# Society for Light Treatment and Biological Rhythms

Program and Abstracts: Volume 25

**25th Annual Meeting**
**June 21-23, 2013**
**Starling Hotel & Convention Center**
**Geneva, Switzerland**
**www.sltbr2013.org**


Matthäus Willeit, SLTBR President 2012-2014

Scientific Committee: Matthäus Willeit (chair), Anna Wirz-Justice, Namni Goel, and Farhad Hafezi

Local arrangements are made courtesy of:
Center for Environmental Therapeutics - Europe &
The University of Geneva

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Contact SLTBR at sltbrinfo@gmail.com www.sltbr.org

**MESSAGE FROM OUR LOCAL HOST**

Dear Friends and Colleagues,

We are delighted to welcome you again to Geneva!

As the local organizing host and together with the program committee members, we look forward to an exciting program that combines multiple disciplines and research topics. I believe that the roundtable will provide interesting discussions about the latest trends and findings in the field.

And, I would like to welcome and thank our first-time sponsors to the meeting – Carex Health Brands (USA), Nature Bright (USA), Von Hoff AG, Valkee Oy, and Sanalux GmbH (Switzerland). I would also like to thank our returning sponsors for their continued support of SLTBR – Phillips (The Netherlands), Lumie (UK), Medi-Lum SàrL (Switzerland), Northern Lights (Canada), and Phytolis AG (Switzerland).

I wish all of you a very productive and enlightening congress and unforgettable moments in Geneva.

Sincerely,

Farhad Hafezi, MD PhD
Professor and Chair of Ophthalmology
University of Geneva

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# SLTBR 25th Annual Meeting Program

## Friday, June 21, 2013

**08:00 Registration Opens** *Foyer Rive Droite*

**09:00 SLTBR Board Meeting (by invitation only)** *Arosa Room*

**11:30 Buffet Lunch/Poster Session** *Pontresina/Foyer Rive Droite*

All presenters will be required to display their posters by 11:30.
Posters will remain on display through Sunday (14:30).

**12:45 Welcome, Introductions & Program Overview** *St. Moritz*

Matthäus Willeit (Austria)
Farhad Hafezi (Switzerland)

**13:00 Keynote Lecture – A New Look at the Eye**

Russell Foster (United Kingdom)

**13:45 Hot Topic - Modelling Photoreceptor Input to Non-Image Forming Responses to Light**

Stuart Peirson (United Kingdom)

### Symposium I

**Blue-Blocking Lens Debate**

Co-Chairs/Moderators:
F. Hafezi (Switzerland) & R. Foster (United Kingdom)

**14:00 Spectral Dependency of Light-Induced Retinal Degeneration**

C. Remé (Switzerland)

**14:20 Pro's and Con's of Blue Filtering Lenses**

S. Downes (United Kingdom)

**14:40 Long-Term Effects of Reducing Blue Light Input on Melatonin and Sleep**

M. Gordijn (The Netherlands)

**15:00** **Light and Dark for Phase Shifting Circadian Rhythms: How to Maximize the Effectiveness of a Light Treatment with Blue-Blocking Lenses**
M. Figueiro (USA)

**15:20** **Coffee Break**

**16.00** **Blue-Blocking Lens Panel Discussion**

**16:30** **Oral Presentations I: Nonvisual Responses to Light**

**16:30** **Modeling Dynamic Aspects of Human Nonvisual Responses to Light**
M. Ámundadóttir (Switzerland)

**16:45** **Blue Light Therapy in The Morning Supports a Sleep Advancing Protocol**
M. Geerdink (The Netherlands)

**17:00** **Effects of Light Wavelengths on Event-Related Desynchronization/Synchronization During a Working Memory Task**
Y. Okamoto (Japan)

**17:15** **Comparison of Non-Visual Light Dependent Functions in Healthy Subjects and Patients with Hereditary Optic Neuropathy**
M. Münch (Switzerland)

**18:00 Welcome Reception (All registered participants welcome)** ***Foyer Rive Droite***

# Saturday June 22, 2013

8:00 Registration & Morning Coffee

## Symposium II

**Chronobiology & Brain Monoamines** ***St. Moritz***

Co-Chairs/Moderators:
M. Willeit (Austria) & A. Wirz-Justice (Switzerland)

**09:00** **A Review of Circadian and Seasonal Changes in Brain Monoamine Function**
M. Willeit (Austria)

**09:30** **Interaction of Methamphetamine-Induced Oscillation and the SCN Circadian Clock**
K. Honma (Japan)

**10:00** **The Circadian Clock and Mood Related Behaviors**
U. Albrecht (Switzerland)

**10:30** **Seasonality in Suicide Research: What Have We Learned in 100 Years?**
N. Kapusta (Austria)

**11:00 Coffee Break & Poster Session**

Presenters with an even number will be asked to remain in front of their posters.
Posters will remain on display through Sunday (1430h).

**12:00 SLTBR 25th Anniversary Lecture**
Michael Terman (USA)

**13:00 Buffet Lunch** ***Patio***

**14:30 Oral Presentations II: Clinical Applications of Light**

**14:30** **Rapid Treatment of Suicidal Symptoms in Drug-Resistant Bipolar Depression with Lithium and Chronotherapeutics (Light and Wake)**
Ch. Locatelli (Italy)

**14:45** **A System for Delivering Prescribed Doses of Circadian Light**
M. Rea (USA)

**15:00** **Long-Term Bright Light Treatment as a Stabilizing Agent of Sleep and Mood**
K. Martiny (Denmark)

**15:15** **A Pilot Randomized Controlled Study of Light Therapy for Sleep-Wake Disturbances In Renal Transplant Recipients**
H. Burkhalter (Switzerland)

**15:30 Coffee Break & Poster Session**
Presenters with both even and odd numbers will be asked to remain in front of their posters. Posters will remain on display through Sunday (1430h).

**19:00 Congress Banquet Dinner (by paid invitation only)** ***Nendaz Room***

# Sunday June 23, 2013

8:00 Registration opens & Morning Coffee

## Symposium III

**Chronobiology, Sleep Loss and Obesity in Humans** ***St. Moritz***

Chair/Moderator:
N. Goel (USA)

**09:00** **Phase-Delayed Eating Patterns in Night Eating Syndrome Patients and in Healthy Sleep-Deprived Adults**
N. Goel (USA)

**09:30** **Impact of Sleep Restriction on Energy Balance**
M. St-Onge (USA)

**10:00** **Importance of Chronotype Preferences in Eating Behavior. Lessons Learned from the Sleep Exension Study, a Randomized, Controlled Study of Sleep Extension in Obese, Chronically Sleep-Deprived Individuals**
G. Cizza (USA)

**10:30** **The Relationship Between Overweight Status and Sleep Problems in Pre-Schoolers**
R. Levitan (Canada)

**11:00** **Coffee Break / Poster Sessions**
Presenters with an odd number will be asked to remain in front of their posters.
Posters will remain on display through Sunday (1430h).

