SLTBR

Society for Light Treatment and Biological Rhythms

Society for Light Treatment and Biological Rhythms (sltbr.org)

Klaus Martiny, MD, PhD, President

Academic and Local Conference Host:
Center for Environmental Therapeutics (cet.org)
Michael Terman, PhD, President

New York State Psychiatric Institute
1051 Riverside Drive
New York City

28th Annual Program and Abstracts
Wednesday, June 29 – Friday, July 1, 2016

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Dear Friends,

On behalf of the Board of Directors, scientific and planning committees, I am delighted to welcome you to the 28th annual meeting of the Society for Light Treatment and Biological Rhythms in New York City.

We are honored and grateful for the opportunity to hold our meeting under the auspices of the Columbia University Department of Psychiatry / New York State Psychiatric Institute, with Professor Michael Terman as academic host.

We are fortunate to be able to offer you a scientific program with top experts who will show the rapidly emerging knowledge in, and importance of, the areas that SLTBR is devoted to furthering. We greatly appreciate their participation in the meeting.

The travel grants and the J. Christian Gillin Young Investigator Award have been major incentives for participation. The number of applicants continues to increase each year.

The Center for Environmental Therapeutics (CET) is again generously offering a teaching course, so clinician members of the New York State Psychological Association can obtain CE credits, thanks to NYSPA's Independent Practice Division, David Byrom, President, and Frank Corigliano, Past President.

Speaking of past presidents, we are very pleased to welcome a record number of SLTBR past presidents to this year's meeting.

I would like to thank our many new and returning corporate sponsors, who have made this meeting possible. With their support, SLTBR has been able to create this exciting scientific program, including travel grants and the J. Christian Gillin Young Investigator award.

Special thanks to Elizabeth Saenger of CET for her intriguing cover design for our program book.

Lastly, I would like to express my gratitude to the members of our Board of Directors, who have devoted countless hours to making this annual meeting possible: Mirjam Münch (incoming president 2016-2018), Ybe Meesters, Konstantin Danilenko, Dorothy Sit (incoming vice president), Kathryn Roecklein, and Matthaeus Willeit (immediate past president). And kudos to Nikki Hafezi, our expert administrative manager, for her dedication to the Society, and John Hanifin, treasurer, for helping to keep us afloat. It is their active involvement and commitment to the Society that creates our solid platform for interaction among researchers, with a unique program focused on lighting technology and therapeutic applications within the conceptual base of chronobiology.

Enjoy the meeting and continue SLTBR's treasured tradition of lively, friendly interaction and debate.

Klaus Martiny, MD, PhD, SLTBR President
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. *J. Christian Gillin Young Investigator Award*

Congratulations, Kim Boddum, PhD!

The overall focus of my research is the investigation of chemical signaling and receptor function, as well as the underlying principles of pathologic dysregulation of neuronal signaling and the resulting disorders. Using electrophysiology, fluorescence, and imaging approaches, I have studied various cellular and animal models. Currently, I am working as a postdoc at the University of Copenhagen, where I am investigating novel compounds and their ability to control ion channel function and consequently cellular excitability.

During my time at Rigshospitalet (The National Hospital of Denmark), I performed electrophysiological *in vivo* studies in genetically modified mice, displaying a narcoleptic phenotype. More precisely, I used electroencephalographic (EEG) and electromyographic (EMG) recordings to monitor the sleep architecture of these animals in to examine the mechanistic background of sleep regulation. I particularly focused on the interplay between sleep and the immune system, as well as the influence of sleep related neuropeptides.

Our work on seasonal variations of hypocretin levels in a human cohort began, while working under the hypothesis that the activity of hypocretin secreting neurons was to some extend regulated by the immune system. We were granted access to the Danish healthcare database to collect patient data. Those data enabled us to show that the cerebrospinal fluid hypocretin-1 level fluctuates with season and correlates with day length.

I graduated with a degree in biology from Aarhus University in 2010. For my master's degree, I developed *in vitro* models of Parkinson's disease to evaluate electrophysiological changes in neuronal functioning. I obtained my PhD degree in neuropharmacology from the University of Copenhagen, Department of Drug Design and Pharmacology. My graduate work centered around extrasynaptic (GABAA) receptors and their therapeutic potential for the treatment of epilepsy, which I investigated using *in vivo* pharmacology, electrophysiology, immunohistochemistry and recombinant expression assays. The experimental work for this PhD project was partly performed at the Institute of Neurology, University College London.

SLTBR SCIENTIFIC PROGRAM

Wednesday, 29 June 2016

We kindly ask you to respect the Institute's regulation that photography or video recording is prohibited within the building, except for Auditorium events

1430-1830	A Tour of New York	Marylou Selo, Guide	
1600-1800	Board of Directors meeting	By invitation	Coogan's
1830-2030	Welcome reception	All participants and spouses are invited.	Coogan's

Thursday, 30 June 2016

0800-0900	Registration & Coffee Service	Pardes Auditorium	
0900-0915	**Welcome, Introduction & Program Overview**	Klaus Martiny, President Michael Terman, Host	Denmark USA
0915-1130	**Teaching course:**	Chair: Michael Terman	 USA
0915-1000	The Biology of Circadian Rhythms	Dan Oren	USA
1000-1045	How to Set Light and Dark for Personal and Work Schedules	Marijke Gordijn	The Netherlands
1045-1130	Psychological factors in the Etiology and Treatment of Seasonal Depression	Michael Young	USA
1130-1330	**Lunch with Poster Session**	Kolb Lobby	
1330-1500	**Symposium 1 Body clocks – Molecular Approaches from Animals to Humans – Consequences of Life Style, Shift Work**	Co-chairs: Steven Brown Urs Albrecht	 Switzerland Switzerland
1330-1400	Long-term Consequences of Abnormal Circadian Lighting: A Question of Epigenetics or Circuits?	Steven Brown	Switzerland
1400-1430	Clock Genes and Mood Related Behavior	Urs Albrecht	Switzerland
1430-1500	Development and Identification of the Melatonin-producing Pinealocyte	Martin Fredensborg Rath	Denmark
1500-1530	Coffee Service	Pardes Auditorium	

Thursday Continued

1530-1630	**Oral Presentation Session 1**	Chair: Namni Goel	 USA
1530-1545	Arctic light exposure at two seasons and effects on mood and recovery	Arne Lowden	Sweden
1545-1600	Melatonin Suppression via Nighttime Light Exposure in Adult Men Stimulates Growth and Metabolism of Tissue-Isolated, Androgen Independent Human Prostate Cancer Xenografts in Nude Rats: Effect of Wavelength	John Hanifin	USA
1600-1615	Systematic Light Exposure Improves Depression among Cancer Survivors	William H. Redd	USA
1615-1630	The Metabolomic Marker Acetylcarnitine Predicts Neurobehavioral Performance during Chronic Sleep Restriction	Namni Goel	USA
1630-1700	**J. Christian Gillin Young Investigator Award Presentation**	Co-Chairs: Mirjam Münch Ybe Meesters	 Germany Netherlands
1635-1700	**Lecture by the Award Recipient** Cerebrospinal Fluid Hypocretin-1 Orexin-A) Level Fluctuates with Season and Correlates with Day Length	Kim Boddum	Denmark
1700-1800	**Poster walk** Presenters should stay with their poster for the poster walk	Kolb Lobby Dorothy Sit Ybe Meesters Klaus Martiny	 USA Netherlands Denmark
1900-2200	**Banquet &** **Invited address**	Banquet speech: Norman Rosenthal	Artie's USA

Friday, 01 July, 2016			
0800-0830	Registration & Coffee service	Pardes Auditorium	
0830-1000	**Symposium 2** **Impact of Light at Night** **– Light at the Wrong Time**	Co-chairs: George Brainard Dieter Kunz	 USA Germany
0830-0900	Living in Biological Darkness	Dieter Kunz	Germany
0900-0930	Light-Induced Circadian/Melatonin Modulation of Responsiveness to Cancer Risk and Therapy	David Blask	USA
0930-1000	Light at Night and Cancer Risk – the Epidemiological Evidence	Eva Schernhammer	USA
1000-1030	Coffee Service	Pardes Auditorium	
1030-1130	**Keynote Address** A Systems Genetics Approach to Understand the Consequences of Sleep Loss	Paul Franken	Switzerland
1130-1230	**Oral Presentation Session 2**	Chair: Ybe Meesters	 Netherlands
1130-1145	Non-Visual Light Sensitivity in Individuals Suffering from a Delayed Sleep Schedule	Christophe Moderie	Canada
1145-1200	Polychromatic Bright Light Exposure Facilitates Recovery of Cognitive Performance and Objective Sleepiness after 40 hours of Extended Wakefulness	Jan de Zeeuw	Germany
1200-1215	Differential Recovery of Behavioral Attention Outcomes, But Not Other Cognitive and Subjective Measures, After Chronic Sleep Restriction and Acute Total Sleep Deprivation	Namni Goel	USA
1215-1230	The Impact of Broad Spectrum Bright Light and Exogenous Melatonin at Night on Plasma Hormones and Metabolites Responses to a Meal	Mohammed Albreiki	UK
1230-1345	**Lunch - Poster Session 1230-1330** **or** **Lunch - Business Meeting 1245-1345**	Kolb Lobby Pardes Auditorium	

Friday Continued

1345-1530	**Symposium 3** **Chronotherapeutics: Bipolar and Treatment Resistant Unipolar Depression**	Co-chairs: Francesco Benedetti Konstantin Danilenko	 Italy Russia
1345-1400	Overview of the Field	Francesco Benedetti	Italy
1400-1430	Light Therapy for Bipolar Depression: Findings from a Randomized Controlled Trial, Dosing Issues, Managing Emergent Mixed or Manic Symptoms	Dorothy Sit	USA
1430-1500	Moving Chronotherapeutics into Outpatient Practice	John Gottlieb	USA
1500-1530	Chronotherapeutics in Unipolar and Treatment Refractory Depression	Jonathan Stewart	USA
1530-1600	Coffee Service	Pardes Auditorium	
1600-1700	**Oral Presentation Session 3**	Chair: Michael Young	 USA
1600-1615	Blue Light Exposure Before Bedtime in Subjects Complaining of a Delayed Sleep Schedule	Solenne van der Maren	Canada
1615-1630	Increased Appetitive Symptoms Differentially Predict Treatment Response to Medication, Light and Placebo in Non-Seasonal Major Depression	Robert Levitan	Canada
1630-1645	Testing Dynamic Solid State Lighting for Improving Circadian Adaption and Sleep in Long Duration Space Flight Missions	George Brainard	USA
1645-1700	Neurotophins/Hematopoietic Growth Factors as Biomarkers of Antidepressant Response to Chronotherapeutics	Francesco Benedetti	Italy
1700-1730	**Poster Prize Presentation,** **Student Grants &** **Final Remarks**	Pardes Auditorium Dorothy Sit Mirjam Münch Klaus Martiny	 USA Germany Denmark

List of Abstracts for Oral Presentations and Posters

THE IMPACT OF BROAD SPECTRUM BRIGHT LIGHT AND EXOGENOUS MELATONIN AT NIGHT ON PLASMA HORMONES AND METABOLITES RESPONSES TO A MEAL

Mohammed Albreiki, Benita Middleton, Shelagh Hampton
University of Surrey, Guildford, UK

Objectives
Our previous study has shown that light at night is associated with changes in glucose, insulin and non-esterified fatty acid (NEFA) levels (Albreiki et al., 2015). This study aims to investigate the impact of light and exogenous melatonin on plasma insulin and metabolites prior to and after an evening meal in healthy male participants.

Methods
A favourable ethical opinion was obtained from the University of Surrey Ethics Committee. Nine healthy males (26 years (SD 4.03) BMI 24.8 kg/m^2 (SD 2.4)) were randomised to a three way cross-over design protocol; light session (LS) (>500 lux), dark session plus exogenous melatonin (DSM) (<5 lux), and light session plus exogenous melatonin (LSM) (>500 lux), separated by at least seven days. Each session started at 18:00h and finished at 06:00h the next day. All participants were sleep deprived and maintained a semi-recumbent position throughout the session. Participants consumed an isocaloric meal (1066 Kcal, 38g protein, 104g CHO, 54g fat, 7g fibre), meal timings were individualised based on melatonin onset. Exogenous melatonin (Circadin tablet 2mg) was administered 90 minutes prior to the evening meal. Plasma and saliva samples were collected at specific time intervals to assess glucose, insulin, NEFAs , triacylglycerides (TAGs) and melatonin levels. Two factors repeated measures ANOVA, followed by post-hoc test, paired student's T-test and total area under the curve (TAUC) were performed.

Results
Salivary melatonin was significantly higher in DSM and LSM than in LS ($p<0.001$), whereas no significant difference was shown between DSM and LSM . Pre-prandial NEFA levels were significantly greater in DSM and LSM than in LS ($p=0.009$). NEFAs levels showed no significant differences between LSM and DSM ($p=0.07$). Postprandial glucose and insulin showed significant increase in LS compared to DSM and LSM ($p=0.01$), whereas no significant differences were shown between DSM and LSM ($p=0.38$). There was a significant increase in postprandial TAGs in LS compared to DSM and LSM ($p<0.01$), whereas no significant differences were shown between DSM and LSM ($p=0.2$). There were significant effects of time in all 5 parameters in all conditions.

Conclusion
Melatonin suppression in LS was due to light intensity, whereas high melatonin levels in LSM and DSM were due to the administration of slow release exogenous melatonin. High postprandial glucose in LS despite the presence of elevated insulin levels indicates changes in insulin sensitivity. It is possible that the significant reduction in insulin levels in LSM and DSM is due to the presence of melatonin (Coomans, et al. 2013; McMullan, et al. 2013). Increased pre-prandial NEFAs in LSM and DSM when melatonin levels were rising suggests that melatonin has a role in lipid metabolism. Postprandial TAGs were greater in LS than in DSM and LSM this could be due to the presence of melatonin inhibiting insulin secretion, influencing lipoprotein lipase production and thus regulating NEFAs and TAGs levels (Bonen et al., 2006). This study confirms our previous findings that reported changes in glucose, insulin and NEFAs responses due to the presence of endogenous melatonin after a late evening meal.

Funding/Disclosures
This study is supported by Abu Dhabi Health Services Company (SEHA).

LONG-TERM CONSEQUENCES OF ABNORMAL CIRCADIAN LIGHT: A QUESTION OF CELLULAR CLOCKS OR CIRCUITS?

Abdelhalim Azzi* (1), Jennifer A. Evans*§ (2), Tanya Leise (3), Jihwan Myung (4), Toru Takumi (4), Alec J. Davidson*§ (5) and Steven A. Brown*§ (1)
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*These authors contributed equally to this work.

Objectives
A circadian clock governs most aspects of mammalian behavior and physiology. Its basic mechanism is cell-autonomous. Although its properties are in part genetically determined, an altered light-dark environment can change circadian period length through a mechanism requiring de novo DNA methylation. However, the downstream consequences of these epigenetic modifications are unclear.

Methods
To test the hypothesis that altered neural networking could contribute to light-mediated circadian plasticity, we examined clock phase in brain slices taken from Per2::luc mice raised in different day lengths, in segmented brain slices, and in slices treated with different neurotransmitter inhibitors.

Results
We show here that epigenetically mediated changes in period are effected not via cell-autonomous clock properties, but rather through altered networking within the suprachiasmatic nuclei (SCN), the circadian "master clock" in the hypothalamus, which is DNA-methylated in a region-specific manner. As a result, circadian phasing within individual cells of the SCN is temporally reorganized to change the period length of the network as a whole. Interruption of neural communication by chemical inhibitors of neuronal firing or by physical cutting suppresses SCN reorganization and restores period. Mathematical modeling suggests, and experiments confirm, that SCN reorganization depends upon GABAergic signaling.

Conclusions
Our results show that basic circadian clock properties like period length in mammals are governed by dynamic interactions among SCN neurons, with neuroadaptations in network function driven by the environment.

Funding/Disclosures
This work has been supported by the Velux Foundation.

CHRONOTHERAPEUTICS: BIPOLAR AND TREATMENT RESISTANT UNIPOLAR DEPRESSION: OVERVIEW OF THE FIELD

Francesco Benedetti
Department of Neuropsychiatric Sciences, Scientific Institute and University Vita-Salute San Raffaele, Milan, Italy.

Psychiatric chronotherapeutics is the controlled exposure to environmental stimuli that act on biological rhythms in order to achieve therapeutic effects in the treatment of psychiatric conditions. In recent years some techniques (mainly light therapy and wake therapy, in the form of total or partial sleep deprivation, or phase advance) have passed the experimental developmental phase and reached the status of powerful and affordable clinical interventions for everyday clinical treatment of depressed patients. These techniques target the same brain neurotransmitter systems and the same brain areas as do antidepressant drugs, and should be administered under careful medical supervision. Their effects are rapid and transient, but can be stabilised by combining techniques among themselves or together with common drug treatments, such as lithium salts.

Antidepressant chronotherapeutics targets the broadly defined depressive syndrome, with response and relapse rates similar to those obtained with antidepressant drugs, and good results are obtained even in difficult-to-treat conditions such as bipolar depression. While disruption of sleep-wake and activity-rest rhythms is known to trigger mood episodes in bipolar disorder, specific combinations of extended wake and light during depression, and extended bedrest and dark during mania, can help to rapidly restore euthymic conditions.

