afternoon stream (48.1 +/– 12.0 vs. 41.7 +/– 10.4 respectively, $p < 0.001$), suggesting that patients do choose the stream most synchronous with their subjective chronotype. An unexpected finding is that actual treatment responses follow the opposite pattern. The MEQ by treatment stream interaction was highly robust using either raw QIDS change scores ($t = –3.49$, $p = 0.001$) or % change scores ($t = –3.47$, $p = 0.001$), with *lower* morningness scores at baseline predicting better treatment responses in the morning IDT stream, and *higher* morningness scores predicting better outcomes in the afternoon stream.

Conclusions: In sum, while MDD patients showed a strong tendency to choose the IDT stream synchronous with their pretreatment MEQ score, the subgroup of patients who chose the IDT stream *asynchronous* to their baseline MEQ score had a much better anti-depressant and quality of life response overall. This suggests that in the IDT context, it is better to be treated at one's less preferred, and not one's preferred time of day for activities. Potential mechanisms to explain this pattern of results will be discussed.

Funding/Disclosures: Dr. Levitan is supported by the Cameron Parker Holcombe Wilson Chair in Depression studies at CAMH and University of Toronto.

A41

Effects of Bright Light Exposure on Alertness Under Forced Desynchrony Conditions

Renske Lok, Tom Woelders, Minke J. van Koningsveld, Klaske Oberman, Sebastiaan G. Fuhler, Domien G.M. Beersma, Roelof A. Hut

University of Groningen, GELIFES, Department of Neurobiology, Groningen, The Netherlands

Objectives: Daily physiological and psychological rhythms, such as body temperature and alertness, are under circadian and homeostatic (i.e. time since wake) influence. Several Forced Desynchrony (FD) experiments successfully quantified the contribution of both processes. In addition, non-image-forming (NIF) effects of light on these parameters have been repeatedly demonstrated. For example, alertness is increased by bright light exposure during the night, when the circadian drive for wakefulness is low, and homeostatic sleep-pressure is high. Such effects on alertness are difficult to demonstrate during daytime, suggesting that these effects of light are modulated by the circadian clock and/or by the amount of accumulated homeostatic sleep pressure. The goal of this FD experiment is to quantify circadian and sleep/wake homeostatic modulation of NIF effects of light on alertness and mental performance.

Methods: An FD experiment was performed under dim and bright white light (<10 lux and 1500 lux) in eight men. The FD principle uses T-cycles outside the range of human light entrainment. Kronauer model based simulation showed lack of entrainment under 1500 lux using an 18 h LD cycles (sleep-wake cycle). Within each light condition, baseline Dim Light Melatonin Onset (DLMO) measurement was followed by 4 x 18 hours FD protocol (5 h sleep, 13 h wake; total 72 hours), followed by 8-h recovery sleep and final DLMO assessment. Participants were exposed to both light conditions in a semi-randomized within subject design. Subjects performed 2-hourly test-sessions for subjective sleepiness (Karolinska Sleepiness Scale), objective sleepiness (Karolinska Drowsiness Test, EEG), sustained attention (psychomotor vigilance task; PVT) and inhibitory control (Go-NoGo task) assessment as well as pupil size and eye-blink rate. Heartrate, skin- and core body temperature (CBT) were measured continuously and saliva samples (for melatonin and cortisol assessment) were collected hourly.

Results: Preliminary analysis of 6 subjects confirms both circadian and homeostatic regulation of most parameters. Our dim/bright light FD paradigm shows that bright light effectively reduced the circadian CBT rhythm amplitude as well as the homeostatic decay of CBT during wake. The effect of light on subjective sleepiness (KSS) mainly depends on elapsed time awake and not on circadian phase. Light made PVT reaction times faster, especially in a small circadian time-window. Homeostatic sleep pressure did not influence the effect of light on reaction time, suggesting different pathways by which light affects subjective sleepiness and sustained attention.

Conclusions: This experiment shows therefore, for the first time, that NIF effects of light on CBT and subjective and objective psychological performance measures are differently modulated by circadian and homeostatic phase.

Funding/Disclosures: None.

A42

Melanopsin Retinal Ganglion Cell Function in Seasonal Mood, Melatonin Regulation and Light Therapy

Helle Ø. Madsen[1], Ida Hageman[1], Shakoor Ba-Ali[2], Henrik Lund-Andersen[2], Klaus Martiny[1]

[1]Mental Health Center Copenhagen, Copenhagen, Denmark; [2]Department of Ophthalmology Rigshospitalet/ Glostrup Hospital, Copenhagen, Denmark

Objectives: The post-illumination pupil response to blue light (PIPR) mediated by the melanopsin containing retinal ganglion cells (mRGCs) is attenuated in depression including seasonal affective disorder (SAD). The proposed decrease in retinal photosensitivity may be of pathogenetic importance in depression. Since glaucoma leads to mRGC degeneration we use glaucoma and visual impairment as a model of mRGC dysfunction to study aspects of SAD. We thus investigate the role of mRGC dysfunction in mood seasonality, seasonal melatonin regulation and response to bright light therapy.

Methods: Study A includes outpatients with glaucoma in a cross-sectional survey using the Global Seasonal Score (GSS) from the Seasonal Pattern Assessment Questionnaire (SPAQ) to assess seasonal variation in sleep length, social activities, mood, energy levels, appetite, and body weight. Correlations between GSS and glaucomatous visual field defects and retinal ganglion cell layer thickness are the main outcomes. Study B performs biannual assessments of salivary melatonin, PIPR and self-assessed mood and sleep (WHO-5, SPAQ, HAM-D_6 and sleep logs) in subjects with advanced glaucoma and control subjects without eye disorder. Saliva is sampled every 4 hours across a 24 hour period. Main outcome is total diurnal melatonin secretion. Study C includes persons with SAD and severe visual impairment in a 6 week trial of morning bright light (10,000 lux, 30 minutes). At inclusion a diagnosis of depression is established by clinical interview and a basic ophthalmologic examination is performed. Before and after treatment, PIPR is measured and depression severity is assessed by a psychiatry consultant blinded to visual function, PIPR and compliance. Main outcome is reduction in depression score.

Results: We will present preliminary results from 99 subjects with glaucoma who completed the SPAQ. Four cases were excluded due to photophobic or allergic summer malaise. In the remaining 54 women and 41 men, mean age was 64 (18–92 years) and mean GSS 4.6 (SD 3.9). There was a negative correlation between age and GSS ($r^2 = 0.122$, $p = 0.03$) only for men. There was no overall correlation between GSS and visual field ($r^2 = 0.001$, $p = 0.7$) but a strong correlation in females under 66 years ($r^2 = 0.35$, $p = 0.004$).

Conclusions: In this limited population we find a correlation between glaucomatous visual field defects and mood seasonality only in selected subgroups. Study B and C are ongoing.

Funding/Disclosures: The study has received funding from the Velux Stiftung, the Augustinus Foundation, the Jascha Foundation and the Ivan Nielsen Foundation. None of the authors report any disclosures.

A43

Dynamics of Subjective Thermal Comfort and Skin Temperatures Under Self-Selected (Day-) Lighting Conditions

Lenka Maierova[1,2] *, Apiparn Borisuit*[1], *Jean-Louis Scartezzini*[1], *Mirjam Münch*[1,3]

[1]Swiss Federal Institute of Technology, Lausanne, Switzerland, Solar Energy and Building Physics Laboratory, Lausanne, Switzerland; [2]Czech Technical University in Prague, UCEEB, Prague, Czech Republic; [3]Current affiliation: Charité Universitätsmedizin Berlin, Institute of Physiology, Sleep Research & Clinical Chronobiology, Berlin, Germany & St. Hedwig Hospital, Clinic for Sleep and Chronomedicine, Berlin, Germany

Objectives: Diurnal changes in physiology and behavior are modulated by external factors such as light or temperature. Our objective was to test whether self-selected office lighting during a habitual waking period (16 hrs) would have an impact on subjective thermal comfort and objective measures of skin temperature in young morning and evening types (16/16), where preferred bed and wake times usually differ by several hours.

Methods: The results obtained under a self-selected lighting condition (SSL; daylight and electrical lighting) were compared with a constant bright light (BL; 1000 lx) and a control condition (DIM, dim light). All participants came three times to the laboratory and remained under controlled constant posture conditions for 16 hrs, where room temperature was kept constant. Subjective thermal comfort was assessed hourly by visual analogue scales and proximal and distal skin temperatures were continuously recorded and expressed relative to midsleep.

Results: Participants felt significantly colder in DIM than in BL or in SSL conditions ($p < 0.05$), and subjective thermal comfort remained stable in BL and SSL conditions. Proximal (clavicula) and distal skin temperatures (hands) were significantly higher for SSL than for DIM or BL conditions. The time course for distal skin temperatures revealed for evening types significantly higher temperatures 5–6.5 h and 9–9.5 h after habitual wake time, but only in BL, and not the other two conditions ($p < 0.05$). The distal-proximal temperature gradient (DPG) was significantly correlated with subjective thermal comfort (Spearman Rho: 0.48, $p < 0.05$).

Conclusion: Self-selection of lighting at work might positively influence thermoregulatory functions regarding inter-individual differences, similar to what we have previously shown for subjective alertness, mood, wellbeing and melatonin secretion (Maierova et al. 2016).

Acknowledgements: Velux Foundation Switzerland.

Disclosure: None.

A44

Extended Photoperiod Alters Circadian Rhythmicity and Expression of Synaptic Plasticity-Associated Genes. The Impact of Blue-Enriched Light

Andrea R. Marti[1]*, *Jorrit Waslander*[1,2]*, *Silje Skrede*[1,3], *Jelena Mrdalj*[1], *Torhild T. Pedersen*[1], *Louise H. Bjerrum*[1], *Kari M. Ersland*[1,4], *Tone E.G. Henriksen*[1,5], *Clive Bramham*[1], *Janne Grønli*[1]

[1]University of Bergen, Bergen, Norway; [2]University of Groningen, Groningen, The Netherlands; [3]Bergen Clinics Foundation, Bergen, Norway; [4]Haukeland University Hospital, Helse Vest, Norway; [5]Valen Hospital, Helse Fonna, Norway; *the authors contributed equally to this work

Objectives: Light can have complex effects on regulation of circadian rhythmicity, mood and cognition. The brain's ability to maintain cognitive function depends on synaptic plasticity – persistent increases or decreases in synaptic strength in response to neural activity patterns. Several immediate early response genes have been implicated in synaptic plasticity, including brain-derived neurotropic factor (BDNF), the activity-regulated cytoskeleton-associated (Arc) protein, Krueppel-like factor 10 (KLF10) and Neuronal PAS domain protein 4 (NPAS4). Here we use a model of prolonged photoperiod (20 h light, 4 h dark; 20:4 LD) with two different spectral qualities (white and blue-enriched light) to examine effects on the circadian rhythm of body temperature (BT), and expression of neuroplasticity markers in the rat brain.

Methods: For recording of BT rhythm, rats ($n = 6$/group) were housed in standard 12:12 LD condition, followed by exposure to 7 days long photoperiod (20:4 LD) in either white or blue-enriched light conditions, and 14 days recovery in standard 12:12 LD condition. Tissue from a separate set of animals ($n = 10$/group) was collected on exposure day 7 (E7), and recovery day 3 (R3), from anterior cingulate cortex (ACC; implicated in mood regulation) and prefrontal cortex (PFC; implicated in mood and cognition). Tissue samples were analyzed with qPCR. Two-tailed student's t-test was used for statistical comparison to 12:12 LD controls ($p < 0.05$).

Results: The rhythm of BT maintained a 24 h period in both blue-enriched and white light conditions during 20:4 LD, although the acrophase was shifted to co-occur with the dark phase. Upon return to 12:12 LD, decreased amplitude and no clear 24 h period was observed for up to 8 days. Extended photoperiod, independently of spectral qualities, decreased expression of Arc (ACC and PFC; $t's_{(15–18)} > –3.74$, $p's < 0.002$) and KLF10 (ACC; $t's_{(17–18)} > –2.51$, $p's < 0.02$) compared to controls at E7. NPAS4 was decreased in the blue-light condition only (PFC; $t_{(15)} = –3.53$, $p = 0.003$). The expression of BDNF was not significantly changed at E7 compared to controls, but increased at R3 in the blue-light-condition only (PFC; $t_{(14)} = 3.80$, $p = 0.002$). No significant differences in expression of Arc, KLF10 or NPAS4 were observed at R3 compared to controls.

Conclusions: Extended photoperiod disrupted the circadian rhythmicity of body temperature, and reduced several markers of

synaptic plasticity in brain regions important for mood and cognitive performance. Furthermore, the effect on synaptic plasticity markers depends on the spectral quality and brain-region.

Funding/Disclosures: The work was funded by Helse Vest (ID HV911 893) and the Faculty of Psychology, University of Bergen (Småforsk, ID 173200-270452; 173200-810298).

A45

Acute Exposure to Blue Light at Night Impairs Glucose Tolerance, Alters Insulin Secretion and Increase Sugar Intake in Diurnal Rodents

Anayanci Masis-Vargas[1,2,3]*, Andries Kalsbeek*[2,3]*, Jorge Mendoza*[1]

[1]Light, Vision and the Brain Team, Institute de Neurosciences Cellulaires et Intégratives (INCI), UPR-3212 CNRS-Université de Strasbourg, Strasbourg, France; [2]Hypothalamic Integration Mechanisms, Netherlands Institute of Neuroscience (NIN), Amsterdam, The Netherlands; [3]Department of Endocrinology and Metabolism, Academic Medical Center (AMC), University of Amsterdam, Amsterdam, The Netherlands

Objectives: To study the acute effects of blue light (BL) in the early night on regular chow or high caloric palatable food intake, and glucose metabolism, in male and female diurnal rodents.

Methods: Female and male diurnal Sudanian grass rats (*Arvicanthis ansorgei*) were exposed to a regular chow or a free choice high fat high sucrose (fcHFHS; sugar and fat exposure in addition to regular chow pellets) diet and assigned to either a dark control or blue light exposure condition. At Zeitgeber time 14 (two hours after lights off in a 12/12 h light-dark cycle) a 1 h pulse of BL ($\lambda = 490 \pm 20$ nm) was given and an oral glucose tolerance test (OGTT) was performed 1 h after (ZT15). One week after, a second light pulse was given and food intake from both diet groups was evaluated every 12 h from the day before and the day after the light exposure. Finally, a week later a third light pulse was given and blood was recovered for glucose, insulin and corticosterone analyses. Locomotor activity of animals was monitored during the whole experiment.