**12:00** **SLTBR Annual Business Meeting**

**13:00** **Buffet Lunch** ***Patio***

**14:30** **ROUNDTABLE: Update on the application of bright light therapy**
Chairs. M. Willeit (Austria) with invited clinicians

**15:45 Oral Presentations III: Broader Implications of Light and Season**

**15:45** **Extraocular Bright Light Exposure in the Evening via the Ear Canals Does Not Affect Melatonin, Sleepiness or Psychomotor Vigilance**
V. Bromundt (Switzerland)

**16:00** **Influence of Artificial Dusk on Sleep**
K. Danilenko (Russia)

**16:15** **Activity Forecast by Season and Weather? Two Years Actigraphy in a Woman with Alzheimer's Disease**
A. Wahnschaffe (Germany)

**16:30** **Seasonal Symptomatology and the Appraisal of Vegetative Symptoms**
M. Young (USA)

**17:00 Final Remarks by SLTBR President / Meeting Closure**
M. Willeit (Austria)

## SOCIETY FOR LIGHT TREATMENT AND BIOLOGICAL RHYTHMS

**Business Meeting**
**Sunday, June 23, 2013 - 1200**
**St. Moritz Room - Starling Convention Center, Geneva, Switzerland**

**AGENDA**

1. **Call to Order**
2. **Approval of the 2012 Business Meeting Minutes**
3. **Introduction of New Board of Directors**
4. **Reports**
   A. Presidential Report on Key Developments: Matthäus Willeit
   B. Financial Report: Matthäus Willeit (for John Hanifin, Treasurer)
   C. Membership/Meeting Registration: Shawn Youngstedt
5. **2014 Annual Meeting Plan**

   Location:

   Dates: Friday, June 20 – Sunday, June 22, 2014 (tentative)

   Program Committee

   Abstract Submission (Timeline)
6. **Floor Open to Membership**

# SLTBR 25th ANNUAL MEETING

## *POSTER PRESENTATIONS*

1. **EFFECTS OF CLOCK GENE VARIANTS ON HOPELESSNESS AND SUICIDALITY IN DRUG-RESISTANT BIPOLAR DEPRESSION.**
   F Benedetti, C Locatelli, R Riccaboni, D Dallaspezia, C Colombo

2. **BRIGHT LIGHT FOR WEIGHT LOSS: RESULTS OF A CONTROLLED CROSSOVER TRIAL**
   KV Danilenko, SV Mustfina, EA Pechenkina

3. **LIGHT ASSOCIATED IMPRINTING AND DISRUPTION OF CIRCADIAN SYSTEMS: WHEN AND HOW SHOULD WE "TRANSLATE" INSIGHTS INTO "PRUDENT AVOIDANCE" – STRATEGIES IN PERINATAL HEALTHCARE?**
   TC Erren, K Trautmann, MME Salz, A Pinger & RJ Reiter

4. **TRANSLATIONAL CHRONOBIOLOGY: AN INITIATIVE TO FACILITATE THE TRANSLATION OF EXPERIMENTAL BIOLOGY RHYTHM RESEARCH INTO EPIDEMIOLOGICAL STUDIES IN HUMANS**
   TC Erren, MME Salz

5. **MINDFULNESS-BASED COGNITIVE THERAPY (MBCT) AS PREVENTION OF WINTER DEPRESSION? A PILOT STUDY.**
   J Fleer, E Geerts, VI Panjer, Y Meesters

6. **CEREBRAL NEUROIMAGING BY FNRIS DURING SLEEP INDUCTION THROUGH TRANSPAPEBRAL NIGHT VISION**
   P-A Grounauer, B Métraux

7. **A PILOT STUDY AIMS TO EXAMINE WHETHER THE EFFICACY OF BRIGHT LIGHT THERAPY (BLT) IS SIMILAR FOR DIFFERENT SUBTYPES OF MOOD DISORDERS.**
   PMJ Haffmans, T Naus, A Burger, J Grant, R van Rutten, B van der Meulen, ML Seelen

8. **A PILOT STUDY WILL EXAMINE THE EFFICACY OF BLT FOR BIPOLAR DEPRESSION.**
   PMJ Haffmans, T Naus, A Burger, J Grant, R van Rutten, B van der Meulen, ML Seelen

9. **A LONGITUDINAL STUDY OF RELATIONSHIPS BETWEEN PHOTOPERIOD, SLEEP TIMING, MOOD AND LIFE SATISFACTION**
   KS Jankowski, M Linke

10. **ONE WEEK OF LIGHT THERAPY SUFFICIENT IN THE TREATMENT OF SEASONAL AFFECTIVE DISORDER?**
    SE Knapen, M van de Werken, MCM Gordijn, Y Meesters

11. **MOTOR SKILL ACQUISITION IN ADHD: TRAINING IN THE EVENING RESULTS IN MORE EFFECTIVE CONSOLIDATION AND BETTER RETENTION THAN TRAINING IN THE MORNING**
    I Levy, O Fox, Y Dagan, M Korman, A Karni

12. **MORNING LIGHT THERAPY IMPROVES MOOD AND SLEEP IN WOMEN WITH BREAST CANCER**
    C Locatelli, S Cantamessa, S Dallaspezia, S Smeraldi, F Benedetti

13. **MODELLING PHOTORECEPTOR INPUT TO NON-IMAGE FORMING RESPONSES TO LIGHT**
    SN Peirson

14. **AN IMMEDIATE EFFECT OF LIGHT ON REPRODUCTIVE HORMONES IN WOMEN: REVISED**
    OY Sergeeva, KV Danilenko

15. **BRIGHT LIGHT AND MENTAL FATIGUE DURING DAYTIME: EXPLORING DAYTIME EFFECTS OF BRIGHT LIGHT EXPOSURE AND INDIVIDUAL'S LIGHT PREFERENCES AFTER MENTAL FATIGUE**
    KCHJ Smolders, YAW de Kort

16. **BRIGHT LIGHT INTERFERES WITH FEAR LEARNING**
    C Stoll, A Wahnschaffe, D Fay, O Pollatos, D Kunz

17. **IMPROVING THE CIRCADIAN RHYTHM OF ADULT PATIENTS WITH ADHD (ATTENTION-DEFICIT HYPERACTIVITIY-DISORDER) USING LIGHT**
    J Thome, M Gross, C Berger, R Wandschneider, A Popa-Wagner, A Coogan

18. **DAWN LIGHT SIMULATION AS A COUNTERMEASURE FOR CARDIOVASCULAR VULNERABILITY SURROUNDING SLEEP TO WAKE TRANSITION**
    AU Viola, V Gabel, C Schmidt, V Hommes, N Montano, C Cajochen.