Chronotherapeutics offers then a benign alternative to more radical treatments for severe depression on psychiatric wards, giving to the patients' similar rates of response but with the advantage of rapidity of onset and lack of side effects, and it has been proven to be feasible and effective in outpatient settings. Recent findings also show that the combination of wake and light can successfully treat the most life-threatening conditions in mood disorders, such as acutely suicidal bipolar depression, and can produce some clinically significant benefit by rapidly decreasing suicidal ideation even in patients who do not achieve a final response. Wake and light therapy can then be proposed as first line treatments for mood disorders.

Funding/Disclosures
None.

NEUROTOPHINS/HEMATOPOIETIC GROWTH FACTORS AS BIOMARKERS OF ANTIDEPRESSANT RESPONSE TO CHRONOTHERAPEUTICS

Francesco Benedetti (1), Sara Poletti (1), Thomas A. Hoogenboezem (2), Clara Locatelli (1), Oliver Ambrée (3), Harm de Wit (2), Annemarie J.M. Wijkhuijs (3), Elena Mazza (1), Chiara Bulgarelli (1), Benedetta Vai (1), Cristina Colombo (1), Enrico Smeraldi (1), Volker Arolt (3), Hemmo A. Drexhage (2)

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Objectives

Growth factors involved in neurogenesis and neuroplasticity could play a role in biological processes that drive depression recovery. Combined total sleep deprivation and morning light therapy (TSD+LT) can acutely reverse depressive symptoms, thus allowing to investigate the neurobiological correlates of antidepressant response.

Methods

We tested if changes on plasma levels of Brain Derived Neurotrophic Factor (BDNF), S100 calcium binding protein B (S100-B), Stem Cell Factor (SCF), Insulin-like Growth Factor-Binding Protein 2 (IGFBP-2), Epidermal Growth Factor (EGF), Platelet-Derived Growth Factor-BB (PDGF-BB), and Vascular Endothelial Growth Factor (VEGF) are associated with response to TSD+LT in 26 inpatients affected by a major depressive episode in the course of bipolar disorder. Regional grey matter (GM) volumes were assessed at baseline, and BOLD fMRI neural responses to a moral valence decision task were recorded before and after treatment.

Results

61.5% of patients responded to treatment. SCF plasma levels increased significantly more in responders, and correlated with GM volumes in frontal and parietal cortical areas. The pattern of change of SCF also associated with both GM volumes and changes of BOLD fMRI neural responses in the anterior cingulate and medial prefrontal cortex.

Conclusions

SCF is both a hematopoietic growth factor and a neurotrophic factor, involved in neuron-neuron and neuron-(micro)glia interactions, fostering neuronal growth and an anti-inflammatory milieu. We correlated SCF levels with antidepressant response and with functional and structural MRI measures in cortical areas that are involved in the cognitive generation and control of affect. SCF may be a candidate growth factor that contributes to neurotrophic and immune effects that are involved in the process of remission/recovery from depression.

Funding/Disclosures

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LIGHT-INDUCED CIRCADIAN/MELATONIN MODULATION OF CANCER RISK AND RESPONSIVENESS TO THERAPY

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Objectives
The central circadian clock within the suprachiasmatic nucleus (SCN) plays an important role in temporally organizing and coordinating many of the processes governing cancer cell signaling, metabolism and proliferation and ultimately cancer tumor growth progression in synchrony with the daily light/dark cycle. Cancer signaling, metabolism and growth activities are dynamically regulated, coordinated and integrated within circadian time structure over a 24-hour light/dark cycle by SCN-driven nocturnal pineal production of the anticancer hormone melatonin.

Methods
Exposure of experimental animals or human subjects to light at night (LAN) of sufficient intensity and appropriate wavelength induces a type of circadian disruption that ranges from total elimination of the nocturnal melatonin signal to a suppression of its circadian amplitude and shortening of its duration without affecting its phasing. For example, in nude female and male nude rats, dim LAN exposure (0.2 lux) results in this latter type of circadian/melatonin disruption that, in turn, disrupts this circadian-regulated host/cancer balance among several important cancer preventative signaling mechanisms, leading to hyperglycemia and hyperinsulinemia in the host. This is accompanied by circadian disruption tumor circadian rhythm of aerobic glycolysis (Warburg effect), lipid metabolism, oncogenic signaling and proliferative activity and runaway tumor growth in tissue-isolated human breast cancer xenografts as compared to tumors exposed to an intact nocturnal melatonin signal under LD,12:12 conditions. Virtually identical effects with LAN are observed in human prostate cancer xenografts.

Results
In female or male human subjects exposed to bright (2800 lux) polychromatic white LAN, nighttime melatonin production is compromised leading to amplitude suppression of the nocturnal circadian melatonin anti-cancer signal. Human breast or prostate cancer xenografts directly perfused *in situ* with blood collected during the night (i.e., high melatonin levels) respond with markedly diminished signaling, metabolic and proliferative activities. Following subject exposure to bright LAN and blood collection (i.e., low melatonin levels) and tumor perfusion with this blood, the signaling and metabolic activities that support rapid cell proliferation during the daytime are re-established. These melatonin suppressive and oncogenic effects of LAN in human subjects are not restricted to bright, polychromatic white light but extend to blue wavelength (480 nm) LAN whereas red wavelength (630 nm) LAN is without effect. When female nude rats bearing tissue-isolated estrogen receptor positive (ERα+) human breast cancer xenografts are exposed to dim LAN, the suppression of the nocturnal melatonin signal leads to their accelerated growth progression and decreased sensitivity/increased resistance to the anti-cancer effects of tamoxifen and doxorubicin.

Conclusions
Our findings strongly argue that exposure to either polychromatic white light or blue wavelength LAN, by disrupting/suppressing the nocturnal circadian melatonin signal, may not only increase the risk of the development and growth of clinically relevant human breast and prostate cancer, but may adversely modulate the responsiveness of breast cancer to standard, first-line endocrine and chemo-therapies by increasing their resistance to therapy and promoting a metastatic phenotype. The detrimental effects of LAN-induced circadian melatonin disruption on cancer risk and response to anti-cancer therapies notwithstanding, we may now be at the point where imaginative strategies are needed for using light to enhance or reinforce healthful circadian melatonin physiology as a novel therapeutic tool to mitigate cancer risk and improve tumor responses to anti-cancer therapies.

Funding/Disclosures
None.

CEREBROSPINAL FLUIDE HYPOCRETIN-1 (OREXIN-A) LEVEL FLUCTURATES WITH SEASON AND CORRELATES WITH DAY LENGTH

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Objectives
The hypocretin/orexin neuropeptides (hcrt) are key players in the control of sleep and wakefulness evidenced by the fact that lack of hcrt leads to the sleep disorder Narcolepsy Type 1. Sleep disturbances are common in mood disorders, and hcrt has been suggested to be poorly regulated in depressed subjects. To study seasonal variation in hcrt levels, we obtained data on hcrt-1 levels in the cerebrospinal fluid (CSF) from 227 human individuals evaluated for central hypersomnias at a Danish sleep center.

Methods
The samples were taken over a 4 year timespan, and obtained in the morning hours, thus avoiding impact of the diurnal hcrt variation. Hcrt-1 concentration was determined in a standardized radioimmunoassay. Using biometric data and sleep parameters, a multivariate regression analysis was performed.

Results
We found that the average monthly CSF hcrt-1 levels varied significantly across the seasons following a sine wave with its peak in the summer (June—July). The amplitude was 19.9 pg hcrt/mL [12.8–26.9] corresponding to a 10.6%increase in midsummer compared to winter. Factors found to significantly predict the hcrt-1 values were day length, presence of snow, and proximity to the Christmas holiday season. The hcrt-1 values from January were much higher than predicted from the model, suggestive of additional factors influencing the CSF hcrt-1 levels such as social interaction.

Conclusions
This study provides evidence that human CSF hcrt-1 levels vary with season, correlating with day length. This finding could have implications for the understanding of winter tiredness, fatigue, and seasonal affective disorder. This is the first time a seasonal variation of hcrt-1 levels has been shown, demonstrating that the hcrt system is, like other neurotransmitter systems, subjected to long term modulation.

Funding/Disclosures
The study was supported by the Lundbeck Foundation.

TESTING DYNAMIC SOLID STATE LIGHTING FOR IMPROVING CIRCADIAN ADAPTATION AND SLEEP N LONG DURATION SPACE FLIGHT MISSIONS

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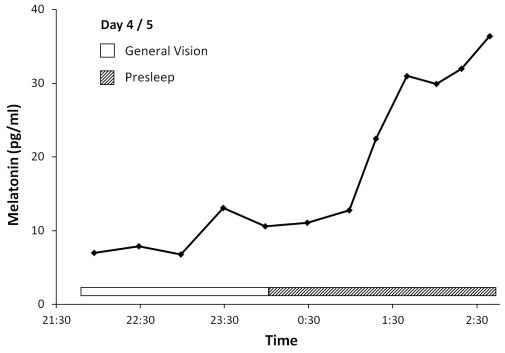
Objectives
Sleep deficiency has been documented in astronauts during space shuttle and International Space Station (ISS) missions (Barger et al., Lancet Neurol., 2014). Light can be a powerful countermeasure for both circadian misalignment and sleepiness. The ISS interior is currently illuminated with fluorescent lamps. From October 2016, there will be a staged replacement of the ISS lighting with Solid-State Light Assemblies (SSLAs) capable of three color temperature modes (NASA Specification S684-13489, 2013). The aim of the following work is to ground test light emitted by SSLAs for their efficacy in supporting astronaut operational tasks as well as effects on circadian, neuroendocrine, neurobehavioral and sleep physiology.

Methods
A Dynamic lighting schedule has been developed based on the spectral and intensity sensitivity of the human circadian photoreceptor system. The SSLAs have three pre-determined light settings, each with a unique intensity and spectrum to optimize their efficacy: 1) a General Illumination setting; 2) an Alertness/Phase Shift setting; and 3) a Pre-Sleep setting. The aim of this project is to conduct a 5-day, controlled inpatient study using astronaut-aged volunteers, to test the efficacy of an SSLA lighting protocol for daily operations. This study is being conducted in the high fidelity ISS analog crew laboratory at Thomas Jefferson University (Brainard et al., Acta Astronautica, 2013). Study subjects are randomly assigned to a 5-day exposure to either the Dynamic lighting schedule or a Static lighting schedule. Methods include visual tests, actigraphy, polysomnography, sampling for melatonin analysis, and neurobehavioral tests.

Results
Recruitment of volunteers will be ongoing until a total of 28 subjects have completed the 5-day study. To date, 10 subjects successfully have completed the study (5 in each lighting condition). This graph shows plasma melatonin values collected during the evening up until the sleep opportunity for a subject exposed to a Dynamic lighting schedule. This test subject had a sleep opportunity nightly at 03:00. Exposure to a Dynamic lighting schedule advanced plasma melatonin levels compared to their own Day 2/3 melatonin values. Comparative melatonin data, along with other empirical results will be presented.



Conclusions
This and other studies will determine if dynamically tuned SSLA lighting can be used to support astronaut vision and serve as a countermeasure for circadian and sleep disruption on the ISS.

Funding/Disclosures
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COGNITIVE PERFORMANCE AND OBJECTIVE SLEEPINESS UNDER POLYCHROMATIC BRIGHT LIGHT EXPOSURE AFTER 40 HOURS OF EXTENDED WAKEFULNESS AND ONE RECOVERY NIGHT

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Objectives
Previous studies showed that after one or multiple recovery nights following acute (i.e. Lamond et al, 2007) or chronic sleep restriction (i.e. Belenky et al, 2003) cognitive performance was still lower than at baseline. We aimed to investigate the effects of bright polychromatic light exposure on different cognitive tests and objective sleepiness after extended wakefulness and one night of recovery sleep.

Methods
Ten healthy participants (male; 25.3 ± 2.8 yrs; mean ± SD) underwent a 40 h constant routine in dim light. Hourly cognitive performance tests were performed and objective sleepiness was assessed in the wake EEG during the constant routine and during 3 h of polychromatic bright white light exposure (≈1.300 lx at the eye level) after recovery sleep.

Results
The impact of extended wakefulness on circadian performance modulation was such that after 24 hrs of wakefulness cognitive performance became worse for sustained attention (Go-Nogo, PVT) and the easier version of the working memory test (2-back; $p<0.001$). The more difficult cognitive tests (3-back, abstract reasoning test) remained at constant performance levels across 40h. Power density of the wake EEG between 0.5-5.8 Hz was significantly higher after 24h awake, indicating higher objective sleepiness ($p<0.05$). During bright light exposure after recovery sleep, performance in all cognitive tests returned to baseline levels. There was no difference in EEG power density between baseline and the light exposure morning ($p>0.1$).

Conclusions
Our results indicate that bright light exposure might facilitate restoration of cognitive performance back to baseline levels after one night of recovery sleep.

Funding/Disclosures
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DIFFERENTIAL RECOVERY OF BEHAVIORAL ATTENTION OUTCOMES, BUT NOT OTHER COGNITIVE AND SUBJECTIVE MEASURES, AFTER CHRONIC SLEEP RESTRICTION AND ACUTE TOTAL SLEEP DEPRIVATION

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Objectives
We determined whether four days of recovery sleep following sleep loss would reveal different neurobehavioral recovery dynamics after chronic sleep restriction (SR) versus after acute total sleep deprivation (TSD).

Methods
89 healthy adults (34.3 ± 9.0y; 39 females) were randomized to receive two baseline nights (BL1-2; 10h-12h time in bed (TIB), 2200h-0800/1000h) followed by five SR nights (n=44; 4h TIB, 0400h-0800h) or 36 hrs. of acute TSD (n=45). After sleep loss, all subjects received four consecutive recovery nights (12h TIB, 2200h-1000h). Neurobehavioral testing included the Psychomotor Vigilance Test (PVT), Digit Symbol Substitution Test (DSST), Karolinska Sleepiness Scale (KSS), and Profile of Mood States [POMS-Fatigue (F)] every 2h during wakefulness. Paired t-tests with corrections for multiple comparisons compared responses between baseline, sleep loss and recovery for each group. Mann-Whitney U tests compared changes in cognitive and subjective measures from baseline to each recovery night (R1-BL2, R2-BL2, etc.) between the chronic SR and acute TSD groups.

Results
As expected, acute TSD and chronic SR produced deficits in cognitive performance (PVT, DSST; p's<0.001) and increases in subjective sleepiness and fatigue (KSS, POMS-F; p's<0.001). Recovery from TSD occurred completely after one night of recovery sleep and was maintained for all neurobehavioral measures (p's<0.001). Recovery from five nights of chronic SR occurred after one night of recovery sleep and was maintained for all cognitive and subjective measures except for PVT lapses and response speed, which failed to show complete recovery after four nights of recovery sleep. Accordingly, after R1 and through R4, the chronic SR group showed significantly greater PVT deficits (more lapses, slower response speed) than the acute TSD group; no other measures differed between groups.

Conclusions
Neurobehavioral recovery from acute total sleep deprivation deficits occurred rapidly and completely across measures. PVT deficits from chronic sleep restriction, however, failed to reverse completely even after four recovery nights. Whether physiological sleep and other physiological and psychological factors contribute to these lingering behavioral attention deficits after chronic sleep restriction requires systematic examination.

Funding/Disclosures
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A SYSTEMS GENETICS APPROACH TO UNDERSTAND THE CONSEQUENCES OF SLEEP LOSS

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Objectives
Experimental and epidemiological evidence demonstrates that disrupted sleep is prevalent in our 24/7 society and can have far-reaching adverse, clinical effects such as increased risk for metabolic disorders. Although the response to sleep loss is known to have strong genetic determinants, genetic heterogeneity, epigenetic interactions, and complex gene-by-gene, and gene-by-environment interactions will ultimately determine vulnerability to disturbed sleep. We took a systems genetics approach in the mouse to map the molecular pathways regulating sleep by combining multi-level information from genotype, transcriptome, metabolome, and sleep-wake phenome with sleep deprivation (SD) as an environmental challenge.

Methods
We interrogated 41 lines of the BXD recombinant inbred mouse panel, a set of well over 100 lines in total in which two fully sequenced genomes (C57Bl/6J and DBA/2J) segregate. High-density genotype maps were constructed (11K SNPs) based on liver and cortex RNAseq and *GeneNetwork* data. We quantified 325 sleep/EEG/activity phenotypes, expression of 14.8K genes in cortex and 12.5K in liver, and 124 plasma metabolites (targeted LC/MS, FIA) under baseline and SD conditions.

Results
Quantitative Trait Locus (QTL) mapping identified 61 genome wide-significant phenotype, 22 metabolic, and several thousand expression QTLs. Also the SD response was under strong genetic control. E.g., recovery of sleep time lost yielded a significant QTL on chromosome 4, for which *Acot11* was identified as a top candidate. A cis-eQTL affecting liver *Acot11* expression, predicted this sleep rebound. Moreover, the fatty acid Phosphatidylcholine_ae_C38:2 mapped to the same QTL and its SD plasma levels strongly correlated with *Acot11* liver expression.

