Program Committee: Kathryn Roecklein (chair), Klaus Martiny, Konstantin Danilenko

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Contact SLTBR at sltbrinfo@gmail.com

Dear Friends & Colleagues,

On behalf of the 2014-2015 organizing committee and board of directors, I would like to welcome you to the 27th Annual Society for Light Treatment and Biological Rhythms meeting! This year, we are honored to collaborate with the Centre for Circadian Rhythms at the University of California San Diego as our academic partner and Professor Michael Gorman as our local organizer. With their support, our scientific program has very exciting topics ranging from basic science to clinical application of chronobiology and chronotherapeutics.

This year, we have compiled oral presentations, invited lectures, poster sessions and, of course, dedicated time for questions and answers. By doing this I hope the tradition of active participation and spontaneous debates from both the participants and the sponsors will continue. This tradition, I believe, is the unique and beneficial characteristic of our organization.

I would also like to thank both our new and returning sponsors, who have made this meeting possible, especially our title sponsor Nature Bright. With their support, SLTBR is able to design and implement a high quality scientific program and support student travel grants.

Last, but certainly not least, I would like to express my gratitude to the SLTBR board of directors: Mirjam Münch (vice-president), Kathryn Roecklein (2015 program chair), Konstantin Danilenko, Ybe Meesters, Dorothy Sit (memberships chair), and Matthaeus Willeit (past president), and our coordinator Nikki Hafezi. Without their active involvement and dedication to the meeting and society, the SLTBR would unable to provide a solid platform needed to promote active discussion and debate in the field of light therapy and biological rhythms.

Thank you again for your support and participation, and I hope that you enjoy this year's meeting!

Enjoy the meeting,

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SLTBR President, 2014-2016

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- **Healthy Aging:**
  How can quality of life at higher age be increased or stabilised?
- **Ophthalmology:**
  What solutions are needed to cure the various diseases of the eye?

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Congratulations!

2015 Young Investigator Award Winner

Virginie Gabel, PhD

Centre for Chronobiology
Psychiatric Hospital
University of Basel
Switzerland

SCIENTIFIC PROGRAM

Friday, June 26, 2015

1500-1700	SLTBR Board Meeting - invitation only	La Jolla Shores	
1730-2000	Welcome Reception - all participants + spouses invited to attend	La Jolla Shores	

Saturday, June 27, 2015

0730-1545	Registration Open		
0730-0745	Shuttle Service from La Jolla Shores to Sanford Consortium		
0800-0805	**Welcome, Introduction & Program Overview**	Klaus Martiny	Denmark
0805-0835	**Introduction to Chronobiology**	Michael Gorman	USA
0835-1135	**CET Teaching Course**: Survey for clinicians, researchers, and corporate members, with emphasis on the therapeutic and physiological effects of light, applications, and caveats		
0835-0930	Melatonin: Endogenous and exogenous processes	Benita Middleton	UK
0930-0955	Melatonin: Naturalistic administration	Michael Terman	USA
0955-1035	Wake Therapy	Francesco Benedetti	Italy
1035-1120	Light Therapy for ADHD	Robert Levitan	Canada
1120-1135	Questions and Answers for CET Teaching Course		
1135-1300	**Lunch**		
1300-1330	**Guest Address: The beginning of light therapy**	Dan Kripke	USA
1330-1510	**Symposium I: Sleep and Circadian Health**		
	Co-moderator	Gena Glickman	USA
	Co-moderator	Ronald Szmusiask	USA
1330-1350	Developing circadian signatures for evaluation of sleep health in the home	Gena Glickman	USA
1350-1410	Behavioral interventions to improve sleep and sleepiness in Bipolar Disorder	Kate Kaplan	USA
1410-1430	Why do people nap? Effects of napping on personality, mood and cognition	Sara Mednick	USA
1430-1450	Effects of light treatment on fatigue, sleep and rhythms in cancer	Sonia Ancoli-Israel	USA
1450-1510	Questions and Answers for Symposium I		
1510-1540	**Coffee Break / Poster Session I** *Presenters remain in front of their posters.*		

1540-1645	**Oral Presentations - Session I**	Barbara Parry	USA
1540-1555	Increasing clock plasticity using exotic light-dark cycles	Michael Gorman	USA
1555-1610	Extreme light suppression of locomotor activity in a Smith-Magenis syndrome (SMS) mouse model	Shanaz Diessler	Switzerland
1610-1625	The dilemma of the isolated night shift and the right light: Should it be orange and bright?	Johannes Regente	Germany
1625-1640	Questions and Answers for Oral Session I		
1645-1700	**Young Researcher Award Presentation**	Mirjam Münch Ybe Meesters	Germany Netherlands
	Young Research Award Lecture	Virginie Gabel	Switzerland
1700-1830	**Poster Walk - Poster Prize Judging** *All poster presenters need to be present at poster during review*	Dorothy Sit	USA
1930-2200	**Congress Dinner - hosted by NatureBright**	Joshua Chen	USA

Sunday, June 28, 2015

0800-1130	Registration Open		
0745-0800	Shuttle Service from La Jolla Shores to Sanford Consortium		
0800-0945	**Symposium II: Chronobiotics**		
	Moderator	Marijke Gordijn	Netherlands
0800-0830	Lithium and other mood stabilizers	Francesco Benedetti	Italy
0830-0900	Chronobiopharmacology basics / Circadian gene expression atlas in mammals	John Hogenesch	USA
0900-0930	Endogenous melatonin and its receptors: implications for chronobiotics	Alfred Lewy	USA
0930-0945	Questions and Answers for Symposium II		
0945-1045	**Keynote Lecture**: The BioClock Studio: students creating innovative content to enhance teaching, research and outreach	Susan Golden	USA
1045-1115	**Coffee Break / Poster Session II** *Presenters remain in front of their posters.*		
1115-1235	**Oral Presentations - Session II**	Michael Young	USA
1115-1130	The pupil light reflex demonstrates seasonal variation in healthy subjects	Mirjam Münch	Germany
1130-1145	Chronotype predicts positive affect rhythms as measured by ecological momentary assessment	Megan A. Miller	USA
1145-1200	The impact of broad spectrum bright light on plasma hormones and metabolites	Mohammed AlBreiki	United Kingdom
1200-1215	Bright light facilitates fear extinction and prefrontal processing for fear extinction in humans	Takuya Yoshiike	Ja[an
1215-1235	Questions and Answers for Oral Session II		
1235-1400	**Lunch** **SLTBR Annual Business Meeting**		

1400-1515	**Symposium III: DSM-5 and Chronobiology**		
	Co-moderator	Kathryn Roecklein	USA
	Co-moderator	Raymond Lam	Canada
1400-1420	Looking into the eye of ADHD	Sandra Kooij	Netherlands
1420-1440	SAD and serotonin	Brenda McMahon	Denmark
1440-1500	Cellular circadian rhythms in bipolar disorder	Michael McCarthy	USA
1500-1515	Questions and Answers for Symposium III		
1515-1545	**Coffee Break / Poster Session III**		
	Presenters remain in front of their posters.		
1545-1645	**Oral Presentations - Session III**		
1545-1600	A randomized, placebo-controlled study of bright light therapy, fluoxetine and the combination, for nonseasonal major depression	Raymond Lam	Canada
1600-1615	Randomized trial of cognitive-behavioral therapy vs. light therapy for Seasonal Affective Disorder	Kelly J. Rohan	USA
1615-1630	Early wake therapy reduces the melatonin onset-sleep onset phase angle and improves mood in depressed pregnant women	Barbara Parry	USA
1630-1645	Questions and Answers for Oral Session III		
1645-1700	**Poster Prize Presentations**	Dorothy Sit	USA
	Travel Grants	Mirjam Münch	Germany
	Students need to be present to receive grants		
1700-1715	**Final Remarks**	Klaus Martiny	Denmark

Poster Presentations

Abstracts of Posters and Presentations (as provided by authors)

(in alphabetical order by first author)

THE IMPACT OF BROAD SPECTRUM BRIGHT LIGHT ON PLASMA HORMONES AND METABOLITES

Mohammed AlBreiki, Benita Middleton, Shelagh Hampton
Department of Biochemistry & Physiology, School of Bioscience & Medicine, Faculty of Health & Medical Science. University of Surrey, UK

Objectives
This study aims to investigate the impact of light and/or melatonin on plasma hormones and metabolites prior to and after a set meal in healthy subjects.

Methods
A favourable ethical opinion was obtained from the University Ethics Committee (EC/2013/93/FHMS). Seventeen healthy participants, 8 females (22.2 ± 2.59 years, body mass index (BMI) 23.62 ± 2.3 kg/m2), 9 males (22.8 ± 3.5 years, BMI 23.8 ± 2.06 kg/m2 (mean ± SD)) were randomised to a two way cross over design protocol; dim light condition (<5 lux) and bright light condition (>500 lux), separated by at least seven days. Each clinical session commenced at 18:00h and finished at 06:00h the next day. Participants consumed an isocaloric and non-carbonated evening meal (1066 Kcal, 38g protein, 104g CHO, 54g fat, 7g fibre. The meal times were individualised based on melatonin onset (dim light onset (DLMO)) estimated from participants' 48h sequential urine collection. Pre-prandial and postprandial plasma samples were collected at specific time intervals to assess glucose, insulin, TAG and NEFAs concentrations. Saliva samples were collected every 30 minutes to assess melatonin levels. Melatonin and insulin were measured using radioimmunoassay (Stockgrand Ltd, EMD Millipore), whereas Glucose, TAG and NEFA were analysed by standard automated enzymatic spectrophotometric methods (ILAB 650). Statistical analysis was carried out using Statsoft STATISTICA with three factor repeated measures ANOVA (gender, time, treatment).

Results
The results of 17 subjects for melatonin, glucose, TAG, NEFAs and insulin are shown below. Salivary melatonin and plasma NEFAs levels were significantly higher in the dim light condition compared to bright light conditions ($p = < 0.001$, $p = < 0.01$) respectively. In contrast, plasma insulin and glucose levels were significantly greater in the bright light condition than in dim light conditions ($p = 0.001$, $p = 0.02$) respectively. No significant difference was seen in plasma TAG. There were significant effects of time in all 5 parameters, whereas no significant effects of gender were shown.

Parameter	Gender	Condition	Time
Melatonin	0.203	<0.001***	<0.001***
Glucose	0.842	0.02*	<0.001***
NEFAs	0.277	0.005**	<0.001***
TAGs	0.213	0.394	<0.001***
Insulin	0.764	0.001**	<0.001***

(* p<0.05, ** p<0.01, *** p<0.001)

Conclusions
Melatonin suppression was expected due to light exposure at night (LAN). It is possible that the significant reduction in insulin levels under the dim light condition is due to the presence of melatonin7, which in turn minimises the inhibitory effects of insulin on hormone sensitive lipase (HSL) resulting in higher NEFAs in dim light than in bright light 8. Plasma glucose levels were greater in bright light than in dim light despite the presence of higher insulin levels in the bright light condition, which could be explained by increased insulin resistance.

Disclosures This study is supported by Abu Dhabi Health Service Company (SEHA) and Abu Dhabi Education Council in United Arab Emirates

EFFECT OF LIGHT TREATMENT ON FATIGUE, CIRCADIAN ACTIVITY RHYTHMS AND QUALITY OF LIFE IN PATIENTS WITH CANCER

Sonia Ancoli-Israel (1,2), Lianqi Liu,(1), Ariel Neikrug,(1), Michelle Rissling (1)
Department of (1) Psychiatry and (2) Medicine, University of California San Diego

Objectives
Fatigue is one of the most disturbing complaints of cancer patients and often is the reason for discontinuing treatment. In addition, during chemotherapy circadian rhythms are commonly disrupted and quality of life (QOL) diminishes. We have previously shown that women with breast cancer (BC) have little exposure to bright light. Yet, decreased exposure to bright light has been associated with depression, fatigue and poor sleep in other chronic illnesses and increased bright light has been shown to improve and strengthens circadian rhythms. This randomized controlled study tested whether increased morning bright light, compared to dim light, would result in less fatigue, more robust circadian activity rhythms (CAR) and better quality of life in women with breast cancer undergoing chemotherapy.

Methods
39 women newly diagnosed with Stage I-III breast cancer were randomized to either bright white light (BWL) or dim red light (DRL) treatment and were instructed to use the light box for 30 minutes every morning throughout the first 4 cycles of chemotherapy. The Multidimensional Fatigue Symptom Inventory (MFSI) and the Functional Assessment of Cancer Therapy-Breast (FACT-B) were administered and 3 consecutive 24-hour periods of wrist actigraphy were recorded at 5 time-points: prior to chemotherapy (baseline), cycle-1 treatment week (C1TW) and recovery week (C1RW), and cycle-4 treatment week (C4TW) and recovery week (C4RW).