19. **INFLUENCE OF BRIGHT LIGHT TREATMENT ON COMBAT-RELATED PTSD**
    SD Youngstedt, JP Ginsberg, SK Crowley, AC Reynolds, CE Kline

# ABSTRACTS 2013

## SOCIETY FOR LIGHT TREATMENT AND BIOLOGICAL RHYTHMS

**TRANSLATIONAL CHRONOBIOLOGY: AN INITIATIVE TO FACILITATE THE TRANSLATION OF EXPERIMENTAL BIOLOGICAL RHYTHM RESEARCH INTO EPIDEMIOLOGICAL STUDIES IN HUMANS**

**T.C. Erren & M.M.E. Salz**
Institute and Policlinic for Occupational Medicine, Environmental Medicine and Prevention Research, University of Cologne, Germany

**Objectives:** Biological rhythm research is providing insights into the architecture and economy of temporal organization at an accelerating pace. Indeed, scientists experimenting at many levels of temporal organization - from sub-cellular biochemistry, to whole cells, to organs, to animals, to (albeit small numbers of) humans - have worked out a cascade of quite precise and partly related causal mechanisms. And yet, since there are rather limited epidemiological studies in humans to "test" whether what is found in experiments is really relevant for health and disease, a targeted initiative to translate experimental biological rhythm research into observational studies in humans may be warranted.

**Methods:** On the basis of a selective literature review, this presentation explores the three main themes of this year's SLTBR meeting with a view to feasible hypothesis-driven epidemiological research in humans: (a) Symposium I ("Blue Blocking Lens Debate" —> ipRGCs), (b) Symposium II ("Chronobiology & Brain Monoamines" —» central circadian clock and mood) and (c) Symposium III ("Chronobiology, Sleep Loss and Obesity in Humans" —> chronotype and sleep).

**Results:** With regard to (a), with the premise that ipRGCs play a key role in circadian organization (including sleep-wake behavior), observational studies in populations with glaucoma or cataracts should "test" the prediction that sleep disturbances are more frequent in populations with critical ganglion cell loss despite ipRGC survival competence than in individuals without ocular diseases. With regard to (b), assuming that perinatal photoperiods imprint circadian system stability, mood disorders should be observed more frequently in populations born in winter months at extreme latitudes than in populations born at other times of the year and/or in locations closer to the Equator. With regard to (c), a thought experiment evinces that studies on and beyond shift-workers may be not interpretable without considering the chronobiological propensity which is critically, but not exclusively, determined by genes and can be influenced by exposure to light. Experimental research also suggests that epidemiology must consider several facets of complex sleep to avoid reductionism, namely the quantity *and* quality *and* timing of sleep.

**Conclusions:** From an epistemological point of view, considerable time elapses before experimental insights in the field of biological rhythm research are translated into observational studies and thus "tested" for their relevance in humans. To facilitate the transfer of experimental results into epidemiological studies, the following approach may be considered: key conferences such as of the ERBS or of the SLTBR could offer a dedicated 'Translating Experimental Biological Rhythm Research into Observational Studies in Humans" session. This format could invite proposals and discussions of experimental research worthwhile for future observational studies, and should contribute to zeroing in on *how* specifically chronobiology-driven hypotheses and predictions could be "tested" by epidemiologists. Moreover, core experimental journals may want to invite commentaries or have a dedicated issue on 'Translating Experimental Chronobiology into Epidemiology". By doing this, experimental and epidemiological research fields may cross-fertilize one another. Since resulting studies of populations would precede or accompany the development of clinical applications for individuals, the suggested initiative seems to be a recipe for the success of "Translational Chronobiology".

**Keywords**: Translational Chronobiology, Biological Rhythm Research, Experiments, Epidemiology, ipRGCs, Central Circadian Clock, Chronotype, Mood, Sleep

**Motor skill acquisition in ADHD: training in the evening results in more effective consolidation and better retention than training in the morning**

**Ishay Levy[1], Orly Fox[1,2], Yaron Dagan[1], Maria Korman[3] & Avi Karni[1, 4]**
[1]The lab of Human Brain & Learning, E.J. Safra Brain Research Center and the Department of Learning Disabilities, the University of Haifa, Haifa, Israel.
[2]The Zinman College of Physical Education & Sport Sciences, the Wingate Institute, Israel.
[3]Department of Occupational Therapy, Faculty of Social Welfare & Health Sciences, University of Haifa, Israel.
[4]The Sagol Department of Neurobiology & Ethology and Department of Human Biology, University of Haifa, Israel.

**Purpose:** to test the effects of the timing of training, comparing evening training to day training, on learning, consolidation and retention of motor skills in young female adults with ADHD. The learning and practice of a given sequence of movements can generate robust procedural memory for the learned sequence. The acquisition of this memory develops in two phases: *i*. gains in speed that emerge concurrently with training, and *ii*. additional gains in speed and accuracy that evolve following the termination of practice (delayed, "offline" gains). Delayed gains in task performance are considered a manifestation of procedural memory consolidation processes, which result in long-lasting retention. The timing of training in relation to sleep may play a role in the development of the offline performance gains. This may be even more critical in individuals with ADHD who are more likely to be evening oriented than adults without ADHD.

**Method:** 50 female students, 24 with ADHD (no stimulant medication) and 26 without ADHD (control group) were trained and tested in performing a five-element finger-to-thumb opposition sequence. During practice, 160 repetitions of the sequence were afforded. Tests, measuring speed and accuracy of self initiated continuous performance of the trained sequence, were made before, immediately after, overnight (a day after) and two weeks after the practice session. Half the participants in each group were trained in the evening, the rest were trained in the morning. The third and fourth tests (overnight, and two weeks later, respectively) took place in the morning.

**Results:** All four groups showed robust within-session gains and well-retained the practiced sequence of finger movements. However, participants with ADHD training at evening time showed significantly higher delayed gains than the morning-trained ADHD participants. No significant differences were found between the performance of the evening-trained ADHD group and the morning and evening trained control groups.

**Conclusion:** Young female adults with ADHD, who are more likely to be evening oriented, express more robust offline, consolidation phase, gains in the performance of a newly learned sequence of movements if trained in the evening. Morning-trained young adults with ADHD may show the smallest offline performance gains and thus less than optimal procedural knowledge.

**CEREBRAL NEUROIMAGING BY fNIRS DURING SLEEP INDUCTION THROUGH TRANSPALPEBRAL NIGHT VISION**

**P-A. Grounauer [1], B. Métraux [2]**
[1]Former Associate University Eye Clinic, Rue Pichard 11, 1003 Lausanne, Switzerland, [2] medical student CHUV Lausanne

**Objectives:** the aims of this applied research are two-fold. Firstly, to demonstrate that it is possible, using fNIRS, to follow the hemodynamic modifications of the prefrontal and occipital visual areas during a visual task. This consists of attentively observing, through closed eyes, the light emitted by a red LED placed on the forehead. Secondly, to show that this visual sensory perception could become a new cognitive behavioral therapy to break the cycle of insomnia.

**Method:** in a dark, silent room, where the subject is sitting, a LED emitting at 605 nm, 5 mcd, varies in intensity sinusoidally for 4 seconds, then switches off for 10 seconds. The subject is a right-handed, medication-free 21 year-old man in good health. The FOIRE 3000 Shimadzu spectroscope is connected to 12 prefrontal and 12 occipital optodes. Two minutes after the test, the result is visible on screen.