Results: Caloric intake increased in animals exposed to fcHFHS diet and the bimodal diurnal pattern of food intake became more accentuated, especially in females. In chow fed animals the AUC of the OGTT was significantly higher in the BL exposed animals of both sexes in comparison to dark controls. This effect was also observed in males, but not females, fed with the fcHFHS diet. BL exposure induced an increase of sucrose intake in male *Arvicanthis* on the night of the BL pulse. Yet a similar effect was observed on the day after on the female group. In both, chow and fcHFHS fed males, a significant decrease in plasmatic insulin concentrations was observed after light exposure.

Conclusions: Exposure to BL at night causes glucose intolerance in diurnal rodents, with a stronger effect in males when they were exposed to a high caloric diet. Moreover, BL at night was sufficient to trigger a higher intake of sugar in both male and female grass rats, and to cause a dampening in the insulin release in a sex dependent manner.

Funding/Disclosures: This work is supported by Erasmus+ NeuroTime Programme, an ANR-14-CE13-0002-01 ADDi-CLOCK JCJC grant and the Institut Danone France-Fondation pour la Recherche Médicale Consortium.

A46

Chronically Disrupted Sleep, Neuronal Plasticity and Depression

Peter Meerlo

University of Groningen, Groningen, The Netherlands

Sleep problems are a common complaint in the majority of people suffering from depression. While sleep complaints were traditionally seen as a symptom of mood disorders, accumulating evidence suggests that in many cases the relationship may be reverse as well. A long list of longitudinal studies shows that sleep complaints often precede the onset of depression and constitute and independent risk factor for the development of the disorder. Additionally, experimental studies in animals show that chronically restricted or disrupted sleep may gradually induce neurobiological changes that are very similar to what has been reported for depressed patients. The mechanisms through which insufficient sleep increases the risk for depression are poorly understood but may include effects of sleep disturbance on neuroendocrine stress systems, serotonergic neurotransmission, and various interacting signaling pathways involved in the regulation of neuronal plasticity and neurogenesis. Because sleep is considered to play a crucial role in regulating neuronal plasticity and synaptic strength, chronically insufficient sleep may contribute to depression through an impairment of these plasticity processes leading to altered connectivity and communication within and between brain regions involved in the regulation of mood.

A48

Dynamics of Daytime Light Exposure Impacts on Sleep Architecture in a Naturalistic Setting

Claudia Nowozin[1,2]*, *Amely Wahnschaffe*[1,2]*, *Jan de Zeeuw*[1], *Alexandra Papakonstantinou*[1,2], *Frederik Bes*[1,2], *Mirjam Münch*[1,2,3], *Dieter Kunz*[1,2]

[1]Charité – Universitätsmedizin Berlin, Corporate Member of Freie Universität Berlin, Humboldt-Universität zu Berlin, and Berlin Institute of Health, Institute of Physiology, Sleep Research & Clinical Chronobiology, Berlin, Gemany; [2]St. Hedwig-Hospital, Clinic for Sleep and Chronomedicine, Berlin, Germany; [3]Charité Universitätsmedizin Berlin, Corporate Member of Freie Universität Berlin, Humboldt-Universität zu Berlin, and Berlin Institute of Health, Institute of Immunology, Berlin, Germany; *equal contribution

Objectives: While rapid eye movement (REM) sleep is predominantly circadian driven, slow wave sleep (SWS) is homeostatically driven. There is also evidence that light during daytime has an impact on subsequent sleep. A recent study by Wams et al. in 2017 found an association between the timing and amount of (natural) light exposure during daytime, REM sleep and SWS accumulation during ambulatory polysomnographically (PSG) recorded sleep episodes. The aim of the current evaluation was to replicate and expand these findings using the data from an older study performed in a semi-natural setting.

Methods: Eleven healthy adults (between 20 and 30 years, intermediate chronotypes, 6 male, 5 female) participated in the study 2008. Individual illuminance was continuously recorded at the eye level between 8 am and 7 pm (Luxblick, TU Ilmenau, Prof. C. Schierz). Four hours before habitual bedtime participants came to the laboratory and remained in dim light (<5 lx). Their sleep episode was recorded with PSG. All PSG recordings (available from 9 participants) were visually scored according to standard criteria and illuminance recordings were collapsed into hourly bins. For analysis non-parametric tests were applied.

Results: Participants spent 59% of their days with illuminance levels lower than 50 lx and 90% below 200 lx. Participants had more SWS during the night when they had a later time of maximum light exposure (min; Rho = 0.733; p = 0.025) and were exposed to more light between 2–3 pm (Rho = 0.70; p = 0.036). Accordingly, a later maximum light exposure was associated with less stage 2 sleep (min; Rho = –0.683; p = 0.042). The fitted slopes from accumulated SWS were significantly steeper and associated with higher illuminance between 4–5 pm (Rho = 0.683; p = 0.042). Regarding REM sleep accumulation, less steep slopes were associated with greater illuminance between 11–12 am (Rho = 0.683, p = 0.042). Finally, longer REM sleep latency was significantly related to higher illuminance levels between 11–12 am (Rho = 0.90; p = 0.001). Shorter REM sleep latency was associated with more light between 4–5 pm (Rho = –0.700; p = 0.036).

Conclusion: Our results support earlier work showing an association of natural daylight exposure and sleep architecture during the subsequent night. Based on the explorative analysis in this small sample we hypothesize a differential impact of light at different times of day on different sleep stages.

Funding/Disclosures: BMBF, German Ministry of Education and Research FKZ: 13N8973.

A49

Advanced Chronotherapeutics for Depression During Pregnancy

Barbara Parry, Charles Meliska, Diane Sorenson, Fernando Martinez, Ana Lopez, Sharron Dawes, Richard Hauger, Daniel Kripke

University of California, San Diego, CA, USA

Objectives: To test the hypothesis that combined wake therapy and light treatment improve depressed mood during pregnancy and postpartum, and that the magnitude of mood change correlates with the magnitude of melatonin and sleep changes.

Methods: Initially 78 women, 35 pregnant (20 normal controls-NC; 15 depressed participants-DP with a major depressive episode-MDE by the Structured Clinical Interview for DSM-IV during pregnancy) and 43 postpartum (24 NCs; 19 DP with onset of a MDE within 3 months postpartum), were randomized to a parallel trial of one night of early-night wake therapy-EWT (wake until 03:00 h, sleep 03:00–07:00 h) + 6 weeks of evening (PM) bright white light-BWL (5.5" x 6.25" Litebook Advantage light box, 60 cool white light-emitting diodes, intensity 1,350 lux, irradiance 2.41 x 10^{-9} w/cm^2 at 21 in, spectral emission peaks 464 nm, 564 nm, The Litebook Company Ltd., Alberta Canada) administered for 60 min starting 90 min before habitual sleep onset time, vs. one night of late-night wake therapy-LWT (sleep 21:00–01:00 h, then wake) + 6 weeks of morning (AM) BWL administered for 60 min within 30 min of habitual wake time. Pre- and post-intervention, clinicians blind to treatment condition assessed mood weekly by the Structured Interview Guide for the Hamilton Rating Scale for Depression with Atypical Depression Supplement (SIGH-ADS), and participants completed the Horne-Ostberg Morningness-Eveningness questionnaire (MEQ), and collected 2 overnight samples (36 hours from 18:00 h-noon the following day) of urine for 6-sulphatoxy melatonin (6-SMT) measures.

Results: SIGH-ADS did not differ at 1, 2 or 6 weeks (p > 0.089). Pregnant DP mood improved more at 2 weeks of EWT+PM BWL (p = 0.016 MEQ covariate); in Postpartum DP it improved more at LWT+AM BWL (p = 0.019). In postpartum DP, phase-advance in 6-SMT offset and acrophase was greater (p < 0.05) after LWT+AM BWL and correlated with improved mood (p = 0.003).

Conclusions: Mood improved more after 2 weeks of EWT + PM BWL in Pregnant DP, and more after LWT + AM BWL in Postpartum DP, which correlated with the magnitude of phase-advance in 6-SMT.

Funding/Disclosures: NIH R01 HD076476.

A50

Bright Light Exposure during Simulated Night Shift Work – Impact on Daytime Sleep

Torhild T. Pedersen[1], Jelena Mrdalj[1], Ståle Pallesen[2], Erlend Sunde[2], Eirunn Thun[2], Tone E.G. Henriksen[1,3,4], Debra J. Skene[5], Janne Grønli[1]

[1]Bergen Stress and Sleep Group, University of Bergen, Bergen, Norway; [2]Department of Psychosocial Science, University of Bergen, Bergen, Norway; [3]Department of Clinical Medicine, Section for Psychiatry, University of Bergen, Bergen, Norway; [4]Division of Mental Health Care, Valen Hospital, Fonna Local Health Authority, Valen, Norway; [5]University of Surrey, Guildford, UK

Objectives: Bright light has been suggested as a countermeasure to sleepiness and cognitive impairment during night shifts, and for improving subsequent sleep. We aimed to investigate how exposure to different light intensities of full spectrum white light during simulated night shifts would affect polysomnographic-assessed sleep parameters following the shift.

Methods: A randomized counterbalanced, controlled, repeated-measurements design was used. To simulate night shift work, participants performed a battery of cognitive tasks in the laboratory from 11 PM to 7 AM for three consecutive nights. The light conditions were full spectrum bright light (mean illuminance: 890.2 lx, SD = 85.9) and dim light (mean illuminance: 88.5 lx, SD = 8.3). Following each night shift participants went home to sleep, and daytime sleep was monitored by the use of polysomnography. Here we report preliminary data on 10 out of 13 participants. Mean ± SEM and Cohen's *d* are used to estimate differences and effects sizes between conditions.

Results: Total daytime sleep following the third night shift was longer when participants were exposed to bright light during the night shift, compared to when participants were exposed to the dim light condition (421.88 ± 30.85 min vs. 324.54 ± 25.19 min, $d = 1.57$. Sleep onset latency was shorter (5.10 ± 1.98 min vs. 8.90 ± 1.50 min, $d = –0.96$) and percentage time in stage N2 was longer (44.23 ± 5.66% vs. 32.06 ± 4.28%, $d = 1.07$ in bright light compared to the dim light condition. Percentage time spent in stage N3 and REM sleep indicated smaller differences (21.50 ± 9.05% vs. 32.57 ± 6.84%, $d = –0.61$, and 24.98 ± 3.77% vs. 25.98 ± 3.07%, $d = –0.14$, respectively).

Conclusions: Exposure to bright light during simulated night shifts increased total daytime sleep compared to lower intensity light.

Funding/Disclosures: The research is funded by" Småforsk" (local research funds nr.173200-270452).

A51

The Efficacy and Safety of Morning Light Therapy for (Winter) Depression in Bipolar Disorder

Lisette Rops[1], Lotte van Hout[2], Marijn Groen[1], Claudia Simons[1]

[1]GGzE, Eindhoven, The Netherlands; [2]Maastricht University, Maastricht, The Netherlands

Objectives: Evaluation of efficacy and safety of light therapy for seasonal (winter)depression in bipolar disorder.

Methods: The study was carried out at a specialized outpatient treatment centre for bipolar disorders. Inclusion criteria were a diagnosis of bipolar AND seasonal affective disorder AND current depression. The scores of Inventory of Depression Symptoms (IDS; used in the period 2015–2017) or Quick Inventory of Depression Scale (QIDS; since 2017 onwards) had to be above remission threshold. Light therapy was given with an intensity of 10,000 lux for 30 minutes in the morning during a period of seven days, after which severity of depressive symptoms was assessed by IDS or QIDS. If remission (based on scores of IDS or QIDS) occurred, light therapy was stopped. In case of non-remission light therapy was continued for seven days followed again by IDS or QIDS assessment. The maximum of light therapy was 21 days. Given that there is ongoing debate about safety of light therapy in bipolar disorder, especially concerns about a switch into mania in morning light therapy, we registered carefully the reason of drop out during the treatment. A multilevel regression analysis was carried out.

Results: We included 31 patients in the winter period between October until March in respectively 2015/2016, 2016/2017 and again 30 patients in the period of October 2017 until March 2018. The results up to and including 2017 are already analyzed. These results showed a significant improvement in depression scores after seven days of light therapy. Only one client had to discontinue light therapy because of hypomanic symptoms (sleep reduction and increased energy). After therapy was discontinued, these symptoms faded away in a few days. The results of October 2017 until March 2018 are now being analyzed and will be presented at the conference.

Conclusions: Morning light therapy seems to be efficacious and safe in patients with bipolar (winter) depression. The risk of switching to (hypo)mania appeared to be limited.

A52

Do Dynamic Changes in Light Level and Spectral Power Distribution Improve Acute Alertness During Daytime?

Inga Rothert, Stephan Völker

Lighting Technology, Technische Universität Berlin, Berlin, Germany

Objectives: Many studies confirm positive acute effects of higher light levels for alertness, while findings concerning the effects of variation of spectral power distribution are inconclusive. Dynamic changes of light level have been shown to improve acute alertness at nighttime. However, are these dynamic changes also beneficial during daytime?

Methods: Acute alertness was measured with a d2R-test and an auditory Go-NoGo task. A questionnaire addressed personal well-being and acceptance of the lighting conditions and the Karolinska Sleepiness Scale (KSS) was used to assess subjective drowsiness. Three light settings were tested: 1) Dim static warm white (200 lx at eye level, 2,200 K), which was expected to be non-effective; 2) Bright static cool white (1,000 lx at eye level, 12,000 K), which was expected to be most effective; 3) A dynamic setting, which changed every 12 min between the two other lighting conditions. A between-subjects design was conducted with 30 participants (18–30 years) for each setting. The experiments took place in groups of up to six participants in a test room without daylight and the light exposure lasted 90 min in the afternoon (post-lunch dip).

Results: Unexpectedly, the results for the d2R-test, the Go-NoGo task and drowsiness on the KSS scale did not show any significant differences between the three lighting conditions. Well-being and acceptance of the lighting conditions are still under investigation. Although this contradicted our working hypothesis, this finding is in line with a number of other recent publications.