Results
Fatigue: The DRL group reported increased fatigue at C1TW ($p=0.003$) and C4TW ($p<0.001$) compared to baseline while there was no significant change from baseline in the BWL group. A secondary analysis showed that the increases in fatigue levels in the DRL group were not mediated through associated with changes in sleep or in CAR.
CAR: The DRL group exhibited significant deterioration in overall rhythm robustness at C1TW, C4TW, and C4RW. Women in the BWL group also showed significant decrease in overall rhythm robustness at treatment weeks C1TW and C4TW, but returned to baseline levels at both recovery weeks.
QOL: Compared to baseline, the DRL group demonstrated significant decline in QOL during the treatment weeks of both cycles (all $p's<0.02$), whereas the BWL group had no significant decline (all $p's>0.05$).

Conclusions
The results of this study suggest that morning bright light treatment may protect women undergoing chemotherapy from fatigue and decline in QOL. The first administration of chemotherapy was associated with transient circadian activity disruption, but repeated administration of chemotherapy resulted in progressively worse and more enduring rhythm impairments.

Disclosures Supported by California Breast Cancer Research Program11IB-0034, a grant from Litebook, Inc, NCI CA112035, NIH M01 RR00827, P60MD00220, The Rebecca and John Moores UCSD Cancer Center (NCI P30 CA23100).

EFFECTS OF CLOCK GENE VARIANTS AND EARLY STRESS ON HOPELESSNESS AND SUICIDE IN BIPOLAR DEPRESSION

Francesco Benedetti, Roberta Riccaboni, Sara Dallaspezia, Cristina Colombo
Ospedale San Raffaele, Milano, Italy

Objectives
Patients with mood disorders show a high dependence of behavior on the molecular characteristics of the biological clock. CLOCK rs1801260 gene polymorphism influences circadian behavior in Bipolar Disorder (BD), with *C carriers showing a delayed sleep onset and increased insomnia. Sleep phase delay and insomnia are associated with suicide in the general population.

Methods
We investigated the effects of rs1801260, and of exposure to stressful life events, on current suicidal ideation and history of suicide attempts in 70 depressed patients with Bipolar Disorder (BD).

Results
rs1801260*C carriers currently showed higher Hamilton Depression Rating Scale scores for suicide, and higher ratings for depressive cognitive distortions. Previous history of attempted suicide was associated with exposure to higher stressful events in early life, with rs1801260*C carriers showing a higher dependence of the modeled probability of attempting suicide on the severity of exposure to early stress.

Conclusions
CLOCK rs1801260 modulated the relationship between early stress, adult history of attempted suicide, and current suicidal ideation. Factors affecting the biological clock can influence "non-clock" core psychopathological features of mood disorders.

A DOUBLE BLIND. PLACEBO CONTROLLED, RANDOMIZED TRIAL OF LIGHT THERAPY FOR NON-SEASONAL BIPOLAR VS UNIPOLAR DEPRESSION

Magdalena Chojnacka (1), Łukasz Święcicki (2)
(1) Department of Affective Disorders, Institute of Psychiatry and Neurology, Warsaw (2) Department of Affective Disorders, Institute of Psychiatry and Neurology, Warsaw

Objectives
Antidepressants are the mainly treatment option for depression. However application of pharmacotherapy is often connected with some limitation. Moreover its treatment efficacy is lower than desired, at the most of 70%. There are ongoing studies on the pathogenesis of depression to search for new therapeutic strategies. In the last decades there is growing interest in the chronobiology. One of the chronotherapeutics is exposure to bright light. Effectiveness and tolerability of bright light therapy (BLT) was confirmed in the treatment of seasonal affective disorders (SAD). Although more and more reports on the use of BLT in nonseasonal depression are published, either as monotherapy or as adjuvant to conventional antidepressants, this method has not been extensively studied yet and the results are unclear. The aim of the study was to examine the efficacy and safety of morning BLT in treatment of patients with bipolar or unipolar affective disorder, depressive phase, without seasonal pattern. It was randomized, double-blind and placebo-controlled trial.

Methods
Adults, ages 18-70 years were randomized to treatment either with BLT or with device called “negative ion generator” (as a placebo control). Patients were administered BLT (exposure for 30 min to a 10 000 lx) in the morning for 2 weeks. Subjects were required to be on stable and therapeutic dose of psychotropic medication for at least 4 weeks prior to enrollment and the treatment was not sufficiently effective. Clinical state was monitored at the baseline and at the end of treatment. The HAMD-21, MADRS, BDI, CGI, PGI were used.

Results
95 patients were enrolled (50 with diagnosis of bipolar disorder and 45- unipolar disorder). 52 patients were randomized to treatment with BLT and 43 were in the placebo group. 83 subjects completed the study. There were 12 dropouts (5 in the light group and 7 in the placebo group). After 14 days of treatment a significant improvement was found in all groups ($p<0,001$). Subjects treated with BLT demonstrated no significantly different improvement compared to patients treated with placebo ($p>0,25$). There was no statistically significant differences between unipolar and bipolar disorders ($p>0,3$). However, the further statistical analysis showed that BLT had a significant effect on the symptoms associated with dysregulated circadian rhythms. Furthermore, there was found that in the group of patients with drug resistant depression BLT was more effective than placebo ($p=0,06$). The results also showed a tendency for a higher remission rate ($p=0,07$) in the light group. BLT was well tolerated. Side effects were rare, mild and disappeared after a few days of treatment beginning. The most common were headache and anxiety.

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

SLEEP HOMEOSTATIC PRESSURE AND PER3 VNTR GENE POLYMORPHISM INFLUENCE ANTIDEPRESSANT RESPONSE IN BIPOLAR DEPRESSION

Sara Dallaspezia, Cristina Colombo, Francesco Benedetti
Ospedale San Raffaele, Milano, Italy

Objectives
Total sleep deprivation (TSD) combined with light therapy (LT) causes a marked and rapid improvement of bipolar depression. Changes of sleep homeostasis have been hypothesized to parallel clinical improvement. The coding region of Per3 gene contains a variable-number tandem-repeat (VNTR) polymorphism, which has been associated with diurnal preference, sleep structure and sleep homeostatic response to sleep deprivation in healthy subjects.

Methods
We administered three consecutive TSD+LT cycles to 90 bipolar depressed patients. Severity of depression was rated on the Hamilton Depression Rating Scale. A group of 60 patients was also studied with wrist actigraphy during treatment.

Results
PER3 VNTR polymorphism influenced changes in total sleep time before/after treatment: while $PER3^{4/4}$ and $PER3^{4/5}$ patients showed a reduction of TST after treatment, and $PER3^{5/5}$ subjects showed an increase of about 45 minutes, suggesting a higher homeostatic pressure. The same polymorphism influenced the change of depressive symptomatology during treatment, with $PER3^{4/4}$ and $PER3^{4/5}$ subjects showing the best reduction of HDRS scores, and $PER3^{5/5}$ lower benefit.

Conclusions
A higher sleep homeostatic pressure is associated with lower antidepressant response to TSD+LT, while an allostatic adaptation to sleep loss is associated with better response. This process appears to be under genetic control. Actigraphic data were recorded through one day after the end of treatment, so we had no information about subsequent changes of sleep pressure during discontinuation.

EXTREME LIGHT SUPPRESSION OF LOCOMOTOR ACTIVITY IN A SMITH-MAGENIS SYNDROME (SMS) MOUSE MODEL

Shanaz Diessler (1), Corinne Kostic (2), Aki Kawasaki (2), Yvan Arsenijevic (2), Paul Franken (1)
(1) Center for Integrative Genomics, University of Lausanne, Switzerland
(2) Jules-Gonin Ophthalmic Hospital, University of Lausanne, Switzerland

Objectives
In addition to its role in vision, light has major effects on behavior, physiology, and cognition. These effects include the role of light as Zeitgeber entraining circadian rhythms as well as the so-called direct effects of light such as, e.g., the promotion of sleep by light in a nocturnal animal. SMS is a multiple congenital anomalies mental-retardation disorder associated with an interstitial deletion on chromosome 17p11.2 or with point mutations in a gene located within the deletion area, Rai1 (Retinoic acid induced 1). Besides characteristic clinical features, the most constant phenotype is a misalignment of sleep evidenced by early on- and offset of sleep, nocturnal awakenings, and excessive daytime sleepiness coupled with an inverted melatonin rhythm, suggesting impaired light perception in SMS. We here aim to determine whether circadian rhythmicity, entrainment, or direct light effects contribute to the SMS phenotype using a mouse model.

Methods
We used male B6(Cg)-Tyrc-2J/J mice heterozygous for a Rai1 deletion (Rai1+/-; Bi et al. Hum Mol Genet 2007) and their wild-type littermates as controls. Activity and sleep-wake patterns were investigated under different light-dark (LD) regimens: LD12h:12h, LD1h:1h, and constant light (LL) and dark (DD) conditions. Electroencephalogram (EEG) and -myogram (EMG) signals were recorded to evaluate sleep, the electroretinogram (ERG) to evaluate retinal activity.

Results
Rai1 haploinsufficiency resulted in hypoactivity with increased levels of EEG delta (1-4 Hz) activity during wakefulness, but not to an important redistribution of sleep-wake and activity patterns under LD12:12. Under DD, Rai1+/- mice showed a pronounced 2.6h decompression of the active period and a 0.5h advance of activity onset relative to LD12:12, while period length did not differ (23.8h for both) indicating that light suppresses activity in Rai1+/- mice. The results of the LD1:1 and LL conditions powerfully illustrate that light indeed strongly suppresses activity independent of circadian time. Wakefulness was much less affected by light underscoring that locomotor activity in the mouse can be a poor indicator of sleep-wake state. In search of mechanism, we found that ERG output was decreased indicating that already at the level of the retina processing of light information is altered in Rai1+/- mice.

Conclusions
Rai1 haploinsufficiency in the nocturnal mouse resulted in a hypersensitivity to light while clock function and entrainment seemed intact. In SMS patients light might have lost its capacity to stimulate active wakefulness contributing to the misalignment of sleep. How reduced rod/cone activity contributes to this extreme phenotype and through which pathways activity, but not wakefulness is supressed, is under investigation.

Disclosures none

RELATIONSHIP BETWEEN CHRONOTYPE, MEAL TIMING, AND BODY MASS IN SEASONAL AFFECTIVE DISORDER

Shannon D. Donofry (1), Gabrielle R. Brinsky (1), Megan A. Miller (1), & Kathryn A. Roecklein (1,2)
(1) Department of Psychology, University of Pittsburgh
(2) Center for the Neural Basis of Cognition

Objectives
Winter seasonal affective disorder (SAD), characterized by the onset of depressive episodes during the winter months that remit in spring or summer, has been associated with winter weight gain and higher prevalence of binge eating. However, the mechanisms underlying seasonal changes in eating and weight are not fully understood. Given that individuals with SAD exhibit circadian delays in both physiology and behavior, it is possible that these individuals tend to eat their meals later in the day, a known risk factor for obesity and binge eating. Therefore, the present study aimed to examine differences in meal timing in winter among individuals with SAD relative to non-seasonal, non-depressed controls.

Methods
Participants included adults (96% female) aged 21-64 years (M = 39.50, SD = 12.34) diagnosed with SAD (n = 16) or with no history of depression (n = 8). Meal timing was assessed using the Pittsburgh Sleep Diary, from which average first meal time was derived. Participants completed the Morningness-Eveningness Questionnaire (MEQ) to determine chronotype. Height and weight were recorded to calculate body mass index (BMI).

Results
Individuals with SAD (beta = 0.382, p = 0.035) and individuals with a more evening chronotype (beta = -0.457, p = 0.014) ate their first meal significantly later in the day than did controls or those with a more morning chronotype. Group, MEQ scores, and timing of first meal did not significantly predict current BMI (F (4, 19) = 1.750, p = 0.18) or maximal lifetime BMI (F (4, 19) = 1.600, p = 0.22) when included in a single model. However, group was significantly correlated with current BMI (r = 0.419, p = 0.02) and maximal lifetime BMI (r = 0.374, p = 0.05), with SAD individuals having higher BMI than healthy individuals. There was no significant correlation between MEQ scores and current BMI (r = -0.339, p = 0.11) or maximal lifetime BMI (r = -0.333, p = 0.11), although individuals with a more evening chronotype had higher mean BMI than those with a more morning chronotype.

Conclusions
The present study provides evidence that individuals with SAD eat their first meal significantly later than those without SAD. Similarly, individuals with an evening chronotype ate their first meal later than those with intermediate or morning chronotype, perhaps reflecting the influence of delayed circadian rhythms. However, contrary to study hypotheses, there were no significant relationships between group, chronotype, timing of first meal, and BMI. Nevertheless, the relationships between group, chronotype, meal timing, and BMI were in the hypothesized direction, and may have reached statistical significance in a larger sample.