**Results:** the results show that it is possible and easy to measure the hemodynamic variations produced by the visual task thanks to the differences in the absorption-reflection of the oxy-desoyhemoglobin. In particular, we notice that a luminous "cloud stimulation" leaves the occipital cortex at rest but that it stimulates asymmetrically the prefrontal cortex to the detriment of the left lobe, which remains silent, while the right is clearly activated.

**Conclusions:** subject to ulterior statistical confirmation, we observe that the fNIRS could become an easy-to-use, inexpensive means, close to clinical reality. In the case of the fight against insomnia using visual CBT, we consider that it could become an elegant way of showing how somnogen visual training functions and illustrating the suggestion "train your mind to change your brain".

**Keywords:** fNIRS, visual CBT, insomnia, somnogen visual training, www.sleapi.com

**MINDFULNESS-BASED COGNITIVE THERAPY (MBCT) AS PREVENTION OF WINTER DEPRESSION? A PILOT STUDY.**

**J. Fleer[1], E.Geerts†, V.I. Panjer [1], Y. Meesters [2]**

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[2] University Medical Center Groningen, Department of Psychiatry, PO Box 30001, 9700 RB Groningen,
The Netherlands

**Aim**

The best available treatment for seasonal affective disorder (SAD) is light therapy. Yet, this acute treatment does not prevent recurrence of depression in subsequent seasons. One of the main public health challenges is, therefore, to develop interventions with enduring effects in the prevention of SAD recurrence. Mindfulness-based cognitive therapy (MBCT) has shown to be effective in the prevention of recurrence of non-seasonal depression, and thus might represent a solution to long-term SAD management.

The aim of this study is to gain preliminary insight in the efficacy of MBCT in the prevention of recurrence of depression in SAD patients in the following winter. The primary endpoints are (1) the moment of relapse and (2) severity of relapse. We hypothesize that patients in the treatment condition experience a later moment of relapse of SAD and that their relapse is less severe.

**Methods**

In April 2011, 152 patients from the SAD outpatient clinic of the University Medical Center Groningen were asked to participate in a randomized controlled pilot study. All were diagnosed with a major depressive disorder with a seasonal pattern according to the DSM-IV. Patients who expressed their interest received a telephone call to assess if they met the inclusion criteria. Eligible patients were randomized to the treatment condition (i.e. receiving 8 sessions of MBCT) or the control condition (i.e. care as usual). Patients in the treatment condition received MBCT in May-June, 2011, when there was no presence of depressive symptoms.

Moment of relapse and severity of relapse were assessed with the Inventory for Depressive Symptomatology Self Report (IDS-SR), which was completed on a weekly basis from September 2011- April 2012 as part a standard clinical care. During the winter of 2011-2012 participants received light therapy according to their clinical needs.

**Results**

Of the 152 approached patients. 91 patients were not interested to participate, and 15 did not fulfil inclusion criteria. The final sample consisted of 46 patients, of whom 23 were randomized to the treatment condition and 23 to the control condition. Analyses showed that there was no difference between groups in either moment of relapse ($t(29) = 1.21$, $p = .23$) or severity of relapse ($t(33) = .58$, $p = .57$).

**Conclusions**

The findings of this pilot study show that when MBCT is offered in a symptom free period (i.e. spring) it is not effective in the prevention of a depressive episode in the following winter period. Both the moment of onset of SAD and the severity of symptoms were similar for the two conditions. From an etiological point of view, an explanation for this lack of effect might be that SAD is more strongly determined by biological aspects than by cognitive aspects. In this case, cognitive interventions like MBCT may not have that large of an effect. However, because of the small sample size of this study, further research is warranted. Future studies might want to consider to provide MBCT shortly before the winter starts, for example in September and October.

**BRIGHT LIGHT AND MENTAL FATIGUE DURING DAYTIME: EXPLORING DAYTIME EFFECTS OF BRIGHT LIGHT EXPOSURE AND INDIVIDUAL'S LIGHT PREFERENCES AFTER MENTAL FATIGUE**

**Karin C. H. J. Smolders & Yvonne A. W. de Kort**
Eindhoven University of Technology, Human Technology Interaction, University of Eindhoven, The Netherlands

**Purpose:** A growing body of research is demonstrating acute activating effects of bright light exposure on indicators of alertness, vitality and performance. But little is known about these alerting and vitalizing effects as a function of antecedent conditions. Studies investigating effects of bright light exposure on human functioning have shown robust effects in the late evening and at night. Yet, to what extent and under what conditions such effects exist during daytime for day-active persons is largely unknown. As humans evolved as a diurnal species, their psychological functioning is primarily less optimal at night or after prolonged wakefulness compared to daytime hours. Nonetheless, persons may also experience sleepiness, a lack of energy and decrements in performance during daytime, even in the absence of sleep deprivation. We investigated whether alerting and vitalizing effects of bright light exposure differ during daytime, depending on individuals' prior mental state. To this end we performed two studies. One experiment investigated whether activating effects are more pronounced under mental fatigue than when rested. The second study investigated whether individuals' preferences for bright light differ depending on prior mental fatigue**.**

**Method Study One:** A 2x2 within-subjects design (N = 28; 106 sessions) was applied to explore effects of two illuminance levels (200 vs. 1000 lx at eye level, 4000 K) after a mental antecedent condition (fatigue vs. control) in experiment One. During 30 minutes of light exposure, subjective measures and cognitive tasks were administered in two repeated measurement blocks and physiological indicators were recorded continuously.

**Method study Two:** Employing a one-factor (fatigue vs. control) within-subjects design (N = 30, 60 sessions), light preferences were investigated after participants had engaged in mentally demanding tasks or had engaged mainly in restorative activities prior to the light exposure. Participants experienced each antecedent condition in separate visits to the laboratory. During each session, participants were asked to select the lighting level they felt would be optimal for performance on a subsequent attention task after the antecedent condition.

**Results:** Study One showed that participants felt less sleepy ($p = .02$), more vital and happier when exposed to bright light (both $p < .01$). These effects were immediate and persistent throughout the light exposure. As hypothesized, effects on self-reported sleepiness and self-control capacity were stronger under mental fatigue. In contrast, vigilance benefitted from bright light exposure, irrespective of antecedent mental condition. Notably however, other tasks showed mixed and sometimes even adverse effects of bright light. Data collection of study Two is currently in progress. These results will be presented at the conference.

**Conclusions:** Results of the subjective indicators in study One suggest that exposure to a higher illuminance level during daytime can replenish mental fatigue. However, the physiological and performance-based measures showed no clear indications for stronger effects of bright light exposure after mental fatigue. Bright light effects on daytime performance appear to depend on duration of exposure and vary with type of task. Together, the results show a complex picture suggesting that the beneficial effects of exposure to bright light at night cannot be directly translated to daytime situations, but need further research. Results of the study Two will provide insights into whether persons feel a need for more intense light when they suffer from mental fatigue. This will illustrate whether individuals' preferences reflect potential alerting and vitalizing effects of light during daytime.