Conclusions: No positive acute effects of dynamic changes in light level and spectral power distribution on alertness during daytime were found. One possible explanation is that short term light exposure for only 90 min might not be long enough to observe effects. Experiments over an entire working day including subsequent sleep quality might give different results. Furthermore, this study included only healthy young students, who seem to be less sensitive to light conditions than other groups, for example sleep deprived, stressed or elderly people. Under non-critical operating environments, however, the effect of light on acute alertness might be less important than often assumed and good standard lighting conditions might be sufficient.

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

A53

Can Bright Light Exposure Function as a Compensation of Midday Nap Deprivation among Habitual Nappers?

Taotao Ru[1,2]*, Karin C.H.J. Smolders*[2]*, Qingwei Chen,*[1]*, Guofu Zhou*[1,3]

[1]National Center for International Research on Green Optoelectronics, South China Normal University, Guangzhou, China; [2]Human Technology Interaction, School of Innovation Sciences, Eindhoven, The Netherlands; [3]Guangdong Provincial Key Laboratory of Optical Information Materials and Technology & Institute of Electronic Paper Displays, South China Academy of Advanced Optoelectronics, South China Normal University, Guangzhou, China

Introduction: It is well documented that a short daytime nap at noon or in the early afternoon could significantly counteract post-lunch dip in alertness and performance. Yet, it is unclear whether a habitual midday nap deprivation would elicit impairment of subsequent alertness and working performance. Moreover, previous studies have suggested the effectiveness of bright light exposure to overcome the decline of alertness and performance under the condition of night sleep deprivation and daily natural post-lunch dip. The potential benefits of bright light exposure following midday nap deprivation among habitual nappers remains to be investigated. Thus, the current study was conducted in an effort to explore whether exposure to bright blue-enriched light (1000 lx at 6500 K at eye level) opposed to practical office setting (165 lx at 4000 K at eye level) could counteract the impairment of alertness, mood and performance induced by a habitual midday nap deprivation among university students.

Objectives: To examine the effects of bright blue-enriched light exposure on subjective alertness, mood and performance following a habitual midday nap deprivation.

Methods: Seventeen university students with the long-term habit of a afternoon nap (around 13:00 h) either took a nap, or served two nap deprivation conditions on three non-consecutive days. After the nap intervention, participants were tested on sustained attention, response inhibition and working memory task under different light conditions. Bright blue light (1000 lx at 6500 K at eye level) was applied in one of two nap deprivation conditions. The changes of subjective sleepiness and mood were measured during experimental session.

Results: Results showed exposure to bright blue-enriched light after nap deprivation significantly decreased subjective sleepiness, negative mood, and enhanced sustained attention, working memory and response inhibition speed.

Conclusions: Bright blue-enriched light exposure is an efficient compensation of a habitual afternoon nap loss.

Funding/Disclosures: This work has been funded by the National Key Research and Development Program of China (No.2016YFB0404202), National Natural Science Foundation of China (Grant No. U1501244, 51561135014), the Top graduate project of South China Normal University (2016090 to T. Ru) and under a program co-financed by Philips Lighting.

A54

The Effects of Bright Light Therapy on Depression, Sleep and Circadian Rhythm in Patients with Parkinson's Disease and a Depressive Disorder: Results of a Double-Blind Randomized Controlled Trial

Sonja Rutten[1,2], *Chris Vriend*[1,2,3], *Jan H. Smit*[1,7], *Henk W. Berendse*[3,4], *Eus J.W. van Someren*[1,5,6], *Adriaan W. Hoogendoorn*[1,7], *Jos W. Twisk*[7,8], *Ysbrand D. van der Werf**[2,3], *Odile A. van den Heuvel**[1,2,3]

[1]Department of Psychiatry, VU University Medical Center/GGZ inGeest, Amsterdam, The Netherlands; [2]Department of Anatomy and Neurosciences, VU University Medical Center, Amsterdam, The Netherlands; [3]Amsterdam Neuroscience, Amsterdam, The Netherlands; [4]Department of Neurology, VU University Medical Center, Amsterdam, The Netherlands; [5]Department of Sleep & Cognition, Netherlands Institute for Neuroscience, Amsterdam, The Netherlands; [6]Department of Integrative Neurophysiology, Center for Neurogenomics and Cognitive Research CNCR), Amsterdam Neuroscience, VU University, Amsterdam, The Netherlands; [7]EMGO Institute for Health and Care Research, VU University Medical Center, Amsterdam, The Netherlands; [8]Department of Epidemiology and Biostatistics, VU University Medical Center, Amsterdam, The Netherlands

Objectives: To assess the efficacy of BLT in reducing depressive symptoms in patients with Parkinson's disease (PD) and Major Depressive disorder (MDD), compared with exposure to a control light.

Methods: In this double-blind controlled trial, PD patients with a MDD were randomized to either BLT or a control light condition. Subjects received 30 minutes of home treatment twice daily for three months, followed by a six-month naturalistic follow-up. The primary outcome of the study was the Hamilton Depression Rating Scale (HDRS) score. Secondary outcomes were ancillary depression measures, objective and subjective sleep parameters, and salivary melatonin and cortisol concentrations. Assessments were repeated halfway and at the end of the treatment phase, and one, three and six months post-treatment. Data were analyzed using a linear mixed model analysis.

Results: Eighty-three subjects were included. There was a strong decrease in HDRS score in the experimental as well as the control group, with a non-significant between-group difference. Subjective sleep improved in both groups, with a significantly larger increase in the subjective sleep rating in the experimental group (B (SE) = 0.36 (0.18), $p < 0.05$). Moreover, the experimental group showed a decrease in total salivary cortisol secretion, while it increased in the control group (B (SE) = –8.11 (3.93), $p = 0.04$). After correction for confounders, this group difference showed a trend towards significance (B (SE) = –13.5 (5.2), $p = 0.10$).

Conclusions: BLT was not more effective in reducing depressive symptoms than a control light. Both groups showed an improvement of mood and subjective sleep. BLT was more effective in improving subjective sleep quality than control light, possibly through a BLT-induced decrease in cortisol levels.

Funding/Disclosures: This study was financially supported by research grants from Hersenstichting Nederland, Stichting Parkinson Fonds and de Parkinson Vereniging.

A55

Evening Chronotype Is Associated with Medical Comorbities and Factor Structure of Depression: A Descriptive Study

Cigdem Sahbaz

Bezmialem Vakıf University, Istanbul, Turkey

Objectives: Substantial evidence suggests that chronotypes and biological rhythm disturbances may affect severity and factor structure of depression. No study has addressed specifically the relationship between circadian preferences and vegetative factors and current medical comorbidities in patients with depression. This study aims to examine the potential association between chronotypes and vegetative symptomatology in patients with depression. The patients with the evening chronotype may have more severe vegetative symptoms and medical comorbidities in depression.

Methods: Drug-naive patients with depression according to DSM-5 criteria from the ages of 17–65 were recruited to this study at the outpatient clinic in the Department of Psychiatry, Bezmialem University Hospital. The Morningness-Eveningness Questionnaire (MEQ) was applied to define chronotypes, biological rhythm disturbances were measured by the Biological Rhythms Interview of Assessment in Neuropsychiatry (BRIAN), and quality of subjective sleep was measured with Pittsburgh Sleep Quality Index (PSQI). Depression levels were evaluated through the use of the Hamilton Rating Scale for Depression (HAM-D). Also, we investigated HAM-D with the three-factor structure: Cognitive, Anxiety, Vegetative depression factors.

Results: 101 patients (mean age = 40.18–11.54, 75% female) with depression were recruited. HAM-D scores (HAM-D total, HAM-D total without sleep cluster) and HAM-D factors (cognitive, affective, vegetative, vegetative without sleep cluster) of patients divided into "morning preference" (MP) and "evening preference" (EP) at the D-MEQ (58MP/43EP) sample median. HAM-D scores were significantly higher in EP than in MP at HAM-D total, HAM-D total-without sleep cluster ($p < 0.05$) and vegetative, vegetative-without sleep cluster scores were extremely significant in EP than MP ($p < 0.001$). According to three groups of MEQ; HAM-D total, HAM-D total-without sleep cluster, HAM-D factors (cognitive, vegetative, vegetative-without sleep cluster) were extremely significant in evening chronotype (E) than in morning chronotype (M) and intermediate chronotype (I) ($p < 0.001$). Furthermore, the medical record of patients evaluated retrospectively, and the ratio of having another chronic illness was found statistically significant among the patients with depression and the evening chronotype ($p < 0.05$). Additionally, BRIAN total, sleep, activity, social and eating scores have highly indicated HAM-D scores and factors.

Conclusions: Evening chronotype may notably associate with vegetative symptomology in patients with depression. General and psychiatric clinical examinations need to be considered with the understanding of biological rhythm disturbances and circadian preferences. The description and understanding of the relationship between biological rhythms, chronotype and factor structures of depression may be useful to enhance the treatment options for depression.

Funding/Disclosures: None.

A56

Investigation of Retinal Spectral-Domain Optical Coherence Tomography (SD-OCT) Findings on Biological Rhythm Perspective

Cigdem Sahbaz

Bezmialem Vakıf University, Istanbul, Turkey

Objectives: Spectral-domain optical coherence tomography (SD-OCT) is a fast, noninvasive imaging technique that provides in vivo imaging of the human retinal layer. Schizophrenia (SCH) and Bipolar Disorder (BD) are associated with several brain deficits in neuroimaging studies, but clinically useful biomarkers are elusive. Retinal neurons originate with distinct layers containing components of grey matter. Therefore, recent studies hypothesized that retina might represent a possible "window" to the brain abnormalities. SD-OCT has been increasingly using to search for available biomarkers of psychiatric diseases. However early findings of SD-OCT investigations looking for SCH and BD biomarkers have been controversial and most studies have had severe methodological limitations such as without consideration of control group matching and covariance factors. We conducted two case-control studies comparing individual retinal layer measurements in patients with SCH (N = 50) and BD (N = 36) with age/gender/BMI matched controls. To address unresolved issues, we determined whether: (1) retinal changes in SCH and BD occurs independently of biological rhythm disturbances and subjective sleep parameters that might affect the retina. (2), Due to defining the effect of sleep disturbances directly on retinal findings, we conducted another case-control study in patients with Primary Insomnia (N:52) excluding the existence of another medical comorbidity.

Methods: A Heidelberg Spectra SD-OCT device was used in both eyes of the 50 patients with schizophrenia, 36 patients with bipolar disorder, 52 patients with primary insomnia and 50 age/gender/BMI matched healthy controls. Manual retinal layer segmentation was performed in 3 macular regions. The Morningness-Eveningness Questionnaire (MEQ), Biological Rhythms Interview of Assessment in Neuropsychiatry (BRIAN), Pittsburgh Sleep Quality Index (PSQI) and Insomnia Severity Index (ISI) were performed.

Results: BRIAN scores (total and sleep, activity, social, eating subscales) and PSQI total scores were found significantly higher both in patients with SCH and BD. In study group with SCH, the Inner Plexiform Layer (IPL) was significantly thinner than controls ($p < 0.02$), but when we conducted in General Linear Model taking PSQI total score as a covariate, this effect did not remain significant. Similarly, in the BD group, total retinal volume was found significantly thinner than controls ($p < 0.005$), but after adjusting BRIAN total score as a covariance in the model, this effect did not remain significant. Also in the Insomnia group, IPL was found extremely significantly thinner than controls ($p < 0.0001$), and Choroidal thickness was significantly higher than controls ($p < 0.004$). Besides these findings, thinning of IPL and thickness of Choroid are associated with severity of insomnia and chronotypes in patients with primary insomnia.

Conclusions: Our findings show that retinal layer thicknesses are affected by biological rhythm changes independently. For future studies, biological rhythm disturbances and sleep quality should be considered as confounding factors in patients with SCH and BD. Also, insomnia and chronotypes might influence SD-OCT indices, and these novel findings warrant the investigations of retinal biomarker research in general medical practice.

Funding/Disclosures: None.

A57

Association of Serum BDNF Levels and BDNF Val66Met Polymorphism with Sleep Habits in Healthy Young Adults

Kaori Saitoh, Ryuji Furihata, Yoshiyuki Kaneko, Masahiro Suzuki, Sakae Takahashi, Makoto Uchiyama

Department of Psychiatry, Nihon University School of Medicine, Tokyo, Japan

Objectives: Brain-derived neurotrophic factor (BDNF) is widely expressed in the brain and plays an important role in neuronal maintenance, plasticity, and neurogenesis. Many reports showed that circulating levels of BDNF or BDNF polymorphism were associated with psychiatric disorders, including depression, bipolar disorder, and schizophrenia. Several reports have pointed out a negative correlation between perceived stress and circulating levels of BDNF in non-clinical populations. Apart from mental conditions, those who suffered from sleep disturbances were reported to be associated with decreased serum BDNF levels. More recently, a study suggested that serum BDNF levels were associated with the severity of insomnia. However, a fundamental understanding of the relation between BDNF and sleep in healthy humans remains unclear. The aim of the present study was to elucidate whether the serum BDNF levels and BDNF genotype were associated with characteristics of sleep habits in healthy young adults.

Methods: Seventy-nine healthy paid volunteers (45 men, 34 women) aged 20 to 29 years were recruited. Serum BDNF levels were measured with an enzyme-linked immunosorbent assay, and a single-nucleotide polymorphism (Val66Met) in the BDNF gene was assessed. Detailed sleep habits were examined using a self-recording 1-week sleep diary.

Results: Serum BDNF levels were significantly associated with several sleep parameters on weekends, whereas no such association was found on weekdays. Longer total sleep time and time in bed, and later mid-sleep time on weekends were associated with lower serum BDNF levels. The discrepancy between mid-sleep time on weekdays and that on weekends, otherwise known as social jetlag, was negatively associated with serum BDNF levels.

Met/Met homozygotes of BDNF Val66Met polymorphism spent significantly longer time in bed on weekends than Val/Val homozygotes. Heterozygotes did not differ from Val/Val homozygotes.

Conclusions: We first found that serum BDNF levels and BDNF Val66Met polymorphism in healthy young adults were associated with sleep habits on weekends but not with those on weekdays, suggesting that the neuronal mechanisms involved in the BDNF control may be rather linked to endogenous sleep characteristics than the socially constrained sleep schedule in healthy young adults.

Funding/Disclosures: This study was supported in part by Health Science Research Grants from the Ministry of Health, Labor and Welfare of the Japanese Government and by a Research Grant from the Japan Society for Promoting Science and Technology Agency.