Conclusions
This example is only one of several illustrating how with this data set, we can readily connect genotype, mRNA, metabolite, and phenotype. Because *Acot11* is involved in fatty acid metabolism and obesity risk, these findings are of importance for the negative impact disturbed sleep can have on energy homeostasis. The results link peripheral fatty acid metabolism with sleep homeostasis and illustrate the power of systems genetics to build hypotheses on mechanistic pathways.

Funding/Disclosures
None.

THE METABOLOMIC MARKER ACETYLCARNITINE PREDICTS NEUROBEHAVIORAL PERFORMANCE DURING CHRONIC SLEEP RESTRICTION

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Objectives
Sleep loss degrades neurobehavioral functions including behavioral attention, cognitive throughput and memory, and increases sleepiness. However, there are stable and trait-like individual differences in such responses to sleep loss: some individuals show few neurobehavioral decrements (resilient), others show intermediate decrements, and others show marked decrements (vulnerable). This study examined whether metabolomic markers could differentiate such vulnerable and resilient individuals, and thus serve as biomarkers for personalized countermeasure implementation.

Methods
Ten healthy subjects (27.5 ± 5.6 y; 5 females) participated in one of two 14-18 day laboratory protocols. Metabolomic blood samples were taken following 10-12h of fasting after: 1. one night of baseline sleep [10h time in bed (TIB), 2200h-0800h]; 2. chronic sleep restriction (5 nights of 4h TIB, 0400h-0800h); and 3. one night of recovery sleep (12h TIB, 2200h-1000h). The Psychomotor Vigilance Test (PVT), the Digit Symbol Substitution Task (DSST), the Digit Span Task (DS), the Karolinska Sleepiness Scale (KSS) and the Profile of Mood States (POMS) were administered every 2h while awake. Orthogonal Partial Least Square (OPLS) regression was used for statistical analysis.

Results
Preliminary data analyses indicate the metabolite acetylcarnitine associated with 6 neurobehavioral variables during sleep loss, but not at baseline or recovery: PVT lapses and errors, PVT response speed (1/RT), DSST total correct, DS total correct, KSS scores, and POMS vigor scores. Higher levels of acetylcarnitine predicted poorer performance on the PVT, DSST, and DS, and higher KSS scores.

Conclusions
This study provides the first experimental evidence that acetylcarnitine may be a predictor of differential neurobehavioral vulnerability to sleep loss in healthy adults. Reliable prediction using valid biomarkers of who is more or less likely to experience neurobehavioral decrements from sleep loss will allow for the development of countermeasures to mitigate the disruptive effects of these changes in a variety of clinical, medical and applied settings.

Funding/Disclosures
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TEACHING COURSE LECTURE:
HOW TO SET LIGHT AND DARK FOR PERSONAL AND WORK SCHEDULES

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The biological clock in our brain determines when it is the optimal time to sleep and when it is the optimal time to work. Light is the main Zeitgeber for the human biological clock; it shifts the clock depending on timing of the exposure. A proper timing of light and darkness is therefore essential for synchronizing work and sleep schedules to the biological day and night. In this presentation the basics of circadian entrainment, the phase response curve to light and how to use this information for personalized advice will be discussed.

In the nucleus suprachiasmaticus in the human brain, about 20,000 neurons form a clock that tells our body what time it is. It regulates periodicity in numerous behavioral and physiological variables, of which the sleep-wake cycle is a very prominent one. This endogenous clock runs with a period slightly deviating from 24h. If not adjusted, behavioral and physiological rhythms will desynchronize with the natural light-dark cycle and our social clock. Light and darkness are the most important signals in the outside world that are able to adjust the phase of the endogenous clock. Light that enters the eye shifts the clock depending on timing, intensity, spectral composition and duration of the light exposure. Especially the short wavelengths of light (blue light, or the blue part of full spectrum light) are most effective in inducing phase shifts. A specialized photoreceptor in the retina contains a photopigment, melanopsin, which is sensitive to the blue part of light. This cell sends the information on environment light to the endogenous clock.

A Phase Response Curve (PRC) describes the relationship between the timing of light exposure relative to the endogenous phase of the clock and its phase shifting effect. Light in the late subjective evening/early night, shortly before the temperature minimum, induces the largest phase delays. Light in the early subjective morning, shortly after the temperature minimum induces the largest phase advances. But at what time is the subjective morning and subjective evening? Differences exist in timing of the sleep-wake cycle between individuals and this result in a wide distribution of so-called chronotypes in society. Some characteristics of the endogenous clock may underlie the individual differences, but exposure to light and darkness may either reinforce or counteracts the differences.

The use of appropriate exposure to light and darkness with the purpose to shift circadian rhythms, or to prevent shifts, needs knowledge of the individual's endogenous phase. The most robust rhythm to measure endogenous phase is the melatonin rhythm. If it is not possible to measure melatonin, the phase of the sleep wake cycle may be used as a reasonable estimate for starting light treatment at a proper phase. Recent data will be discussed showing the use of light treatment to induce phase shifts and the misuse of light resulting in desynchronization.

Funding/Disclosures
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MOVING CHRONOTHERAPEUTICS INTO OUTPATIENT PRACTICE

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Objectives
The science of chronobiology and the practice of psychiatric chronotherapeutics has failed to diffuse into mainstream mental health care. This failure is especially apparent in the outpatient sector where more rapid and effective treatments are so urgently needed. This presentation will consider some underlying causes for this state of affairs, discuss some corrective actions to facilitate a more rational deployment of outpatient chronotherapeutic practices, and identify particular conditions whose treatment may encourage adoption of chronobiologically-based interventions.

Methods
The clinical experience of this author, in his role as Medical Director of an outpatient practice specializing in the evaluation and treatment of cyclic affective disorders, will be reviewed. Systematic observations, anecdotal experience, case reports, and referral patterns will be used to address the potential role of chronotherapeutics in outpatient psychiatric practice.

Results
Chronotherapeutics has a vital, indispensable role to play in the outpatient management of recurrent affective illness. This especially applies to the following specific conditions: rapid cycling, mixed states, mood syndromes with seasonal features, disorders requiring rapid amelioration, and in those individuals who are averse and/or unable to use pharmacotherapy or psychotherapy. Practice structures that emphasize general clinical expertise over particular modalities or treatment approaches support the incorporation and utilization of chronotherapeutic methods.

Conclusions
Chronotherapeutic practices can be successfully exported into mainstream mental health care through careful focus on specific conditions and with a practice organization that emphasizes superior clinical care and outcomes instead of singular therapeutic approaches.

Funding/Disclosures
None.

MELATONIN SUPPRESSION VIA NIGHTTIME LIGHT EXPOSURE IN ADULT MEN STIMULATES GROWTH AND METABOLISM OF TISSUE-ISOLATED, ANDROGEN INDEPENDENT HUMAN PROSTATE CANCER XENOGRAFTS IN NUDE RATS: EFFECT OF WAVELENGTH

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Objectives
Humans are regularly exposed to varying degrees of electrical lighting at night. Light exposure at night disrupts the central circadian timing system located in the suprachiasmatic nucleus (SCN) within the hypothalamus of the brain. The most reliable circadian output signal of the SCN is the nighttime pineal gland production of melatonin. The endogenous circadian melatonin signal is a potent inhibitor of the processes governing prostate carcinogenesis. Melatonin is suppressed in a wavelength, duration and intensity-dependent manner when exposing the eyes to light at night. This study preliminarily examined, within subjects, the effects of equal photon exposures to monochromatic light at wavelengths of 480 and 630 nm during darkness on blood melatonin levels, prostate tumor signal transduction, metabolism and growth.

Methods
On each test day, each subject (N=3) donated a total of 3 blood samples: one during daylight hours in the early afternoon, one at night following 2 hours of exposure to complete darkness at 0200 h and one again after a 90 minute exposure to one of the equal photon flux of monochromatic light (480 or 630 nm) conditions or a dark control condition. Blood samples were shipped to Tulane University overnight on ice where tumor perfusions were completed on tissue-isolated PC3 human prostate xenografts growing in male nude rats.

Results
Perfusion results showed substantial reductions in tumor cAMP levels, total fatty acid and linoleic acid uptake, 13-hydroxyoctadecadienoic acid production, glucose uptake, O_2 consumption and CO_2 production, and [^{3}H] thymidine incorporation into tumor DNA for melatonin-rich dark control and nighttime/630 nm light exposure-collected samples compared to tumors perfused with daytime and nighttime/480 nm light exposure-collected, melatonin-diminished blood samples.

Conclusions
These findings show that blood collected from human subjects exposed to short wavelength (480 nm) light at night markedly stimulates human prostate cancer growth, signal transduction and metabolic activity when compared to long wavelength light (630 nm) or darkness. These changes likely occur via suppression of the nocturnal circadian melatonin signal.

Funding/Disclosures
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LIVING IN BIOLOGICAL DARKNESS

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Objectives
Light during the day and darkness at night are crucial factors for proper adaptation of the human circadian system to the 24h-day. We tested whether bright blue-enriched morning light over several days could counteract detrimental effects from inadequate daytime and evening lighting.

Methods
In a semi-naturalistic within-subject study design, 18 young participants were exposed to three different (bright blue-enriched, bright orange, dim) lighting conditions in the evenings and to two different lighting conditions (bright blue-enriched and control light) in the morning. The control lighting condition in the morning mimicked low daytime lighting conditions. Subjective sleepiness, reaction times, salivary melatonin concentrations and nighttime sleep using polysomnography were assessed.

Results
Acute effects of the blue-enriched morning lighting included wake-promoting and faster response times ($F>19.8$; $p<0.0001$). Also, in the early evenings, participants performed faster in the PVT when they had the blue-enriched morning lighting condition, compared to the control ($F_{3,341}=3.49$; $p=0.02$). Participants had more light sleep (N2) and less EEG power density in higher frequencies (14.2-16.8 Hz; 17.4-18 Hz; 19.4 and 19.8 Hz) during their night sleep episodes after the bright morning lighting condition ($p<0.05$). Most importantly, the summated circadian phase shifting effects, induced by combinations of different evening and the two morning lighting conditions, were significantly smaller with the blue-enriched morning light ($F_{1,43}=5.78$; $p=0.02$; $N=10$).

Conclusions
Bright blue-enriched morning light has positive repercussions on morning and evening performance and stabilizes the circadian phase across several days. It could be an effective counterstrategy for insufficient lighting during the day or light at the wrong time.

Funding/Disclosures
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INCREASED APPETITIVE SYMPTOMS DIFFERENTIALLY PREDICT TREATMENT RESPONSE TO MEDICATION, LIGHT AND PLACEBO IN NON-SEASONAL MAJOR DEPRESSION

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Objectives
Our recent randomized placebo-controlled study reported that bright light treatment is efficacious in adults with non-seasonal major depression (JAMA PSYCHIATRY, Jan. 2016). As increased appetitive symptoms predict response to light therapy in seasonal affective disorder (SAD), we examined whether the same held true in these non-seasonal patients.

Methods
In total, 122 patients with non-seasonal MDD were randomly assigned to light monotherapy, fluoxetine, combination light and fluoxetine or double-placebo. Multiple regression assessed the percentage change in MADRS scores based on treatment condition, overeating symptom score (sum of 3 items on the SIGH-SAD), and the condition by overeating interaction.

Results
The treatment condition by overeating interaction was a strong predictor of MADRS change scores (t=2.65, p=.009). The relationship between overeating scores and drop in depression scores was strongly negative in the placebo group (i.e. more overeating symptoms, less response; beta = -2.50, SE =1.45) and strongly positive in the group receiving both fluoxetine and light therapy (beta = 3.49, SE 1.77) or fluoxetine alone (beta = 2.79, SE 1.86). In contrast to established work in seasonal affective disorder, the group that received light therapy alone did not show a strong relationship between overeating symptoms and treatment outcome.

Conclusions
Increased appetitive symptoms at baseline predicted treatment response differentially across the four treatment groups. Contrary to prior findings in SAD, this moderating effect was strongest for patients receiving medication with or without light therapy, but was not manifest in the light therapy only group. A further novel finding was the negative relationship between increased appetitive symptoms and treatment outcome in the double-placebo group.

Funding/Disclosures
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ARCTIC LIGHT EXPOSURE AT TWO SEASONS AND EFFECT ON MOOD AND RECOVERY

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Objectives
The importance of light in regulation of circadian rhythms has been known as a crucial influence on life, however, little is known about seasonal differences related to daylight exposure. The aim was to test how daylight exposure influences sleep in shift and daytime work. We saw a unique opportunity to examine the scarcity of light in northern Sweden (latitude 67°86'), above the Arctic Circle.

Methods
1800 miners working both above and underground were invited to participate in a sleep and light questionnaire study in winter (n=1291) and summer (n=909) using a paired t-test to study mean seasonal differences.

Results
Shift workers (3-shift and 2-shift) but not daytime workers consistently followed the same regular sleep patterns (sleep timing and sleep length) regardless of season at different shifts. Daytime workers slept longer in winter on days off ($p<0.01$) mainly due to later waking (winter 08:33 hr ± 0.49; summer 08:05 hr ± 0.59; $p<0.001$). Both shift workers and daytime workers reported sleep in winter more often being interrupted by awakenings ($p<0.016$), contained more premature awakenings and workers feeling less refreshed by sleep ($p<0.001$). Also more sleepiness, fatigue and lack of energy during work were reported in winter ($p<0.01$) in all groups.
60% felt seasonal changes and increases of low mood and fatigue in winter. Light exposure in connection to both workdays and days off in winter was associated with lowered mood and fatigue. A regression analysis demonstrated that the likelihood to develop winter problems was reduced by 30% for every extra half hour workers spent out-doors.

Conclusion
The dark period of the year is reported to increase with mood and sleep complaints that possible are associated with daylight exposure. We show that shift workers had a more stable seasonal sleep than daytime workers but sleep quality was lowered in winter independent of work hours. Most likely the day light influence in the summer supports sleep quality and daytime alertness that compensate despite the observed sleep loss for day workers.

Funding/Disclosures
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NON-VISUAL LIGHT SENSITIVITY IN INDIVIDUALS SUFFERING FROM A DELAYED SLEEP SCHEDULE

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Objectives
Inability to advance bedtime to meet social requirements is associated with a late circadian phase. Evening light exposure delays circadian rhythms with maximal effect with blue light (460-480nm) to which the non-visual system of light perception is most sensitive. Hence, increased sensitivity to evening blue light may contribute to the late circadian phase in individuals suffering from delayed sleep schedule. We used a test of melatonin suppression to examine circadian sensitivity to blue light in healthy young subjects complaining of a late sleep schedule, compared with subjects with a more adapted sleep schedule.

Methods
14 young adults (19-28 y.; 8F/6M) complaining of delayed sleep schedule were compared to matched subjects with an adapted sleep schedule. Habitual bedtime (HB) was after midnight in all delayed subjects (01:36± 1:14h) and before midnight in all adapted subjects (23:15± 0:14h). Subjects followed their HB (±1h) for one week and the laboratory protocol was individually adjusted to HB. Subjects were admitted 5h before HB and kept in dim light (<5 lux) for 6h. They were then exposed for 1.5h to blue light using light panels with inserted blue filters (280µW/cm2, 6.8x1014 ph/cm2/sec at 460 nm), for a photometric illuminance of ~500 lux. Salivary melatonin and subjective sleepiness (KSS) were assessed every 30 min. Melatonin suppression was computed after 30, 60 and 90 min of light exposure. Dim light melatonin onset (DLMO) was used to estimate circadian phase.

Results
DLMO was later in the delayed than in the adapted group (23:03± 01:27h *vs*. 21:13± 1:00h, p=0.001). There was no difference for melatonin suppression averaged over the 1.5h of light exposure (delayed: 36.2± 29.0%, adapted: 38.6± 26.6%, p=0.98). However, in the delayed group, there was a significant correlation between DLMO and melatonin suppression after 30 (r= 0.58, p= 0.04) and 60 min (r=0.66, p= 0.02), but not after 90 min (r=0. 47, p= 0.12) of light exposure. There was a smaller increase of subjective sleepiness in the delayed subjects than in the adapted subjects before HB, but no difference during blue light exposure.

Conclusions
Results do not support the hypothesis that individuals complaining of a late sleep schedule are more sensitive to blue light compared to volunteers having an adapted sleep schedule. However, among delayed subjects, enhanced sensitivity to blue light may contribute to the severity of the circadian phase delay. The slower increase of subjective sleepiness before HB in delayed subjects may also contribute to the maintenance of a late sleep schedule.

Funding/Disclosures
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TEACHING COURSE LECTURE: THE BIOLOGY OF CIRCADIAN RHYTHMS

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Objectives
This session will describe the physical and biological principles underlying circadian rhythms and light's antidepressant effects. Specific factors that will be detailed include the photoreceptor cells and molecules, the wavelengths of light thought to regulate these processes, the anatomic organs and neurological pathways that mediate these processes, and the chemical output of these pathways.

Methods
A synthetic review for teaching purposes.