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**A LONGITUDINAL STUDY OF RELATIONSHIPS BETWEEN PHOTOPERIOD, SLEEP TIMING, MOOD AND LIFE SATISFACTION**

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A number of studies have shown that more evening oriented subjects exhibit less advantageous psychological functioning, as compared to more morning-oriented individuals. Such relationships have been shown, amongst others, for mood and life satisfaction. Consequently, it has been proposed that a shift toward morningness could improve psychological well-being. However, the above proposition has been inferred from intra-individual research and it is not clear whether it is in fact valid in intra-individual level. The aim of the present research was to test whether shift toward morningness in response to prolongation of photoperiod is accompanied by improvement of psychological functioning. Self-reported sleep timing parameters (for working and free days), energetic arousal, tense arousal, hedonic tone and life satisfaction were measured four times in three week intervals, in successively increasing photoperiod in a sample of 96 university students. Regression analyses for within subjects design indicated that longer photoperiod was related to earlier bed time ($r$ = -.19; $p$ < .01), sleep-onset ($r$ = -.21; $p$ < .001), wake time ($r$ = -.27; $p$ < .001), mid-sleep time ($r$ = -.31; $p$ < .001) (all variables referring to free days), shorter sleep latency on free ($r$ = .21; $p$ < .001) and working ($r$ = .29; $p$ < .001) days, smaller social jetlag ($r$ = -.30; $p$ < .001) and greater tension arousal ($r$ = .17; $p$ < .01). Shift toward morningness (earlier mid-sleep time on free days) was related to earlier bedtimes on free ($r$ = .73; $p$ < .001) and working ($r$ = .22; $p$ < .001) days, sleep-onset on free ($r$ = .75; $p$ < .001) and working ($r$ = .29; $p$ < .001) days, mid-sleep time on working days ($r$ = .18; $p$ < .01), shorter sleep latency on free ($r$ = .15; $p$ < .001) and working ($r$ = .16; $p$ < .001) days, smaller social jetlag ($r$ = .76; $p$ < .001) and sleep debt ($r$ = .19; $p$ < .01), longer sleep duration on working days ($r$ = -.19; $p$ < .01), whereas for psychological outcomes associations were statistically non-significant. None statistically significant relationship between psychological variables and social jetlag, sleep duration or other studied sleep parameters was observed. The results indicate that increasing photoperiod is related to shift toward morningness, however increasing morningness or change in other studied sleep parameters were not related to alteration in psychological outcomes. As shift toward morningness was not accompanied by alteration in mood and life satisfaction, it is possible that some third factor underlies association between eveninngess and disadvantageous psychological functioning revealed in between subject comparisons and recommendations inferred from such studies may not be valid.

**BRIGHT LIGHT INTERFERES WITH FEAR LEARNING**

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***Purpose***
In an fMRI study it has been demonstrated that blue light increases amygdala activity when compared to green light (Vandewalle, et al.). The amygdala is involved in processing of emotional stimuli and salience learning (Phelps & LeDoux, 2005), especially stimuli that are threatening in their nature (Sato et al, 2011). The aim of the current study is to examine the influence of bright blue-enriched light on the processing of threatening stimuli. It is hypothesized that bright blue-enriched light activating amygdalic regions interferes with processing of threatening stimuli.

***Method***
In a balanced design pictures with neutral, positive and negative connotations were shown to participants (n=16). A recognition task was conducted after an hour of bright blue-enriched light exposure (or control condition), measuring accuracy and reaction times.

***Results***
Results showed that the benefit of bright light on reaction times was present for neutral (-46 ±176ms) and positive (-56 ±109ms) pictures, but there was no benefit of bright light for reaction times to negative pictures (21 ±148ms). A significant difference in the change of reaction times was found between the positive and negative categories (paired t-test; $p < 0.05$).

***Conclusion***
Considering that bright light not only activates amygdalic regions but also cortical networks that might be responsible for general decreased reaction times, current data confirm the hypothesis that bright blue-enriched light interferes with processing of negative stimuli. The current study was conducted in the evening hours when light is biologically unnatural. Further research should investigate this relationship in a daytime setting.

**ONE WEEK OF LIGHT THERAPY SUFFICIENT IN THE TREATMENT OF SEASONAL AFFECTIVE DISORDER?**

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**Aim:** Seasonal Affective Disorder (SAD) is characterized by recurrent episodes of major depression occurring with a seasonal pattern. Prevalence is around 2-10% in western countries. Light therapy (LT) is the treatment of choice for winter SAD and treatment duration ranges from one to eight weeks. Previous studies showed no difference in outcome between two and five weeks of LT[1]. We aim to investigate retrospectively whether only a single week of LT is as effective as two weeks in treating winter SAD, whether males and females respond differently and if there is an effect of expectations as assessed before treatment.

**Methods:** Patients (83 women and 25 men, mean ± SD, 37.6 ± 12.1 years) who received either one week (group 1, n = 42) or two weeks (group 2, n = 68) of LT were included in 3 studies[2–4]. Depression severity was determined by a structured interview (SIGH-SAD) prior to LT, after one week of LT, after two weeks of LT (only group 2), and one week after having finished LT. Prior to LT patients' expectations on therapy success were determined with a questionnaire containing three questions on the expectations of therapy success.

**Results:** Depression severity was similar in both groups prior to treatment (mean ± SE 25.3 ± 0.5) and decreased significantly during treatment ($F_{2,106}$ = 174.8, $p < 0.001$). No significant difference in therapy outcome 1 week after treatment between the different groups was found (percentage SIGH-SAD score reduction 67.1 ± 2.9; $F_{1,106}$ = 0.71, ns). A significant effect of LT duration over the weeks of treatment was found ($F_{2,105}$ = 3.2, p = 0.046). No significant effect of duration of treatment was found in men ($F_{2,21}$ = 0.69, ns); in women there was a significant effect of duration ($F_{2,79}$ = 4.1, p = 0.019) showing that women in the 2 week LT condition responded more slowly compared to women in the one week LT condition.

On average men and women had similar expectations on therapy success. In men there was no significant correlation between expectations and therapy outcome (Spearman correlation, ρ = 0.284, ns). In women there was a significant positive correlation in expectations and therapy success (ρ = 0.238, p = 0.03).

**Conclusions:** There is no difference in therapeutic response after one week of LT compared to the response of 2 weeks LT. Our results actually show that women have a slower response of two weeks of LT compared to one week of LT. This slower response seems to be attributable to therapy expectations. Since one week of light therapy is both cost and time saving compared to longer treatment, we propose to use one week of LT.

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**BRIGHT LIGHT FOR WEIGHT LOSS: RESULTS OF A CONTROLLED CROSSOVER TRIAL**

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**Objective:** One study showed that daily bright light treatment combined with moderate exercise reduced body fat in overweight/obese non-seasonal subjects compared to the exercise alone [1]. Our previous study did not find a difference in body mass change following mild hypocaloric diet combined with bright light treatment vs. placebo [2]. The aim was to investigate whether light treatment may indeed reduce body mass.