A58

Development of the Dutch Guideline for Light Therapy in Patients with Bipolar Depression

Peter F.J. Schulte[1], Loes Kaarsgaren[2] & the Working Group for Chronotherapy of the Dutch Foundation for Bipolar Disorder

[1]Mental Health Service Noord-Holland-Noord, Alkmaar, The Netherlands; [2]Independent Psychiatrist, Amsterdam, The Netherlands

Objectives: Current treatments for depressive episodes in bipolar disorder are often ineffective and/or intolerable. In unipolar depression light therapy is a treatment option for seasonal and non-seasonal depression. We intended 1) to review the efficacy and tolerability of light therapy in bipolar depression with or without a seasonal pattern; 2) to develop a guideline for light therapy in bipolar depression.

Methods: Narrative review of the pertinent literature and discussion in a panel of experts.

Results: A systematic review and meta-analysis of efficacy of light therapy in bipolar depression found four controlled trials with a medium effect size of improvement of depression (Tseng et al. 2016). Recently, three randomized controlled trials were published which compared bright light with dim red placebo light in non-seasonal bipolar depression (Sit et al. 2018, Yorguner Kupeli et al. 2018, Zhou et al. 2018). All of them found superior efficacy of bright light compared to the dim red placebo condition and a very low risk of switch into (hypo-) mania. A systematic review of 41 studies did not find a higher risk of (hypo-) mania than in the control condition, except for patients with rapid cycling (Benedetti 2018). There are no controlled trials of light therapy in bipolar seasonal (winter-) depression. But in practice, light therapy is administered successfully for this indication in many outpatient clinics. Early trials for light therapy in winter depression did not exclude patients with bipolar II depression. Therefore the Dutch Multidisciplinary Guideline for Bipolar Disorders states that light therapy is an option for patients with bipolar winter depression (Kupka et al. 2015). A systematic review found negligible evidence for harmfulness of light therapy for the retina of patients using psychopharmaceuticals (Brouwer et al. 2017). The guideline for light therapy in bipolar depression differs only slightly from those for unipolar depression: a) for patients with bipolar I disorder a mood stabilizer is recommended in order to prevent a manic switch, b) a depressive episode with mixed features is a relative contra-indication, c) psychopharmaceuticals are no absolute contra-indication for light therapy. The patient is informed about potential risks and decides about referral for an ophthalmological consultation.

Conclusions: Light therapy is a treatment option for patients with bipolar seasonal and non-seasonal depression.

Funding/Disclosures: None.

A59

Towards an Understanding of Circadian and Seasonal Clocks

William J. Schwartz

The University of Texas at Austin, Austin, TX, USA

Since the formation of the SLTBR in 1988, our understanding of circadian and seasonal clocks – at multiple levels of biological organization – has evolved enormously. At the molecular level, the concept of a cell-autonomous, transcription-translation feedback loop as the basic timing machine emerged, generating new tools for both monitoring and breaking the clock. At the cellular level, the heterogeneity of suprachiasmatic nucleus neurons and their dynamic coupling became known, revealing intercellular mechanisms for plasticity and adaptation. At the organismal level, the physiological consequences of a dissociable multi-organ network for internal time were appreciated, reformulating ideas on disease etiopathogenesis. And at the societal level, the effects of abiotic and biotic environmental factors on the phase of entrainment of the clock were highlighted, raising ecological and public health implications. All of this in just 30 years! In this overview, we will consider how these advances have altered our metaphors for conceptualizing the clockworks, complicated our experimental designs and interpretations, and provided new opportunities for translational science.

Funding/Disclosures: None.

A60

A Pilot Study of Adjunctive Personalized Integrated Chronotherapy for Perinatal Mood Disorders

Katherine M. Sharkey[1,2], *Jason T. Machan*[1,2], *Janine Bacic*[1], *Carmen Monzon*[1,3], *Ellen Flynn*[1,3], *Julie Quattrucci*[2], *Sarah Carr*[3], *Sharon Vessella*[3], *Teri Pearlstein*[1,3]

[1]Alpert Medical School of Brown University, Providence, RI, USA; [2]Rhode Island Hospital, Providence, RI, USA; [3]Women's Medicine Collaborative, Providence, RI, USA

Objectives: Changes in women's sleep patterns across the perinatal period affect circadian rhythms and are related to postpartum mood; this pilot randomized controlled trial tested a personalized integrated chronotherapy (PIC) intervention, consisting of morning bright light, sleep restriction, and an advanced sleep-wake schedule, added to usual care (UC, i.e., medications and/or psychotherapy) versus UC alone, for treatment of perinatal mood disorders.

Methods: 39 pregnant women with major depressive disorder and/or an anxiety disorder confirmed with the Structured Clinical Interview for DSM-5 were randomized to UC or PIC+UC. Sleep timing/duration and light levels were estimated with 1 week of wrist actigraphy during pregnancy at baseline (24–28 weeks gestation), 33 weeks, 36 weeks, and during postpartum weeks 2 and 6. After baseline, the starting sleep/light prescription for PIC+UC patients was 7.5 hours time in bed, a 1-hour advance of wake time, and 30 minutes of 10,000 lux white light in the first hour after waking. Salivary dim light melatonin onset (DLMO) was assessed at baseline, 36 weeks, and 6 weeks. Mood was measured with the Hamilton Depression Scale ($HAMD_{17}$) by a blinded rater and patients reported pre-sleep arousal on a nightly sleep diary.

Results: So far, 28 women have completed the study. Hourly morning light levels (6 am–12 pm) decreased across the perinatal period in the UC group, but remained stable in the PIC+UC group ($p < 0.001$). Baseline HAMD scores did not differ between groups: UC = 12.4 (95% CI = 10.7–14.1); PIC+UC = 14.2 (95% CI = 12.3–16.0). At postpartum week 6, the HAMD score decreased to 5.3 (95% CI = 3.7–7.0) in the PIC+UC group and to 8.4 (95% CI = 6.5–10.4) in the UC group ($p = 0.004$). Pre-sleep arousal decreased from 28.4 at baseline (95% CI = 25.8–31.4) to 23.4 (95% CI = 21.3–26.2) at 6 weeks postpartum in UC patients and from 27.6 (95% CI = 24.5–31.6) to 19.6 (95% CI = 18.0–22.3) in PIC+UC patients ($p = 0.058$). Compared to baseline DLMO, PIC+UC women tended to phase advance in pregnancy ($p = 0.059$) with a return to baseline DLMO at postpartum week 6, whereas the UC group had a persistent DLMO delay across the perinatal period. Shift to an earlier wake time was associated with greater HAMD decrease ($p = 0.0203$). Decreased morning light from baseline to 6 weeks postpartum was associated with less HAMD improvement ($p = 0.0097$).

Conclusions: Women with depression/anxiety in pregnancy who received PIC+UC had a greater decrease in depressive symptoms and pre-sleep arousal than women receiving UC alone. Further, our data indicate that changes in sleep timing and light levels were associated with mood improvements.

Funding/Disclosures: R34-MH104377andU54GM115677 (NIH), and a Seleni Institute Grant

A61

Temporal Dynamics in Light Exposure, Wellbeing, and Sleep among Independent Living Elderly

Karin C.H.J. Smolders[1], *R. van der Sande*[1,2], *Yvonne A.W. de Kort*[1]

[1]Eindhoven University of Technology, Eindhoven, The Netherlands; [2]Vilans, Utrecht, The Netherlands

Objectives: The elderly may suffer from sleep problems and experience challenges with respect to their level of vitality and mood. While it is well known that light is a powerful tool to align sleep-wake patterns with environmental demands and can benefit wellbeing, studies investigating non-image forming effects of light on sleep and wellbeing have been mainly performed among young participants, demented elderly or persons with SAD. The aim of the current field study was to 1) monitor and quantify light exposure and sleep-wake patterns, 2) investigate potential (bi-directional) correlations between these patterns, and 3) explore the effect of these patterns on well-being among healthy independent living elderly subjects in real-life situations.

Methods: A field study was performed in which twenty elderly volunteers (12 males; mean age of 71, range 65–79) participated. During one sampling week, wearable measurement devices (light sensors and activity trackers) were used to quantify participants' light exposure patterns, physical activity, and sleep-wake timing. These measurements were combined with a sleep diary to asses self-reported sleep timing and sleep quality, and an experience sampling protocol to probe subjective vitality and mood throughout the waking episode of their daily routine. Prior to the start of the sampling week, participants reported on their general sleep quality and habitual sleep-wake timing. Multilevel analyses were performed to quantify inter-individual and intra-individual variations in light exposure, sleep and affective state, and to test correlations between these variables of interest.

Results: Preliminary results revealed that participants were, on average, exposed to relatively high intensity levels with exposure to more than 1000 lux close to their eyes for about 25% of their waking episode. Intra-class correlations for light exposure showed particularly intra-individual variations, with structural variations in the amount of light exposed to as a function of time of day. Most of the variance in sleep timing occurred on a day-to-day basis, while sleep quality mainly varied between participants. Multilevel analyses investigating the relationship between light and sleep revealed that, in contrast to the average light dosage, the amount of light exposure in the morning and evening were significantly related to sleep quality and sleep duration respectively. Moreover, subjective vitality and mood showed significant and positive correlations with the average light dosage in the morning. In addition, participants reported more positive affect when exposed to more intense light in the afternoon.

Conclusions: Overall, the findings of the current study provide insights into the light exposure patterns and their effects on

well-being and sleep among healthy independent living elderly, and could be used to provide tuned lighting scenarios to steer a healthy lighting and sleep regime in order to prevent or reduce sleep problems and to support well-being in elderly. This knowledge is particularly relevant in view of the aging of the population.

Funding/Disclosures: Project funded by 4TU.NIRICT.

A62

Visual and Non-Visual Responses to Short-Wavelength Light

Manuel Spitschan

Department of Experimental Psychology, University of Oxford, Oxford, UK

Objectives: The human retina contains five photoreceptors: The three spectral classes of cones — the S cones (peak spectral sensitivity λ_{max} ~420 nm), the M cones (λ_{max} ~530 nm), the L cones (λ_{max} ~558 nm) — , rods (λ_{max} ~495 nm), and melanopsin (λ_{max} ~480 nm). Short-wavelength light is known have important effects on what is conventionally called "non-image-forming" visual function, including circadian photoentrainment, phase shifting and the pupillary light reflex.

Methods: By presenting stimuli which are matched in the activation of a given set of photoreceptors (so-called metamers) but differ in activation of the target photoreceptors, the contributions of the different photoreceptors can be mapped out. We have previously used this method to examine the properties of the human pupillary light reflex, and encoding of melanopsin-targeted stimuli in human visual cortex (using fMRI). Here, we are examining metameric illuminants at five chromaticities along the daylight locus (correlated colour temperatures 25,000K, 10,000K, 6,500K, 5,000K and 4,000K) differing in melanopsin activation by 200% and measuring the pupil size in human observers under naturalistic viewing conditions.

Results: While the colour rendering properties of these metameric illuminants are generally poor, they elicit physiologically differentiable pupil sizes by up to 20%. This is not a surprising result, as it is known that melanopsin contributes to the pupil under conditions of silent substitution; but it provides evidence that large melanopsin contrast in isolation seen in naturalistic viewing conditions has a tangible physiological effect.

Conclusions: This research represents a step towards producing carefully controlled metameric melanopsin-targeted stimuli under naturalistic (e.g. sleep lab, home setting, office) viewing conditions with a demonstrable physiological effect.

Funding/Disclosures: Wellcome Trust 204686/Z/16/Z.

A63

The Relationship between Melatonin and Cortisol Profiles with Cancer Related Fatigue: A Study Protocol

Daniëlle E.J. Starreveld[1], Laurien A. Daniels[2], Flora E. van Leeuwen[1], Eveline M.A. Bleiker[1]

[1]Psychosocial Research and Epidemiology, Netherlands Cancer Institute, Amsterdam, The Netherlands; [2]Clinical Oncology, Leiden University Medical Center, Leiden, The Netherlands.

Objectives: Fatigue is one of the most reported complaints by cancer survivors. Pilot studies showed promising results for light therapy as a novel intervention for this complaint. However, the working mechanisms remain unknown. It is hypothesized that light therapy decreases Cancer Related Fatigue (CRF) via the entrainment of circadian rhythms. Previous results showed an association between desynchronized circadian activity rhythms and fatigue symptoms. Other studies showed an association between elevated levels of nocturnal cortisol with CRF. Yet, as far as we know, there is no published research on an association between melatonin profiles and CRF. The current study aims to investigate the associations between (disruptions in) circadian rhythms of cortisol and melatonin with CRF and the efficacy of light therapy to synchronize these rhythms. Based on the positive effects of light therapy on CRF, it is expected that these circadian rhythm are disrupted in survivors with fatigue compared to survivors without fatigue.

Methods: This study invites survivors of Hodgkin lymphoma (HL) with fatigue (n = 50), and a matched group of survivors of HL without fatigue (n = 25). All participants complete questionnaires on chronotype and fatigue. Saliva is collected to assess cortisol and melatonin levels at ten different time points during a 24 h period: at awakening, 30 min after awakening, 45 minutes after awakening, at 4 pm, five, four, three, two, and one hour prior to bed time, and at bedtime. Cortisol levels will be determined with an electrochemiluminescence immunoassay. Outcome variables include the cortisol awakening response, diurnal cortisol slope and area under the curve. The Dim Light Melatonin Onset will be determined with a direct saliva melatonin radioimmunoassay.

Results: This study is ongoing.

Conclusions: The finding of an association between disrupted circadian rhythms of cortisol and melatonin with CRF will provide more information on potential working mechanisms of light therapy as a treatment for cancer related fatigue. Moreover, it will add a new insight on a potential causative factor of CRF.

Funding/Disclosures: This trial is funded by the Dutch Cancer Society and is registered at clinicaltrials.gov (clinical trials ID: NCT03242902).

A64

Does Early Response Predict Subsequent Remission in Bipolar Depression Treated with Three Cycles of Total Sleep Deprivation Combined with Light Therapy and Lithium?

Masahiro Suzuki[1,2], *Sara Dallaspezia*[1], *Clara Locatelli*[1], *Makoto Uchiyama*[2], *Cristina Colombo*[1], *Francesco Benedetti*[1]

[1]Department of Clinical Neurosciences, Scientific Institute and University Vita-Salute San Raffaele, Milan, Italy; [2]Department of Psychiatry, Nihon University School of Medicine, Tokyo, Japan

Objectives: The combination of three cycles of sleep deprivation (SD) with light therapy (LT) and lithium has recently been proposed as a possible first-line treatment for bipolar depression. However, it is unclear whether early improvement predicts final response/remission in bipolar depression treated with this regimen.