Disclosures None

GENDER-RELATED ALTERATIONS IN SUBJECTIVE WELL-BEING UNDER MODERATELY BRIGHT LIGHT DURING 40-H OF SUSTAINED WAKEFULNESS

Virginie Gabel (1), Carolin Reichert (1), Micheline Maire (1), Christina Schmidt (2), Christian Cajochen (1), Antoine U. Viola (1)
(1)Centre for Chronobiology, Psychiatric Hospital of the University of Basel, Switzerland
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Objectives
It was shown that subjective well-being is modulated by circadian phase, sleep pressure and also gender (Birchler-Pedross et al., 2009). However, it is not yet known, whether circadian and sleep-wake homeostatic modulation of subjective well-being is different in men and women under differential light conditions. Thus, we examined gender-related effects of extended light exposure during 40h of sleep deprivation on well-being, in comparison to subjective sleepiness, melatonin and cortisol levels.

Methods
Twenty six young participants (15 young men (24.47 ± 0.67) and 11 young women (25.64 ± 1.04)) underwent 40-hours of extended wakefulness once under dim light (DL: 8 lux), and once under either white light (WL: 250 lux) or blue-enriched white light (BL: 250 lux) exposure. Subjective sleepiness and well-being was assessed hourly along with melatonin and cortisol assays. Mixed-model analyses of variance for repeated measures were applied for statistical analyses.

Results
Subjective well-being exhibited a clear circadian modulation with lower values during the biological night than during the biological day in both gender, while well-being did not worsen or improve with increasing sleep pressure. However, a significant effect for the factor gender was found for well-being, which indicated that men felt generally better under 40-h of sustained wakefulness than women under all light conditions. Furthermore the significant interaction gender x light condition, indicated that men felt better under both moderately bright light sources compared to dim light, whereas women only showed a significant improvement in well-being under the blue-enriched light condition. Bright light during 40 hours of sustained wakefulness induced a significant decrease in subjective sleepiness. However, only at the trend level women felt sleepier than men under all light conditions with no significant interaction term gender x light condition. Melatonin levels were in general significantly higher in women than to men, with no significant gender difference in the suppressing effect of both moderately bright light conditions. In contrast to melatonin, there was no main effect of gender for the cortisol profile, but a significant interaction term gender x light which yielded higher cortisol levels in women compared to men under the white light condition.

Conclusions
Our data indicate that constant exposure to moderately bright light during 40 hours of extended wakefulness has gender specific effects on well-being and cortisol secretion. Thus, when implementing new light solutions in institutions requiring night shift work (e.g. hospitals), the gender composition of the workforce should be considered.

Disclosures None

DAWN SIMULATION AS A PROTECTIVE CONTEXT FOR CARDIOVASCULAR VULNERABILITY SURROUNDING SLEEP-TO-WAKE TRANSITION

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Objectives
We consciously control our sleep-wake timing, by the use of alarm clocks to wake-up in the morning. Increases of major cardiovascular events in the morning hours represent a common feature and are thought to be partially due to abrupt changes in the sympatho-vagal balance, namely sympathetic surges during the transition from sleep to wakefulness. Here, we explored whether a more gradient transition from sleep to wakefulness via a dawn simulation light around awakening has the potential to reduce morning cardio-vascular vulnerability.

Methods
After a night of 6-h sleep restriction, participants were awakened 2 hours before their habitual wake-time. In a counterbalanced within-subject design, we applied a habitual auditory alarm clock or a dawn simulation light alarm clock (DSL) starting 30-minutes before and ending 30-minutes after scheduled wake-up time. Importantly, for both conditions participants remained in bed in a supine position until 30-minutes following their awakening. Seventeen healthy young men met the inclusion criteria.

Results
We observed a significant gradient reduction in heart rate during the transition from sleep to wakefulness when applying DSL as compared to the classical alarm clock. Likewise, Heart-rate-variability smoothly increased throughout the 30-min sleep episode preceding scheduled wake-up in the DSL condition.

Conclusions
Dawn simulation might protect the heart by an evolving preparation of cardiac physiology for the wake-up process. Application of a dawn simulation, which more closely approximates natural lighting conditions in the morning, might therefore be considered as an effective tool to help waking up reducing the cardiovascular vulnerability of the waking up process.

SLEEP AND CIRCADIAN HEALTH IN ACTIVE DUTY MILITARY ELITE

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Objectives
Sleep problems are frequently reported by active duty military members and result in a host of negative health and warfighter readiness consequences. Evidence suggests our Naval Special Warfare Operators (SEALS), among those with the highest operational demands, are not immune to sleep disturbances; however, objective studies of sleep in these elite military members have been limited. We were tasked with rigorously characterizing sleep and circadian health in this unique population.

Methods
Continuous actigraphy recordings were collected for 7 days with concurrent serial sampling of saliva at 10 time points (upon waking, 30 and 60 min post-waking, 1600 and 2100) across the first two days in post-deployed SEALs (n=45). Sleep onsets/offsets, total sleep time (TST), waking after sleep onset (WASO) and sleep efficiency were determined with actigraphy. Subjective sleep quality scores (1-10 scale, with 1 being poorest) were also obtained. Salivary data were adjusted for volume and flow rate, with assessment of dehydroepiandrosterone (DHEA), testosterone, and cortisol via enzyme immunoassay. Hormones were calculated as a percentage of individual mean for each day, and cosinor analysis determined the presence/absence of a circadian rhythm in each biomarker ($p<0.05$) as well as key parameters (mesor, amplitude, acrophase). Mid-sleep times and acrophases for the three hormones were used for phase angle comparisons within and between individuals, and differences >1.5 hours were considered misaligned.

Results
Mean TST was 6.13 hours, with a mid-sleep time of 0224. The mean acrophases for DHEA, testosterone and cortisol were 0707, 0710 and 0717, respectively. Comparison of individual data found the vast majority of subjects (89%) demonstrate at least one 24 h rhythm; however, among those, ~50% show some circadian misalignment between hormones and/or mid-sleep times. Those who do not show a 24 h rhythm in any of the 3 salivary markers demonstrate 59% greater WASO, 5% lower sleep efficiency score and significantly earlier mid-sleep times. In contrast, mean TST and subjective sleep quality scores were not statistically different between rhythmic and arrhythmic subjects.

Conclusions
Our study reveals the pervasive nature of sleep and circadian disturbance in SEALs, even post-deployment. In addition, two of the main metrics used to determine sleep health (TST and subjective sleep quality) failed to identify those with the most extreme neuroendocrine abnormalities, though those individuals also had greater qualitative sleep disturbances based on WASO and sleep efficiency scores. Future assessment of sleep and circadian health within this elite military population should include multiple objective outputs.

INCREASING FLEXIBILITY OF CIRCADIAN ENTRAINMENT WITH EXOTIC LIGHT MANIPULATIONS

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Objectives
In response to shift-work or rapid time zone travel, circadian rhythms are very slow to shift. Here we investigate methods to achieve rapid resetting and stable entrainment of mice and hamsters to extraordinary lighting conditions.

Methods
Rodents are maintained in running wheel cages and exposed to 24 h and non 24 h light:dark:light:dark (LDLD) cycles with or without incorporation of very dim (< 0.1 lux) light during scotophases.

Results
In LDLD cycles with dim nocturnal illumination, rodents undergo a rhythm “bifurcation” such that they experience two subjective days and two subjective nights per 24 h. Once bifurcated, rhythms of mice and hamsters may be reset nearly instantly to a conventional LD cycle in any phase. Moreover, bifurcated animals will successfully adjust to lighting cycles far from the conventional range of entrainment (e.g., 18 h – 30 h days).

Conclusions
The circadian systems of rodents are far more flexible than previously anticipated. An understanding of the modulation of circadian flexibility may enable human circadian clocks to be more easily manipulated to avoid circadian disruption.

Disclosures: Funded by the Office of Naval Research (N000141310285) to MRG

VISUAL PERCEPTION REQUIRES PHOTORECEPTION: SUBJECTIVE REPORT OF LIGHT IN THE SLEEP ENVIRONMENT

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Objectives
The vast majority (84%) of American adults have light-emitting technology in their room at night (2014 Sleep in America Poll). Light is the primary synchronizing cue for the circadian timing system, and even relatively dim light, such as that emitted by e-readers, can markedly alter the body's clock (Chang et al., 2014). Thus, consideration of ambient light is critical in the assessment of sleep health. Sleep diaries are commonly utilized to examine sleep patterns and habits, yet they do not typically include information about the lighting environment. Some wrist-worn actigraphy devices contain light sensors, though precision and cost both limit the scope of application. The addition of a few sleep diary questions pertaining to perception of light in the sleep environment may aid in the differential diagnosis of circadian and sleep disorders, provide information regarding sleep hygiene and compliance, and even provide a crude metric of relative photic intensity and photoreceptor stimulation, at virtually no cost.

Methods
Diary and actigraphic measures were used to quantify sleep in active duty military service members (n=17) for 6 nights per individual in the home (102 nights total). Participants completed the sleep diary each morning upon waking, and the following questions were included to probe light intensity and photoreceptor activation in the sleep environment: 1) After turning off the light, was there any light still visible in your room?; 2) Were you able to see objects in your room?; and 3) If you could see objects, did they appear in shades of grey or in color (even if less vivid)? Nightly data were divided into two groups (affirmative or negative responses) for each of the three light-based questions. These were then compared to diary- and actigraphy-derived measures of sleep. Statistical analyses corrected for unequal samples sizes where appropriate.

Results
On nights when visible light was reported (Question #1), reported sleep latency was longer (15 vs. 9.27 min; $p<0.05$) and reported sleep quality was poorer (6.77 vs. 7.75; $p<0.05$); however, no group differences were found for reported number of awakenings nor for any actigraphic measures. Similarly, no differences on any sleep measure were found for nights when objects could be seen in the room (Question #2). Group differences were found on both diary- and actigraphy-based measures for Question #3, regarding objects appearing in shades of grey or color. On nights when objects were reported as appearing in color (indicative of relatively increased intensity and activation of cones), there were more reported awakenings (3.56 vs. 2.21; $p<0.05$), and actigraphy showed greater wake after sleep onset (WASO; 123.63 vs. 57.68 min; $p<0.05$) with a corresponding reduction in sleep efficiency (69.90 vs. 80.80%; $p<0.05$).

Conclusions
The addition of only a few items to sleep diaries may provide meaningful information about light in the sleep environment. In addition, responses to these questions appear to relate to clinically relevant measures of sleep. Further data collection and analysis is underway, including examination of the relationship between perceptual information and actigraph photosensor measures.

SLEEP AND CIRCADIAN DISRUPTION IN HOSPITAL EMERGENCY PHYSICIANS

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Objectives
To maintain around-the-clock care, Emergency physicians (EPs) work rotating shifts, often divided into three scheduled 8 h shifts across the 24 h day (day, swing, and night). Rotating shiftwork causes profound circadian disruption, with consequent decrements in health and performance. Further, shiftwork has been cited as a primary reason for leaving the specialty. We aim to quantify the circadian and sleep disruption that results from current EP scheduling practices and sleep strategies, with the goal of identifying strategies that mitigate symptoms of disruption.

Methods
In Experiment 1, subjective measures of sleep and alertness in emergency medicine residents (EMRs) at an urban training program were reported across the three different shift types (n= 31). The survey included The Survey of Shiftworkers and the reduced Horne-Ostberg Morningness Eveningness Questionnaire (rMEQ). In Experiment 2, which is ongoing, sleep and vigilance across different shift types are assessed objectively in both EMRs and attending physicians (n=7). Actigraphy is collected for 28 days during a month-long rotation. Participants are asked to complete the Psychomotor Vigilance Task (PVT) and the Karolinska Sleepiness Scale at the beginning, end, and during any break throughout each shift. In a novel assay, predicted sleep strategies for coping with the rotation are collected and directly compared to actigraphy and a sleep log data collected throughout the actual rotation.

Results
Thirty-one EMRs with a mean exposure to shift work of 2.2 ± 0.2 years participated in Experiment 1 (13 female; mean age 30.7 ± 0.4 y). Total reported sleep time was highest between consecutive days off, lower in succession from swing to day to night shifts, and lowest after the final night shift (9.21, 7.81, 7.40, 6.66 and 4.88 hours, respectively; RM-ANOVA, $p<0.0001$; all $p<0.05$ excepting day vs. swing and night shifts). Sleep quality between successive shifts was rated highest between days off, worse between day and swing shifts and worst between night shifts (RM-ANOVA, $p<0.0001$; all $p<0.05$ except day vs. swing shift). Subjectively-reported alertness was significantly lower on night shifts than on day or swing (RM-ANOVA, $p<0.0001$). Finally, chronotype predicted total sleep time on day and swing shifts: morningness was associated with more sleep on day shifts ($r=0.40$; $p<0.05$), with the opposite pattern for the swing shift ($r= -0.40$; $p<0.05$). Data collection and analysis for Experiment 2 is in progress. Preliminary results suggest that alertness as measured by median reaction time on the PVT is significantly lower on night shifts than on day or swing ($p<0.05$).