**Methods:** A crossover, placebo-controlled, randomized clinical trial was performed between November and April in Novosibirsk (55° N). The trial comprised a 3-week in-home session of morning bright light treatment using a device of light-emitting diodes (Lumie SADlight) and a 3-week placebo session by means of a deactivated ion generator, separated by an off-protocol period of at least 23 days. The number of placebo and light sessions was matched with respect to season. Data were obtained from 34 overweight women, aged 20–54 years, 10 were seasonal-dependent (= light-dependent) according to the Seasonal Pattern Assessment Questionnaire. Weekly measures included body weight, percentage body fat by bioimpedancemetry, and subjective scores (appetite, mood, energy levels).

**Results:** Motivation and expectation towards weight loss were similar for the two intervention sessions. With light, compared to the placebo session, weight did not reduce significantly, but percentage fat, fat mass, and appetite were significantly lower (average fat reduction 0.35 kg). The latter two results remained significant after excluding seasonal-dependent subjects from the analysis. Irrespective of the type of intervention, seasonal-dependent subjects had greater weight and fat mass changes during treatment (decline $p < 0.036$) or between sessions (regain $p < 0.003$). Photoperiod ($p = 0.0041$), air temperature to a lesser extent ($p = 0.012$), but not sunshine ($p = 0.29$) was associated with the weight change (greater weight reduction if the second session was in spring).

**Conclusion:** Morning bright light treatment reduces body fat and appetite in overweight women and may be included in weight control programs.

**Keywords:** Overweight, Bright Light Treatment, Body Fat, Appetite, Seasonality

**Funding support:** Lumie® (Cambridge, England).

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**EFFECTS OF CLOCK GENE VARIANTS ON HOPELESSNESS AND SUICIDALITY IN DRUG-RESISTANT BIPOLAR DEPRESSION**

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**Purpose**. Previous researches by our group showed that clock genes can bias both clock and non-clock brain functions in patients with Bipolar Disorder, such as neural responses to positive and negative moral stimuli, instability of circadian rhythms, insomnia, recurrence of illness. The aim of the present study is to investigate the role of CLOCK gene in influencing suicidality and cognitive distortions in BD.

**Methods**. We studied 123 consecutively admitted inpatients with a major depressive episode in course of BD. Severity of depression was rated on the Hamilton depression rating scale (HDRS) and Beck depression inventory (BDI). Cognitive distortion was assessed through the Cognition Questionnaire (CQ) and Adverse Childhood Experiences were assessed through the Risky Family Questionnaire (RFQ).

**Results**. CLOCK mutants have a worse tendency toward the generalization across time of negative distortions, with worse hopelessness, higher ratings on the suicide item of the Hamilton rating scale, and a diminished resilience as shown by a stronger relationship between early life stress and current suicidality.

**Conclusion**. These psychopatological features are state-dependent and closely linked with the overall negative distortion in the generation and cognitive control of affects which parallels the waxing and waning of depression. Chronotherapeutic antidepressant interventions, that directly target the clock, cause indeed an immediate decrease of suicidality and hopelessness which is independent of CLOCK genotype. Drug-resistant bipolar depressed patients respond equally well.

**MORNING LIGHT THERAPY IMPROVES MOOD AND SLEEP IN WOMEN WITH BREAST CANCER**

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**Purpose**. Patients with breast cancer suffer from fatigue generally before, during and after chemotherapy. The syndrome shows negative effects on physical functioning, quality of life, and correlates directly with sleep disruption and inversely with bright light exposure. Light therapy is effective for circadian rhythm related disorders in consolidation sleep and in improving the strength of circadian rhythms. The aim of the study is to investigate if light therapy can be effective in reducing fatigue in cancer disease.

**Methods**. To counteract cancer-related fatigue and sleep disturbances, we administered morning light therapy (dawn-simulation, ranging from 0 to 400 lux for 30 minutes in the morning) for the first two weeks of chemotherapy cycle to patients affected by breast cancer. We treated 10 women with stage I-III breast cancer during neo-adjuvant or adjuvant anthracycline-based chemotherapy, and rated quality of life, fatigue, mood and quality of sleep with self-and observed ratings. Activity-rest and sleep-wake rhythms were monitored using actigraphic support before and after the treatment. Data were analyzed in the context of the General Linear Model.

**Results**. Treatment was associated with a progressive improvement of perceived mood. This change was influenced by cancer stage and by the degree of phase advance of the activity-rest rhythm: the more light advanced the rhythms the better the mood improved. This was also associated with significantly early sleep onset and better sleep efficiency.

**Conclusion**. Moring light therapy with dawn simulation, that produces an immediate amelioration of circadian rhythm abnormalities (insomnia, sleepiness, ect) through the synchronization of these rhythms, can be an effective treatment for breast cancer-related disturbances of mood and sleep.

**AN IMMEDIATE EFFECT OF LIGHT ON REPRODUCTIVE HORMONES IN WOMEN: REVISED**

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**Objectives**: In 2010, we reported an immediate effect of light on reproductive hormones, addressing the role of blue-sensitive (~480 nm) melanopsin-based photoreception mediating the non-visual effects of light [1]. The results of that study were conflicting. We discovered later, that hormonal serum samples obtained from a single woman were assayed in different biochemical runs, thus there might be a confounding effect of interassay variability. Here we report the results following the hormonal re-measurements.

**Methods:** In April-May 2009, 16 healthy women (age 20-44 y) came to the laboratory twice in 1-3 days (median = 2 days) during the follicular phase of their menstrual cycle. They arrived ~07:30 shortly after waking and wore sunglasses (<10 lux) during the 5-10 minute walk from their home to the laboratory. During one session, a broad-spectrum white-appearing light with a superimposed peak at 469 nm was presented; during the other session, short-spectrum red light with a peak at 651 nm was used (crossover, counter-balanced order). The study used light-emitting diode units (Lumie SADlight) matched for irradiance levels (~7.0 $W/m^2$ at a distance of 50 and 45 cm, respectively). In photopic units, the lights were 1300 vs. 1100 lux presented against 5-10 lux background. Venous blood was taken at 0, 20 and 45 minutes of light exposure to measure concentrations of follicle-stimulating hormone (FSH), luteinizing hormone (LH), prolactin, estradiol, progesterone, melatonin and cortisol. Melatonin was measured as a recognized indicator of the specific spectral action of light (control). All 6 serum samples obtained from each woman were assayed in a single run.

**Results:** As expected, melatonin levels were lower with white vs. red light; the significance became negligible after 45 min of exposure, possibly due to low levels of melatonin at that time of day. The levels of other hormones did not differ between the two conditions. Levels of all hormones decreased during the first 20 min of light exposure. In the case of melatonin and prolactin, this may reflect the natural morning decay (circadian-dependent); data on cortisol levels (which usually increase in the morning) and the remaining hormones (which have no distinct circadian variations) point to a confounding effect of transition from walk to sedentary position on hormone blood concentration [2].