Methods: We studied 220 consecutively admitted inpatients with a major depressive episode in the course of bipolar disorder. The relation between response to first SD and response/remission at the end of the treatment (day 6) was analyzed using logistic regression analysis. Severity of depression was rated using the Hamilton Depression Rating Scale (HDRS). Clinical response was defined as a ≥50% reduction in HDRS scores, and remission was defined as an HDRS score of ≤7.

Results: Among the 217 completers, 67.7% showed response and 54.4% reached remission at the end of the treatment. Multiple logistic regression analysis revealed that response after first recovery sleep (day 2) predicted final response and remission at the end of the treatment with high odds ratios (10.9 for response and 8.2 for remission); however, response immediately after the first SD (day 1) did not predict final response or remission.

Conclusions: Clinical status after first recovery sleep is a strong predictor of successful final outcome in patients with bipolar depression treated with the combination of repeated SD, LT, and lithium. Recovery sleep may play a role in inducing the antidepressant effect associated with the success of treatment.

Funding/Disclosures: This study was supported by JSPS KAKENHI (grant number JP25861032) and AMED (grant number JP17hk0102041).

A65

Melatonin, Body Temperature and Alertness Response to Late Evening Light Are Reduced by Prior Early Evening Light Exposure

Marije te Kulve[1], *Luc Schlangen*[2], *Wouter van Marken Lichtenbelt*[1]

[1]Department of Human Biology & Movement Sciences, NUTRIM, Maastricht University; [2]Philips Lighting Research, Eindhoven, The Netherlands

Objectives: Evening light can acutely affect melatonin levels, sleepiness and body temperatures. The objective of the current study was to test whether responses to one-hour evening light exposure are reduced when these are preceded by bright light exposure instead of dim light exposure during the beginning of the evening.

Methods: In a randomized crossover study, twelve healthy females participated in four sessions during which melatonin, subjective sleepiness and body temperature were measured. Three evening sessions were scheduled to compare the effects of dim light (A), a one-hour evening light pulse (750 lx, 4000 K starting at 22.30) (B), and the same evening light pulse (750 lx, 4000 K starting at 22.30) but now preceded by 2.5-hours of bright light (1200 lx, 4000 K starting at 18:30) (C). One morning session (D) used the same one-hour light pulse as in session B, but now starting at 10.30.

Results: As expected, the melatonin levels and subjective sleepiness were reduced, and the change in the (absolute value of the) skin temperature gradients was larger, during the one-hour evening light exposure (B) as compared to dim light exposure (A). When the one-hour light exposure was preceded by 2.5-hour exposure to bright light (C), the effects of the one-hour evening light pulse on melatonin and body temperatures were significantly reduced and the reduction in subjective sleepiness was absent. During the morning (D), melatonin levels were significantly lower compared to the evening (B). Morning and evening light effects on skin temperature gradients and sleepiness did not significantly differ.

Conclusions: The study results demonstrate that 2.5-hour bright light exposure at the beginning of the evening, can reduce the response to a 1-hour light pulse in the late evening. The effects of the light pulse on melatonin, subjective sleepiness and skin temperature gradients were reduced when this was preceded by bright light instead of dim light. By itself, a 2.5-hour bright light exposure in the early evening can already reduce the sleep-disruptive influence of light exposure in the late evening. Future studies are required to test whether prior (daytime) light exposure can also reduce the circadian phase delaying response to evening light.

Funding/Disclosures: This project was funded by the STW–Philips Electronics Nederland B.V. Partnership Program 'Advanced Sustainable Lighting Solutions' (no. 12733). Luc JM Schlangen is an employee of Philips Lighting Research, the Netherlands.

A66

SLTBR: Who We Were, Are, and Might Become

Michael Terman

Columbia University Department of Psychiatry and Center for Environmental Therapeutics, New York, NY, USA

1982. The U.S. National Institute of Mental Health (NIMH) publishes a case study of a patient with bipolar disorder who shows recurrent annual depressions as day length decreases. Stretching the day artificially with morning and evening light exposure proves therapeutic.

1984. They immediately proceed to a controlled clinical trial for patients with winter depression, sparking replications and extensions by 15 independent groups in the U.S. and Europe.

1987. The "seasonal pattern" specifier for recurrent major depression quickly enters the Diagnostic Manual of the American Psychiatric Association (APA). The NIMH sponsors a workshop on seasonal affective disorder (SAD), bringing in researchers on photoperiodism and circadian rhythms to help frame a conceptual structure.

1988. SLTBR is formed at a sit-down beer fest of around 30 researchers and clinicians at the APA annual meeting. A bulletin of news and comment follows, to be published for 16 years.

1989. Our first annual meeting, with around 130 colleagues and students, is hosted by the NIMH, with 34 presentations (28 of them focused on SAD), along with innovative pilot studies of night shift work, premenstrual depression, bipolar depression, and alcohol abuse and dependence. The time of day for effective light therapy (morning, midday, evening), and the differentiation from placebo response, surface as key points of debate. A work group examines the role of the nascent light box industry and confronts its presumed authority to make clinical claims and instruct doctors, patients and consumers in use of the devices.

. . . 2017. The 29th annual meeting in Berlin draws 116 attendees. There are 61 presentations (only 2 focused on SAD), with a broad range of basic and applied topics including melatonin, cortisol, melanopsin, metabolism, sleep, major depression, bipolar depression, cognitive performance, the built environment, and more.

2018. Early themes resurface: concern about light device claims and clinical guidelines issued by manufacturers; and the time of day of light treatment, with a focus on bipolar disorder (this time not SAD, for which morning light has become the standard intervention). The first task force on chronotherapy is appointed by the International Society for Bipolar Disorders. We begin to ask how, beyond our research, can SLTBR advocate light therapy in mainstream medicine as a valuable adjunct for the treatment of sleep and mood disorders.

2018+. Clearly, SLTBR has staying power, but we need to define our role more clearly and actively vis-à-vis societies with overlapping interests. The challenge is to build on our unique strengths. These include a wide mix of specialties (e.g., chronobiology, lighting science, psychiatry, human factors, and architecture), coupled with manageable size. Our informality is infectious, and encourages new collaborations, close attention to student contributions, and open brainstorming. These are precious assets that can accelerate discovery and minimize the competitive one-upmanship all too familiar in larger international venues.

Funding/Disclosures: None.

A67

The Effect of Chronic Sleep Deprivation on Cognition in Healthy Middle Aged Men

Jana Thomas[1,2,3], *Sharon Ooms*[1,2,3], *Jetteke Doornbosch*[1], *Sebastiaan Overeem*[4,6], *Marcel Verbeek*[2,3,5], *Marcel Olde Rikkert*[1,2,3], *Roy Kessels*[1,2,3] *Jurgen Claassen*[1,2,3]

[1]Department of Geriatric Medicine, Radboud University Medical Centre, Nijmegen, The Netherlands; [2]Radboud Alzheimer Centre, Nijmegen, The Netherlands; [3]Donders Institute for Brain, Cognition and Behavior, Nijmegen, The Netherlands; [4]Sleep Medicine Centre Kempenhaeghe, Heeze, The Netherlands; [5]Department of Neurology, Radboud University Medical Centre, Nijmegen, The Netherlands; [6]Eindhoven University of Technology, Eindhoven, The Netherlands

Objectives: Recent evidence indicates a bi-directional relation between poor sleep and the development of Alzheimer's disease (AD). Poor sleep may play a causal role in the pathology of AD by influencing the clearance and production of the amyloid beta (Aβ) protein. Previous studies have shown that one night of total sleep deprivation increases Aβ concentrations. This led to the hypothesis that extended periods (>10 years) of disturbed sleep could lead to Aβ accumulation with subsequent cognitive decline in the context of AD. The present study was conducted to study the relationship between chronic sleep disturbances due to an extrinsic cause and cognitive function among healthy middle aged men to investigate the hypothesis that prolonged abnormal sleep behavior increases the risk of AD-related cognitive decline.

Methods: Our study population consisted of male volunteers (n = 19), aged 50 to 60 years, who show divergent and fragmented sleeping patterns due to irregular work schedules. This chronic sleep deprivation group was compared to a group of healthy volunteers (n = 19) with normal sleep, matched in gender, education and age. All participants underwent one night of standard polysomnography (PSG), preceded by approximately 10 days of actigraphy (Actiwatch 2, Philips Respironics) and maintenance of a sleep-wake diary. Cognitive function (including memory consolidation) was assessed with a neuropsychological test battery.

Results: The chronic sleep deprivation group showed more slow wave sleep (N3 = 16.4% (± 7.39)) compared to the healthy controls (N3 = 12% (± 5.61)), but no difference in cognitive test scores were found. The chronic sleep deprivation group performed only significantly (p = 0.007) better on a memory consolidation test (short delay) (A' = 0.92 (± 0.03); hits = 27.4 (± 1.5)) than the controls (A' = 0.88 (± 0.05); hits = 25.8 (± 2.11)).

Conclusions: Identifying poor sleep as one of the preventable risk factors for the development of AD could create more awareness about individual sleeping behavior. However, we found no negative effects of poor sleep on cognitive function in the

chronic sleep deprivation group. This could be related to the finding of enhanced slow wave sleep in this group, which might serve as a compensatory mechanism for years of sleep disturbances. This requires further exploration in follow-up research.

Funding/Disclosures: None.

A68

Programmed Environmental Illumination during Autologous Stem Cell Transplantation Hospitalization for the Treatment of Multiple Myeloma Reduces Severity of Depression

Heiddis Valdimarsdottir[1], Mariana Figuero[2], Williiam Holden[1], Susan Lutgendorf[3], Lisa M. Wu[4], Sonia Ancoli-Israel[5], Jason Chen[1], Ariella Hoffman-Peterson[1], Julia Granski[1], Nina Prescott[1], Alejandro Vega[1], Natalie Stern[1], Gary Winkel[1], William H. Redd[1]

[1]Icahn School of Medicine at Mount Sinai, New York, NY, USA; [2]Rensselaer Polytechnic Institute, Troy, NY, USA; [3]University of Iowa College of Liberal Arts and Sciences, Iowa, IA, USA; [4]Northwestern University Feinberg School of Medicine, Chicago, Il, USA; [5]University of California San Diego, San Diego, CA, USA

Background: Over a third of multiple myeloma (MM) patients report clinical levels of depression during autologous stem cell transplant (ASCT) hospitalization. We report results from a randomized clinical trial investigating effects of Programmed Environmental Illumination (PEI) of hospital rooms on depression.

Methods: Patients (N = 187) scheduled to receive an ASCT were assessed for eligibility. Those who met study eligibility criteria (n = 44) were randomly assigned to one of two PEI conditions involving delivery of either circadian active bright white light (BWL) or circadian inactive dim white light (DWL) throughout the room from 7 to 10 AM daily during hospitalization. Patients completed the Center for Epidemiological Studies Depression Scale (CES-D) prior to hospitalization, at days 2 and 7 post-transplant, and on the third day of engraftment.

Results: General Linear Model analyses revealed no difference between the groups in CES-D total score at baseline (p = 0.7859). A longitudinal linear mixed model analysis revealed a significant interaction between time of assessment and light condition [$F(3,107) = 2.90$; $p = 0.0386$; $eta^2 = 0.08$)]. PEI prevented development of depression during hospitalization, with effects reaching significance by the third day of engraftment. At the third day of engraftment, 68.4% of the participants in the DWL comparison condition met the criteria for clinically significant depression compared to 42.1% in the BWL condition.

Conclusion: These findings demonstrate that PEI using BWL during MM ASCT hospitalization is effective in reducing the development of depression. Future studies should examine the mechanisms whereby PEI improves depression.

A69

Chronotype and Depressive Symptoms in Students: An Investigation of Possible Mechanisms

Julia F. van den Berg, Liia Kivelä, Niki Antypa

Leiden University, Leiden, The Netherlands

Objectives: Individuals with an evening chronotype are at increased risk of experiencing emotional problems, including depressive symptoms. However, the mechanisms underlying these associations remain unclear. The present study aimed to determine whether poor sleep quality, substance use, and cognitive emotion regulation difficulties – which have been implicated in the etiology of depression – mediate the relationship between chronotype and depressive symptoms in a student sample, which was assessed cross-sectionally and after one year.

Methods: A total of 742 Dutch students (75% women, mean age 21.4 ± 2.9 years) completed the Quick Inventory of Depressive Symptomatology, the Morningness-Eveningness Questionnaire, the Pittsburgh Sleep Quality Index, a questionnaire assessing alcohol, caffeine consumption, smoking tobacco and cannabis use, the Cognitive Emotion Regulation Questionnaire and the Behavioral Inhibition/Activation Scale. A subsample (n = 115) was assessed one year later with the same questionnaires.

Results: Cross-sectional analyses showed that evening chronotype was associated with more depressive symptoms, adjusted for age and gender ($\beta = -0.082$, $p = 0.028$). The relationship between eveningness and depressive symptoms was mediated by sleep quality, alcohol consumption, and the cognitive emotion regulation strategies of self-blame and positive reappraisal. In longitudinal analyses, eveningness at baseline predicted more depressive symptoms at follow-up, adjusted for age and gender ($\beta = -0.29$, $p = 0.002$), and only poor sleep quality at follow-up was a significant mediator of this relationship.

Conclusions: Eveningness is related to depressive symptoms and this relationship is mediated by poor sleep quality, also in a prospective design. Self-blame and reduced positive reappraisal are correlated with eveningness. The integration of chronotherapeutic interventions together with sleep education and cognitive approaches is of high importance for targeting depression in such populations.

Funding/Disclosures: None.

A70

Is Insomnia a Disorder of Rhythm or Sleep, and Is Chronotherapy Useful?

Eus J.W. van Someren

Department Sleep & Cognition, Netherlands Institute for Neuroscience, Amsterdam, The Netherlands

Sleep regulation is known to involve a circadian and a homeostatic component: process C and process S. In spite of the strong and wide support of these factors in the regulation of normal sleep, there is little support for their primary involvement in *insomnia* –

which is both the most prevalent sleep disorder and second-most costly mental disorder.