Results
Living organisms are made up of millions of cells with their own biological clocks. Many physical aspects of the biological clock in humans and other mammals have been identified. Components include input pathways from the eyes to the master clock in the suprachiasmatic nuclei (SCN), gene regulation within the SCN, electrical signaling from the SCN to the pineal gland via a specialized spinal tract, and release of melatonin to circulate in the body via the bloodstream. Melanopsin, and rod and cone photoreceptors all contribute to detecting the presence of clock-regulating external light. And yet these cells are not the only known biological clock regulating photoreceptors, at least in the retina. Separately, humoral phototransductive mechanisms suggesting a role for CO as a transducer is beginning to emerge. The SCN is a color and irradiance signal processor, capable of synthesizing external environment intensities and wavelengths of light detected via intrinsically photosensitive retinal ganglion cells into a coherent clock signal. The SCN synchronizes peripheral clocks via humoral and neuronal outputs. As it is itself a collection of independent clocks (bilaterally distributed in the hypothalamus), its coordination is driven by LHX1 protein. Its anatomy includes a shell and core with likely different pacemaker and phase-shifting functions. The clock in the SCN and most mammalian cells operates via a negative feedback loop between production of CLOCK and Bmal1 transcription factors and clock-controlled genes including Per1, Per2, Cry1, and Cry2.

Conclusions
Core aspects of the "time-setting knob", the "internal hardware", and the "hands" of the biological clock are now well understood. Yet, there are interspecies differences in anatomy and mechanisms. New aspects and nuances (including hitherto unappreciated differences between the anatomy of diurnal and nocturnal animals) are continually being discovered.

Funding/Disclosures
None.

DEVELOPMENT AND IDENTIFICATION OF THE MELATONIN-PRODUCING PINEALOCYTE

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Objectives
The pineal gland is a neuroendocrine organ responsible for nocturnal synthesis of melatonin. During early development of the rodent pineal gland from the roof of the diencephalon, a number of homeobox gene-encoded transcription factors are expressed in the gland; these are essential for normal pineal development consistent with the well-established role that homeobox genes play in developmental processes. However, the pineal gland appears to be unusual because strong homeobox gene expression persists in the pineal gland of the adult rodent brain. Accordingly, in addition to developmental functions, homeobox genes appear to be key regulators in postnatal phenotype maintenance of the principal cell type of the pineal gland, the pinealocyte. Production of melatonin is believed to be a defining characteristic of this postnatal pinealocyte phenotype; however, melatonin synthesis in the rodent pineal gland has not been localized at the cellular level.

Methods
The work is based on knowledge from detailed developmental and daily gene expression analyses, immunohistochemical colocalization studies, pineal phenotypes of knock out mice, and shRNA studies on cultured pinealocytes.

Results
The presented results will focus on ontogenetic aspects of pineal development and recent progress in demonstrating the involvement of homeobox gene-encoded transcription factors in rodent pineal development and adult function. A working model is proposed for understanding the sequential action of genes in controlling development and mature circadian function of the mammalian pinealocyte. Further, to characterize the phenotype of the mature pineaolcyte, novel advances in our understanding of the cellular localization and heterogeneous distribution of melatonin synthesis in the gland will be presented.

Conclusions
Our model depicts that homebox gene-encoded transcription factors represent a molecular link between cell development and cellular melatonin synthesis. However, the mature pinealocyte phenotype appears to represent diverse molecular and metabolic cellular identities with only a subpopulation of pinealocytes devoted to final melatonin production.

Funding/Disclosures
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LIGHT AND NIGHT AND CANCER RISK: THE EPIDEMIOLOGICAL EVIDENCE

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Melatonin (5-methoxytryptamine) is an indoleamine produced primarily by the pineal gland, which is secreted exclusively during the dark phase of the light-dark cycle in humans. Several decades ago, reports indicated that melatonin possesses oncostatic properties, leading to novel hypotheses that diminished secretion of melatonin might promote the development of cancer. Growing evidence also demonstrates that visible light, including electric light, can acutely suppress melatonin production– a phenomenon often referred to as "circadian disruption" particularly if it occurs at night, as commonly observed in shift workers.

In 2007, the International Agency for Research on Cancer classified shift work as a possible carcinogen, based on convincing experimental evidence and supportive, but still limited, epidemiologic data. Indeed, experimental data has consistently demonstrated that circadian disruption can promote carcinogenesis in animals; specifically, exposure to light at night and phase shifts in the light-dark cycle have accelerated tumor development in rodents (reviewed in). In humans, epidemiologic data continues to accumulate, with the majority of existing studies indicating that shift work is related to a modest increase in the risk of breast cancer. A recent systematic review and meta-analysis, published in 2013, found that women with a history of night shift work had a 21% higher risk of breast cancer compared to women without night work experience (RR=1.21, 95% CI=1.00-1.47). Initial studies have identified links between shift work and other cancers as well, although this evidence is very limited.

Increasing evidence also suggests that shift workers are more often obese than non-shift workers, which has been attributed, in part, to the negative effects of circadian disruption on glucose and lipid metabolism and reduced thermogenesis related to eating food at night. The direct effects of circadian clock genes have been implicated in metabolism and therefore may contribute to these mechanisms as well. In addition, obesity is an important risk factor for many cancers, including breast cancer, endometrial cancer, colorectal cancer, among others. As a result, obesity is a potential mediator of the observed association between shift work and cancer risk, and it is important to appraise whether previous analyses have evaluated this hypothesis. In this presentation, I will provide an overview of the underlying biology and review epidemiologic studies of shift work and cancer risk, with additional emphasis on the role of sleep, chronotype, metabolism and obesity in this association.

Funding/Disclosures
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MICE LACKING CIRCADIAN CLOCK COMPONENTS DISPLAY DIFFERENT MOOD-RELATED BEHAVIORS AND DO NOT RESPOND UNIFORMLY TO CHRONIC LITHIUM TREATMENT

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Objectives
Genomic studies suggest an association of circadian clock genes with bipolar disorder (BD) and lithium response in humans.

Methods
We tested mice mutant in various clock genes before and after lithium treatment in the forced swim test (FST).

Results
We find that expression of circadian clock components, including *Per2*, *Cry1* and *Rev-erbα*, is affected by lithium treatment. In particular we observed that *Cry1* is important at specific times of the day to transmit lithium-mediated effects. Interestingly, the pathways involving *Per2* and *Cry1* are distinct as evidenced by the phosphorylation of GSK3β after lithium treatment and the modulation of dopamine levels in the striatum. Furthermore, we observed the co-existence of depressive and mania-like symptoms in *Cry1* knock-out mice, which resembles the so-called mixed state seen in BD patients.

Conclusions
Per2, *Cry1* and *Rev-erbα* may modulate the beneficial effects of lithium therapy. The results strengthen the concept that a defective circadian timing system may impact directly or indirectly on mood-related behaviors.

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LIGHT THERAPY FOR BIPOLAR DEPRESSION:
A RANDOMIZED, PLACEBO-CONTROLLED TRIAL

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Objectives
Building on our pilot findings, we conducted a 6-week randomized, double-blind, placebo-controlled trial to investigate the efficacy of midday light therapy for bipolar depression. We examined the change in depression levels and remission rates in patients randomized to active-light versus the inactive comparator.

Methods
We included depressed adults with SCID-confirmed BD-Type I or II, on stable-dosed antimanic medication. Patients were randomized to 7000lux broad-spectrum light therapy OR 50lux dim red light. Weekly, we assessed depression levels with the Structured Interview Guide for the Hamilton Depression Scale with Atypical Depression Supplement (SIGH-ADS), emergent mania with the Mania Rating Scale, suicidality with the Scale for Suicidal Ideation and sleep disturbances which affect sleep quality on the Pittsburgh Sleep Quality Index.

Results
We randomized 23 patients to the broad-spectrum light and 23, the inactive-control. The baseline SIGH-ADS indicated moderately-severe to severe depression levels in the active-light and control groups (26.1±5.2 and 30.1±6.1, U(1)=5.68, p=0.02, respectively). Thirty-seven (80%) patients completed the study. At Week 6, patients in the active-light versus control groups had significantly reduced SIGH-ADS (10.4±8.1 vs 17.3±9.53; U(1)=5.651, p=0.0053, f=0.41, large effect), and higher remission rates (SIGH-ADS<8)(56.5% ,13/26 and 14.3%, 3/26, OR=8.264, p=0.005) respectively. None experienced a mood polarity switch or emergent mania. Treatment expectations did not differ significantly between groups. From Week 0 to 6, patients in both groups reported increased in sleep quality (8.31±3.45 vs 6.54±3.07) and reduced suicidal ideation (11/46=24% vs 5/46 =11%), respectively.

Conclusions
Original findings indicated bright light therapy was effective for the treatment of bipolar major depression. After 6-weeks, patients randomized to midday light therapy experienced significantly higher rates of remission and a significant reduction in depression symptoms compared to patients randomized to the inactive-control. The decrease in suicidal ideation and improved sleep quality reported by patients in both treatment groups suggested non-specific effects may contribute to clinical improvement.

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CHRONOTHERAPY FOR TREATMENT RESISTANT DEPRESSION?

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Objectives
To gain an initial sense of whether chronotherapy can be effective treatment for nonbipolar depression which has not responded to adequate trials with antidepressant medications.

Methods
Study #1: Physically healthy, non-psychotic, non-substance using adults aged 18-60 who had not benefited sufficiently from ≥ 4 weeks taking ≥ ⅔ PDR maximum dose of two antidepressant medications thought to have different mechanisms and meeting DSM-IV criteria for a nonbipolar affective disorder completed sleep logs for 1-2 weeks and the Morningness-Eveningness Questionnaire (MEQ) and determined their desired sleep time. They entered the hospital where three Wake Nights alternated with 8 hours of allowed sleep (6 hours pre-desired, then 3 hours pre-desired, then desired thereafter). From the morning following their initial Wake Night, they sat in front of 10,000 Lux light for ½ hour at their desired wake-up time. Throughout, standard mood ratings were obtained, daily for the first week and otherwise weekly.
Study #2: Physically healthy, non-psychotic, non-substance using adults aged 18-65 meeting DSM-5 criteria for non-bipolar affective disorder completed the MEQ and the ATHF, determined their desired sleep time, then remained awake (at home) approximately 36 hours following which they were allowed to sleep desired – 6 hours, desired – 3 hours and desired sleep time thereafter. Throughout, sleep logs and activity monitoring were collected as well as weekly mood ratings and daily mood ratings during the week following their Wake Night. We will report on those who had not benefited from 1 or more adequate trial of an antidepressant medication (TRD).

Results
Study #1: N = 8; 3 (38%) were remitted at 1 and 6 weeks; 50% responded.

Study #2: N = 10, including 3 with TRD; 2 (67%) were remitted at 1 and 6 weeks; 67% responded. 1 (9%) of the 11 patients was remitted on the day following his Wake Night.

Conclusions
To the extent conclusions can be drawn from open treatment, it appears that about half the patients with TRD may benefit from Chronotherapy, but not over night as occurs in about 60% of depressed patients who have bipolar disorder. Chronotherapy Lite (i.e., a single Wake Night) is doable on an outpatient basis and is worthy of further research.

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SYSTEMATIC LIGHT EXPOSURE IMPROVES DEPRESSION AMONG CANCER SURVIVORS

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Objectives
Depression is one of the biggest challenges faced by cancer survivors even 10 years after all treatment has ended. These survivors might benefit from systematic light exposure (sLE) using bright white light as it has been found to be effective in reducing depression among other populations suffering from depression. sLE has also been found to normalize circadian activity rhythms which are disrupted both among cancer patients/survivors and depressed individuals. The aim of the present study was, therefore, to examine the effectiveness of sLE in reducing depression and restoring circadian activity rhythms among cancer survivors.

Methods
Fifty-four cancer survivors were randomized to either a BWL (n=28) or a standard comparison group – dim red light (DRL) (n=26) exposure. Participants were instructed to self-administer the light, using Litebook®, for 30 minutes every morning throughout the four-week intervention period. Depression (Brief Symptom Inventory) and circadian activity rhythms (actigraphs) were assessed at: Baseline, 2-weeks into the intervention, at the end of the 4-week intervention, and three weeks after the completion of the intervention.

Results
A Linear Mixed Model (LMM) analysis of depression revealed that the group by time interaction was significant [$F(3,44) = 3.43$; $p = 0.025$] with depression being significantly lower in the BWL group compared to the DRL group at the end of the intervention and at the final assessment. The LMM analysis of overall rhythmicity (f-statistic) indicated that the group by time interaction was significant [$F(3,43) = 5.39$; $p = 0.0031$] with the BWL group having a significantly higher f-statistic (more rhythmicity) than the DRL group by the final assessment

Conclusions
Providing sLE via bright white light may provide a non-invasive, innovative way to decrease depression among cancer survivors and normalize circadian rhythms, which are vital for health and well-being.

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BLUE LIGHT EXPOSURE BEFORE BEDTIME IN SUBJECTS COMPLAINING OF A DELAYED SLEEP SCHEDULE

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Objectives
Young adults frequently show sub-clinical features of delayed sleep phase disorder characterized by a chronic inability to advance the timing of their sleep episode to accommodate standard work schedules. Exposure to evening light, especially blue light (~480 nm), produces a circadian phase delay and may therefore be involved in the late increase of sleep propensity observed in individuals suffering from a delayed sleep schedule. The objective of this study was to compare blue light exposure in relation to habitual bedtime (HB) between young adults complaining of a delayed sleep schedule and age-matched volunteers having an adapted sleep schedule.

Methods
14 young adults (19-28 y.; 8F/6M) complaining of a delayed sleep schedule (bedtime: 01:36 ± 0:14h) were matched to 14 volunteers with an adapted sleep schedule (bedtime: 23:15 ± 1:14h). Subjects wore an ambulatory light monitor (Actiwatch Spectrum) as a pendent or pinned at the shoulder to record 24-h light exposure for 7 consecutive days. Subjects kept their HB (±1h) all week and filled out a sleep/light diary in which they reported the use of light-emitting devices (TV, computer, tablets, and cellphones) in the 3 h before bedtime. Data from the blue sensor were adjusted to a peak sensitivity at 480nm (Price et al, 2012) and log-transformed. Hourly means in relation to HB were averaged over the 7 days of recording and expressed as % of the 24-h mean to show the results as 24-h profiles of blue light exposure. Groups were compared using a 2x24 ANOVA and correlations between HB and light exposure before bedtime were computed.

Results
Subjects with an adapted sleep schedule were relatively more exposed to blue light in the daytime (4 to 9h before HB), whereas delayed individuals were relatively more exposed to blue light in the evening, during the 1-to-2h interval before HB. There was a positive correlation between HB and relative blue light exposure in the 1-to-2h interval before HB ($r=0.37$; $p=0.05$). Delayed subjects used more light-emitting devices during the 3 h before bedtime ($p=0.01$). A positive correlation was found between relative blue light exposure in the 1-to-2 h interval before bedtime and duration of computer use during the second hour prior to bedtime ($r=0.50$; $p=.007$).

Conclusions
Results support the hypothesis that individuals complaining of a late sleep schedule are relatively more exposed to blue light before bedtime compared to participants having an adapted sleep schedule. This light profile favors a late circadian phase and a delay in the circadian increase of sleep propensity. Increased exposure to evening blue light was associated with a greater use of light-emitting devices, mostly computers, which could contribute to a delayed sleep schedule.

Funding/Disclosures
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TEACHING COURSE LECTURE:
PSYCHOLGICAL FACTORS IN THE ETIOLOGY AND TREATMENT OF SEASONAL DEPRESSION

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Objectives
1. The participant will be able to describe the mechanisms by which depressive cognitive processes contribute to the symptomatology of SAD.
2. The participant will be able to plan behavioral strategies to maximize the effectiveness of light treatment for SAD.
3. The participant will be able to plan modifications of cognitive behavioral therapy for use with SAD clients.

Research on winter depression (including diagnosable seasonal affective disorder) has generally focused on biological processes. However, over 2 decades of research indicates that psychological depressive processes that are well-documented in unipolar depression also play a role in the etiology of SAD. These processes include rumination, negative causal attributional style, and loss of reinforcement contingency. Several randomized clinical trials have shown that interventions based on these processes can be applied to reduce seasonal symptomatology. This variant of cognitive behavioral therapy is straightforward for therapists trained in CBT to learn. In addition, as with many medical interventions, much of the success of light treatment depends on adherence to the treatment protocol and accurate feedback from the patient to the clinician. Enhancing adherence can be achieved through the use of psychoeducation, motivation enhancement, effective scheduling, and self-monitoring. Procedures for working with patients in these areas are part of standard clinical skills for behavioral health psychologists and are skills that can be learned with and intentionally applied by clinicians using light therapy.

Conclusions
Understanding the role of psychological factors enhances our ability to understand the etiology of seasonal depression as well as improve the outcomes of our patients.

Funding/Disclosures
None.

PRELIMINARY DATA ON TREATMENT RESPONSE AND FEASIBILITY OF OUTPATIENT TRIPLE CHRONOTHERAPY

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Objectives
Present preliminary data on treatment response and feasibility of an intensive-outpatient triple chronotherapy treatment program for the treatment of unipolar and bipolar depression. A case will be presented and the following topics discussed: potential barriers, use of novel monitoring methodologies, protocol development/implementation, and future directions. Primary objective in sharing this information is to inform others of this potential treatment option and to promote the development of further research programs aimed at extending these findings.