**Conclusions:** Moderately bright blue-enhanced white light, compared to matched-by-irradiance red light, was not found to alter reproductive hormones blood levels after 20 or 45 minutes of light exposure in healthy women.

**Keywords:** Women, Light, Reproductive Hormones

**Funding support:** The study was supported by Lumie®. OYS was paid by grant EUCLOCK (the EU 6th Framework Project No. 018741).

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**LIGHT-ASSOCIATED IMRPINTING AND DISRUPTION OF CIRCADIAN SYSTEMS: WHEN AND HOW SHOULD WE "TRANSLATE" INSIGHTS INTO "PRUDENT AVOIDANCE" STRATEGIES IN PERINATAL HEALTHCARE?**

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**Background & Objectives**: Experimental evidence suggests the possibility that pre- and post-natal light exposure of fetus and infant may be more important for the later well-being than has been appreciated so far. First empirical evidence in rodents suggests that perinatal light exposure patterns may critically imprint circadian system stability – hereinafter referred to as the "perinatal light imprinting circadian system" hypothesis [PLICS hypothesis, 1; 2]: – and may be associated with health or disease in later life stages. With regard to exposing adults to light at biologically unusual times, IARC [International Agency for Research on Cancer] classified shift work involving circadian disruption as being probably carcinogenic to humans – hereinafter referred to as the "chronodisruption cancer theory" [CDCT, 3]. Assuming that the hypothesized chains of causation were not falsified, this presentation intends to stimulate discussion regarding when, and if so, how it may be appropriate to translate possible insights into "prudent avoidance" strategies in perinatal healthcare.
**Methods**: On the basis of a selective literature review, this presentation explores further empirical background to perinatal light exposure and the development of circadian "vision" and systems, on the one hand, and shift work and circadian disruption, on the other. Perspectives for practical preventative options are developed with a view to perinatal healthcare.
**Results**: The PLICS hypothesis is in line with additional circumstantial evidence: melanopsin-containing retinal ganglion cells (ipRGCs) as critical interfaces of environmental light with circadian systems respond to light immediately after birth [4] and non-image forming circuits can contribute to "circadian vision" [5] before the "classical" image-forming pathways work. After IARC's classification, more experimental and increasing epidemiological evidence appears compatible with the CDCT. With regard to "populations" which may benefit from preventative measures, there are the (a) unborn and neonates; (b) pregnant and breast-feeding mothers; (c) nurses and doctors at neonatal intensive care units (NICUs). With regard to light-associated diseases, we are confronted with suspected diseases which are not confined to cancer [6] in adults whose work at biologically unusual times exposes them to circadian disruption. On the basis of the PLICS hypothesis, light-associated late sequelae, possibly including mood or neurobehavioral disorders such as seasonal affective disorders (SAD) or attention deficit hyperactivity disorder (ADHD) [7;8] and cancer are conceivable in neonates, particularly in those who need intensive care in early developmental stages.
**Suggestions & Conclusions**: The following measures may be considered to foster perinatal care of population (a): Since the mothers' melatonin can be critical for the pre- and post-natal maturing of circadian systems, both pregnant and breast-feeding mothers may want to seek out cyclic light conditions of 16:8 L:D ratios. Moreover, in average homes and – whenever feasible in NICUs – newborns and infants should be exposed to cyclic light conditions of 16:8 L:D ratios; 24:0 L:D ratios as well as constant dimness should be avoided [9, 10] wherever and whenever possible. To protect populations (b) and (c), both may benefit from paying attention to their individual chronotype [11]. Mothers as well as NICU personnel may choose their activities in time windows which are – according to their genetically determined propensity for sleep and wake – chronobiologically convenient and least demanding for them. Overall, as long as the proposed causal links of light-associated disease endpoints are not falsified in any one of the three "populations", the preventative measures above regarding what light is needed and when by (a), (b) and (c) should be discussed and possibly balanced in the suggested way. Clearly, light interacts with other Zeitgebers, including social time cues, food provision, ambient noise and physical activities. And yet, the suggested focus on "light" to foster neonatal non-image forming photosensitivity, on the one hand, and to protect mothers, nurses and doctors from circadian disruption, on the other, does not appear to be a reductionist approach but may constitute a promising prospect for targeted research and prevention.

**Keywords**: Translational Chronobiology, Perinatal Light; Perinatal L:D Patterns, Imprinting of Circadian Systems, ipRGCs, Circadian Disruption, Chronotype, ADHD, Mood, Sleep, Cancer, Prudent Avoidance, Prevention

**A PILOT STUDY AIMS TO EXAMINE WHETHER THE EFFICACY OF BRIGHT LIGHT THERAPY (BLT) IS SIMILAR FOR DIFFERENT SUBTYPES OF MOOD DISORDERS**

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***Background**:* There is growing interest in the possible applications of Bright Light Therapy (BLT). BLT might be a valid alternative or add-on treatment for many other psychiatric disorders beyond Seasonal Affective Disorder. This pilot study aims to examine whether the efficacy of Bright Light Therapy (BLT) is similar for different subtypes of mood disorders.

***Methods**:* Participants were 48 new outpatients with major depressive disorder with either melancholic features (*n* = 20) or atypical features (*n* = 28). Morning BLT was administered daily for 30 minutes at 5.000-10.000 lux on working days for up to three consecutive weeks.

***Results**:* Participants' depressive symptoms improved significantly after BLT ($p < .05$). The effects of BLT remained stable across a four week follow-up. There were no significant differences in efficacy of BLT between groups ($p > .05$). No effect of seasonality on the improvement in depressive symptoms after BLT was found, ($p = .781$).

***Limitations**:* The study had a small sample size and lacked a control condition.

***Conclusions**:* This pilot study provides preliminary evidence that BLT could be a promising treatment for depression, regardless of the melancholic or atypical character of the depressive symptoms.

**Keywords:** bright light therapy– major depression – seasonality

**A PILOT STUDY WILL EXAMINE THE EFFICACY OF BLT FOR BIPOLAR DEPRESSION**

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**General Summary**

The depressive episodes in bipolar disorder are the leading cause of impairment and death among these patients. The treatment of bipolar depression is a major problem since the few existing treatment options have not been proven to be safe or effective.

Bipolar disorder is associated with deregulated biological rhythms, in both depressive and (hypo)manic as well as euthymic episodes, suggesting that bright light therapy (BLT) might be a particularly appropriate and effective alternative treatment option for bipolar depression. BLT is a relatively inexpensive, fast-acting, non-invasive and easy to use procedure with few side-effects, but definite information about the feasibility, efficacy and most optimal method of implementation is lacking. Therefore, this pilot study will examine the efficacy of BLT for bipolar depression. The results will lead to more optimal (cost) effective treatment implementation because of the expected decrease in the use of more expensive and time consuming treatments. This research might make BLT better acceptable for patients, clinicians, and mental healthcare institutions alike and will function as a foundation for the development of a guideline. Most importantly, it may lead to improvement of the quality of life of many patients.