It will be shown that insomnia is not a single disorder, but rather represents previously unrecognized subtypes that are stable over years. The presentation briefly reviews the disappointing findings on process C and S involvement in insomnia to continue with a new perspective on its etiopathology. From an evolutionary survival perspective one can ask the question: if clock and homeostat say: "sleep!" could there be any reason not to do so and stay in part alert at night? Indeed, from the perspective that sensorimotor integration is the primary function of the brain, there could be reasons, respectively: (1) *sensory*: environmental and internal monitoring of needs, threats and opportunities: awareness of situation and surroundings; (2) *motor*: action preparation: being optimally prepared if needs, threats or opportunities occur and (3) *integration*: making use of cognition: what prior learning about safety and threats has engraved in the brain? These qualities for survival in unsafe environments have the downside of not being compatible with sound sleep.

Examples from HD-EEG, MRI, genetic, developmental and psychometric studies will be provided that provide converging support for the idea that the insomniac brain is radically different from the sleep deprived brain of a good sleeper: hyper-alert versus hardly alert.

The fragmented sleep that is characteristic of people suffering from insomnia does not only interfere with the normal overnight resolving of distress after a negative emotional experience, but may in fact even *increase* distress as compared to staying awake. A developmental model will be presented, proposing that genetic predispositions in combination with childhood adversity can promote the development of a brain that is optimally wired for staying alert (in a possibly unsafe environment) and remember distress, at the cost of suffering from insomnia.

So can we ignore light and other chronotherapeutic approaches to insomnia? Not so! We found that intense environmental light ameliorates deficient subjective 'liking' in insomnia. Moreover, the addition of the chronotherapeutic interventions of timed light, physical activity or warm baths solidified the benefits of cognitive behavior therapy for insomnia on the long term. Chronobiological interventions are of use in spite of the limited support for a role of the clock in the underlying causes of insomnia. Just like headache doesn't have to be caused by a 'lack of acetaminophen' for paracetamol to work!

Further Reading: Stoffers, Brain 2014;137:610; Wassing, PNAS 2016;113:2538; Benjamins, Sleep Med Rev 2017;36:71; Hammerschlag, Nat Genet 2017;49:1584; Jansen bioRxiv 2018;DOI: 10.1101/214973; Te Lindert, Sleep 2018;41:zsy022.

A71

Triple Chronotherapy for Depression – Experience in the UK

David Veale

Kings College, London & South London and Maudsley Trust & The Priory Hospital North London, London, UK

Objectives: 1) To describe a service evaluation and case series of inpatients with depression in a private hospital in the UK by triple chronotherapy.

2) To describe a protocol and recruitment so far of outpatients with unipolar depression in a RCT of triple chronotherapy in the UK.

Methods: 1) Service evaluation – patients with unipolar or bipolar depression admitted to the Priory Hospital North London are invited to participate in triple chronotherapy. Patients are deprived of sleep on the first night with the support of nursing staff followed by phase advance of sleep for the following four days. Blue blocking glasses are used for at least 3 hours prior to sleep time. Bright Light (10,000 Lux) is given for 30 minutes, timing is optimised according to the Morningness Eveningness Questionnaire and recommended to be continued on discharge.

2) A protocol with the inclusion/exclusion criteria and outcome measures will be described for a feasibility study evaluating Triple Chronotherapy vs. a control group in a randomised controlled trial of out-patients recruited at the Maudsley Hospital. Sleep deprivation occurs with the support of an occupational therapist for the first two nights before being monitored at home.

The study is aiming to recruit 30 patients with unipolar depression in each group to determine the feasibility of recruiting for a larger RCT of the clinical and cost effectiveness of triple chronotherapy in outpatients with depression.

Results: 1) Service evaluation – the demographics, diagnoses and outcomes will be described according to the 6 item Hamilton Depression Rating Scale, Clinical Global Impression, and Quick Inventory of Depressive Symptomatology (QIDS) self-report.

2) Protocol – The numbers recruited in a Consort flow chart and the experience of treating out-patients in the RCT so far will be described.

Conclusions: The UK has lagged behind in the development of chronotherapy and it is hoped that these initiatives will start to contribute to the evidence base.

Funding/Disclosures: None.

A72

Room-Light 1:1 – Light Simulation Using a Mock-Up of Patient Bedrooms in the Projected New Psychiatric Hospital Bispebjerg

Carlo Volf[1], Carsten Dam-Hansen[2], Paul Michael Petersen[2], Signe Dunker Svendsen[1], Jais Elvekjær[3] Kjeld Johnsen[4], Klaus Martiny[1]

[1]Psychiatric Center Copenhagen, University of Copenhagen, Rigshospitalet, Copenhagen, Denmark; [2]Department of Photonics Engineering, Technical University of Denmark, Copenhagen, Denmark; [3]New Psychiatry Bispebjerg, Mental Health Services in the Capital Region of Denmark, Copenhagen, Denmark; [4]The Danish Building Research Institute, Copenhagen, Denmark

Objectives: There is a growing focus on daylight and artificial light in the fields of health and psychiatry as elements that can support conventional medical treatment. In the treatment of patients with depression, new knowledge suggests that both daylight and dynamic LED technology can help to improve their overall condition. The purpose of this project is to build a 1:1 mock-up of a patient bedroom, as is projected in The New Psychiatry Bispebjerg, to be completed in 2021. The rotatable mock-up will measure daylight intensity and spectral distribution when pointing to different geographical directions during the seasons. From these measures, we can calculate the optimal dynamic LED artificial light. This will secure the best possible zeitgeber signal to the inner clock to induce a maximum antidepressant effect and stabilisation of the sleep-wake cycle. To formalize this we have coined the concept: Latitude Compensated Architectural Lighting (L-CAL) aiming at supplying daylight with dosed dynamic LED lighting, to secure an optimum illumination in rooms regardless of their orientation relative to the geographical orientation. A north-facing room will thus ideally have as good a lighting condition as a south-facing room.

Methods: We are currently building a rotatable 1:1 mock-up of a patient bedroom, in cooperation with the building projector, mounted on top of a parking house to secure the full influx of daylight. We will use a highly specialized measurement method developed in collaboration with DTU Photonics, which examines the total amount of light intensity as well as the spectral distribution of light, and relates this to the expected biological effect on the brain.

Results: The mock-up is under construction and will be finished by April 2018. We will be will able to provide light measurement data and calculations on window characteristics and artificial lighting.

Conclusions: Based on the data from the measurements of light in the mock-up we will be able to offer a qualified suggestion for window characteristics, regarding transmittance properties and size, and based on this, the total lighting schedule for the artificial light in the bedrooms in the New Psychiatry Bispebjerg. We hope to be able to implement this in the final construction.

Funding/Disclosures: The project is funded by Danish Energy – Research and Development, ELFORSK. No further disclosures.

A73

EPFL Smart Glass Field Study

Forrest S. Webler, Victoria Soto Magan

Ecole Polytechnique Fédérale de Lausanne (EPFL), Lausanne, Switzerland

Objectives: The objectives of this study are to evaluate (1) direct non-visual effects of red-impoverished daylight on circadian resetting and alertness and (2) the daily light-exposure pattern on indirect–circadian–effects. The novelty of this study is that it will be conducted on the EPFL campus in two identical classrooms outfitted with electrochromic windows from SageGlass. Studying non-visual effects under real-life conditions is essential to better understand the role of an adaptive glazing to improve alertness in the context of a classroom. We will also log irradiance and illuminance at eye level in order to document light received at the eye over two 6-day trials. We hope that recording light exposure during wake hours will help us to better understand the type of light people receive on a daily basis and if adaptive glazing technologies can help mitigate negative physiological responses normal working hours.

Methods: Participants will be selected using recruitment forms and excluded for health problems, sleep irregularity and use of drugs or stimulants. During the study, participants will be asked to wear an integrated spectrometer and luxmeter mounted discretely on a pair of glasses frames, and iButtons to measure skin temperature for two 6-day periods with a one-week break in-between. Participants will be split into intervention and control groups on with the electrochromic glazing turned on and the other turned off and be asked to fill out questionnaires every hour and take a PVT test to establish quantitative assessment of alertness. In addition, they will wear a heart rate variability monitor. After the supervised hours are finished, participants will be allowed to go about their normal life but will be asked to continue monitoring eye-level irradiance and skin temperature. At the end of the study, participants will return the hardware, be compensated for their time, and debriefed.

Results: Timing and the physical properties of light are essential in inducing direct and indirect non-visual effects. We expect to see increased alertness in the intervention group after the first week since the light will be bluer and more stimulating to the non-visual system. Similarly, brighter light should induce more alerting effects which may or may not be a direct response of NIF effects. Light exposure over time will also elucidate the type of light received by students and if it could cause disruptions to circadian phase.

Conclusions: Tracking light exposure over time is the first step to evaluate the importance of lighting conditions in the built environment. Both direct and indirect non-visual effects are important to understand in the context of real architectural spaces. We hope this is the first study of many to take an applied approach in the field and study the effects of daylight on health and wellbeing.

Funding/Disclosures: St Gobain, who manufactures SageGlass, will fund part of this study.

A74

Lunar Mood Cycles and Their Relationship to Seasonal Mood Cycles

Thomas A. Wehr

Intramural Research Program, NIMH, Bethesda, MD, USA

In previous research, we showed that humans, in the course of their evolution, have conserved a regulatory mechanism homologous to one that enables other animals to regulate the timing of seasonal cycles in their behavior by tracking seasonal changes in the length of the day. This is accomplished by neural networks in the suprachiasmatic nucleus of the hypothalamus that separately track the changing times of dusk and dawn through the course of the year. One network is entrained to dusk and controls timing of the nightly onset of sleep and melatonin secretion, while the other is entrained to dawn and controls timing of the daily onset of wakefulness and cessation of melatonin secretion. Changes in the duration of melatonin secretion that result from these adjustments serve as a chemical signal that causes the organisms to undergo seasonal changes in their behavior.

That finding followed our earlier finding that human melatonin secretion can be suppressed with light, an observation that showed that the neural pathway that passes from the eye via the suprachiasmatic nucleus (SCN) to the pineal gland is intact and functional in humans.

In view of their role in seasonal rhythms in other animals, it is likely that the same networks and pathways regulate seasonal rhythms in humans. In this regard, we presented some evidence that changes in day-length, acting on the SCN's neural networks, regulate the timing of mood cycles in individuals with seasonal affective disorder.

Recently, we found that these neural networks also may play a role in the pathogenesis of rapid cycling bipolar disorder. In 19 patients, we found that their mood cycles oscillated in synchrony with bi-weekly lunar cycles that modulate the amplitude of the moon's gravimetric tidal cycles.

In two cases, longitudinal records of sleep provided clues to the mechanism through which the tidal cycles may have acted upon the mood cycles. In each case, the lunar tidal day (period of recurrence of every second 12.4-hour tidal cycle) appeared to entrain the oscillations of one of the SCN's neural networks to the tidal day's 24.8-hour rhythm. As the network entrained to the lunar tidal day went in and out of phase with the network that remained entrained to the 24-hour solar day, it gave rise to multi-week cycles in the timing and duration of sleep and in mood. Results of previous experiments suggest that the changes in sleep caused the changes in mood.

Taken together the present results, and the recent finding that light can be used to treat non-seasonal forms of bipolar disorder, raise the possibility that several types of mood disorders may have a common neural substrate in the neural networks of the SCN that track seasonal changes in duration of the photoperiod.

Funding/Disclosures: None.

A75

Seasonal Affective Disorder and Non-Seasonal Affective Disorders: Results from the NESDA Study

Wim H. Winthorst[1], Annelieke M. Roest[2], Elisabeth H. Bos[2], Ybe Meesters[1], Brenda W.J.H. Penninx[3], Willem A. Nolen[1], Peter de Jonge[2]

[1]Interdisciplinary Center Psychopathology and Emotion Regulation, University of Groningen, University Medical Center Groningen, Groningen, The Netherlands; [2]Department of Developmental Psychology, University of Groningen, Groningen, The Netherlands; [3]Department of Psychiatry/EMGO Institute for Health and Care Research, VU University Medical Center, Amsterdam, The Netherlands

Objectives: To compare the clinical picture and the seasonal distribution of major depressive episodes of participants with seasonal affective disorder (SAD) to non-seasonal affective disorder (non-SAD).

Methods: The Composite International Diagnostic Interview (CIDI) (WHO version 2.1) was used to establish current (last month) and lifetime diagnoses of depressive and anxiety disorders according to DSM-IV criteria in 2185 participants of the Netherlands Study of Depression and Anxiety. The Seasonal Pattern Assessment Questionnaire was administered to diagnose SAD. Symptoms of depression and anxiety were measured with the Inventory of Depressive Symptoms (IDS), the Beck Anxiety Inventory (BAI) and the Fear Questionnaire (FQ).

Results: Of the participants with a lifetime depressive disorder 3.9% fulfilled the Kasper criteria for SAD (and 5.9% for sub-SAD). These percentages were 1.7% (6.6% sub-SAD) for participants with any lifetime anxiety disorder, 6.8% (8.8% sub-SAD) for participants with a lifetime comorbid anxiety and depressive disorder, 12.1% (12.1% sub-SAD) for participants with a lifetime bipolar disorder and 0.4% (2.3% sub-SAD) for healthy controls. Participants diagnosed with SAD, with a lifetime bipolar disorder (and no SAD or sub-SAD), or a lifetime comorbid anxiety and depressive disorder (and no SAD or sub-SAD) scored highest in terms of current or persistent anxiety or depressive disorders (DSM IV diagnoses) in the last year and the last month at the time of the 2 year follow-up measurement. Participants in the SAD group and in the bipolar group scored higher than participants with a lifetime depressive disorder or a lifetime comorbid anxiety and depressive disorder (and no SAD or sub-SAD) on the IDS, BAI and FQ. There was no overall seasonal effect (no difference between the seasons) in mean scores on the IDS and BAI for the participants with SAD versus the participants with a lifetime depressive disorder or a lifetime comorbid anxiety and depressive disorder (and no SAD or sub-SAD). The seasonal distribution of major depressive episodes was not different for participants with or without SAD.

Conclusions: SAD may be a measure of severity of depression with a subjectively perceived worsening of symptoms in the winter months.