Methods
Adult subjects with current unipolar or bipolar depressive episode recruited via local treatment providers. Measurements obtained at: intake, days 2-5 of protocol, 7-day follow-up, and 28-day follow-up. Measures utilized include: ASRM, HAM-D6, MEQ, MINI-v5, QIDS-SR16, SIGH-ADS, and YMRS. Subjects wore actigraphic monitoring device (ActTrust, Condor Instruments) to capture data on light, activity, and temperature from intake through 7-day follow-up. Active treatment phase is approx. 4 days in duration: 1 night of total sleep deprivation (TSD) followed by 3 nights of sleep phase advance (SPA; 6PM-1AM, 8PM-3AM, 10PM-5AM). Bright light therapy (BLT) administered after TSD and each morning afterward (30' per day at MEQ-based time for unipolar subjects; 5-10' at 12 noon for bipolar subjects). Twice daily measurements obtained on all active treatment phase days: modified ASRM at 7 am and at 1 pm with modified modified HAM-D6. Adherence and safety monitoring conducted via optional use of medication-monitoring application in addition to twice-daily phone check-ins.

Results
Remission, defined as HAM-D6 score below 7, typically obtained in active treatment phase. Remission maintained at 7- and 28-day follow-up. Inverse relationship between HAM-D6 and ASRM scores observed. No adverse reactions observed.

Conclusions
Preliminary results indicate consistent, rapid reduction in depressive symptomatology to remission with maintenance through 28-day follow-up period for bipolar depression. Results suggest protocol may function as cost-effective outpatient version of comparable and well-researched in-patient triple chronotherapy treatment programs. Future research is essential in confirming these and other findings to ensure treatment safety and efficacy for use with outpatient clinical populations.

Funding/Disclosures
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NIGHT SLEEP INFLUENCES WHITE MATTER MICROSTRUCTURE IN BIPOLAR DEPRESSION

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Objectives
Alteration of circadian rhythms and sleep disruption are prominent trait-like features of bipolar disorder (BD). Diffusion tensor imaging (DTI) measures suggest a widespread alteration of white matter (WM) microstructure in patients with BD. Sleep promotes myelination and oligodendrocyte precursor cells proliferation. We hypothesized a possible association between DTI measures of WM microstructure and sleep quantity measures in BD.

Methods
We studied 69 inpatients affected by a depressive episode in course of type I BD. We used whole brain tract-based spatial statistics on DTI measures of WM microstructure: axial, radial, and mean diffusivity (AD, RD, MD), and fractional anisotropy (FA). Self-assessed measures of time asleep (TA) and total sleep time (TST) were extracted from the Pittsburgh Sleep Quality Index (PSQI). Actigraphic recordings were performed on a subsample of 23 patients. Self-assessment of TA and TST on PSQI significantly correlated with actigraphic measurements (TA $r=0.51$, $p=0.026$; TST $r=0.6$, $p=0.007$).

Results
We observed a positive correlation between DTI measures of fractional anisotropy (FA) and subjective measures of TB and objective measures of TST, that were also both inversely correlated with radial diffusivity (RD). Several WM tracts were involved, including left superior and inferior longitudinal and fronto-occipital fasciculi, anterior thalamic radiation, reticular part of internal capsule and corticospinal tract.

Conclusions
This is the first study investigating the role of sleep duration in affecting the WM microstructure integrity in BD. Reduced FA with increased RD and MD suggests dismyelination or demyelination. Our findings indicate that the trait-like alteration of sleep, typical of this disorder, could lead to detrimental changes of oligodendrocyte precursor cells proliferation and myelination of white matter tracts which underpin the functional connectivity of the brain.

Funding/Disclosures
None.

CLOCK GENES ASSOCIATE WITH WHITE MATTER INTEGRITY IN DEPRESSED BIPOLAR PATIENTS

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Objectives
Bipolar disorder (BD) is a progressive and disabling psychiatric condition associated with neurostructural changes and disruption of circadian rhythms. CLOCK and Period3 (PER3) genes are involved in the control system of circadian rhythms. A single nucleotide polymorphism in the 3' flanking region of CLOCK (3111 T/C; rs1801260) is known to influence occurrence of insomnia, response to treatment of sleep complaints, and lifetime recurrence rate of illness episodes in patients affected by BD. A variable-number tandem-repeat polymorphism of PER3 ($PER3^{4/5}$) was found to influence age at onset in bipolar patients and characteristics of temperament and cognitive performance in response to sleep loss in healthy subjects. Diffusion tensor imaging (DTI) measures suggest a widespread alteration of white matter (WM) microstructure in patients with BD. We hypothesized that these two polymorphisms of the biological clock could be associated with WM microstructure integrity in bipolar patients.

Methods
We studied the relationship between CLOCK and PER3 polymorphisms with WM integrity in a sample of 98 depressed bipolar patients. First we compared the DTI measures of patients carriers of the mutant C allele and of T homozygotes for CLOCK gene. Then we analyzed differences in WM microstructure between the two homozygote groups for $PER3^4$ and $PER3^5$ polymorphisms. We used whole brain tract-based spatial statistics in the WM skeleton with threshold-free cluster enhancement on the DTI measures: axial, radial, and mean diffusivity, and fractional anisotropy.

Results
In regard to CLOCK gene, we found that, compared to T homozygotes, C carriers showed a widespread increase of mean diffusivity in several WM tracts, including superior and inferior longitudinal fasciculus, corpus callosum, uncinate fasciculus, medullary lamina of thalamus, and corona radiata. No significant difference has been observed for fractional anisotropy, axial, and radial diffusivity. Additionally, $PER3^4$ homozygotes showed reduced fractional anisotropy and increased radial diffusivity compared to $PER3^5$ homozygotes in several WM tracts, including thalamic radiations, inferior longitudinal and fronto-occipital fasciculus, and internal capsule.

Conclusions
Mean diffusivity (MD) measures the magnitude of water molecules diffusion and correlate with membrane density and myelin integrity. Increased MD indicates myelin degeneration. Radial diffusivity associates the integrity of myelin sheaths, while fractional anisotropy reflects the structure of axonal cell membranes, myelin sheaths, and bundle coherence within the WM tracts. Therefore, our result highlights greater damages to myelin in C carriers for CLOCK gene, and to $PER3^4$ homozygotes in regard to PER3. This finding suggests that CLOCK and PER3 genes could enhance the negative influence of BD on WM microstructure, with specific detriments resulting from effects on specific WM tracts contributing to the functional integrity of the brain and involving critical networks for bipolar symptomatology.

Funding/Disclosures
None.

ABNORMAL BRAIN OSCILLATIONS PERSIST AFTER RECOVERY FROM BIPOLAR DEPRESSION

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Objectives
Fast EEG neural oscillations have been found to be markedly reduced in schizophrenia, bipolar disorder and major depressive disorder, suggesting a common neurobiological mechanism of cortico-thalamic impairment. However, it still remains unclear if these abnormalities change over time, and no longitudinal study has yet assessed high-frequency oscillations in bipolar disorder (BD) before and after response to antidepressants.

Methods
Here we employed TMS/EEG to assess the frontal natural oscillatory activity in eighteen BD patients before and after antidepressant treatments (sleep deprivation and light therapy), relative to nine healthy controls. Event related spectral perturbations (ERSP) were obtained for each participant and from each TMS/EEG session, using wavelet decomposition. The main frequency at which a system oscillates was selected by the frequency showing the largest activity across time.

Results
Severity of depression markedly decreased after treatment with 12 patients achieving response and 9 patients achieving remission. TMS resulted in a significant activation of the Beta/Gamma band response (21-50 Hz) in healthy controls. In patients, the main frequencies of frontal EEG responses to TMS did not significantly change before/after treatment and at both time points were significantly lower than those of controls (11-27 Hz) and comparable in patients achieving remission and in those not responding to treatment.

Conclusions
In the first longitudinal study to assess natural frequencies before/after antidepressant response in BD, we did not observe any change over time. Evoked brain oscillations remained lower than those of healthy controls, and comparable in patients achieving remission and in those not responding to treatment. This suggests that the reduction of natural frequencies is a trait marker of BD, independent from the clinical status of the patients. The present results reveal important aspects of the neurobiological underpinning of severe psychiatric disorders and demonstrate that the combination of TMS/EEG represents a unique tool to develop biomarkers.

Funding/Disclosures
None.

LIGHT THERAPY AND MOOD IN BREAST CANCER

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Objectives
There is evidence suggesting that breast cancer patients constitute the subgroup of neoplastic patients most at risk for experiencing sleep difficulties, fatigue and depressive symptoms. Depressive symptoms reduce cancer patient understanding of and adherence to medical interventions, decrease quality of life and increase suicide rates. No study has yet focused on the effect of light therapy (LT) on mood in breast cancer patients.

Methods
We recruited 10 women affected by breast cancer under anthracycline-based chemotherapy treatment with a negative history of psychiatric and neurological disorders. Patients were administered Dawn LT in early morning for two weeks (white light up to 400 lux). Daily sleep quality was assessed by Pittsburgh Sleep Quality Index (PSQI). Patients were administered with an Italian version of the Functional Assessment of Cancer Therapy General Version 3 (FACT-G) scale at the beginning and after the end of LT. During the three days before the beginning of the study and the three days after the end of the chronobiological treatment, patients self-assessed subjective mood levels with a Visual Analogue Scale (VAS).

Results
All the considered variables respected the normality assumption (Kolmogorov-Smirnov test). T-test analysis on the sample before and after dawn treatment found no significant differences in FACT-G scale total score but significant variations were found in emotional ($t=2.57$; $p=0.0029$) and social($t=3.7$; $p=0.0049$) dimensions. No difference was found in PSQI total score, but a significant reduction after treatment was found in sleep latency ($t=2.7$; $p=0.024$) and on the ratio between time asleep and time in bed ($t=2.54$; $p=0.032$). For each patient we calculated a mean of VAS scores of the three days before and after treatment. Significant variations in perceived mood ($t=-3.55$; $p=0.0062$) with therapy leading to a positive effect were found. We then analyzed data in the context of the General Linear Model with a repeated measure ANOVA. Treatment was associated with a progressive improvement of perceived mood ($F= 2.54$; d.f. 18,7; $p=0.0013$). This change was influenced by the change in sleep quality ($F= 1.77$; d.f. 18,7; $p=0.036$) and not by the change of FACT-G scale scores.

Conclusions
Our results not only confirmed the usefulness of light therapy as a supportive care for patients affected breast cancer but also suggested the chronobiological intervention as a promising treatment for depressive syndromes in neoplastic patients under chemotherapy. Indeed, in patients assuming chemotherapy, the use of antidepressant drugs may be linked to various drug–drug interactions leading to an increase in side effects, influencing continuation rates and outcomes

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None.

ANTIDEPRESSANT CHRONOTHERAPEUTICS IN A GROUP OF DRUG FREE OUTPATIENTS

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Objectives
The combination of Total Sleep Deprivation (TSD) and Light Therapy (LT) has been shown to
prevent the early relapses characterizing response to TSD. Despite their proved efficacy, TSD and LT are still far from being considered standard therapy in the inpatient units and no study has assessed their efficacy and feasibility in outpatient settings.

Methods
We studied 27 drug-free out-patients affected by Major Depression, divided in 7 groups according to the date of the wake night. Patients were administered one night of TSD and received LT during consecutive mornings. Severity of depression was rated on Back Depression Inventory Scale (BDI) at baseline, one week and three months after the end of treatment.

Results
BDI scores significantly decreased during treatment (Friedman's ANOVA: $\chi 2 = 31.26$, $p<0.00001$) with no difference between the seven consecutively treated groups of patients ($F=0.57$; $p=0.85$). Post-hoc Newman-Keuls test confirmed significant differences in BDI scores between the baseline and one week ($p=0.00011$) or three months ($p=0.00012$) after the end of treatment.

Conclusions
TSD and LT caused a significant amelioration of depressive symptoms in an outpatient setting.
Similar effects were observed in seven independent groups, suggesting that there is repeatability in findings. Chronotherapeutics confirmed their efficacy in the treatment of depression

Funding/Disclosures:
None.

THE EFFECT OF COLORED SURFACE IN TERMS OF BIOLOGICAL RESPONSE IN INTERNAL SPACES

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Objectives
An experimental study was designed to confirm that the actual regulations, focusing solely on the visual comfort, may not be satisfactory as far as the biological stimulation is concerned.

Methods
Four same sized models of an office room exposed only to natural daylight were manufactured, each having its internal surfaces painted by different combination of colors. The spectral distribution of light and illuminance were measured at positions along the room and the potential biological response of subjects was evaluated by an evaluation model of circadian light (Rea et.al). The measurements showed that colored surfaces - especially yellow color - can provide satisfactory visual comfort, but simultaneously decrease the biological stimulation by daylight. Mainly in the winter period the biological response to daylight can be low even at medium illuminance levels. Thus, sufficient daylight and proper choice of internal surfaces' colors are important to avoid the potential negative health effects. The light conditions were measured by portable spectrophotometer Konica Minolta CL 500A and the data were processed in terms of SPD levels, Illuminance levels, Circadian light levels (CLA) and Circadian stimulus levels to assess the influence of surface colours.

Results
The result showed that there is a difference between visual and circadian measures along the range of the models. Colored surfaces – yellow, blue, gray - influenced the spectral light composition in the space when compared to the reference – white - one. The greatest values of CLA were recorded for the reference model due to the highest absolute reflectance levels and to the fact that it is spectrally neutral, thus it homogeneously reflect all wave lengths. The model with yellow walls, which provided the second highest levels of photopic illuminance for all measurement positions, produced low values of circadian light levels CLA. The model with grey wallpaper provided lower levels of CLA than the yellow one, as well as it provided low levels of photopic illuminance. The blue part of the daylight spectrum was decreasing at room depths that are commonly occupied by employees in offices. This might potentially result in insufficient biological stimulation.

Conclusions
The results of the present experiment emphasize the important effect of proper selection of internal surface color on the spectral characteristics of natural daylight penetrating through a clear window glass. The spaces with bigger depth and smaller windows should be equipped by light surface colors, such as white or light grey to provide uniform spectral reflectance.

Funding/Disclosures
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STATE-DEPENDENT ALTERATIONS IN INHIBITORY CONTROL AND IDENTIFICATION OF EMOTIONAL FACES IN SEASONAL AFFECTIVE DISORDER

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Objectives

Depressed individuals often exhibit impaired inhibition to negative input and identification of positive stimuli, but it is unclear whether this is a state or a trait feature. We aimed to examine seasonal changes in inhibitory control and identification of emotional faces in individuals with Seasonal Affective Disorder (SAD).

Methods

Twenty-nine individuals diagnosed with winter-SAD and 30 controls with no seasonality symptoms completed an emotional Go/NoGo task and an emotional face identification task twice; in winter and summer.

Results

In winter, SAD individuals showed impaired ability to inhibit prepotent responses to angry (P=.0006) and sad faces (P =.011), and decreased identification of happy faces (P=.032) compared to controls. In summer, SAD individuals and controls performed similarly on these tasks (Ps>.24).

Conclusions

We provide novel evidence that inhibition of angry and sad faces and identification of happy faces are impaired in SAD in the symptomatic phase, but not in remitted phase. These affective biases in cognitive processing constitute state-dependent features of SAD.

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ACUTE POSITIVE, BUT DELAYED, NEGATIVE SUBJECTIVE NON-IMAGE FORMING EFFECTS OF MORNING BRIGHT LIGHT EXPOSURE IN HEALTHY DAY-ACTIVE STUDENTS

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Objectives
Recent studies revealed acute activating effects of bright light exposure (BLE) on subjective feelings of alertness during daytime among healthy, non-sleep deprived participants. However, subjective aftereffects of BLE are largely unknown. The current study tested acute non-image forming (NIF) effects of morning and afternoon bright vs. normal light exposure on subjective alertness, vitality, tension and mood in healthy day-active students, but also explored delayed effects on these indicators as well as subjective sleep quality during the subsequent night.

Methods
This study employed a counterbalanced design with Light intensity (165 vs. 1700 lux at eye level, 60-minute exposure) manipulated within and Local clock time (morning vs. afternoon) between subjects. Thirty-four participants (15 male, M_{age} = 20.59; SE_{age} = 0.38) came to the lab on two separate occasions at the same time of the day (either 9 AM - 10:30 AM or 3:45 PM - 5:15 PM). Questionnaires on state subjective alertness, vitality, tension and mood were completed after the baseline phase (120 lux ate eye level) and after the lighting condition. Each laboratory session was combined with an Experience Sampling Method (ESM) to probe participants' level of alertness, vitality, mood and tension at fixed moments during the remainder of their day. The morning after each laboratory visit, participants reported on their sleep timing and quality via a sleep diary questionnaire. Multilevel analyses, corrected for participants' chorotypes and multiple testing (Bonferroni), were conducted for each outcome measure.

Results
Results on the acute NIF effects of light intensity in the laboratory revealed significant Light*Time of day interactions for subjective alertness ($F(1,34) = 11.06$, $p = 0.002$) and vitality ($F(1,33) = 8.85$, $p = 0.005$), indicating that participants felt more alert ($p < 0.001$) and vital ($p = 0.001$) after 1-hour 1700 vs. 165 lux exposure in the morning. ESM data revealed continued increased vitality up to 30 minutes after morning BLE ($p = 0.02$), yet these vitalizing effects dissipated quickly afterwards. ESM data further showed significantly more tension at the end of the day (5:30 PM - 10:00 PM, $p = 0.007$) after morning BLE. Sleep diary data suggested that participants reported to have slept significantly less calm ($p = 0.009$) and reported to be significantly less happy the next morning after morning 1700 lux vs. 165 lux exposure ($p = 0.01$). No acute or delayed differences on subjective indicators were found for afternoon BLE.