Conclusions
These data suggest decreased sleep quantity, quality, and levels of alertness in EMRs during night shifts, with decreased measures over successive night shifts. They also suggest that consideration of chronotype in scheduling may lead to improved sleep in EMRs. Subsequent analyses of sleep and sleep strategies may lead to additional scheduling recommendations.

Disclosures None.

IMMEDIATE INFLUENCE OF BRIGHT WHITE VS. DIM RED LIGHT ON METABOLISM IN SAD AND HEALTHY CONTROLS : A CROSSOVER STUDY

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Objectives
Previous studies have shown a decrease in body (fat) mass following bright light treatment in overweight women irrespective of their season(light)-dependence. Possible explanations included (a) appetite decrease, (b) metabolism increase, (?) normalization of diurnal rhythm of eating behaviour, and (d) increase of a drive to weight loss. Whereas (a) was supported and (d) - rather not, the (b) – metabolism changes - were undefined in those studies. The previous studies investigating metabolism following light treatment brought contradictory results: in one study, a decrease of enhanced metabolic rate (according to oxyspirography) following a week of light therapy was observed in winter depressives (SAD) [1], in another, an increase has been reported, both in winter depressives and healthy controls [2]. This study investigated an immediate effect of bright light on metabolism and, additionally - on resting system tone and arousal levels.

Methods
The study was performed in January-March 2014 in Novosibirsk (55°N). Ten DSM-IV-diagnosed SAD women (age 22-63 y) who previously benefitted from the bright light therapy (and were not necessarily currently depressed) and ten matched by age, BMI and menopausal status non-seasonal women attended the Institute in the morning twice within 1-5 days. During one session, bright luminescent light 4300 lux was presented for 30 minutes (Lumie® Arabica light box), during the other session, the light from similar light box dimmed by red filter to 100 lux ('placebo') was used. After the initial 15 minutes of a quiet sitting in an experimental chamber with low light level, the 10-min measurements were done before, at the end and 15 minutes after the 30-min light exposure while subjects remained seated for 80 minutes in total. The measurements included 5-min oxyspyrography (for O2 and CO2 consumption and heart rate), VAS-based self-rating for mood, energy and sleepiness, and saliva sampling for the estimation of cortisol and a-amylase concentration.

Results
None of the measured parameters differed significantly between the bright light and dim red light sessions, although some differences were in a predictable direction (e.g., higher a-amylase levels following bright white light). The group-specific effects (seasonals vs. non-seasonals) were also non-significant.

Conclusions
This study failed to show an immediate effect of morning artificial bright light, in comparison with red light, on metabolism, resting system tone and arousal levels in seasonal-dependent and seasonal-independent women. A possibility exists that the effect may be indeed revealed at night or in laboratory well-controlled conditions.

Funding: The study was supported by Lumie®.

EVENINGNESS AND INSOMNIA: INDEPENDENT RISK FACTORS OF NONREMISSION IN MAJOR DEPRESSIVE DISORDER

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Objectives
It is unclear whether there is an association between chronotype and nonremission of depression, and whether the association is related to the confounding effect of insomnia.

Methods:
A cohort of patients with major depressive disorder were assessed for chronotype (by Morningness-Eveningness Questinnaire [MEQ]), depressive symptoms, insomnia severity and clinical outcomes in a naturalistic follow-up study.

Results
Of the 253 recruited subjects (age 50.8 ± 10.2 y; female: 82.6%; response rate 90.0%), 19.4%, 56.1% and 24.5% patients were classified as eveningness, intermediate, and morningness, respectively. Evening-type subjects had higher insomnia severity, more severe depressive symptoms, and higher suicidality. Eveningness was associated with nonremission of depression with an odds ratio (OR) of 3.36 (95% confidence interval [CI] 1.35-8.34, $P < 0.01$), independent of insomnia severity. In addition, insomnia was an independent significant factor in contributing to nonremission of depression (OR = 1.12; 95% CI 1.05-1.19, $P < 0.001$).

Conclusions
The independent association of eveningness with nonremission of depression suggested a significant underpinning of circadian involvement in major depressive disorder. Our findings support the need for a comprehensive assessment of sleep and circadian disturbances as well as integration of sleep and chronotherapeutic intervention in the management of depression.
This study is published in: Chan, J. W. Y., Lam, S. P., Li, S. X., Yu, M. W. M., Chan, N. Y., Zhang, J., & Wing, Y.-K. (2014). Eveningness and Insomnia: Independent Risk Factors of Nonremission in Major Depressive Disorder. Sleep, 37(5), 911–917.

Disclosures None

BEHAVIORAL INTERVENTIONS TO IMPROVE SLEEP AND SLEEPINESS IN BIPOLAR DISORDER

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Objectives
Objective: The present research sought to characterize the safety and efficacy of Cognitive Behavioral Therapy for Insomnia (CBTI) in individuals with insomnia comorbid Bipolar I Disorder, as well as to introduce a novel treatment component aimed at reducing morning sleepiness. Given that two primary components of CBTI, sleep restriction and stimulus control, involve short-term sleep deprivation, and given that sleep deprivation has been linked to escalation of manic symptomatology, the safety of this intervention in a bipolar population is unknown. Within the parent CBTI trial, we also sought to develop and evaluate a routine designed to reduce morning sleepiness in this population.

Methods
Methods: Individuals meeting DSM-IV-TR criteria for Bipolar I Disorder and Research Diagnostic Criteria for Insomnia, all euthymic at study entry, were randomized to receive 8 weeks of CBTI or psychoeducation. All participants completed weekly semi-structured and self-report assessments of depressive and manic symptomatology, along with daily sleep diaries, which were used to determine the relationship between treatment components, sleep duration, and symptom exacerbation. Furthermore, all CBTI participants were introduced in the first session to a brisk wake-up routine designed to decrease morning sleepiness. Sleep diaries, wrist actigraphy, and ecological momentary assessment, whereby participants reported on sleepiness one hour and three hours after waking, were collected in the week prior to and following the routine.

Results
Results: Regularizing bedtimes and risetimes as a first step in CBTI was often sufficient to bring about improvements in sleep. Two of 15 individuals noted mild increases in hypomanic symptoms following stimulus control instruction, but this was unrelated to changes in total sleep time; two of five individuals who underwent sleep restriction noted mild escalations in manic symptoms that were also unrelated to sleep time. Mixed model analyses revealed the brisk wake-up routine increased activity and decreased subjective sleepiness in the first few hours after waking.

Conclusions
Conclusions: CBTI appears to be safe and efficacious in treating insomnia in bipolar disorder, with stabilizing sleep / wake rhythm a promising first step. Furthermore, introducing a brisk wake-up routine as a component of CBTI appears useful to reduce subjective morning sleepiness. Further research is warranted to ascertain whether reducing morning sleepiness increases compliance with subsequent CBTI recommendations.

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VISUAL AND NONVISUAL EFFECTS OF MONOCHROMATIC PULSED LIGHT ON PHYSIOLOGICAL FUNCTIONS AND SUBJECTIVE EVALUATIONS

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Objectives
The intrinsically photosensitive retinal ganglion cells (ipRGCs) affect the suprachiasmatic nucleus (SCN) and act as the primary photoreceptor for nonvisual effects such as melatonin suppression and pupillary constriction (miosis). We found previously that the miosis under a 100-μs pulsed blue light condition was significantly greater than that under a steady blue light condition; the two conditions had equal blue light components (Katsuura et al., 2012). Figueiro et al. (2008) found that simultaneous exposure to blue and green light resulted in less melatonin suppression than monochromatic light exposure to blue or green light. Here we conducted an experiment using blue and green-pulsed lights to examine the visual and nonvisual effects on miosis, electroretinogram (ERG), and visual evoked potential (VEP) and subjective evaluations.

Methods
Twelve healthy young males participated. The subject being tested sat on a chair with his eyes facing an integrating sphere. After 10 min of light adaptation, the subject was exposed to three light conditions: blue-pulsed light (464 nm), green-pulsed light (526 nm) of 2.5 ms pulse width with 1.6 x 10^15 photons/cm^2/s irradiance intensity, and simultaneous blue + green-pulsed light (3.2 x 10^15 photons/cm^2/s) with white background light (2287 K, 30 cd/m^2). We measured the subject's pupil diameter three times in each condition. Then, after 10 min of rest, the subject was exposed to the same three light conditions. We measured the averaged ERG, VEP and the visual analog scale (VAS) for subjective evaluations of "bluish" and "greenish" during 210 pulsed-light exposures in each condition. The order of the three light conditions was counterbalanced among the subjects.

Results
The miosis during the blue light exposure was more remarkable than that during the simultaneous exposure to blue + green light, despite the double irradiance intensity of the combination. We also found that the b/a wave of ERG during blue light was higher than that during the blue + green light. We confirmed the "subadditive" response to pulsed light on miosis and ERG. However, the P100 of the VEP during the blue light was smaller than those during the blue + green light and green light, indicating that the P100 amplitude might depend on the luminance of light. There were no significant differences of subjective evaluation of "bluish" and "greenish."

Conclusions
The effects of ipRGCs by the blue light exposure are apparently reduced by the simultaneous irradiation of green light. The blue versus yellow (b/y) bipolar cells in the retina might be responsible for this phenomenon.

Disclosures Our findings demonstrated the effect of the "subadditive" response to pulsed light on miosis and ERG responses.

ASSOCIATION BETWEEN CIRCADIAN GENES AND CHRONOTYPE IN A LARGE DUTCH SAMPLE

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Objectives
The term chronotype has a long history. It indicates whether a person is an evening or a morning person, however, the underlying biological mechanisms are still largely unclear. Circadian genes are part of the biological clock, which is centered in the suprachiasmatic nucleus (SCN) of the hypothalamus, and are likely involved in a person's chronotype. This study aims to associate single nucleotide polymorphisms (SNPs) in these circadian genes to chronotype in the Netherlands Study of Depression and Anxiety (NESDA) cohort (n=2981).

Methods
A set of 351 circadian genes was selected for association analysis with mid sleep on free days (sleep corrected) (MSFsc), as assessed by the Munich Chronotype Questionnaire in the NESDA cohort (n=1571). For 1119 of them genome-wide data was available, which were imputed to the 1000G global reference set using minimac (Howie et al. 2012; Fuchsberger et al. 2014). Associations were tested using SNPtest v2.5 (Marchini et al. 2012). Correction for multiple comparisons was applied resulting in a significance cut-off value of $p < 0.00014$ (0.05/351 circadian genes).

Results
From the NESDA GWAS database 342750 SNPs were extracted based on their position within 10kb of the selected genes. Nine of these SNPs showed a significant association with chronotype: one in the CYP3A5 gene (p=0.00011) one in the GLRA1 gene (p=0.000059), one in the PMP22 gene (p=0.000035), two in the MPDZ gene (both $p < 0.00004$) and four in the OMD gene (all $p<0.00005$).

Conclusions
This is the first study to analyze association between known circadian genes and a circadian phenotype, a person's chronotype. Significant associations were found for five genes (CYP3A5, GLRA1, MPDZ, PMP22 and OMD). These SNPs or linked functional polymorphisms might provide a biological basis for the different chronotypes in humans and as such also a liability to develop depression.

Disclosures None to report

PATIENTS' EXPERIENCES WITH WAKE AND LIGHT THERAPY

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Objectives
Wake therapy can reduce depressive symptoms within days, and response rates are high. Patients participating in wake therapy stay awake for a night and the following day, in all 36 hours. The effect of wake therapy can be transitory, but recent studies indicate that wake therapy in combination with other chronotherapeutic interventions, as for instance light therapy, can produce a sustained antidepressant effect. To achieve this sustained effect patients' adherence is pivotal; however, adherence in long-term treatments is often low. According to WHO no intervention strategies towards adherence have shown to be effective across all patients, conditions and settings. Interventions targeting improved adherence must therefore be aimed at treatment-related factors as the patients experience them. Very few previous studies have focused on patients' experience with chronotherapeutic treatments.
The aim of this study is to illuminate the patients' experiences with wake and light therapy with focus on factors related to the patients' adherence.

Methods
Qualitative methods are used, as they are suitable in situations where existing knowledge is limited. Approximately ten in-patients with major depression will be included, and they participate in an intervention consisting of three wake therapies during the first week, 30 minutes daily light treatment for the following nine weeks, and ongoing psychoeducation regarding good sleep hygiene and maintaining a stable circadian rhythm. Patients are requested to keep a diary, and by the end of the wake therapy (after one week) and the light therapy (after 9 weeks), individual semi-structured interviews will be conducted. Data from interviews and patient dairies will be analyzed using qualitative content analysis with both a manifest analysis (describes the content) and latent analysis (seeks to discern its meaning). According to the manifest content, the text is divided into meaning units, which are sorted into categories. Next, themes are identified in the categorized data, and based on theses an interpretation of the meaning is reached.