Funding/Disclosures: This is an edited abstract of an article with the same title, published in BJPsych Open (2017) 3, 196–203. doi: 10.1192/bjpo.bp.116.004960. Y.M. has received re-

search funding and served as a consultant for Royal Philips Electronics NV and The Litebook Company Ltd. W.A.N. has received grants from the Netherlands Organization for Health Research and Development, the European Union, the Stanley Medical Research Institute, Astra Zeneca, Eli Lilly, GlaxoSmithKline and Wyeth; has received honoraria/speaker's fees from Astra Zeneca, Pfizer, Servier and Wyeth; and has served in advisory boards for Astra Zeneca, Pfizer and Servier.

A76

Seasonality of Negative and Positive Affect in a Large Crowdsourcing Study in the Netherlands (HowNutsAreTheDutch)

Wim H. Winthorst[1], Annelieke M. Roest[2], Elisabeth H. Bos[2], Ybe Meesters[1], Peter de Jonge[2]

[1]University of Groningen, University Medical Center Groningen, Department of Psychiatry, Interdisciplinary Center Psychopathology and Emotion Regulation, Groningen, The Netherlands; [2]Department of Developmental Psychology, University of Groningen, Groningen, The Netherlands

Objectives: Seasonal changes in mood and behaviour are considered to be common in the general population. In most studies only complaints (symptoms), but not positive affect of individuals are measured. This leads to the question whether positive affect and negative affect are equally influenced by the seasons. We formulated the following research questions: 1) Are there seasonal differences on a population level in the domains of positive affect, negative affect and depressive symptoms? 2) Can a within-person pattern of seasonality be shown in the domains of positive affect, negative affect and depressive symptoms in the subgroup of respondents who filled out the questionnaires twice? We will also investigate the role of neuroticisms as a potential moderating factor.

Methods: We will use the data of HowNutsAreTheDutch (Dutch: HoeGekIsNL). In this national internet-based crowdsourcing project individuals were invited to visit the website www.hownutsarethedutch.com and to assess themselves on several domains of mental health. The present study is based upon the 8414 individuals who participated between December 19th 2013 (launching date of the internet platform) and December 19th 2017 and filled out the Quick Inventory of Depressive Symptomatology (QIDS), the Positive and Negative Affect Schedule (PANAS) and the NEO-FFI-3 personality inventory. We will use ANCOVA to test for differences between the seasons in mean scores on the QIDS and the PANAS, with age and gender as covariates. For the second research question we will perform mixed linear models on data of participants who filled out the questionnaires twice.

Results: We are currently analyzing the results, which will be available in June 2018 during the SLTBR meeting.

Funding/Disclosures: None.

A77

Prevalence of Winter Depression in a Prospective Cohort Study

Anna Wirz-Justice[1], Vladeta Ajdacic[2], Wulf Rössler[2,3], Hans-Christoph Steinhausen[4,5,6,7], Jules Angst[2]

[1]Centre for Chronobiology, Psychiatric Clinics, University of Basel, Basel, Switzerland; [2]Department of Psychiatry, Psychotherapy and Psychosomatics, University of Zurich, Zurich, Switzerland; [3]Department of Psychiatry and Psychotherapy, Charité University Medicine Berlin, Berlin, Germany; [4]Department of Child and Adolescent Psychiatry, University of Zurich, Zurich, Switzerland; [5]Clinical Psychology and Epidemiology, Institute of Psychology, University of Basel, Basel, Switzerland; [6]Child and Adolescent Mental Health, Capital Region Psychiatry, Copenhagen, Denmark; [7]Department of Child and Adolescent Psychiatry, University of Southern Denmark, Odense, Denmark

Objectives: To document the prevalence of autumn/winter seasonality in depression in the longitudinal Zurich cohort study.

Methods: The initial sample (1978) of 4547 subjects representative of the canton of Zurich was screened with the Symptom Checklist 90-R and a stratified sample (N = 591, 20/21–49/50 y) selected for interviews (1979, 1981, 1986, 1988, 1993, 1999 and 2008). This analysis presents data on depression (DSM-III criteria) from the 5 later interviews where questions about seasonality had been introduced (1986–2008, N = 499).

Results: A weighted prevalence of 3.02% in major depressive disorder and 1.89% in bipolar depression was found. In total, 7.52% suffered from seasonality in major and minor depressive mood states. Weighted prevalence rates for major depressive episode (MDE) were calculated for those with ≥2 episodes in autumn &/or winter (**MDE wi rep**), those with a single autumn &/or winter episode (**MDE wi one**), and compared with episodes at other times of year and non-seasonal (**MDE other**) (Table 1).

Unweighted frequencies: Chi^2 $p < 0.0008$

In terms of clinical characteristics, **MDE wi rep** significantly differed from the others with respect to higher rates of social anxiety disorder, agoraphobia, and atypical depression (DSM-5), as well as diurnal variation of mood (morning worse) and oversensitivity to external stimuli.

Conclusions: This is the first documentation of the prevalence of autumn/winter seasonality in depression in a longitudinal cohort characterised by comprehensive semi-structured professional diagnostic interviews at intervals over more than twenty

Table 1.

Prevalence %, *n*	MDE wi rep	MDE wi one	MDE other	All others
M	1.12 (12)	5.43 (17)	14.90 (36)	78.45 (182)
F	5.75 (31)	14.46 (32)	12.43 (41)	67.36 (148)
Total	3.44 (43)	9.96 (49)	13.66 (77)	72.94 (330)

years. Our long-term large data base confirms the importance of MDE wi rep (which approaches the DSM criterion for SAD of "at least two consecutive winter depressive episodes") as a diagnosis with striking gender differences, classic diurnal variation of mood, as well as a novel finding of oversensitivity to light, noise, or smell. The high comorbidity with social anxiety disorder and agoraphobia has never been described. The concordance found in MDE wi rep with the syndrome of atypical depression strengthens prior descriptions of SAD as presenting mostly atypical symptoms.

Funding/Disclosures: These studies were funded by the Swiss National Science Foundation.

A78

Thirty Years Ago and Now: The Amazing and Wonderful World of Light

Anna Wirz-Justice

Centre for Chronobiology, Psychiatric Clinics, University of Basel, Switzerland

And there was light. Day and night. And light during the day and darkness at night was the environmental signal throughout evolution. In antiquity, fire, oil lamps and candles prolonged the day, though only around 1800 did the first gas lighting begin the era of humans being able to define their individual, work, and social light-dark cycles. Although circadian rhythm research in mammalian species established the formal properties of light (PRC, Aschoff's Rule, after-effects of photoperiod, range of entrainment etc.), social cues, not light were considered to be the primary zeitgeber in humans. Lewy's pioneer study of daylight suppression of melatonin secretion changed everything. Rosenthal, Wehr and Lewy initiated the studies of SAD and light therapy that – looking back – could be said to have invented a new field that explores the dual action of light in humans: the zeitgeber function for the circadian system as well as direct effects on mood, alertness, cognitive function, performance, pupillary response, sleep, etc. The applications of light have rapidly expanded to non-seasonal depression, sleep disorders in other psychiatric syndromes and in medical illness. However, we are still at a stage where we need further large N studies to provide unequivocal evidence that will move light therapy from a still-exotic "alternative" to an established methodology incorporated into treatment guidelines. In contrast, the extraordinarily rich data set on how light affects human physiology has already entered the lighting industry ("human-centric lighting") together with the development of new norms that consider both visual and non-visual aspects. This knowledge is even beginning to change architectural practice. Additionally, animal models have shown a direct relationship between irregular light exposure and aberrant mood and impaired learning. In thirty years of the SLTBR we have seen an extraordinary growth in circadian biology research together with the implementation of light in clinical practice – yet we are still far from being able to prevent and treat pathology of the body clock.

Funding/Disclosures: The author's work on light therapy has been funded over many years mainly by the Swiss National Science Foundation and the Velux Stiftung.

A79

Light Therapy for Women with Perinatal Depression

Katherine L. Wisner

Northwestern University, Chicago, IL, USA

Objectives: 1. Studies of light therapy (LT) in pregnancy will be reviewed. 2. Little information is available about women's preferences for perinatal depression treatment despite the positive impact of providing the preferred treatment on adherence, therapeutic alliance, and symptom reduction. New data on the acceptability of LT in perinatal women will be presented.

Methods: 1. The author was involved in all published studies of LT in pregnancy: an open trial, a small RCT and the protocol design for a larger RCT. 2. The acceptability study was conducted as a survey of women who received treatment for perinatal depression. The survey was posted on a web-based educational website.

Results: 1. The first study was an open A-B-A single-blind study conducted for 3–5 weeks in 16 pregnant patients with 60 minutes of 10,000 lux morning LT. The mean SIGH-SAD scores decreased by 50%. In the second, subjects were randomized to daily LT (7000 lux, n = 5) or dim (500 lux; n = 5) LT. Eight women completed 5 weeks of LT, while 2 subjects in the placebo group withdrew due to nonresponse. The bright LT group had a 10-point drop in mean depression score at week 1 while the dim light group improved by 5 points. A third, randomized trial included pregnant women who were assigned to 7000 lux LT or 70 lux dim red light for 1 hour daily for 5 weeks. The response rate (HAMD 17) was significantly greater for LT (13/24; 54.2%) than for placebo light (5/22; 22.7%) ($p = 0.029$). Remission was attained by 11/24 (45.8%) vs. 4/22 (18.2%), respectively ($p = 0.045$). The weekly decline in depressive symptoms with bright white LT was linear through 5 weeks; in contrast, the dim red LT effect declined in parallel to that of bright white LT until week 2, then plateaued. The trajectory of improvement suggested that symptom reduction would continue beyond 5 weeks. There were no switches into hypomania and side effects were minimal.

2. Non-pharmacologic treatments that can be delivered in the woman's home reduce barriers to depression care, which include the shortage of therapists, travel to the clinician's office, lack of childcare and treatment costs. Respondents who had experienced perinatal depression (N = 111) were asked to choose all acceptable treatments among four options (interpersonal psychotherapy = IPT, the antidepressant sertraline = SERT, the antidepressant bupropion = BUP, and LT). A brief description of each intervention was included in the survey. LT was a highly acceptable option for treatment (87.4% of respondents): IPT, SERT, BUP and LT (44.1%); IPT, SERT, LT (34.2%); IPT, BUP, LT (2.7%); IPT, LT (6.3%); LT only (0%).

Conclusions: LT is an effective inexpensive, low-risk treatment for perinatal depression with high acceptability. Training clinicians and implementation of LT into psychiatric, primary care and women's health practices is essential to advance care for depressed pregnant women.

Funding/Disclosures: None.

A80

Pupil Responses to Colour: A Novel Insight Into the Wiring of the Human Retina

Tom Woelders[1], *Thomas Leenheers*[1], *Marijke C.M. Gordijn*[1,2], *Roelof A. Hut*[1], *Domien G.M. Beersma*[1], *Emma J. Wams*[1]

[1]Rijksuniversiteit Groningen, GeLifes institute, Chronobiology Unit, Groningen, The Netherlands; [2]Chrono@Work B.V., Groningen, The Netherlands

Objectives: It has been established that melanopsin-expressing intrinsically photosensitive retinal ganglion cells (ipRGCs) are of major importance in mediating nonvisual effects of light in the mammalian brain. These cells are especially well-equipped to signal absolute levels of light intensity to the circadian clock, a feature that is necessary to provide our clocks with a sinusoidal Zeitgeber signal to entrain to. Recently it has been shown that the mouse circadian system is not only sensitive to light intensity, but also to colour. This is most likely due to the fact that ipRGCs receive input from cones; the photoreceptors in the mammalian retina that encode colour. Evidence regarding colour coding in human ipRGCs is limited. As it is thought that our pupillary control brain area receives its input mainly from ipRGCs, we decided to study colour coding by the pupil as a proxy of colour coding by ipRGCs. The human retina contains three cone types involved in colour coding, namely short-, mid- and long-wavelength sensitive cones (S-, M- and L-cones). Therefore, we designed an experiment to test how S-cones, M-cones and L-cones contribute to the pupillary light response in humans.

Methods: With the silent substation method, one can design two light spectra that both activate all but one photoreceptor type identically. When these two spectra are temporally alternated, the activation of one photoreceptor type is selectively modulated. We designed 4 pairs of such spectra, granting control over the modulation of either S-, M-, L-cone or melanopsin activity. Sixteen participants viewed the S-, M-, L- or melanopsin spectra, alternating at a frequency of 0.25–4 HZ over a 30-minute interval, during which pupil size was recorded.

Results: Results indicate that selective decrements in M-cone or S-cone activity lead to a paradoxical pupil constriction, whereas selective L-cone or melanopsin increments resulted in pupil constriction.

Conclusions: These findings suggest that human ipRGCs encode color by spectral opponent inputs from different cone types, with inhibitory roles for S- and M-cones and excitatory roles for L-cones and the intrinsic melanopsin-mediated response.

Funding/Disclosures: STW OnTime Project Grant.

A81

The Effect of Systematic Light Exposure on Sleep and Sleep Quality in a Mixed Group of Fatigued Cancer Survivors

Lisa M. Wu[1,2], *Ali Amidi*[3], *Heiddis Valdimarsdottir*[1,4], *Sonia Ancoli-Israel*[5], *Lianqi Liu*[5], *Gary Winkel*[1], *Emily E. Byrne*[1], *Ana Vallejo Sefair*[7], *Alejandro Vega*[1], *Katrin Bovbjerg*[2], *Wiliam H. Redd*[1]

[1]Department of Oncological Sciences, Icahn School of Medicine at Mount Sinai, New York, NY, USA; [2]Department of Medical Social Sciences, Northwestern University Feinberg School of Medicine, Chicago, IL, USA; [3]Department of Oncology, Aarhus University Hospital, Aarhus, Denmark; [4]Department of Psychology, Reykjavik University, Reykjavik, Iceland; [5]Department of Psychiatry, University of California, San Diego, CA, USA; [6]Department of Medicine, University of California, San Diego, CA, USA; [7]Department of Clinical and Social Psychology, University of Rochester, Rochester, NY, USA

Objectives: Sleep disturbances are commonly reported by cancer survivors. Systematic light exposure using bright light has been used to improve sleep in other populations. In this secondary data analysis, the effect of morning administration of bright light on sleep and sleep quality was examined in a mixed group of fatigued cancer survivors.

Methods: Forty-four cancer survivors screened for cancer-related fatigue were randomized to either a bright white light or a comparison dim red light condition. Participants were instructed to use a light box every morning for 30 minutes for 4 weeks. Wrist actigraphy and the Pittsburgh Sleep Quality Index were administered at 4 time points: prior to light treatment (baseline), 2 weeks into the intervention, during the last week of the intervention, and 3 weeks postintervention. Thirty-seven participants completed the end-of-intervention assessment.