Conclusions
Although healthy day-active young people may experience acute vitalizing effects from morning BLE, they may experience negative effects in terms of tension later that day and decreased sleep quality during the subsequent night. This calls for more attention towards such aftereffects.

Funding/Disclosures
None.

ACROSS MOOD DISORDERS:
COMPARISON BETWEEN UNI- AND BIPOLAR MOOD DISORDERS AND HEALTHY CONTROLS

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Objectives
Chronotype, being a morning or an evening type varies between individuals. Patients with mood disorders, such as bipolar disorder (BD) and unipolar depression (MDD) often have a later Chronotype. It has been suggested that in bipolar disorder the evening Chronotype is more pronounced than in unipolar depression, but this has hardly been investigated. This study aims to investigate the difference in Chronotype between BD, MDD and healthy controls.

Methods
This study combines two large databases in order to compare MDD, BD and healthy controls. MDD patients are derived from the Netherlands Study of Depression and Anxiety (NESDA), BD patients from the Dutch Bipolar Cohort (DBC) study and healthy controls from both databases. Chronotype was assessed using the Munich Chronotype Questionnaire (MCTQ) and calculated as the midpoint of sleep on free days (MSFsc). Chronotype is compared between groups, adjusted for sex, age, BMI, alcohol use and external timing.

Results
1613 subjects were included (1048 women, average age±SD: 43±13), 1041 MDD patients, 107 BD patients and 465 healthy controls. There was a main effect of diagnosis on MSFsc $F(2,1604)=3.1$, $p=0.04$. MSFsc was 3.74 for healthy controls, 3.84 for MDD patients and 3.97 for BD patients. Post-hoc testing showed MDD and BD differed significantly from healthy controls ($p=0.04$ and $p=0.03$), but they did not differ from each other.

Conclusions
Both MDD and BD patients have a later Chronotype compared to healthy controls, but Chronotype does not differ between the mood disorders. Similar Chronotype indicates a similar circadian mechanism may underlie the problems in timing in mood disorders.

Funding/Disclosures
None.

INFLUENCE OF DAWN SIMULATION ON SLEEP STAGE PRIOR TO AWAKENING

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Objectives
The aim of this study was to test the hypothesis that dawn simulation alleviates sleep inertia by promotion of a light sleep stage prior to awakening. Previous laboratory 1-2 day studies were not conclusive (Noguchi et al., 2001; van de Werken et al., 2010; Gabel et al., 2013).

Methods
The study was performed in Febuary–December 2015 (with the exclusion of summer months) in Novosibirsk (55°N). Selection criteria required that subjects worked 5-6 days a week, needed to wake at a certain time on a work day and slept alone. Following 2 adaptation nights during baseline week, they underwent 5 days of 30-min dawn simulation (Lumie Bodyclock IRIS) during one week and 5 days of no dawn (the bedside simulator set for the alarm ring only) during another week (counter-balanced crossover). Measurements included all-night polysomnography (PSG; SOMNOwatch plus EEG6), actimetry (Motion Watch 8), visual analogue scales for sleepiness, mood and energy before and after sleep during the 3 weeks. After receiving instructions in the lab, participants positioned PSG electrodes themselves on the forehead (1 EEG and 1 reference), near the eyes (2 ocular) and behind the ear (1 ground), read out and sent the data to investigator each day. Sleep stages were determined at half-minute interval according to standard criteria.

Results
Twenty four subjects entered the study and 18 completed, male:female ratio – 4:14, age – 27.0 ± 7.1 (SD), range 19–46 years. Of the total target 180 registration nights, 19 (10.6%) were lost due to technical reasons. The subjects rarely awoke before the alarm ring (32 vs. 129 times) and this did not depend on the condition (dawn vs. no dawn, Chi-square p=0.34). The distribution of the last, pre-awakening sleep stages was as follows: REM – 90 cases (56%), stage II – 66 cases (41%), stage III – 5 cases (3%). When analyzing only spontaneous awakenings (N=32), the REM phase (the most physiological for the pre-awakening) was observed more often at dawn vs. no dawn sessions (12 vs. 5), but this was not significant. The analysis of data is continuing.

Conclusions
These preliminary results do not indicate that dawn simulation promotes a certain sleep phase prior to the target awakening time.

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DEPRESSIVE PATIENTS' EXPERIENCES OF WAKE- AND LIGHT THERAPY – A QUALITATIVE STUDY

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Objectives
Wake therapy can reduce depressive symptoms within days, and response rates are high. To sustain the effect of wake therapy it is often combined with light therapy. Few studies have focused on factors related to patients´ adherence, and no studies have examined the patients´ experience of these combined interventions using qualitative methods. The aim of the study was to clarify the patients' experiences with wake and light therapy and factors related to the patients' adherence.

Methods
Thirteen in-patients with major depression were included. They participated in an intervention consisting of three wake therapies during the first week, 30 minutes daily light treatment for the entire nine weeks, and ongoing psychoeducation regarding good sleep hygiene. Patients´ kept diary, and individual semi-structured interviews was conducted. Data was analyzed using qualitative content analysis.

Results
The participants overall experience with the treatment was positive. Some experienced a remarkable and rapid antidepressant effect whereas others described more long-term benefits as improved sleep and diurnal rhythm. Yet, the recovery was fragile and the participants' optimism was cautious. Prior to participation, many had been through several conventional pharmacological and psychotherapeutic treatments with limited effect, and they were getting desperate. The non-pharmacological nature of the treatment made it particularly attractive to the participants. Further, they appreciated being active in their own treatment, and by participating they regained confidence in their recovery. The emerging hope kept the participants motivated, and during the project period, many focused on changing sleeping habits and daily routines. Social support was important for keeping up the motivation for staying awake and taking the daily light therapy. Overall participants found the treatment worthwhile. Not all would repeat it; however, all would recommend it to other patients with major depression. The study revealed a lack in knowledge among the participants on the connection between regular sleep patterns and depression.

Conclusions
This study provides insight into patients' experiences, and knowledge that can contribute to guidelines for future adherence-promoting organization of wake and light therapy.

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SLEEP AND MOOD FOR PATIENTS WITH MAJOR DEPRESSION WHEN DISCHARGED FROM INPATIENT WARDS

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Objectives
Very little is known of depressed patients' mental state after being discharged from inpatient wards where they are provided with a sheltered environment with stable sleep wake cycle, regular meals, and regular physical activities. We hypothesized that this stability might be lost after discharge.

Methods
Patients referred to an intensive outpatient service from affective disorders inpatient wards, were included in the study. All patients registered, on a daily basis, sleep parameters and mood in the Daybuilder computer application, beginning shortly before discharge and continued for 4 weeks. Clinicians were enabled to see patients' registration and phoned patients weekly.

Results
In total, 45 patients were included and showed large day-to-day variations of mood and sleep, with 31 % of patients experiencing days with severe depression in the week after discharge. For the whole 28 days monitoring self-assessed mood was unchanged ($p = 0.08$). Sleep onset was delayed from 23:30 (SE 0:09) to 24:00 (SE 0:14) ($p=0.006$), sleep offset from 7:42 (SE 0:09) to 8:30 (SE 0:14) ($p=0.004$), and sleep midpoint from 3:36 (SE 0:08) to 4:15 (SE 0:13) ($p=0.004$) hour: minutes. Delay of sleep onset had a significant negative effect on mood ($p = 0.009$). Hamilton scores changed from 18.0 (6.5) to 13.3 (7.3) ($p < 0.01$). The Daybuilder System Usability score (SUS) application was 86.2 (9.7, range 65-100), (high usability).

Conclusions
Electronic monitoring with the Daybuilder application was feasible. Self-assessed mood was not improved. Patients' sleep was significantly delayed with a negative impact on mood. More intensive feedback with day-to-day observation of patients' data might help patients stabilize sleep and avoid sleep delay thus probably preventing relapse. A follow-up study is planned with sleep phase advance compared to standard sleep regime in a similar set-up with depressed patients discharged from inpatient wards.

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None.

THE EFFECTS OF WHITE LIGHT WITHOUT BLUE AND GREEN COMPONENTS ON PUPIL DIAMETER AND ELECTROENCEPHALOGRAM

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Objectives
It was well known that the intrinsically photosensitive retinal ganglion cells (ipRGCs) affect the suprachiasmatic nucleus (SCN) and act as the primary photoreceptors for nonvisual effects such as melatonin suppression and pupillary constriction. In our previous studies, we verified that simultaneous exposure to blue and green light resulted in less pupillary constriction than that in response to exposure to monochromatic blue or green-pulsed light (subadditive response). However, we wondered whether the subadditive response could still be observed when using white light without the blue and green components. Therefore, we conducted an experiment using optical filters that cut the blue (480 nm) or green (560 nm) bandwidths and examined the nonvisual effects of this light on pupillary constriction and electroencephalogram and subjective evaluations.

Methods
Ten healthy young men participated in this study. The subject sat on a chair with his eyes facing an integrating sphere. After 10 min of light adaptation, the subject's left eye was exposed to white pulsed light (1000 lx; pulse width: 2.5 ms) every 10 s with a blue-cut filter lens, a green-cut filter lens, or without filters (control condition), and pupillary constriction was measured. Then, after a 10-min pause, the subject was exposed a continuous white light of 1000 lx with a blue-cut filter lens, a green-cut filter lens, or without a filter lens and electroencephalogram was performed.

Results
In assessments of pupillary constriction, light without the green bandwidth showed more remarkable findings than that without the blue bandwidth and the normal white light.

Conclusions
A reduction in the green bandwidth component (with a green-cut filter lens) facilitated pupillary constriction. Thus, the effects of the blue bandwidth component on ipRGCs are apparently reduced by simultaneous irradiation with the green bandwidth component. We confirmed that there was a sub additive response on pupillary constriction after removal of the blue and green components from white light.

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SLEEP DURATION, EXERCISE, SHIFT WORK AND POLYCYSTIC OVARY SYNDROME-RELATED OUTCOMES IN A HEALTHY POPULATION

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Objectives
To examine whether lifestyle factors, including short sleep duration, insufficient exercise, and shiftwork, alone or in combination, are associated with the reproductive and metabolic abnormalities typical of PCOS in a healthy population.

Methods
A prospective cross-sectional study of 231 women was conducted at the National University Hospital, Singapore, from 2011 to 2015. The women completed a questionnaire, including their menstrual cycle length, sleep length, and frequency of exercise and shift work. Hyperandrogenism (hirsutism score, testosterone, sex hormone binding globulin (SHBG)), ovarian morphology and function (anthral follicle count, ovarian volume, anti-mullerian hormone (AMH) and metabolic measures (body mass index (BMI), waist hip ratio (WHR), blood pressure, fasting glucose, fasting insulin and fasting lipids) were examined through anthropometric measurements, transvaginal ultrasound scans, and blood tests.

Results
No significant associations were observed between shift work, exercise or sleep duration and the androgenic and ovarian measures that define PCOS. However, women reporting fewer than 6 hours of sleep were more likely to report abnormal (short or long) menstrual cycle lengths (OR=2.1; 95% CI, 1.1 to 4.2). Women who reported fewer than 6 hours of sleep had increased fasting insulin levels (difference in means = 2.13; 95% CI, 0.27 to 3.99 mU/L) and higher odds of insulin resistance (OR=2.58; CI, 1.16 to 5.76). Lack of regular exercise was associated with higher mean fasting insulin (difference in means = 2.3 mU/L; 95% CI, 0.5 to 4.1) and HOMA-IR (difference in means = 0.49; 95% CI, 0.09 to 0.90) levels.

Conclusions
Women with insufficient sleep are at increased risk of menstrual disturbances and insulin resistance, but do not have the hyperandrogenism and polycystic ovarian morphology typical of PCOS. Improved sleep duration may help reduce the risks of diabetes or infertility. Shift work, exercise or sleep duration appear not to impact the androgenic and ovarian measures that define PCOS.

Funding/Disclosures
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STAY ALERT: NOVEL WAYS OF OBJECTIVE QUANTIFICATION

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Objectives
Contemporary developments, such as the emergence of the 24-hour society, pose unique physiological challenges on alertness. Identifying a mechanism to modulate alertness during waking hours is critical to prevent or alleviate problems which are coupled to decreasing alertness. The first step in this development is to objectively quantify alertness.
The goal of these experiments was to investigate whether blink frequency and duration could function as objective parameters of alertness. In addition, sensitivity of these parameters was tested.

Methods
6 participants were subjected to a paradigm lasting from 8 pm till 3 am, in which hourly the Karolinska Sleepiness Scale was filled in. Subsequently, pupillary parameters were measured using an eye tracking device (Eye Tribe Tracker, ET1000). An eye blink was defined as a diameter of 0 pixels for <1 second.

To determine validity and sensitivity of pupillary parameters, a second experiment was designed in which 5 participants were subjected to a paradigm lasting from 11 am to 5 pm. They completed the Karolinska Sleepiness Scale and performed a Sustained Attention to Response task once every 90 minutes. Pupillary parameters were measured thereafter.

Results
During the nighttime experiment, sleepiness increased significantly according to the KSS ($p<0.001$). There was a significant increase in both blink frequency ($p<0.05$, $R^2=0.54$) as well as duration ($p<0.001$, $R^2=0.67$) and the product of the both ($p<0.001$, $R^2=0.22$), tested with a linear mixed model analysis. The daytime experiment revealed a significant correlation between KSS-scores and blink frequency ($p<0.001$, $R^2=0.55$) and between errors of commission and blink frequency ($p<0.05$, $R^2= 0.69$).

Conclusions
The nighttime experiment indicates that blink frequency and – duration could function as parameters of alertness and the daytime experiment suggests, that these parameters are sensitive enough to detect relatively small fluctuations in alertness. Taken together, these studies indicate that blink frequency and duration, especially in combination with other measures of alertness, can quantify alertness.

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None.

DIURNAL VARIATIONS OF HORMONAL SECRETION, ALERTNESS AND COGNITION IN EXTREME CHRONOTYPES UNDER DIFFERENT LIGHTING CONDITIONS

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Objectives

Diurnal changes in physiology and behavior are modulated by external factors such as light or temperature. We aimed to test whether self-selected office lighting during a habitual waking period would have an impact on alertness, cognitive performance and hormonal secretion in young morning and evening types (16/16), where preferred bed and wake times usually differ by several hours.

Methods

The self-selected lighting condition (daylight and electrical lighting) was compared with a constant bright light and a control condition (dim light). Saliva samples for hormonal analyses, subjective ratings of alertness, wellbeing and visual comfort as well as cognitive performance were regularly assessed.

Results

The dim light melatonin onset (=DLMO) revealed a similar timing and circadian phase angle relative to wake time in both chronotypes. When we tested the melatonin secretion onset in the evenings within each chronotype separately, we found that it occurred in both chronotypes significantly later under the constant bright light condition when compared to dim light, indication an acute suppression by bright lighting. Only evening, but not morning types revealed also an earlier melatonin onset in the self-selected lighting, when compared to bright light ($p<0.05$). Morning types showed a steeper increase of sleepiness during the day than evening types, and they reported greater mental effort, also reflected in higher cortisol secretion ($p<0.05$). Wellbeing, mood and performance in more difficult cognitive tasks were better in the bright and the self-selected lighting than in dim light for both chronotypes, whereas visual comfort was best in the self-selected lighting.

Conclusion

To conclude; self-selection of lighting at work might positively influence biological and cognitive functions regarding inter-individual differences.

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INDIVIDUALS DISPLAY ROBUST STABILITY OF TRAIT-LIKE VULNERABILITY OR RESILIENCE TO DIFFERENT TYPES OF SLEEP LOSS AND DIFFERENT NEUROBEHAVIORAL MEASURES

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Objectives
We determined whether trait-like responses are observed after chronic sleep restriction (SR) and acute total sleep deprivation (TSD) separated by recovery sleep in the same protocol, and determined the consistency of such responses among different neurobehavioral measures.

Methods
83 healthy adults (34.7 ± 8.9y; 36 females) completed 2 baseline nights (10h-12h time in bed, TIB) followed by 5 chronic SR nights (4h TIB) or 36h of acute TSD. Subjects then received 4 recovery (12h TIB) nights followed by 5 chronic SR nights or 36h of acute TSD, in counterbalanced order to the first sleep loss condition sequence. Neurobehavioral outcomes included the Psychomotor Vigilance Test (PVT), Digit Symbol Substitution Test (DSST), Digit Span (DS), Karolinska Sleepiness Scale (KSS), and Profile of Mood States (POMS) every 2h during wakefulness. Intraclass correlation coefficients (ICCs) were computed as the ratio of between-subjects variance to the sum of the between- and within-subjects variances using data from 0800h/1000h to 2000h after the fifth chronic SR night and data from 2200h/0000h to 2000h of acute TSD. Spearman's rho assessed the relative rank of individuals' averaged chronic SR-acute TSD responses across neurobehavioral measures.

Results
Regardless of sleep loss order, subjects who displayed vulnerability to acute TSD also displayed vulnerability to chronic SR, evidenced by substantial ICCs: PVT lapses, ICC=0.806; PVT response speed, ICC=0.896; DSST correct, ICC=0.885; DS correct, ICC=0.922; KSS, ICC=0.837; POMS fatigue, ICC=0.787. Notably, individuals exhibited significant consistency of responses within cognitive performance (PVT, DS, DSST; p's<0.001) and within subjective (KSS, POMS; p's<0.001) measurement domains, but not between domains (p's>0.05).