Results
The project was initiated in 2014, and the final interviews will be completed within months. The transcribed interviews and the diaries indicate that patients generally are positive towards wake and light therapy. Furthermore, the patients point out several factors that promote and impede adherence. E.g., support from staff, family and fellow-patients and physical surroundings at the wards.

Conclusions
This study will provide insight into patients' experiences and hopefully contribute to an organization of wake and light therapy that promotes adherence, thereby improving the effect of chronotherapetic interventions.

Disclosures none

THE BEGINNINGS OF LIGHT THERAPY FOR DEPRESSION

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Objectives
A 35-year account of modern bright light treatment.

Methods
Personal observations and historical data assembled by Tom Wehr

Results
Observations that bright daylight reduces depression can be found in some of the earliest recorded history and were familiar to ancient physicians. Artificial electric light was employed to treat depression by the end of the 19th century. Halberg suggested that circadian disturbances cause depression, a topic I was studying when Roger A. Hoffman visited me to suggest that work with Reiter on rodent photoperiodism might be relevant. Encouraged by the report of Lewy et al. that bright light could suppress human melatonin, we started a small placebo-controlled trial of bright light for non-seasonal depression, calling our first paper "Photoperiodic mechanisms for depression and its treatment." The response to 1-hour of treatment was only a significant 15% better than placebo. Few realized that bright light's one-hour response was comparable to the response of outpatients to 8 weeks of fluoxetine.

Lewy, Wehr, and Rosenthal began studying Herb Kern's case-history response to light for SAD at about the same time and published their first placebo-controlled clinical trial of bright light three years later. The excitement of the large initial effect sizes reported for SAD treatment, combined with NIMH prestige and the unique plausibility of increasing light for winter depression, produced over a decade of focus on SAD with few nonseasonal studies.

More recently, Martiny, Benedetti, and Van Someren''s groups, along with others, have provided increasing evidence for the efficacy of bright light treatment in various forms of nonseasonal depression. In the next few months, we will see publication of much stronger clinical trials highlighting the value of bright light treatment combined with antidepressants for nonseasonal depression. We are also seeing increasing evidence that combining bright light treatment with sleep restriction and sleep interval phase advances can yield very rapid clinical benefits, though I have not yet seen enough evidence that the triple treatment added to antidepressants is better than antidepressants combined with bright light alone. In any case, we can now be confident that the combination of bright light and antidepressants with or without the triple intervention is a breakthrough in augmenting clinical treatment of most depression.

Finally, we have waited 30 years for a detailed understanding of how photoperiodism mediates bright light responses. We may now rejoice that new studies show the cellular and molecular mechanisms by which morning bright light elevates our moods.

A RANDOMIZED PLACEBO-CONTROLLED STUDY OF BRIGHT ;IGHT THERAPY, FLUOXETINE AND THE COMBINATION FOR NONSEASONAL MAJOR DEPRESSION

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Objectives
Bright light therapy is an evidence-based treatment for seasonal depression, but there is limited evidence for its efficacy in nonseasonal major depressive disorder (MDD). Our aim was to determine the efficacy of light therapy, alone and in combination with fluoxetine, for nonseasonal MDD.

Methods
This double-blind, randomized, placebo-controlled 8-week trial involved 3 Canadian centres. Entry criteria included DSM-IV criteria for MDD of at least moderate severity. Active medical illness or substance use, bipolar disorder, psychosis, seasonal pattern and treatment-resistance were excluded. Patients were randomly assigned to 1 of 4 conditions: (1) active light monotherapy (active 10,000 lux fluorescent white light box for 30 minutes daily) plus placebo pill; (2) active antidepressant monotherapy (placebo inactive negative ion generator for 30 minutes daily plus fluoxetine 20 mg); (3) combined light and antidepressant (active light box plus fluoxetine); and (4) placebo (placebo inactive negative ion generator plus placebo pill). The primary outcome was change score on the Montgomery-Asberg Depression Rating Scale (MADRS), with secondary outcomes of response (MADRS>=50% reduction) and remission (MADRS<=12). Statistical analysis was conducted with ANCOVA and Bonferroni post hoc tests for change scores, and with chi square tests for categorical outcomes.

Results
131 patients were screened and 122 randomized. The overall ANCOVA for change score on the MADRS was significant, with post hoc tests showing that light monotherapy (p=0.025) and light+fluoxetine combination (p=0.001) were superior to placebo, while fluoxetine monotherapy was not; light+fluoxetine combination was also superior to fluoxetine monotherapy (p=0.028). Similarly, combination light+fluoxetine was superior to both placebo and fluoxetine monotherapy for response and remission rates, while light monotherapy was superior to placebo.

Conclusions
Light therapy, both as monotherapy and in combination with fluoxetine, was found to be efficacious in the treatment of patients with nonseasonal MDD. The combination of light and fluoxetine appeared to have the greatest efficacy.

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THE EFFECT OF LIGHT AND SEXUAL CYCLE ON WOMEN'S TIME SENSATION

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Objectives
We have two endogenous timekeeping systems for a circadian clock and an interval timing clock. Especially, it has known that the perception of short-interval timing, or the time sensation is affected by several psychological and physiological factors - e.g., age, time of day, menstrual cycle, light condition. However, there are still few reports on women's time sensation of the combined effects of light and sexual cycle. Therefore, in the present study, we clarify the effect of light and sexual cycle on women's time sensation.

Methods
Eight female subjects participated in this study. They were exposed to red-light (669 nm) and blue-light (457 nm) environments in the period of follicular phase and luteal phase respectively. The subjects completed five consecutive sessions. The five consecutive sessions were consisted of a 20-min rest, a 20-min oddball task, a 20-min pause, a 20-min rest and a 20-min oddball task. We evaluated the time sensation by time-production tests of 180 s, and measured the P300 event-related potentials during the auditory oddball tasks, the state-trait anxiety inventory (STAI), salivary progesterone and subjective evaluation.

Results
There was no significant effect of light condition on the time sensation. However, the time sensation in the follicular phase condition was significantly longer than that in the luteal phase condition.
On the other hand, the peak amplitude and the latency of P300 were not significantly different. In the brightness of subjective evaluation, the follicular phase condition was brighter than that in the luteal phase condition.

Conclusions
From these results, we estimate that time sensation of women is not involved with light condition and is only affected the sexual cycle.

Disclosures none

CLINICAL IMPLICATIONS OF THE MELATONIN PHASE RESPONSE CURVE

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Objectives
To assess the possibility that endogenous levels of melatonin and melatonin receptors could be mediating the circadian phase-shifting effects of melatonin agonists and agents that affect melatonin production.

Methods
1) Low doses of melatonin were tested in humans in two ways. In sighted humans, four daily doses of 0.5 mg melatonin were given to 12 individuals at 12 times of the day about two hours apart following a placebo-control week. Three dim light melatonin onsets (DLMOs) were obtained (before each week and at the end of week two of the study). Phase shifts were binned at two-hour intervals. The first DLMO was designated circadian time (CT) 14, and administration times were expressed as CT. 2) As previously published [Lewy et al., Chron. Int. 22:1093-1106 (2005)], ten blind people were given several doses of melatonin to determine the lowest dose capable of entrainment. The lowest entraining dose was then plotted against tau at entrainment phase (TEP) established during longitudinal assessment pre-treatment. (TEP takes into account relative coordination to unknown weak zeitgebers and is the best estimate of the required daily phase advance for steady-state entrainment.)

Results
1) The resulting phase response curve (PRC) was similar to previous PRCs, but even more clearly indicated that the melatonin PRC is 12 hours out of phase with the PRC to light. 2) In the range of 20-300 youngs a log-linear dose-response curve. The smallest dose caused a daily phase advance of 0.15 h and the largest dose caused a daily phase advance of 0.9 h.

Conclusions
Low, near-physiological doses of melatonin are capable of causing circadian phase shifts in humans. Therefore, any agent (such as bright light or beta-blockers) that can discretely decrease melatonin levels on either the phase advance zone or phase delay zone of the melatonin PRC has the potential of utilizing this mechanism as part of its phase-resetting action. Furthermore, melatonin agonists exert their phase-shifting effects by acting on endogenous melatonin receptors, according to the melatonin PRC. Thus, a number of therapeutic agents may prove useful for treating disorders related to circadian rhythms. It should also be noted that studies of blind people have shown: 1) higher doses of melatonin than tested above may be less effective, due to "spillover" onto the wrong zone of the melatonin PRC; and 2) "overlap" between the exogenous dose and the endogenous melatonin profile may facilitate phase shifting.

Disclosures Dr. Lewy has consulted for pharmaceutical companies, such as Servier. Dr. Lewy is co-inventor on several process patents owned by OHSU and currently not licensed to any company.

SLEEPINESS DURING WAKE THERAPY AND RELATION TO ANTIDEPRESSANT RESPONSE

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Objectives
Patients doing wake therapy, experience incremental increases in sleepiness during the night, but with a large inter-individual variation. Depression has been hypothesized as a state with insufficient built-up of sleep pressure and wake therapy to work through restoring sleep pressure (process S) to normal levels. Clinically, this is substantiated by the often low levels of sleepiness seen in depressed patients during wake. We wanted to examine whether the degree of sleepiness was related to the antidepressant response to wake therapy.

Methods
In all, 32 patients doing total wake therapy, as part of a randomized controlled trial (compared to exercise), filled in the Standford Sleepiness Scale hourly from 11 pm to 8 am on the wake night (score range 1 = no sleepiness to 7 = falling asleep). Daily sleep logs had been filled in the preceding week. Depression severity was assessed after end of wake therapies with the Hamilton Depression rating scale (HAM-D17).

Results
Sleepiness was distributed through the night in a curvilinear way rising to a maximum of 3.9 (1.3) points at 4 AM and decreasing for the rest of the night. The mean sleepiness during the night was 3.3 points (1.1) [range 1.2-6.2] and strongly negatively associated to depression outcome (parameter estimate 0.36, $R2= 0.31$, $p<0.001$) at next weekly assessment. Using the 1th (score = 24.5) and 3th sleepiness percentiles (score = 38.5) scores as anchor points for analyses , patients with a 1th percentile sleepiness (low sleepiness) had a HAM-D17 score of 9.9 at the following assessment and patient with a 3th percentile sleepiness (high sleepiness) a corresponding score of 14.9. Sleep midpoint in the preceding week was at 3:48 PM (1:06) and only weakly associated to depression outcome (parameter estimate -0.03, $R2 = 0.11$, $p = 0.06$).

Conclusions
The sleep pressure hypothesis could not be substantiated as high level of sleepiness during wake was found to be a significant negative predictor for depression outcome.The risk of naps is related to sleepiness and as naps during wake are known to reduce the antidepressant effect this might explain the poorer outcome for patients with more sleepiness during wake. Sleepiness during wake could be used as a warning of poor outcome. Thus, clinicians should assess sleepiness on wake nights and take preventive measures for the next wake night to avoid napping for example by increasing ambient light levels or support any kind of activities during the night.

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CELLULAR CIRCADIAN RHYTHMS IN BIPOLAR DISORDER

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Objectives
Bipolar disorder (BD) is associated with low amplitude circadian rhythms, a partly reversible illness feature that is corrected by lithium. Previously, we demonstrated that fibroblasts grown from BD patients show a weak amplification of rhythms in response to lithium. However, the mechanism underlying this observation is not understood. Calcium has actions upon the circadian clock, and L-type calcium channel (LTCCs) variants have emerged as risk factors for BD. ERK is a downstream signaling pathway activated by calcium. Therefore, we examined whether genetic variants in LTCCs and ERK account for the attenuated cellular response to lithium in BD.

Methods
We used fluorescent and bioluminescent reporters to measure Ca2+ and gene expression rhythms in fibroblasts from BD patients, healthy controls, and mice while pharmacologically or genetically manipulating LTCCs and the ERK pathway.

Results
Independently of LTCCs, acute lithium stimulated intracellular Ca2+ more effectively in control vs. BD fibroblasts. In longitudinal studies, pharmacological inhibition of LTCCs or siRNA knockdown of CACNA1C, an LTCCs genes affected circadian rhythm amplitude. Diltiazem and knockdown of CACNA1C eliminated lithium's ability to amplify rhythms. CACNA1C genotype predicted amplitude response to lithium. Inhibitors of ERK attenuated the amplitude response to lithium. Knockdown of DUSP6, an inhibitor of ERK sensitized cells to lithium and induced responsiveness to lithium in BD cells that failed to amplify rhythms previously.

Conclusions
The acute Ca2+ response to lithium is abnormal in BD. LTCCs contribute to lithium's effect on rhythms and harbor genetic variants linked to low rhythm amplification and may work through the ERK pathway.

Disclosures None

PATIENTS WITH SEASONAL AFFECTIVE DISORDER SHOW SEASONAL FLUCTUATIONS IN CEREBRAL SEROTONIN TRANSPORTER BINDING

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Objectives
Seasonal variation in different aspects of the serotonin system has previously been reported i.e. studies in healthy (but unscreened) individuals have demonstrated a significant environment-genotype interaction on the serotonin transporter (SERT) binding, with carriers of the short 5-HTTLPR polymorphism (S-carriers) showing a larger season variation in cerebral SERT compared to LALA homozygote individuals. We here investigated for the first time cerebral serotonin transporter binding in individuals with and without symptoms of SAD, both in the winter and the summer.