Results: Repeated-measures linear mixed models indicated a statistically significant time × treatment group interaction effect with sleep efficiency improving more in the bright light condition over time compared with the dim light condition ($F_{3,42} = 5.55$; $p = 0.003$) with a large effect size (partial $\eta^2 = 0.28$). By the end of the intervention and 3 weeks postintervention, mean sleep efficiency in the bright light group was in the normal range. Medium to large effect sizes were also seen in sleep quality, total sleep time, and wake after sleep onset for participants favoring the bright light condition.

Conclusions: The results suggest that systematic bright light exposure in the morning may have beneficial effects on sleep in fatigued cancer survivors. Larger scale efficacy trials are warranted.

Funding/Disclosures: This work was supported by the National Cancer Institute of the National Institutes of Health (W.H.R., grant# R21CA158954 and K05CA108955; and L.W., grant #5K07CA184145-03). Dr. Amidi's work was supported by the Danish Council of Independent Research (DFF – 5053-00220).

A82

Systematic Light Exposure and Cognition in Hematopoietic Stem Cell Transplant Survivors: A Pilot Study

Lisa M. Wu[1,2], *Ali Amidi*[3,4], *Heiddis Valdimarsdottir*[1,5], *Sonia Ancoli-Israel*[6], *Gary Winkel*[1], *Ariella Hoffman-Peterson*[1], *William H. Redd*[1]

[1]Icahn School of Medicine at Mount Sinai, New York, NY, USA; [2]Northwestern University Feinberg School of Medicine, Chicago, IL, USA; [3]Aarhus University, Aarhus, Denmark; [4]Aarhus University Hospital, Aarhus, Denmark; [5]Reykjavik University, Reykjavik, Iceland; [6]University of California, San Diego, CA, USA

Objectives: Hematopoietic cell transplant (HCT) survivors may experience a range of co-occurring cancer-related symptoms including cognitive impairment (CRCI). Systematic light exposure using bright white light (BWL) has shown promise as a treatment for cancer-related symptoms (e.g, fatigue). This study investigated preliminary efficacy of BWL to treat CRCI and assessed treatment satisfaction.

Methods: Fifty-six HCT survivors 1–5 years post-transplant (mean age 60) screened for mild cognitive impairment using computerized neuropsychological tests (i.e., ≥1 SD below the mean on ≥1 subtest) were randomized to BWL or an established comparison dim red light (DRL) condition. Participants were instructed to use the light box for 30 minutes/morning for 28 days. Standardized measures of objective (primary outcome) and self-reported cognitive functioning (secondary outcome) were administered at baseline, the end of the intervention, and 3-weeks post-intervention. Preliminary efficacy was examined using linear mixed models. Treatment satisfaction was assessed using an established 4 point Likert-scale question.

Results: There were statistically significant improvements over time in both groups in objective ($p < 0.0001$) and self-reported cognition ($p = 0.034$). Linear mixed models indicated no significant time by group effects for objective ($p = 0.20$) nor self-reported cognition ($p = 0.41$). Seventy-two percent of participants were satisfied with the intervention to some extent (scores between 2 and 4) with no significant difference between groups ($p = 0.87$).

Conclusions: Although improvements to objective and self-reported cognition were evident in both groups, there was no specific hypothesized effect of BWL over DRL. It is unclear whether changes over time were due to placebo effects, real therapeutic effects of both light conditions, changes unique to each group and unrelated to the intervention, or in the case of objective cognitive functioning, whether both groups were simply displaying practice effects. Due to the small sample size, follow-up research is warranted potentially with a usual care group.

Funding/Disclosures: This work was supported by the National Cancer Institution of the National Institutes of Health (W.H.R., grant# 5 R21 CA178307 02 and K05 CA108955; and L.W., grant#5K07 CA184145 03).

A83

Living in the Photon Space – The Biological Value of Daylight for Human Wellbeing

Katharina Wulff, Joachim Stormly Hansen

Nuffield Department of Clinical Neurosciences, University of Oxford, Oxford, UK

Objectives: (1) Quantification of the variation in daylight properties across day-night cycles in two very different environments – an all-glass house and a brick building, (2) documenting behavioural and physiological responses to the light exposure from living in these spaces.

Methods: A transparent, 35 m^2 large, all-glass building (the 'Photon Space', PS) with natural light penetrating from the roof and all sides down to floor level and with an indoor climate to live-in across all seasons, has been constructed on the Island of Bornholm, Denmark. A randomised, cross-over designed study (data collection from September to March) with fifteen participants spending three days (18:00 to 10:00 compulsory) in the glass house and three days in an ordinary bungalow ('Villa') nearby was employed to investigate participants' alertness, colour perception, visual comfort and emotional well-being several times a day, while rest-activity patterns and light exposure were actigraphically monitored throughout. Sensors continuously monitored external and indoor climate (light, humidity, temperature) over prolonged periods and seasons. Immediately after living in the PS or the Villa, each participant underwent 18 hours of an adapted constant routine under dim (<3 lux) light, in which alertness and melatonin concentration was assessed in hourly intervals with napping permitted between sampling to minimise sleep deprivation. A 48-hour washout period with no assessments was scheduled between conditions.

Results: In the PS, light intensity from twilight until final waking differed by the factor of 100 from that in the Villa. Within subjects, Dim Light Melatonin Onset (DLMOn) was similar regardless of having lived in the PS or Villa before. In 75% of the participants, DLMOffset was earlier after living in the PS compared to the Villa. Participants in the PS also woke up earlier by 27 min on average. Timing of final wake relative to DLMOffset was inconsistent in both environments. Morning light levels, including twilight, was correlated with earlier final wake and greater alertness in the morning, at the time of living in the PS. Under dim light constant conditions, however, there was a trend for greater alertness in the morning and afternoon, when participants had been in the PS beforehand as compared to having been in the Villa.

Conclusions: Current data are suggestive of daylight, from as early as twilight, having a measurable influence on human physiology and behaviour when exposed to the entire 24-hour natural light-dark cycle.

Funding/Disclosures: This research study is partly supported by the UK National Institute for Health Research *(NIHR)* Oxford Biomedical Research Centre (KW: A92181), the UK-based Architectural Glass Manufacturer *CANTIFIX,* and the *Green Solution House* on Bornholm.

A84

Late Sleep, Early Decline: Late Sleep Is Associated with Increased Cellular Aging

Dora S. Wynchank[1], *Denise Bijlenga*[1], *Brenda W.J.H. Penninx*[2], *Femke Lamers*[2], *Aartjan T.F. Beekman*[2], *J.J. Sandra Kooij*[1,2], *Josine E. Verhoeven*[2]

[1]PsyQ Expertise Center Adult ADHD, The Hague, The Netherlands; [2]Department of Psychiatry, Amsterdam Public Health Research Institute, VU University Medical Center, Amsterdam, The Netherlands

Objectives: We evaluated the relationship between leukocyte telomere length (LTL) and sleep duration, insomnia symptoms, and circadian rhythms, to test whether sleep and chronobiological dysregulation are associated with cellular aging.

Methods: Data from the Netherlands Study of Depression and Anxiety cohort (N = 2,936) were used at two waves six years apart, to measure LTL. Telomeres protect DNA, shorten during the lifespan and are important biomarkers for cellular aging. LTL was assessed by qualitative polymerase chain reaction and converted into number of base pairs. Sleep parameters were sleep duration and insomnia symptoms from the Insomnia Rating Scale. Circadian rhythm variables were: an indication of the Delayed Sleep Phase Syndrome (DSPS), mid-sleep corrected for sleep debt on free days (MSFsc), sleep-onset time, and self-reported chronotype in adulthood and childhood, from the Munich Chronotype Questionnaire. Generalized estimating equation models were used to examine the associations between LTL, sleep and chronobiological factors.

Results: Indicators of delayed circadian rhythm showed a strong and consistent effect on LTL, after adjustment for sociodemographic and health indicators. Late MSFsc ($B = -48.5$, $p = 0.005$), late sleep-onset time ($B = -32.0$, $p = 0.001$), indication of DSPS ($B = -71.8$, $p = 0.040$) and moderately late chronotype in adulthood ($B = -72.8$, $p = 0.002$) were associated with significantly shorter LTL across both waves; whereas sleep duration and insomnia symptoms were not. Extremely early chronotype showed significantly longer mean LTL ($B = 157.5$, $p = 0.042$). No sleep or chronobiological predictors showed accelerated LTL attrition rate over 6 years.

Conclusions: Individuals with indicators of delayed circadian rhythm have significantly shorter LTL, but not faster LTL attrition rates.

Funding/Disclosures: Study is supported by an NWO-VICI grant (number 91811602). Infrastructure for the Netherlands Study of Depression and Anxiety (www.nesda.nl) funded through Geestkracht program of the Netherlands Organization for Health Research and Development (Zon-Mw, grant number 10-000-1002) and financial contributions by participating universities and mental health care organizations.

A85

Bright Light Exposure Triggers Earlier Onset of Selective Consolidation of Motor-skill Accuracy in Humans

Takuya Yoshiike[1,2,3], *Motoyasu Honma*[4], *Naoto Yamada*[1], *Kenichi Kuriyama*[1,2]

[1]Department of Psychiatry, Shiga University of Medical Science, Otsu, Japan; [2]Department of Adult Mental Health, NIMH, NCNP, Tokyo, Japan; [3]Psychiatry and Clinical Psychobiology, Division of Neuroscience, Scientific Institute Ospedale San Raffaele, Milano, Italy; [4]Department of Cell Physiology, Kyorin University School of Medicine, Tokyo, Japan

Objectives: A growing literature suggests that ambient light is a critical determinant of successful memory acquisition. Nevertheless, while sleep is known to selectively enhance newly acquired memories according to their future relevance, the potential role of ambient light in this memory triage remains unknown. Here, we investigate how bright light (BL), given within encoding, affects acquisition and subsequent consolidation of motor-sequence learning, and whether BL differentially prompts given finger transitions in accord with individual benefits.

Methods: Twenty-four healthy human subjects were exposed to either BL (8943 ± 291 lux) or control light (CL; 438 ± 31 lux for 15 min, while acquiring motor-skill procedures at 13:00 h when the circadian phase response to light is expected to be minimized, and then performed 24 h retest. The effects of light intensity on immediate and overnight performance gains were evaluated by accuracy and speed.

Results: Practice-dependent immediate accuracy gains were found to be significantly higher in BL group than in CL group, while across a subsequent night of sleep, overnight accuracy gains were lower in the BL group than in CL group. In addition, individual transitions that appeared most difficult at the early phase of training showed a significant increase in accuracy during training in BL group, while in CL group those transitions showed a significant increase in accuracy overnight. Accuracy of individual transitions that were most easily performed, however, was not influenced by light conditions or learning processes. No effects of light intensity were seen on performance speed, or subjective ratings of alertness or mood.

Conclusions: Our findings suggest that brief BL exposure during training triggers the earlier onset of selective consolidation processes that maximally meet individual demands for accuracy of procedural motor-skills, which should have been driven by post-training sleep. This view may offer a new way of enhancing brain plasticity, for instance by compensating for impaired sleep-dependent memory consolidation in neuropsychiatric disorders.

Funding/Disclosures: This work was supported by JSPS KAKENHI JP16K19794 and the SENSHIN Medical Research Foundation. The authors declare no competing financial interests.

A86

Peripheral micro RNAs Are Altered by Total Sleep Deprivation and Psychological Stress and Predict Cognitive Performance in Humans

Michelle J. Zajko[1], *Deanne M. Taylor*[1], *Jiah Pearson-Leary*[2,3], *Seema Bhatnagar*[2,3], *Namni Goel*[4]

[1]Department of Biomedical and Health Informatics, The Children's Hospital of Philadelphia, Philadelphia, PA, USA; [2]Department of Anesthesiology, The Children's Hospital of Philadelphia, Philadelphia, PA, USA; [3]Department of Anesthesiology, University of Pennsylvania Perelman School of Medicine, Philadelphia, PA, USA; [4]Division of Sleep and Chronobiology, Department of Psychiatry, University of Pennsylvania Perelman School of Medicine, Philadelphia, PA, USA

Objectives: Sleep loss is associated with cancer, cardiovascular disease, and Alzheimer's disease and psychiatric disorders, and also impairs cognitive performance, although there are individual differences in such deficits. MicroRNAs (miRNAs), small non-coding RNAs that are important regulators of gene expression, typically repress expression of their target mRNAs. It remains unknown whether sleep deprivation or the adverse combination of sleep deprivation and psychological stress affect miRNA responses in humans, and whether these responses predict cognitive performance during sleep deprivation.

Methods: Thirty-two healthy adults (ages 27–53; mean ± SD, 35.1 ± 7.1 y; 14 women) participated in a five-day experiment consisting of two 8 h time-in-bed (TIB) baseline nights, followed by 39 h of total sleep deprivation (TSD) and two 8 h–10 h TIB recovery nights. A modified Trier Social Stress Test was conducted on the day after TSD to induce psychological stress. The Psychomotor Vigilance Test (PVT), Digit Symbol Substitution Task (DSST), and Digit Span Task (DS), were administered throughout the experiment. Blood samples were taken at 6 time points and miRNAs from plasma were analyzed via Affymetrix microarrays. Linear mixed models with Z-score log2 fold change cutoffs of ± 1.645 and greater (FDR <0.05) and pathway analysis using the random forest method were used for statistical analysis.

Results: Compared to the pre-study time point, 10 miRNAs showed fold changes with TSD alone and 18 miRNAs showed fold changes with TSD and psychological stress; these miRNAs targeted 2309 and 2823 genes, respectively, with 700 overlapping targets. Notably, at pre study, 14 miRNAs predicted PVT lapses and errors during TSD, 7 miRNAs predicted DSST performance and 10 miRNAs predicted DS performance.

Conclusions: For the first time we show that peripheral miRNAs can track responses to total sleep deprivation and its detrimental combination with psychological stress and predict individual differences in cognitive performance. As such, peripheral miRNAs are viable epigenetic biomarkers of sleep deprivation, psychological stress, and cognitive vulnerability in humans.

Funding/Disclosures: This work was supported by NASA NNX14AN49G.

Author Index

Neuropsychobiology

Number refers to abstract number

KARGER

E-Mail karger@karger.com
www.karger.com/nps