Conclusions
Vulnerability to chronic SR and TSD showed trait-like stability in neurobehavioral measures as evidenced by substantial inter-individual variance (79%-92% across measures). Moreover, individuals displayed consistent, but different, vulnerability within performance and subjective domains. Interestingly, cognitive performance vulnerability did not predict subjective vulnerability or vice versa. These data highlight the remarkable stability of phenotypic neurobehavioral responses across different types of sleep loss and across different performance and subjective measures.

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IS THERE A RELATION BETWEEN VEGETARIANISM AND SEASONAL AFFECTIVE DISORDER?

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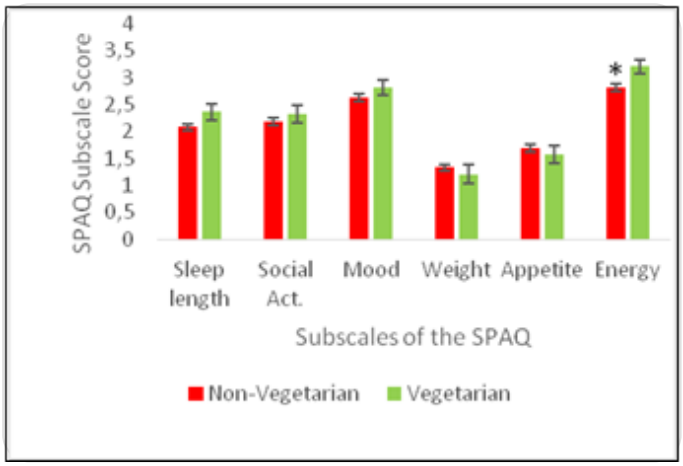
Objectives
Patients with SAD selectively eat more carbohydrates during their depressive episode in winter. Kraüchi et al. found that they eat more sweets, but also more starch-rich food and relatively less proteins. Clarys et al. showed that vegetarians also eat less protein and fats and more carbohydrates and fibre. In the Netherlands 4.5% of the adult population is vegetarian. This raises the question whether vegetarians are more prone to develop SAD than non-vegetarians.

Methods
In the winter seasons of September 2013 to April 2016 every patient visiting the outpatient clinic of the UMCG filled out a SPAQ. We added an extra question asking 257 patients whether they were vegetarian or not (71 males, age= 39.7 ±15.5; 186 females, age =36.7±12.8). Descriptive statistics and Mann-Whitney U test were carried out with SPSS v21.

Results
When we compare the 33 vegetarian patients (12.8%) to non-vegetarians, a significant difference was found on the energy questionnaire (Mann-Whitney U=2886, z = -2,137 p=0.03, 2-tailed). Calculating the effect size (r= z/√n= -0.13). Although not significant, the seasonal difference on the appetite and weight questions of the SPAQ in the vegetarian group was less pronounced than in the non-vegetarians; on the other questions and on the GSS-score vegetarians scored higher (n.s.).



Conclusions
These results may indicate that there are relatively more vegetarians in the SAD group than in the general population. Vegetarian SAD patients report more seasonal energy problems than non-vegetarian SAD patients. These results should be interpreted very carefully though, because of the small effect size and a selection bias. A possible explanation for the energy difference may be that vegetarians have a deficiency of essential nutrients. The higher percentage of vegetarians might be explained by the fact that vegetarians are more concerned with health in general and therefore may prefer LT over medicine. These results are by no means final, but a starting point for further research.

Funding/Disclosures
None.

THE EFFECTS OF A NEW DAWN-DUSK SIMULATOR ON CIRCADIAN REST-ACTIVITY CYCLES, SLEEP, MOOD AND WELL-BEING IN DEMENTIA PATIENTS – A PILOT STUDY

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Objectives
Simulating dawn and dusk provides a naturalistic light therapy shown to improve sleep quality and mood. We investigated the effects of a newly designed dusk and dawn simulator (DDS) on circadian rest-activity cycles, sleep, mood, agitation, well-being and self-reliant activities of daily life in institutionalised older people with severe dementia.

Methods
After one baseline week, 20 older subjects with dementia (86 ± 6 yrs; 17f) were exposed to an individually timed DDS for 8 weeks (7 weeks for 10 patients) and were studied without the DDS during another 8 weeks, in a counterbalanced crossover design. Dusk and dawn were simulated from 0.001 - 80 lx by a concave, diffused white LED panel (4000 K), placed above the bed-head. Circadian rest-activity cycles and sleep were analysed from actimetric recordings over 17 weeks. Cognitive functioning, mood, agitation, self-reliant activities of daily life were assessed by standardised questionnaires and visual analogue scales, regularly rated by the nurses (daily to two-weekly).

Results
The patients showed more self-reliant activities of daily life during the first 4 weeks with the DDS compared to no DDS (main effect of condition; $p=0.02$). Those participants with greater cognitive impairment (as assessed in the Severe Mini-Mental State Examination; N=10) were judged to have significantly more cheerfulness ($p=0.03$) and wellbeing ($p=0.04$) in the morning after getting up with DDS than without (main effect of condition). Rest-activity cycles and sleep showed no significant difference between the two conditions.

Conclusion
A few but promising effects of the new DDS placed above the bed-head of residents of a nursing home were found in this pilot study. Older people suffering from dementia showed better mood and well-being after waking up when using the DDS, and remained more self-reliant in their activities of daily life.

Funding/Disclosures
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PHYSICAL CHARACTERISTICS OF LIGHT EMITTED BY COMMERCIALLY AVAILABLE LIGHT TREATMENT DEVICES

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Objectives
Multiple consumer light therapy devices (LTDs) are currently available, including light boxes, desk lamps, light visors, or compact devices with light-emitting diodes (LEDs). There has been no formal review of light-emitting properties or tolerability of common, commercially available LTDs. We evaluated the spectral power distribution (SPD) by spectrophotometer, illuminance (lux intensity), and subjective glare of 23 LTDs including 9 light boxes, 4 desk lamps, 10 LED devices, and 2 light visors, as well as several commercially-available lighting fixtures.

Methods
For each device we recorded the SPD at the manufacturer's recommended distance (MRD), perpendicular to LTD center. We measured photopic lux across a 24" x 20" plane at MRD to assess degree of light dispersion. To assess for the effect of distance, we measured photopic lux at the surface center of LTD and up to 3' from the surface at 6" intervals. As a measure of tolerability, 14 volunteers rated each LTD for glare at MRD using 1 to 5 analog scale.

Results
MRD ranged from 7" to 30". Among white-light LTDs, 44% of LED LTDs (4/9), 63% of light boxes (5/8), 50% of desk lamps (2/4), and 1 light visor emitted 10,000 ± 1,500 lux at MRD. Evaluation of brightness in the plane at MRD revealed that LED lights and smaller light-emitting surface area lead to marked lux diminution when deviating only inches off-center. With increased distance from the device, smaller devices approximated the inverse square law and larger devices demonstrated generally linear decrements in illuminance within two feet of the device surface. Devices varied greatly in rated tolerability, with means from 2.04 to 4.50 on the analog scale. All LED devices we tested excluded a diffusion screen, and all were rated among the more glaring devices tested. Diffusion screens were associated with greater tolerability. Devices were based on either fluorescent or LED light sources, and thus varied greatly in irradiance in the shorter wavelength, melanopsin-activating, spectral regions.

Conclusions
LDs vary in several key features including SPD, light-emitting surface area, collimation, and glare. Given current recommendations for 10,000 lux white light, it is clear that both distance from device and deviation off-center leads to very significant illumination drop-off. LED devices, which emit light with greater collimation, are less-susceptible to light drop-off with distance but require that they be viewed from within inches of the light center (where glare is maximal). Many commercial LTDs do not meet standards for light emission that are supported by research findings. These findings are critical for clinicians recommending light therapy as they will influence effectiveness and tolerability.

Funding/Disclosures
None.

RETINAL VENOUS CARBON MONOXIDE RESPONSE TO BRIGHT LIGHT IN MALE PIGS

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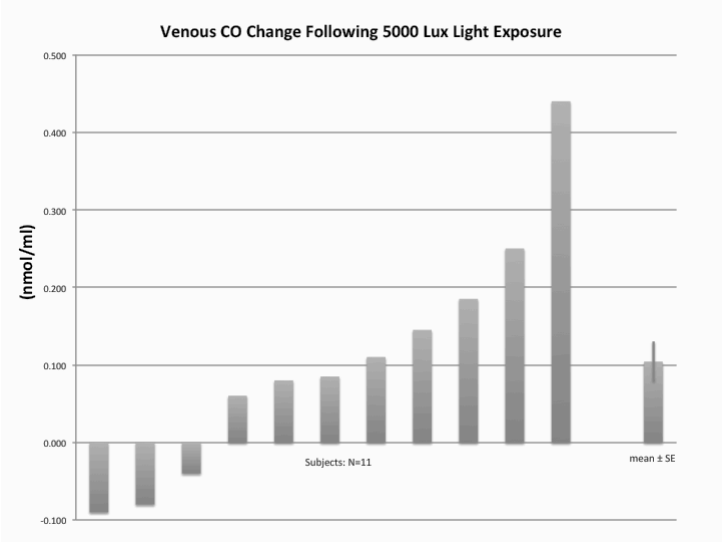
Objectives
The physical mechanism by which light is absorbed and has antidepressant and energizing effects in Seasonal Affective Disorder is of scientific interest. This study was designed to explore one specific aspect of the proposed humoral photo transduction model, namely that carbon monoxide (CO) levels increase in retinal venous blood in response to bright light.

Methods
Eleven mature male pigs approximately six months of age were kept in darkness and fasted for 12 hours prior to surgery. Following mild sedation, anesthesia was induced. Silastic catheters were inserted into the dorsal nasal vein in a cephalic direction through the angular vein of the eye to reach the ophthalmic sinus, from which venous blood was collected. The animals were exposed to 5000 lux of fluorescent-generated white light. CO levels in the blood were analyzed by gas chromatography before and after 80 minutes of light exposure.



Results
At baseline, mean CO levels in the retinal venous blood were 0.43 ± 0.05 (SE) nmol/ml. After bright light, mean CO levels increased to 0.54 ± 0.06 nmol/ml (two-tailed t-test p = 0.05).

Conclusions
This study provides preliminary evidence in a mammal that acute bright light exposure raises carbon monoxide levels in blood draining from the eye.

Funding/Disclosures
None.

ANTIDEPRESSANT TREATMENT WITH TOTAL SLEEP DEPRIVATION INDUCES CHANGES IN WHITE MATTER MICROSTRUCTURE IN BIPOLAR DISORDER

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Objectives
Bipolar disorder (BD) is characterized by changes of white matter (WM) microstructure and by a disruption of circadian rhythms. The chronotherapeutic combination of repeated total sleep deprivation and morning light therapy (TSD+LT) not only can acutely reverse depressive symptoms in approximately 60% of patients, but it also reduces the high percentage of relapses seen after the recovery night. Specific effects of sleep deprivation on the brain have been found by different brain imaging studies showing an association with functional and metabolic changes in specific brain areas of the corticolimbic circuit. Following this line of reasoning the aim of the study is to investigate the effect of chronoterapeutic treatment on WM microstructure in BD.

Methods
Twenty-four patients affected by a major depressive episode without psychotic features, with a diagnosis of BD type I were administered one week of chronotherapeutic treatment through TSD+LT. On a 3.0 Tesla scanner (Gyroscan Intera, Philips, Netherlands) using a 6 channels SENSE head coil scanner were acquired diffusion tensor images (DTI) with 35 gradient directions. Voxelwise DTI analyses were performed using Tract-Based Spatial Statistics using TFCE correction (p=0.05). A paired t-test on DTI measures of WM integrity (axial, radial, and mean diffusivity, and fractional anisotropy) was performed between patients at baseline and after one week of TSD+LT treatment.

Results
Seventeen out of 24 patients successfully responded to TSD+LT. After chronotherapeutic treatment patients showed increased axial diffusivity (AD) and mean diffusivity (MD) in corpus callosum, corona radiata, superior longitudinal fasciculus, corticospinal tract and anterior thalamic radiation. All tracts were localized in the right hemisphere.

Conclusions
The chronotherapeutic treatment is associated to increased AD and MD in several fibre tracts contributing to the functional integrity of the brain. The increase of MD was likely driven by the increase of AD. AD represents the water diffusivity parallel to the axonal fibers, reflecting the greater freedom of water to diffuse along the principal fiber axis rather than to travel across the surrounding myelin sheaths thus reflecting fiber integrity. The right lateralization of the effect is in agreement with a suggested dominant role of the right hemisphere in mood regulation. We suggest that chronotherapeutic treatment could counteract part of the detrimental influences of BD on WM structure, with specific benefits resulting for the patients from effects on WM tracts previously associated to BD and involving inter-hemispheric, and frontal connections.

Funding/Disclosures
None.

TEMPORAL AND LIGHT-INDUCED DYNAMICS IN SELF-CONTROL AND COGNITIVE PERFORMANCE IN REAL LIFE SITUATIONS

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Objectives
To date, light-induced and temporal variations in cognitive performance have mainly been studied under well-controlled conditions in the laboratory. These studies have provided relevant insights in whether and how light and time systematically impact human performance. Yet, how light and time influence performance under the dynamic conditions in daily life is largely unknown. Moreover, little is known about the impact of light, local clock time and Chronotype on individuals' level of self-control. Self-control is a psychological construct related to cognitive task performance. It refers to the capacity to change one's behavior according to standards (Baumeister et al, 2007), and is important to achieve long-term goals and success in daily life. The current study provides a first exploration into structural variations in self-control and cognitive task performance as a function of light exposure, local clock time, and Chronotype during individuals' daily routine in real life.

Methods
We employed wearable light sensors (Daysimeter worn at eye level and Actiwatch worn at wrist) combined with an experience sampling method to track light intensity levels, cognitive task performance and subjective self-control during individuals' daily routine (between 8 am and 8 pm) for three consecutive days. Thirty-one subjects participated in the study (17 male, M_{age} = 24, SD = 8.5; M_{MSFsc} = 4.68, SD = .90). Short performance tasks were administered semi-randomly over the day by means of an app to assess sustained attention (PVT), inhibitory capacity (Go-NoGo task), and working memory (2-Back task). Self-control was assessed hourly with three self-report items (α = .68). Multilevel analyses were performed to model temporal variations, and test the effect of the average light intensity during the prior hour and Chronotype.

Results
Results revealed significant variations in state self-control as a function of local clock time with lower self-control in the early morning and early afternoon. Chronotype and hourly light intensity explained additional variance in state self-control (β = -.19 and β = .07 respectively, both $p < .05$). None of the performance indicators showed significant structural patterns with time of day or Chronotype. Effects of light on performance indicators revealed mixed results: Reaction times on the Go-NoGo task were shorter (β = -.24, $p < .01$), yet the accuracy on the 2-Back task was lower (β = -.12, $p < .05$), when participants were exposed to more intense light during the hour prior to the task. Additional analyses will be presented at the SLTBR meeting.

Conclusions
The results showed systematic variations in self-control as a function of local clock time, Chronotype, and light exposure. Temporal and light-induced variations in performance established in the laboratory cannot be directly translated to real-life situations, and require additional research.

Funding/Disclosures
None

MELATONIN SUPPRESSION AND ALERTNESS UNDER EVENING EXPOSURE TO BLUE-DEPLETED/VIOLET-ENRICHED WHITE LIGHT

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Objectives
Nocturnal light exposure suppresses melatonin production. Several studies have shown that filtering out short wavelengths can reduce melatonin suppression. However, this high pass filtering comes at the cost of the quality of light, since it makes the light much yellower, with a lower color temperature (CCT). We tested whether it is possible to define a polychromatic white light spectrum that reduces melatonin suppression while retaining the same CCT and photopic illuminance as a standard reference light source.

Methods
In a pilot study, we found that adding violet light (405 nm) to amber light (595 nm) did not affect melatonin production. Hence, we added violet light to retain the CCT of polychromatic white light while filtering out the blue part of the spectrum thought to be most responsible for melatonin suppression. 16 Participants were exposed to different light conditions on three evenings, separated by one week. On each evening, they were exposed to 3 hours of either dim light (3600 K, < 5 lx), bright white light (3600 K, 250 lx) or bright white light band-stop filtered between 460 and 480 nm with extra violet to maintain CCT (3600 K, 250 lx). These filter characteristics were based on the studies by Rahman et al. (2011, 2013), which suggest that light in this wavelength region substantially contributes to melatonin suppression. Salivary melatonin, subjective alertness (KSS) and PVT reaction time performance were measured throughout the evening.

Results
The results showed no significant differences on any of the dependent variables between the two bright light conditions. In both conditions, melatonin suppression was significantly higher than in the dim light condition. Moreover, participants reported in both conditions to feel less sleepy than in the dim light condition. No significant effects on PVT performance were observed.

Conclusions
The combination of boosting energy in the very short wavelengths and band-stop filtering 460 – 480 nm is not sufficient to substantially reduce melatonin suppression compared with a reference white light spectrum with the same CCT and illuminance.