Methods
We included a total of 131 11C-DASB positron emission tomography (PET) scans to established changes in cerebral serotonin transporter binding in SAD and in individuals characterized by low seasonality scores (non-SAD) in winter and in summer. Individuals with SAD were diagnosed by trained psychiatrists and depressive symptoms were asses by the Structured Interview Guide for the Hamilton Rating Scale for Depression - Seasonal Affective Disorder version (SIGH-SAD).

Results
No difference was found in global cerebral serotonin transporter binding between SAD and Non-SADs, regardless of season. The longitudinal data showed, however, that females with SAD regulated their SERT differently than Non-SAD females. Likewise, S-carriers had a significantly larger seasonal change in BPND than did LA/LA carriers. Moreover, the seasonal change in SERT binding successfully predicted the progression of depressive symptoms.

Conclusions
We find evidence that the development of depressive symptoms in winter is due to a failure to down-regulate SERT appropriately during exposure to the environmental stress of winter, especially in individual with high risk profiles for affective disorders.

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WHY DO PEOPLE NAP? EFFECTS OF NAPPING ON PERSONALITY, MOOD AND COGNITION

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Objectives:
Napping is a culturally embedded, lifespan-developmental phenomenon. Napping in infants and young children is very common cross-culturally, but by adulthood cultural practices influence napping behaviors, with the frequency of napping at least once per week varying between 36% to 80%. Napping has recently received increased attention because of its associations with health and its use as a tool to understand the function of sleep, with both areas of research showing conflicting associations with well-being. In the epidemiology and public health literature, some studies show that napping is associated with increased mortality risk, but this literature is limited by confounds, disparate approaches to controlling for comorbid illnesses, and different definitions for napping which make it difficult to compare the results of studies. Understanding the reasons why people nap, as well as the correlates of these napping behaviors, can provide insights into normal and pathological nap behaviors in healthy and unhealthy populations.

Methods:
We systematically assessed the reasons people nap by creating an inventory of reasons for napping and determining the underlying structure using factor analysis. These results are summarized in our five-factor model with the acronym DREAM: Dysregulative, Restorative, Emotional, Appetitive, and Mindful. In my talk, I will describe each factor and the psychological, health, and sleep profiles that were related to each factor.

Results:
We demonstrate that use of the DREAM model shows differential associations between reasons for napping and psychological, social, and physical health variables, thus helping to clarify discrepancies in the literature.

Conclusions:
I will conclude by exploring how this novel application of factor analysis to reasons for napping raises exciting possibilities for future research, such as examining the stability and structure of reasons for napping throughout the lifespan, as well as the psychological, social, and health processes associated with napping behaviors.

Disclosures: None

CHRONOTYPE PREDICTS POSITIVE AFFECT RHYTHMS AS MEASURED BY ECOLOGICAL MOMENTARY ASSESSMENT

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Objectives
Evening chronotype, a correlate of delayed circadian rhythms, is associated with depression. Altered positive affect (PA) rhythms may mediate the association between evening chronotype and depression severity. A better understanding of the relationship between chronotype and PA may therefore aid in understanding the etiology of depression. Recent studies have found that individuals with evening chronotype show delayed and blunted PA rhythms, although these studies are relatively limited in sample size, representativeness, and number of daily affect measures.

Methods
A large sample of healthy non-depressed adults (*n* = 408) completed self-report affect and chronotype questionnaires. Using personal data assistants, positive and negative affect were measured hourly while awake for at least two workdays and one non-workday by ecological momentary assessment (EMA). A cosinor variant of multilevel modeling was used to model individual and chronotype group rhythms and to calculate two variables, (1) amplitude of positive affect, or the absolute amount of daily variation from peak to trough during one period of the rhythm, and (2) acrophase, or the time at which the peak amplitude of affect rhythms occurred.

Results
On workdays, individuals with evening chronotype had significantly lower PA amplitudes (0.59, *SE* = 0.18) than their morning type counterparts (1.09, *SE* = 0.06, *z* = -2.56, *p* = 0.01). Similarly, evening chronotype individuals had a significantly later PA acrophase (14:57, *SE* = 0:59) compared to the morning types (12:31, *SE* = 00:11, *z* = 2.43, *p* = 0.02) on workdays. In contrast, non-workday findings revealed non-significant differences in PA amplitude or acrophase which, may be due to fewer non-workday PA measures relative to workday.

Conclusions
The association of chronotype and PA rhythms on workdays in healthy adults is consistent with the hypothesis that evening chronotype may create vulnerability to depression via delayed and blunted PA rhythms. Future research should examine if chronotherapeutic interventions that shift PA rhythms toward those exhibited by non-depressed individuals can attenuate depressive symptoms.

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THE PUPIL LIGHT REFLEX DEMONSTRATES SEASONAL VARIATION IN HEALTHY SUBJECTS

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Objectives
Photoreceptors in the human retina process light for visual function and entrainment of circadian rhythms. Seasonal retinal sensitivity changes have been assumed to contribute to seasonal affective disorder and responses to phototherapy. We examined retinal sensitivity governed by rods, cones and intrinsically photosensitive retinal ganglion cells (ipRGC) by using the pupil light reflex to determine seasonal differences in retinal photoreception of healthy subjects.

Methods
A total of 37 healthy adults (mean age: 30.6 yrs; ± 8.7 yrs; 26 women, 11 men) were tested twice, during the shortest and longest annual photoperiods. The subjects completed the seasonal pattern assessment questionnaire (SPAQ), and a series of daytime pupil responses to red and blue narrowband-width light stimuli were recorded using an automated pupillometer.

Results
Pupil constriction amplitudes to scotopic and photopic light stimuli were significantly greater in summer than winter ($p<0.05$). The post-illuminatory pupil response (PIPR), considered an indicator of melanopsin contribution, was also greater in summer, but only after prior light adaptation.

Conclusions
Pupil responses of the three photoreceptor system including the PIPR were greater in summer than winter, indicating greater sensitivity during summer. This is different to what was previously shown in the electroretinogramm for rods and cones, suggesting a more central change of seasonal threshold regulation of the pupil which might be associated with other seasonal changes.

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MECHANISMS OF FAST RESETTING OF CLOCKS FOLLOWING RHYTHM BIFURCATION

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Objectives
The suprachiasmatic nucleus (SCN), a master circadian clock in the hypothalamus, controls circadian rhythms of the whole body through multiple output systems including the nervous innervation, the endocrine system, and body temperature cycles. Under a permissive 24-h light:dark:light:dark (LDLD) cycle, rodents show bifurcation in activity patterns and melatonin release, and altered SCN oscillatory patterns. Following bifurcation, animals rapidly re-entrain to new LD cycles and can entrain to extreme T-cycles.

Methods
In this study, we examined oscillatory stability of the SCN and peripheral tissues in LDLD-bifurcated PER2::Luciferase (PER2::LUC) knock-in mice using the dissection procedure as an external stimulus. The mice were entrained to either LDLD or a normal LD cycle. The SCN, lung, liver, and adrenal gland were extracted at various time points in a day.

Results
Although the SCN explants of bifurcated animals showed bimodal per1 activity in a previous study using per1::luc transgenic mice, none of the SCN explants showed bimodal PER2 expression in our study. Interestingly, however, the phases of explants were significantly affected by dissection time. Specifically, the phase of the SCN and the lung explants were strongly set by dissection in LDLD mice but not in normal LD mice. The phase of liver explants showed variable resetting patterns in LDLD mice but was independent of dissection time in normal LD mice. The phase of adrenal glands was strongly set by dissection in both LDLD and LD mice. Furthermore, we examined expression patterns of canonical clock genes in the lung, liver, and kidney under LDLD and LD by real-time PCR. Rhythmicity of all three peripheral organs in LDLD was significantly weaker than in LD.

Conclusions
In accord with mathematical modeling, these results suggest that decreased oscillatory amplitude caused by bifurcation facilitates resetting of cultured tissues.

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AUTOMATIC SLEEP MONITORING VS. SELF-MONITORING

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Objectives
Depression is a serious mental illness with a lifetime prevalence of up to 9%. Insomnia is a trigger for depression and 65% of depressive episodes present with comorbid insomnia. Studies have shown that the treatment of depression can be supported with good sleep hygiene. The authors have previously developed a self-registration platform, called Daybuilder, to support the outpatient treatment of depression in a clinical context. The first step towards good sleep hygiene is knowledge of one's sleep patterns, which Daybuilder can already help with through self-registration of sleep. The objective of this pilot study was to investigate if sleep registration in Daybuilder can be improved through the addition of an objective sleep sensor system. Specifically the study was aiming to clarify the feasibility of using a non-invasive sleep sensor in a home setting, as part of depression treatment supported by Daybuilder.

Methods
A comprehensive literature study was conducted with a systematic search for papers on telemedicine related to sleep and depression. A non-invasive sensor system based on ballistocardiography (BCG), called Beddit, was chosen for the study. The study was a randomized within-subject study where each participant used Daybuilder for 2 weeks, 1 week with Beddit and 1 week without. Six males and six females (M=28.6 years, SD=9.9 years), with good or excellent knowledge of IT, were recruited. Quantitative data were collected about participant's use of Daybuilder, the System Usability Scale (SUS) and 2 study-specific questionnaires about sleep registration and usability. Qualitative data were collected through 4 semi-structured interviews with 2 male and 2 female participants.

Results
(A) There was no significant difference in SUS scores when using Daybuilder with Beddit (M=71.7, SD=14.4) and without Beddit (M=73.6, SD=15.9), ($p = 0.632 > 0.0063$). (B) The sleep onset and sleep offset times self-reported by participants were significantly correlated with the Beddit-reported times with a correlation coefficient of 0.73 for sleep onset and 0.80 for sleep offset, ($p < 0.0063$). (C) The number of wake-ups reported by Beddit were not significantly correlated with the number of self-reported number of wakeups ($p = 0.540 > 0.0063$). (D) There was no significant difference in log-in compliance when using Daybuilder with and without Beddit ($p = 0.80 > 0.0063$). Nor was there any significant difference in self-registration compliance when using Daybuilder with and without Beddit ($p = 0.80 > 0.0063$). (E) Interviews and questionnaires showed that participants were not negatively affected by using Beddit.

Conclusions
We have shown the feasibility of the approach of using sensors for sleep monitoring to support the treatment of depression with a web-based tool. The study suffered from selection bias as participants were mostly young, and all were healthy and experienced in using IT, diminishing the external validity of the study. This pilot study points at the possibility of improving an existing online system supporting the treatment of depression, but more research is needed. A larger study of BCG-based systems with real patients to investigate the clinical benefits of using sleep monitoring sensors to support the treatment of depression could potentially open up a new way of using sleep monitoring sensors clinically, outside of sleep disorders per se.

Disclosures Daybuilder was partially developed for the studies 'SAFE' and 'SAFE II' at Psykiatrisk Center, Copenhagen, both funded by Trygfonden. The study was supported by University of Copenhagen and Daybuilder Solutions.

EARLY WAKE THERAPY REDUCES THE MELATONIN ONSET-SLEEP ONSET PHASE ANGLE AND IMPROVES MOOD IN DEPRESSED PREGNANT WOMEN

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Objectives
Previously we found that melatonin circadian rhythms were phase-advanced in pregnant depressed women (DW) and phase-delayed in postpartum DW. Thus, we sought to test the hypothesis that delaying sleep with early-night wake therapy (EWT) would benefit mood in pregnant DW more than advancing sleep with late-night wake therapy (LWT).

Methods
In 58 women, 31 pregnant (7 DW; 24 healthy women-HW) and 27 postpartum (14 DW; 13 HW), we measured plasma melatonin every 30 minutes in dim (<30 lux)/dark conditions from 18:00-11:00 h. In a cross-over design, we randomized 21 DW (7 pregnant, 14 postpartum) and 37 HW (24 pregnant, 13 postpartum), mean age 28 years, to EWT (sleep 03:00-07:00 h) vs. LWT (sleep 21:00-01:00 h) followed by a night of recovery sleep (RS; 22:30-06:30 h). A clinician administered mood ratings (Hamilton Depression Rating Scale; HDRS) pre- and post-treatment (after RS).

Results
Melatonin onset time advanced significantly at baseline in pregnant vs. postpartum DW (p=.012). Mood score by HDRS was inversely correlated with Total Sleep Time in both Pregnant (p=.042) and Postpartum (p=.028) DW, and mood improvement after EWT was positively correlated with increased TST in pregnant DW (p=.017), and in postpartum DW (p=.014) when we controlled for hours of darkness during testing. EWT improved mood scores by 53.4% in pregnant and by 33.9% in postpartum DW. EWT phase delayed melatonin onset (p=.019), phase advanced sleep onset (p=.028), and reduced the (melatonin onset-sleep onset) phase angle (MOT_SOT PAD; p=.010). In the combined perinatal groups, greater mood improvement was associated with greater reduction in MOT_SOT PAD after EWT.

Conclusions
Both EWT and LWT reduced depressive symptoms in perinatal women. In pregnant (but not postpartum) DW, EWT phase-delayed melatonin onset, phase-advanced sleep onset, and improved sleep and mood.

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THE DILEMMA OF THE ISOLATED NIGHT SHIFT AND THE RIGHT LIGHT: SHOULD IT BE ORANGE AND BRIGHT?

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Objectives
Nearly all night shift studies are focusing on consecutive night shifts and therefore aim to phase shift circadian rhythms to adjust for several shifts. For isolated (single) night shifts, such phase shifting effects cause mainly detrimental effects because of circadian misalignment during the next day(s) since most workers return to their normal diurnal activity patterns right after one night shift. In order to solve this problem, we proposed the following: Firstly, there should be no phase shifting effect of the light, which could be achieved by filtering out the short-wavelength (=blue) portion of light that most strongly mediates the circadian effects of light. Secondly, the light should be of high intensity since the vigilance-increasing effect of light is not only wavelength- but also dose-dependent.

Methods
Twenty-four healthy subjects (mean age 22.58 ± 1.61 years) participated in two simulated night shifts. Each participant underwent one night shift under a dim light (DL) condition (<5 lx) and one night under the filtered bright light (FBL) condition (300 lx, wavelengths below 520 nm were filtered out) in a randomized order. Vigilance was measured using the Psychomotor Vigilance Test (PVT). The recovery daytime sleep was polysomnographically recorded (see abstract J. de Zeeuw et. al). Salivary melatonin concentrations were regularly assessed during both night shifts and the dim light melatonin onset (DLMO) was determined on the evening before and after the night shift.

Results
The FBL condition increased vigilance during the night shift regarding the 10% fastest reaction times ($p=0.045$, $n=24$). At the same time, salivary melatonin concentrations showed similar dynamics during the night shift under the FBL and DL condition (area under the curve: $p=0.193$, $n=23$). Finally, there was no phase shifting effect of FBL as there were no significant differences of the DLMOs between the evenings before and after the night shifts under FBL ($p=0.129$, $n=11$).

Conclusions
Concerning the problem of isolated night shifts, FBL is a valuable solution to increase night time vigilance and thereby reducing errors and accidents on the job without shifting circadian phase. It is therefore not causing detrimental effects like shift-lag on the following day(s). The comparison between FBL and conventional bright white light regarding the vigilance-increasing effect was shown in previous studies (Kayumov et al., 2005, van de Werken et al., 2013, Rahman et al., 2013), resulting in similar effects of both lighting conditions.

Disclosures Disclosures
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RANDOMIZED TRIAL OF COGNITIVE-BEHAVIORAL THERAPY VS. LIGHT THERAPY FOR SEASONAL AFFECTIVE DISORDER

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Objectives
In contrast to considerable evidence supporting light therapy (LT) as an efficacious treatment for winter seasonal affective disorder (SAD), data on cognitive-behavioral therapy for SAD (CBT-SAD) are promising but preliminary. Pilot studies suggest that CBT-SAD and LT are comparable acute treatments, but that long-term outcomes are better following CBT-SAD than LT. This study is a large, more definitive test that (1) estimates the difference between CBT-SAD and LT on post-treatment outcomes and (2) compares these treatments on outcomes one and two winters after acute treatment.

Methods
177 community adults with Major Depression, Recurrent with Seasonal Pattern, currently in episode participated in this head-to-head randomized clinical trial comparing 6-weeks of CBT-SAD (n=88) vs. LT (n=89). LT consisted of 10,000-lux cool-white florescent light, initiated at 30 minutes/day each morning and adjusted per treatment algorithm based on response and side effects. CBT-SAD consisted of our 12-session group-format, SAD-tailored protocol, administered by one of three Ph.D. psychologists at a frequency of two 1-½ hr sessions/week. Post-treatment outcomes were continuous depression scores on the Structured Interview Guide for the Hamilton Rating Scale for Depression-SAD Version (SIGH-SAD, administered weekly) and the Beck Depression Inventory-Second Edition (BDI-II, administered at pre-/mid-/post-treatment) as well as post-treatment remission status based on cutpoints. Subjects were followed one and two winters after treatment. Prospective followup visits occurred in January or February of each year, and major depression status was assessed by phone in October and December of the first year. The primary outcome was winter depression recurrence status on the SIGH-SAD.

Results
Depression severity on the SIGH-SAD and BDI-II improved significantly and comparably during both CBT-SAD and LT. Presence of a baseline comorbid diagnosis was associated with higher depression scores across all timepoints in both treatments. The treatments did not differ in proportions of remissions on the SIGH-SAD (47.6% in CBT-SAD vs. 47.2% in LT) or the BDI-II (56.0% in CBT-SAD vs. 63.6% in LT) at post-treatment. The treatments did not differ on any outcome during the first year of followup. At the second winter, CBT-SAD was associated with a smaller proportion of recurrences on the SIGH-SAD (27.3% vs. 45.6%) and all alternate recurrence measures, significantly less severe depressive symptoms on both the SIGH-SAD and the BDI-II, and a larger proportion of remissions defined as BDI-II<8 (63.3% vs. 43.9%) than light therapy.

Conclusions
CBT-SAD and LT are comparably effective for SAD during an acute episode, and both may be considered as acute treatment options. CBT-SAD was superior to light therapy approximately two years following acute treatment, suggesting greater durability for CBT-SAD.

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CHRONOTHERAPEUTICS: AN ANALYSIS OF CLINICAL TREATMENT EFFECTIVENESS IN MAJOR DEPRESSIVE DISORDER AND BIPOLAR DISORDER

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Objectives
Recent research has provided strong evidence that a combination of chronotherapeutics for the treatment of a depressive episode, consisting of sleep deprivation, light therapy, sleep phase advancement and medication, yields better short-term and long-term results, even when other treatment options have failed (Benedetti 2005, Casher 2012, Echizenya 2013). While a scientific bases for combined chronotherapy exists, studies investigating the clinical relevance of the therapy are rare. Our research is focussed on determining the effectiveness of chronotherapy in a general clinical setting.

Methods
Data of 26 patients (16 unipolar depressed patients, 10 bipolar depressed patients) that received chronotherapy at the UMCG in the period between October 2013 and October 2014 were collected and informed consent was obtained to anonymously use diagnostic and treatment outcome data. Patients participated in a 14 day program, consisting of three sleep deprivation nights, with a recovery night in between, and 10 light therapy sessions. Throughout the two weeks patients continued medication use. All unipolar patients continued the use of an anti-depressant (tricyclic antidepressant are excluded), bipolar patients continued the use of a mood stabilizer, in most cases lithium. Sleep phase advancement was supported by light treatment in the early morning between 6:30-7:00 a.m. The baseline IDS-C score was determined 3-5 days before the initiation of chronotherapy and was repeated 1 week, 2 weeks and 4 weeks after the start of the treatment.
Paired t-tests were done to compare IDS-C scores before, during -and after treatment.

Results
The average pre-treatment IDS-C score was 39.3 points (+/- 9.5), indicating severe depression (Rush et al. 2003, Trivedi et al. 2004). After two weeks of chronotherapy the average IDS-C score had dropped to 28. 6 points (+/- 13.7), which is a statistical significant ($p<0.01$) reduction in severity. A follow-up interview two weeks after completing the chronotherapy showed an average IDS-C score of 28.6 (+/- 14.0), suggesting long-term effectiveness. The treatment effectiveness for unipolar depressions and bipolar depressions was also assessed separately. Patients with unipolar depression had an average reduction in IDS-C score of 8.8 points, with an average baseline of 37.3 (+/- 7.6) and an average 4 week follow-up score of 28.5 (+/- 9.7). Patients with bipolar depression had an average reduction in IDS-C score of 13.8, with an average baseline of 42.6 (+/- 11.1) points and an average follow-up score of 28.8 (+/- 18.1). Patients with psychiatric co-morbidity, e.g. social phobia, agoraphobia, obsessive compulsive disorder (OCD) or panic disorder, were also assessed separately. Patients without psychiatric co-morbidity had a significant reduction ($p<0.01$) in IDS-C scores of 15.6 points, while patients with psychiatric co-morbidity had a reduction of 7 points ($p<0.05$). Patients were also separately assessed according to the presence of diurnal mood variation. Patients who reported diurnal variation had a significant reduction in IDS-C scores of 14.1 points ($p<0.01$), while patients who reported no diurnal mood variation had no significant reduction in IDS-C scores.

Conclusions
Chronotherapy seems to be an effective treatment in both patients with major depressive disorder and bipolar disorder. Patients with psychiatric comorbidity e.g. social phobia, agoraphobia, obsessive compulsive disorder (OCD) or panic disorder, had a lower reduction in IDS-C scores but still experienced a significant drop in depression severity. Furthermore daily variations in mood, as indicated in question 9 of the IDS-C, seems to be a predictor for better therapy effectiveness, as suggested in other research (Reinink et al. 1993).

Disclosures none

SEASONAL VARIATION IN SEROTONIN TRANSPORTER BINDING IN SEASONAL AFFECTIVE DISORDER AND HEALTH: A [11C]DASB POSITRON EMISSION TOMOGRAPHY STUDY

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Objectives
SAD affects 1-6% of individuals and rates are higher at more Northern latitudes. Serotonin transporter binding potential (5-HTT BPND), as measured with [11C]DASB PET, is an index of 5-HTT levels and 5-HTT BPND has been found to be higher across multiple brain regions in the fall-winter relative to the spring-summer; a finding replicated by four independent research groups. DASB binds preferentially to 5-HTT on outer cell membranes. As such, it is likely that changes in 5-HTT BPND observed in vivo using [11C]DASB PET reflect 5-HTT protein levels at the cell surface where serotonin re-uptake occurs. The purpose of this study was to determine if the magnitude of seasonal variation in 5-HTT BPND, an index of 5-HTT levels, was greater throughout the brain in individuals with SAD as compared to healthy volunteers. A secondary hypothesis was that seasonal change in 5-HTT BPND would positively correlate with severity in both the prefrontal and anterior cingulate cortices (PFC and ACC, respectively), which include brain regions involved in mood-regulation.

Methods
12 SAD (7 women and 5 men, mean age: 31.8 [4.9] years) and 13 healthy participants (7 women and 6 men; mean age 28.9 [3.9] years) underwent [11C]DASB PET and MRI scans in both summer and winter, in randomized order, to measure seasonal change in 5-HTT BPND. All participants were non-smoking, had no history of major medical or additional psychiatric illness, nor history of substance abuse, and all were medication free. Severity of seasonality was measured with the Seasonal Pattern Assessment Questionnaire (SPAQ) to assess change in seasonal depressive symptoms applying a summed global seasonality score (GSS) to determine degree of seasonality (i.e. seasonal change in sleep, mood, energy, appetite, weight and social activity). Regions assayed included the PFC, ACC, thalamus, caudate, putamen, temporal cortex, midbrain, striatum and hippocampus.

Results
In winter, as compared to summer, a global elevation in 5-HTT BPND was observed in SAD as compared to health (magnitude, 16% vs. -0.85%, MANOVA, $F(9,15)=7.11$, $p=0.001$). A similar trend was also detected in individual brain regions assayed (univariate ANOVA, $F(1,23)=1.16$-7.55, $p=0.01$-0.29), with the exception of the hippocampus ($F(1,23)=0.12$, $p=0.74$). A positive correlation was observed between severity of SAD (measured with the SPAQ) and seasonal change in 5-HTT BPND which was significant in the PFC ($r=0.66$, $p=0.02$), and trend-level in the ACC ($r=0.48$, $p=0.11$).

Conclusions
Since greater seasonal fluctuation in 5-HTT BPND is associated with SAD, and the severity of SAD, this suggests that fluctuation in levels of 5-HTT, most likely in the PFC, represents a component of the phenotype of SAD. This has pathophysiological implications since overexpression of 5-HTT is associated with reduced extracellular serotonin and [11C]DASB has strong preferential binding for the 5-HTT on outer cell membranes. To our knowledge this is the first brain marker of SAD so future study should investigate markers of other phenotypes implicated in mood disorders.

Disclosures This work was supported by funding from the Canadian Institutes of Health Research (CIHR) (grant number: RN158849 & 274056) and student salary support from Brain Canada.**ENABLING**

ENTRAINMENT TO NON-24H LIGHT CYCLES WITH SIMPLE LIGHT MANIPULATIONS.