Funding/Disclosures
This project was funded by Philips Electronics Nederland B.V. All authors are employed by Philips Electronics or Philips Lighting.

DISCREPANCY BETWEEN SUBJECTIVE AND OBJECTIVE SEVERITY AS A PREDICTOR OF RESPONSE TO CHRONOTHERAPEUTICS IN BIPOLAR DEPRESSION

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Objectives
Chronotherapeutic techniques (sleep deprivation and light therapy) are effective treatments for bipolar depression, but viable predictors of response for the daily clinical practice have not yet been established. The discrepancy between subjective and objective severity of the depressive syndrome has been proposed as a possible predictor of treatment outcome in depression. This study examined whether this discrepancy could predict response to chronotherapeutics in bipolar depression.

Methods
We studied 149 consecutively admitted inpatients with a major depressive episode in course of bipolar disorder. Patients were treated with the combination of repeated sleep deprivation and bright light therapy. Severity of depression was evaluated using self-rated (Beck Depression Inventory: BDI) and observer-rated (Hamilton Depression Rating Scale: HDRS) measures. BDI-HDRS discrepancy score at baseline was calculated, and its associations with clinical response and with depressive cognitive distortions, as measured on the Cognitions Questionnaire, were examined.

Results
Among the 147 completers, 66% responded to treatment (50% reduction of HDRS score). The response rate in patients with low discrepancy scores and in patients with high discrepancy scores were 80.2% and 48.5%, respectively. High BDI-HDRS discrepancy predicted negative response to treatment with odds ratio of 3.85 (95%CI: 1.74-8.51). BDI-HDRS discrepancy was positively associated with depressive cognitive distortions.

Conclusions
Higher BDI-HDRS discrepancy can predict poorer response to chronotherapeutics in bipolar depression.

Funding/Disclosures
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EFFECT OF CYTOKINES ON SLEEP IN BIPOLAR DEPRESSION: A PRELIMINARY STUDY

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Objectives
Sleep disturbance is prevalent and clinically significant symptom of bipolar disorder (BD). Although evidence suggests that immune abnormalities are important features of pathophysiology of BD, little is known about effect of cytokines on sleep in BD. We investigated effect of cytokines on sleep in patients affected by a major depressive episode in course of BD (bipolar depression).

Methods
We measured the serum levels of Interleukin (IL)-1β, IL-2, IL-6, IL-8, IL-10, interferon γ and tumor necrosis factor (TNF)-α in 25 patients with a major depressive episode in course of bipolar disorder, and examined their relation to sleep quality and sleep disturbances.

Results
Hierarchical multiple regression analyses showed that serum IL-1β, IL-2 and TNF-α levels were negatively correlated with Pittsburgh Sleep Quality Index global scores. Serum TNF-α levels were positively correlated with hypersomnia.

Conclusions
This preliminary study suggests that IL-1β, IL-2 and TNF-α promote sleep in bipolar depression, and excessive production of TNF-α might be associated with hypersomnia. Given the high prevalence of sleep problems in BD, interest for further studies in larger samples is warranted.

Funding/Disclosures
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CLOCK GENE VARIANTS ASSOCIATE WITH DISCREPANCY BETWEEN SUBJECTIVE AND OBJECTIVE SEVERITY IN BIPOLAR DEPRESSION

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Objectives
Discrepancy between subjective and objective severity of the depressive syndrome has been proposed as a predictor of treatment outcome in depression, and is associated with depressive cognitive distortions. A recent study reported that evening-type depressed patients showed higher depressive cognitions than morning-type patients. Therefore, it can be hypothesized that genetic factors affecting evening preference, such as carrying the CLOCK rs1801260*C allele, could influence this discrepancy.

Methods
We investigated the effect of rs1801260 on discrepancy between subjective and objective severity in 130 depressed patients with bipolar disorder. Severity of depression was evaluated using self-rated (Beck Depression Inventory: BDI) and observer-rated (Hamilton Depression Rating Scale: HDRS) measures. BDI-HDRS discrepancy score was calculated, and the effect of rs1801260 polymorphism on this score was examined.

Results
rs1801260 *C carriers showed higher BDI-HDRS discrepancy than T/T homozygotes (t=-2.252, p=0.026).

Conclusions
Our result suggests that CLOCK gene variants influence on discrepancy between subjective and objective severity in bipolar depression. The relationship between rs1801260 polymorphism and clinical outcome should be investigated in future studies.

Funding/Disclosures
This study was supported by the Italian Ministry of Health RF-2011-02350980 project. M.S. is supported by the Nihon University Overseas Researchers Fund.

CAN ELECTRONIC SELF-MONITORING WITH FEEDBACK FOCUSING ON THE SLEEP-WAKE CYCLE REDUCE RELAPSE OF DEPRESSION AFTER DISCHARGE

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Objectives
Very little is known about depressed patients' mental state after discharge from inpatient wards. During hospitalization patients are provided with a sheltered environment. The period after discharge represent a vulnerable period with potential negative impact on recovery from depression. Our previous study, SAFE I, showed that electronic self-monitoring was useful to gain insight into patients' condition after discharge. Results showed that patients over a four week period had significant day to day variations in self-rated mood and that the patients' sleep were delayed (sleep offset) with 48.2 (SE 12.2) minutes (p=0.0004)). In SAFE II, we investigate whether an intervention focusing on zeitgebers such as daylight exposure, timing of sleep, meals, and social and physical activity, coined *Circadian Reinforcement Therapy* (*CRT*), can lead to a faster recovery and prevent relapse into depression.

Methods
150 patients referred to an outpatient service from inpatient wards will be included while still admitted. Patients will be randomized to either: *Standard Care* (SC) or *Circadian Reinforcement Therapy* (CRT). All the patients will register on a daily basis: sleep, mood, exercise, and medicine compliance, in the Monsenso Daybuilder computer system. The intervention period begins shortly before discharge, continues for 4 weeks and includes weekly telephone contact. The CRT aims at improving sleep and reducing instability in the sleep-wake cycle and by this hopefully prevent relapse of depression. Patient registration will be monitored on a daily basis and contacted if registrations indicate aggravation of depressive symptoms or unstable circadian rhythm. A subset will be assessed with Dim Light Melatonin Onset (DLMO) as a validator of the circadian timing. The primary outcome will be self-rated levels of depression. Secondary outcomes changes in scores on the MDI, WHO-5 index, MEQ, PSQI and Hamilton depression rating scale. The project will run from 2016-2019.

Results
The study is ongoing.

Conclusion
If the interventions are beneficial, we expect to implement the intervention more systematically.

Funding/Disclosures
The study is funded by Trygfonden, Denmark.

EFFECTS OF LIGHT AND TEMPERATURE ON ALERTNESS AND THERMOPHYSIOLOGY

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Objectives
Light and ambient temperature both influence alertness and productivity of building occupants. Effects of the light condition vary over the time of the day. In the evening and night, alerting effects of light go along with a change in physiology, as reflected in skin temperatures, core body temperature and melatonin. The aim of this experiment is to study the effect of light intensity and temperature in the morning on thermophysiology and how this relates to alertness.

Methods
A randomized crossover design was performed in which 19 healthy female subjects participated. The study consisted of two sessions: a bright (1200 lux) and dim (5 lux) light session, both with a correlated colour temperature of 4000K. During each session three different room temperatures were offered: cool (26˚C), neutral (29˚C) and warm (32˚C). Subjects were in semi-supine position and wore underwear. Skin temperatures, core temperature, cortisol and alertness are the main outcome variables. Statistics are performed using a random intercept model in SPSS 23.

Results
Self-assessed alertness was influenced by both light intensity and room temperature. Bright light resulted in a higher self-assessed alertness ($p=0.038$) compared to dim light, irrespective of the ambient temperature. Subjects indicated to feel most alert in the cool temperature ($p<0.01$). Reaction time was only influenced by ambient temperature, not by light, and was slowest during the warm condition ($p<0.01$). Physiological data shows a higher core temperature ($p=0.013$) and proximal skin temperature ($p<0.01$) during dim light session. There was no interaction between light and room temperature. Proximal-distal temperature gradient was larger during dim light ($p=0.01$). Cortisol level was higher at the end of the dim session compared to bright ($p=0.04$) and preliminary results indicate a larger increase of adrenaline during dim light ($p=0.04$).

Conclusions
The three different ambient temperatures result in similar effects of morning light intensity on thermophysiology. However, these effects were opposite to thermo physiological effects reported in literature for evening/nighttime light exposure. At all ambient temperatures studied here, morning bright light increased self-assessed alertness as compared to dim light. This indicates that the relation between thermophysiology and alertness in the morning and evening are of a different nature, warranting further studies.

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GLASS QUALITY AND HEALTH IN PUBLIC HOUSING

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Objectives
The objective of this study is to investigate the health impact of two kinds of window glass on healthy individuals in a public housing in Denmark. Since the invention of the *insulating glass units* (IGUs) in the 1970s, a lot of innovative effort and talent has been put into optimizing the performance of window glass as climate screens. Unfortunately these efforts have served only one purpose: energy, a development which seems to continue in the build environment in the near future, and seems to be the most rational choice, if we do not consider other parameters, such as health. Spending on average 90 % of our time in the indoor environment, the quality of the window glass plays an important and yet overlooked role for our circadian rhythm, sleep, mood, wakefulness and levels of vitamin D. Recent discoveries about the missing piece in the lighting puzzle, the non-visual ipRGCs, put emphasis on natural daylight and its beneficial effects as an efficient *Zeitgeber*, but until now studies have only focused on artificial lighting.

Methods
This randomized controlled study will investigate the effect of the daylight quality, establishing two different indoor daylight conditions by using two different types of window glass in building blocks housing a total of 140 persons in 72 apartments. As part of a building renovation, all windows will be renewed. Tenants that will participate in the study will have their apartment randomized to either: a) Two layered clear low iron glass (Lt = 0,81) that allows ultraviolet and blue light to pass or b) Three layered float glass (Lt = 0,41) that limits the blue and ultraviolet part of the daylight. Spectral power composition (SPC) and transmittance of both glass types will be measured in a controlled environment. Subsequently the study will collect information on wellbeing, mood, sleep, health, and self-reported days of illness. Also D-vitamin will be measured across seasons. All tenants will be asked to take part in the study. The study will sample data during 4 seasons (autumn, winter, spring, summer). Primary outcomes will be self-ratings of sleep, well-being and circadian rhythms. Secondary outcomes will be levels of vitamin D (25-OHD) measured in the blood with a baseline in September before intervention and a measurement after implementation September the following year. Exploratory outcomes will be self-reported days of sick leave and cause of the illness.

Results
Expected results in September 2018.

Conclusions
The hypothesis of the study is that different glass types by a differential transmittance of light, will affect human wellbeing, sleep, illness, and the levels of D-vitamin. The exact effect of different window glass types will, for the first time ever, be examined in a real environment in healthy individuals. Based on the results, we hope to be able to introduce a new concept – a *Healthiness Factor* of glass – in the built environment.

Funding/Disclosures
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CIRCADIAN RHYTHMS, ADHD AND SEASONALITY

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Objectives
We undertook this study to investigate whether indicators of a delayed circadian rhythm (sleep onset, sleep onset and mid sleep) as well as short sleep duration mediated in the relationship between ADHD symptoms and seasonal depressive symptoms.

Methods
Data of 2,239 persons from the Netherlands Study of Depression and Anxiety (NESDA) were used. Two groups were compared: clinically significant ADHD symptoms (N=175) and No ADHD symptoms (N=2064). Sleep parameters were sleep-onset time and sleep duration on free days from the Munich Chronotype Questionnaire. We identified the prevalence of probable SAD and subsyndromal SAD using the Seasonal Pattern Assessment Questionnaire (SPAQ). Clinically significant ADHD symptoms were identified by using a *T* score>65 and the Total score on the Conners Adult ADHD Rating Scale.

Results
The prevalence of probable SAD was estimated at 9.9% in the ADHD group (vs. 3.3% in the No ADHD group) and of probable s-SAD at 12.5% in the ADHD group (vs 4.6% in the No ADHD group). Regression analyses showed consistently significant associations between ADHD symptoms and probable SAD, even after adjustment for current depression and anxiety, age, sex, education, use of antidepressants and benzodiazepines (B=1.81, p<.001). Late self-reported sleep onset was an important mediator in the significant relationship between ADHD symptoms and probable SAD, even after correction for confounders (total model effects: B=0.14, p≤.001).

Conclusions
Both seasonal and circadian rhythm disturbances are significantly associated with ADHD symptoms. Delayed sleep onset time in ADHD may explain the increase in SAD symptoms. Treating patients with SAD for possible ADHD and delayed sleep onset time may reduce symptom severity in these complex patients.

Funding/Disclosures
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LIGHT THERAPY, INITIAL TREATMENT FOR SEASONAL AFFECTIVE DISORDER (SAD)

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Objectives
The purpose of this systematic review is to explore the initial treatment with light therapy alone more effective than combination therapy.

Methods
The World Health Organization (WHO) estimates 350 million people, globally, suffer from depression (WHO, 2015). Mood disorders are a category of illnesses that describe a serious change in mood. Illnesses under mood disorders include major depressive disorder, bipolar disorder, persistent depressive disorder, cyclothymic disorder, and seasonal affective disorder. This debilitating illness causes mental anguish and physical ailments. Mood disorders can increase a person's risk for heart disease, diabetes, and other diseases (Mood Disorders: Medline Plus (n.d.), 2016). Seasonal Affective Disorder (SAD), also known as seasonal depression and seasonal mood disorder, is the result of seasonal patterns that affect biological and mood disturbances. Typically, the patterns occur through fall and winter months with moods returning back to normal by the spring and summer months. Seasonal Affective Disorder (SAD) is a serious mental health issue influencing approximately five percent of the U.S. population (Kurlansik, 2012). The burden of depressive illnesses, such as SAD, is enormous.

A systematic review was conducted comparing various research studies including ten scholarly articles from 2010 to 2015. The results of the review showed evidence suggesting a widespread consensus among experts that daily exposure to light therapy is more effective than combination therapies for treating SAD. Recognizing and understanding SAD in a clinical practice, as well as a variety of effective therapies, are positive implications for improved quality of life.

A systematic review was conducted comparing various research studies for relevance in answering the question: Is the initial treatment with light therapy alone more effective than combination therapy? The criteria used in selecting the studies included publications within the last five years, ranging from 2010 to 2015. The study criteria focused on light therapy, cognitive behavioral therapy, and pharmacotherapies for treating SAD. Out of 25 research articles and studies, including peer reviews, 10 were selected based on the focused criteria. The participants in the studies included women and men with ages ranging from 18 to 60 years of age and met DSM-5 criteria for depressive disorder.

Results
The results of the review showed evidence suggesting a widespread consensus among experts that daily exposure to light therapy is more effective than combination therapies for treating SAD.

Conclusions
Studies varied and supported the hypotheses that light therapy positively influences the brain chemicals responsible for mood changes and depressive symptoms (Osborn, 2014). Bright light therapy showed patients had earlier responses to treatment and less adverse effects than pharmacological groups, using SSRI's and groups using cognitive behavioral therapy (CBT). Studies suggest patients improve within one to two weeks of starting light treatment while using SSRI's take an average of two to four weeks to be effective and CBT can take up to 12 sessions to get results. The effectiveness of light therapy is well established; however, consensus on the duration of treatment required to be effective is not conclusive. Light therapy can be used as an alternative method for those unwilling to use medications or who do not respond to pharmacologic treatments (American Academy of Family Physicians, 2012). CBT requires time and practice to make behavioral changes to reduce symptoms. Preventing recurrences of SAD in second and third winter seasons is limited with light therapy and a repeat of treatments is required.

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None.

BRIGHT LIGHT ENHANCES MOTOR SKILL ACQUISITION IN HUMANS

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Objectives
Bright light (BL) has been known to facilitate human cognition, including emotion and procedural memory without any circadian entrainments. However, although procedural memory is acquired without sharing neural substrates of emotional processing, it remains to be seen how BL affects the consolidation of procedural memory.

Methods
To determine if BL facilitates motor learning, 23 healthy humans randomly assigned to BL (approx. 9,000 lux) or controlled light (CL, approx. 450 lux) group performed a finger tapping task over 2 consecutive days. On day 1 participants were exposed to BL for 20 minutes during performing 12 training finger tapping trials at 1 p.m. corresponding to a nadir of human phase response curve in circadian rhythm for light. They performed 3 retest finger tapping trials on day 2. Immediate and delayed effects of BL on motor skill performance were assessed by its accuracy and speed.

Results
Immediate improvements in accuracy ($p < .0001$) and speed ($p = .007$) were observed in both groups during the training trials. Moreover, the improvement in accuracy in the BL group was found to be greater than that in the CL group ($p < .0001$). Overnight improvements in speed were observed in both groups ($p < .0001$) between the post-training trials and retest. Additionally, the improvement in accuracy in the BL group was found to be less than that in the CL group
($p < .0001$). No between-group difference was found in alertness across the training and retest sessions.

Conclusions
Results demonstrate that BL immediately facilitates motor skill accuracy without speed deterioration, whereas immediate BL facilitation of motor skill accuracy counteracts the delayed effect of the motor skill training. These suggest that BL takes an equivalent delayed improvement in motor skills in advance, which could be acquired overnight, and may suggest that BL drives a potential consolidation process for human motor skill learning.

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