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Objectives
In most natural conditions a stable circadian system is advantageous, but in time zone travel or shift work a more flexible clock could be beneficial. Typical photic phase response curves do not have amplitudes of more and 3 hours; therefore, in standard light:dark conditions rodents do not entrain to light cycles that are more than a few hours longer or shorter than 24 hours. In hamsters, green dim light at night (<0.1 lux) and rhythm bifurcation (i.e. a light cycle with an additional light and dark episode every 24 hours) have been demonstrated to facilitate greater range of entrainment. We tested whether these factors would enable mice (C57Bl/6J, males/females) to entrain to non-24h cycles of 18, 21, 30 and 36 hour durations.

Methods
We used two different paradigms to enhance flexibility of the circadian system and lead to entrainment of running wheel behavior in unnatural light cycles. One group of mice started in long days (19:5) with green dim light at night (light:dim), while another group started in bifurcation (7:5:7:5, light:dim:light:dim). Photophase were progressively shortened and lengthened respectively to reach 13:5 (light-dim) over 8 weeks.

Results
Both groups of mice entrained wheel-running behavior, with almost all activity in the dim lit scotophases. In contrast, body temperature was not fully entrained and showed an additional free running component of slightly more than 24 hours.

Conclusions
Therefore, we propose that facilitation of extreme light cycle entrainment potentially acts through decoupling between multiple oscillator systems. We can conclude that bifurcation and green dim light enable running wheel entrainment to T18. Follow up studies will determine their separate influences. These findings could lead to promising therapies that allow faster adaptation to new environments.

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No conflicts of interest

THE PHOTO AUTONOMIC EFFECT

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Objectives
The autonomic neuroscience of photoperiodic physiology has been classically described as a 24-hour circadian dark-light-dark periodic cycle at the vertebrate Retinohypothalamic (RHT) level. Sleep-wake-sleep polysomnography (PSG), as well as autonomic heart rate variability (HRV), also follow this dark-light-dark cycle. The objective of this exploratory Study was to experimentally characterize the HRV time-frequency spectrum as a function of human visible spectrum time-luminance, time-chrominance and time-color temperature spectrums as a power spectral density (PSD) PhotoAutonomic Transfer Function.

Methods
The visual stimulus followed 1964 CIE 10° Color Standards at 1nm color wavelength, 1°K color temperature and 1 Lx luminance continuous resolutions viewed in a ~0 Lx ambient 10° field of view at 50 cm. The MATLAB„¢ PsychToolBox generated RGB color balanced 21" CRT visual stimulus was presented over three conditions: MonoChromatic [0-100-0 Lx], PolyChromatic [360-555-740 nm] and a Naturalistic Daytime Skylight Thermo Chromatic (Color Temperature) [1000°K-13000°K-1000°K] ranges sweeping over a 60:1 ratio time compressed 1 Minute/Hour simulated 12 Hour Daytime scale. HRV RR inter-beat-intervals were recorded by a Polar RS800CX Thoracic ECG Sensor and imported into Polar ProTrainer software. The RR Data was filtered by windowed linear interpolation, displayed and exported as text. The RR intervals were imported into the VivoSense„¢ analysis system and further filtered with its automatic artifact system by windowed spline interpolation. The resulting RR Tachograms were <1% artifact and detrended for baseline wander. The Standard 1996 Task Force HRV frequency bands were displayed and exported as comma separated variables to Excel„¢ over 12 time points of the experimental sessions with 6 Study Subjects in a cross-over design. Additionally, RR Interval data were exported into the open-source HRVAS time-frequency analysis system and displayed as continuous wavelet transformed (CWT) HRV spectrograms for scientific visualization. During the three Experimental Sessions, the three visual stimulus conditions (1) MonoChromatic/PolyLuminant; (2) PolyChromatic/MonoLuminant; (3) PolyChromatic/PolyLuminant DataSets were analyzed by 3- (stimuli conditions) X 12- (data points) by repeated measures analysis of variance (ANOVA). The Standard 1996 Task Force power spectral density (PSD) parameters were selected from normalized HRV very low (VLF), low frequency (LF) and high frequency (HF) bands to control for 1/f ultra low frequency (ULF) autonomic thermoregulatory processes.

Results
There was a trend effect for HF ($F=5.466$, $p<0.067$) such that HF was highest under the mono condition, then poly condition, and lowest for the thermo condition. There was a main effect for LF/HF ($F=7.23$, $p<0.05$) such that it increased over time for mono and poly conditions but decreased for the thermo condition. The CWT HRV time-frequency spectrograms were heterogeneous and complex, revealing subtle signatures of Human HRV.

Conclusions
These observations of programmed illumination modulating the HRV PSD demonstrate photoautonomic transduction with differential sub-ultradian dynamics over monochromatic-polyluminant, polychromatic monoluminant and polychromatic-polyluminant color temperature stimuli. This exploratory investigational Study characterized a psychophysical stimulus with its psychophysiological response. Further research into clinical-translational photoautonomic neuroscience promises a more nuanced understanding.

Disclosures None.

GLASS QUALITY AND DEPRESSION

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Objectives
Depressive patients at psychiatric inpatients wards often find it difficult to maintain a stable sleep-wake rhythm. Recent discoveries about the missing piece in the lighting puzzle, the non-visual ipRGC in the retina, have put emphasis on light and its beneficial effects as an efficient zeitgeber able to entrain the sleep-wake cycle. Light is also an acknowledged antidepressant agent and alerting agent. Artificial lighting, such as LED-lighting, rich in the blue, short-waved spectral area, can play an important role in effective chronotherapy by inducing a regular sleep-wake cycle, but natural sunlight is far more optimal regarding both spectral composition and the timing of intensity in relation to the sleep-wake cycle. As patients spend a lot of time in the indoor environment, the glass quality at the ward may play a very important role for patients circadian rhythm, sleep, and wakefulness.

Methods
The ipRGC melanopsin receptors in the retina, regulates, among other things, the sleep-wake and melatonin rhythms, and are most sensitive to light in the blue region of the spectral area, approx. at 460 - 480 nm. This study compared the light transmittance (Lt) of five different glass types typically used in windows today. The transmittance of the glass types was measured in a dark room, with each glass type mounted, one by one, providing a closed envelope to the daylight outside, filtering the natural light into the room. The spectral composition of the transmitted light was subsequently measured, using UPRTek units with test glass compared to a reference (no glass).

Results
The study showed that the glass types had a major filtering effect on the short-waved light, thus theoretically reducing the entraining effect of light on the sleep-wake cycle. Clear, low-iron glass had the lowest filtering effect of the tested glass types. Furthermore, there was a large difference in the transmission of UVA and UVB light. The UVB is especially absorbed and reflected in most common glass-types. Only low-iron glass transmits UVB-light, however this glass-type is very seldom used in new architecture. This may be an explanation on the often very low D3-Vitamine levels seen in the patients, spending much time in the indoor environment due to their mental condition.

Conclusions
The differential ability of glass to transmit light may affect the human sleep-wake-cycle and the level of D3-vitamine. Lower transmittances thus affect health-parameters negatively. Glass seems to play a very important and overlooked role when it comes to planning a healthy indoor environment at psychiatric wards. By reducing the shortwave light and the UVB-light, stimulation of the circadian rhythm and transformation to active D3-vitamine in the blood is disturbed. We suggest from the results from this study that an Unhealthiness Factor of glass is introduced, or at least discussed at hospitals and at psychiatric wards. The exact effect of different glass types remains to be studied in humans, relating the glass quality to levels of depression and D3-vitamine in the blood. We therefore suggest further controlled studies at psychiatric in-patients wards.

Disclosures None

BRIGHT LIGHT FACILITATES FEAR EXTINCTION AND PREFRONTAL PROCESSING FOR FEAR EXTINCTION IN HUMANS

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Objectives
Bright light (BL) acts as not only a powerful entrainer of circadian rhythm but also a potent enhancer of human emotion and cognition such as alertness, attention, and memory. Although it has been well known that BL achieves antidepressant effects without any circadian entrainments, it is uncertain whether BL can enhance emotional memory processing, which is intimately involved in the pathophysiology of anxiety and stress-related mental disorders, including post-traumatic stress disorder. Extinction of conditioned fear is a key treatment strategy (i.e. exposure-based cognitive-behavioral therapies) for such disorders and it can be achieved through the prefrontal inhibitory control of limbic activities associated with fear. Here, we investigate whether BL can facilitate fear extinction and prefrontal inhibition of limbic activities in healthy humans using a cued fear conditioning paradigm.

Methods
Twenty-five healthy volunteers (21.4 ± 0.8 years, 9 women) were exposed to BL (8,966 ± 924 lux) or control light (431 ± 114 lux) for 15 minutes during a fear extinction training performed at 1 p.m. in order to examine BL effects on fear extinction and minimize light-induced circadian entrainments. A recognition test was performed after 24 hours following the fear extinction training to evaluate a delayed influence of BL on extinction of conditioned fear. Changes in prefrontal activities and skin conductance responses (SCRs) during the fear extinction training and delayed fear recognition test were measured by using a functional near-infrared spectroscopy and a resistance meter via electrodes attached to the fingers of the non-dominant hand, respectively.

Results
BL significantly reduced the SCR levels during the delayed fear recognition test ($p = .030$). BL significantly reduced prefrontal activities during not only the fear extinction training ($p = .020$) but the fear recognition test ($p = .007$). In addition, these BL effects were achieved without any influences on subjective ratings of mood or actigraphically evaluated sleep-wake rhythm.

Conclusions
Acute exposure to BL facilitates delayed consolidation of fear extinction and could streamline prefrontal inhibitory control via direct suppression of limbic activities including the amygdala. Furthermore, results implicate a clinical benefit of BL as an adjunct to exposure-based cognitive-behavioral therapies for anxiety and stress-related mental disorders.

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DAYTIME SLEEP AFTER A SIMULATED NIGHT SHIFT IN FILTERED BRIGHT LIGHT

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Objectives
The world has more and more turned into a 24/7 society. An increasing number of people are working during night time. Yet, a single night of staying awake can already have detrimental effects on daytime performance, shift circadian phase and affect the sleep of the following day. Since bright blue-enriched light has the greatest effects on the circadian timing system, we investigated the impact of a bright light source where blue wavelengths were filtered out. Our objective was to test whether daytime sleep after an isolated simulated night shift under such filtered bright light conditions was comparable with a daytime sleep episode after a night shift in dim light.

Methods
Twenty-four young subjects (age: 22.58 ± 1.61; mean ± SD) came to our sleep laboratory for one baseline night and two nights in which they worked for 10-hrs on a simulated night shift (separated by one week). After spending a night awake in either dim light (DL; <5 lx) or filtered bright light (FBL; wavelengths below 520 nm were filtered out), the sleep episodes during the following day were polysomnographically recorded and visually scored. The C3-A2 EEG channel was subjected to spectral analysis (Fast-Fourier Transformation) in the range between 0.6 and 25 Hz. A subjective sleep quality questionnaire was given after each sleep episode. For other parameters like melatonin secretion, phase shift and vigilance see the abstract of Regente et al..

Results
There were no significant differences in total sleep time (DL 323.23 ± 30.58 min; FBL 311.96 ± 46.44 min; mean ± SD), sleep latencies or REM sleep latencies between both lighting conditions. A significant lower percentage of time spent in stage 2 sleep ($p = 0.01$) was found after a night in FBL (41.69% ± 8.10%), compared to DL (45.11% ± 8.31%). There was a trend towards more stage 3 sleep after FBL, when compared to DL ($p = 0.07$). Spectral analysis revealed higher EEG power density in both daytime sleep episodes than for night time sleep in the EEG delta and theta frequency range (<7 Hz). There were no significant differences between the two daytime sleep episodes. Subjective sleep quality did not show significant differences either.

Conclusions
Daytime sleep after an isolated night shift under FBL or DL did not substantially differ. Exposure to FBL during an isolated night shift seems not to have any detrimental effects on the subsequent daytime sleep episode when compared to night shifts in DL, confirming recent reports (Rahman et al. 2013 and van de Werken et al. 2013).

Disclosures We are grateful to INTELLUX GmbH, Germany for financial support of the study.

AN ATLAS OF CIRCADIAN GENE EXPRESSION: IMPLICATIONS FOR BIOLOGY AND MEDICINE

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The circadian clock regulates daily rhythms in behavior and physiology throughout the body. Many groups have sought to characterize clock-regulated gene expression as a way to understand its tissue specific roles. However, most of these studies focused on one or two organs. Here we report a survey of the mouse from 12 separate brain regions and organs using both DNA arrays at 2 hr resolution and RNA-seq at 6 hr resolution. We find that 43% of the protein encoding transcriptome is clock regulated, including the majority of human disease genes and drug targets, including targets for 56 of the top 100 best-selling drugs. Most of these transcripts peak in anticipation of dusk and dawn in transcriptional "rush hours". We also find that conserved ncRNAs are substantially more like to cycle than non-conserved ncRNAs. We describe and use a new method, Phase Set Enrichment, which is optimized to detect pathway level enrichment for periodic data. Collectively, these results highlight the importance of the circadian clock and suggest ways to leverage biological time in medicine.

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