**Keywords**

bipolar disorder | bright light therapy | clinical efficacy | biological rhythm | seasonality

**DAWN LIGHT SIMULATION AS A COUNTERMEASURE FOR CARDIOVASCULAR VULNERABILITY SURROUNDING SLEEP TO WAKE TRANSITION**

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**Purpose:** There is a large body of evidence that all major adverse cardiovascular events peak in the morning hours. Abrupt changes in sympatho-vagal balance, namely sympathetic surges during the transition from sleep to wakefulness may partly contribute to this morning accumulation of these adverse events. To prevent these abrupt sympatho-vagal shifts, we propose to reduce the gradient of the transition mimicking the biota wake-up conditions using a dawn simulating light (DSL) alarm clock.

**Methods:** After a 6-h sleep restriction night, participants were woken-up 2-h before their habitual wake time. We applied a habitual auditory alarm clock or a DSL starting 30 minutes (polychromatic light increasing from 1.2 lux, 1.9E+16/ $m^2$*s, 1090K, 0.2 m-lux to -250 lux, 2.4E+18/ $m^2$*s, 2750K , 620 m-lux) before scheduled wake-up time in a balanced cross-over design. In both conditions the participant remained in bed, in a supine position during the 30 min following the awakening. We compared the two type of wake-up episodes during 30 min of sleep in a still dark environment, 30 min of sleep during the gradual DSL exposure and 30 min of wakefulness after wake-up in a supine position in bed.

**Results:** Seventeen healthy men (mean [SE] age 23.12[0.82] years sleep quality index (PSQI) 2.88 [0.27]; body mass index 22.86 [0.35] kg/$m^2$ met the inclusion criteria. The R-R intervals (i.e., the length of time between the R peaks of consecutive QRS complexes) were calculated and checked for artefacts. Power spectral analysis of each consecutive 150 R-R intervals recording was performed sequentially with a fast Fourier transform based on a nonparametric algorithm. The cardiac sympathetic modulation was estimated by the power densities ratio LF/(LF+HF) [LF=0.04 to 0.15 Hz; HF=0.15 to 0.50 Hz]. During the transition from sleep to wakefulness, the classical alarm clock evoked a HR increase from 60.6+2.5 at to 89.7+3.7 bpm, while in the DSL condition, HR increased from 67.5+4.8 to 78.4+5.0, resulting in a significant gradient reduction ($p < 0.05$). This finding was corroborated by a significant increase of sympathetic modulation during the 30 minutes of sleep with a gradual DSL, that did not raise further during the following wakefulness.

**Conclusion:** Dawn light simulation before scheduled wake-up in the morning prepares cardiac physiology to awakening by “smoothing” the abruptness of sympathetic surge. This reduction seems to be due to a pre-stimulation of the sympathetic activity during sleep induced by DSL. These data indicate that DSL may have cardiovascular protective effect and counteract the usual “off/on” awake.

**INFLUENCE OF BRIGHT LIGHT TREATMENT ON COMBAT-RELATED PTSD**

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**Objectives:** Posttraumatic stress disorder (PTSD) is the most common mental health diagnosis of veterans of the recent wars in Afghanistan [Operation Enduring Freedom (OEF)] and Iraq [Operation Iraqi Freedom (OIF), Operation New Dawn (OND)]. Current treatments for PTSD have had limited efficacy. Rationales for potential efficacy of bright light treatment for PTSD include (1) evidence of anxiolytic effects of bright light; (2) serotonergic mechanisms of bright light treatment are consistent with common treatment of PTSD with SSRIs; (3) evidence that PTSD is associated with a delayed circadian system; and efficacy of bright light for alleviating multiple comorbidities of PTSD, including depression, sleep disturbance, and cognitive impairment. The aim of this randomized controlled trial was to examine the effects of bright light on combat-related PTSD and associated morbidities in veterans.

**Methods:** Following extensive screening and a 1-week baseline period, participants (n=65) with combat-related PTSD were randomized to one of two 4-wk treatments: (1) morning bright light (30 min/day at 10,000 lux); or (2) placebo (30 min/day) consisting of an inactivated negative ion generator. Before and after the intervention, participants received a blinded clinical evaluation of PTSD severity (CAPS-2) and global impressions of severity and improvement (CGI), and participants self-rated their PTSD severity (Posttraumatic Stress Disorder Checklist: PCL-M). Sleep was assessed continuously via wrist acigraphy. Weekly questionnaires included the Beck Depression Inventory (BDI), the Spielberger State Anxiety Inventory, and the Pittsburgh Sleep Quality Inventory, including an Addendum which targeted PTSD-related sleep complaints.

**Results:** Clinical ratings of PTSD severity (CAPS-2) improved significantly more (p=0.02) following bright light [from 63.0±3.6 to 42.9±4.5] compared with placebo (62.3±4.7 to 53.4±4.5). Clinical ratings of global impressions of improvement from baseline improved significantly more (p=0.03) following bright light (from 4.3±0.2 to 2.6±0.2) compared with placebo (from 4.2±0.3 to 3.2±0.2). Self ratings of PTSD severity (PCL-M) improved significantly more (p=0.03) following bright light (from 45.3±1.8 to 34.5±2.1) compared with placebo (47.2±2.7 to 40.8±2.3).

**Conclusions**: The results suggest benefits of bright light treatment for PTSD.

**Keywords:** PTSD, Depression, Veterans

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**IMPROVING THE CIRCADIAN RHYTHM OF ADULT PATIENTS WITH ADHD (ATTENTION-DEFICIT HYPERACTIVITY-DISORDER) USING LIGHT**

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**Purpose**: Based on our previous findings that the circadian rhythm of adult patients suffering from ADHD is altered at the behavioural, endocrine and molecular levels (Baird et al. 2012, Mol Psychiatry 17: 988-995) and that drugs used in the treatment of ADHD impact on the CLOCK-gene system (Baird et al. 2013, Brain Res: in press), we presently aim at using chronotherapeutic strategies in order to improve the patients' condition (Coogan and Thome 2011, World J Biol Psychiatry 12, S1: 40-43). One way of doing so, is to explore the possibility of using light in order to alter the circadian rhythm of adult ADHD patients.

**Methods:** After obtaining informed consent, patients and matched controls are provided with mobile light sources (10,000 lux) and instructed to them daily for a period of five weeks for 30 minutes in the morning. Before and after this intervention, saliva samples are collected over a 24h period in regular intervals of four hours (hourly sampling between 8pm and 1am for DLMO (dim-light melatonin-onset) assessement). Melatonin and cortisol levels are determined using standard ELISA kits. All participants are also asked to fill the German version of the morningness-eveningness questionnaire (dMEQ) (Horne and Östberg 1976, Int J Chronobiol 4: 97-110). The study was approved by the local Ethics Committee.

**Results:** Patients and controls exhibit statistically significant differences in their time-of-day preferences with a clear tendency towards evening preference in individuals diagnosed with ADHD. Additionally, there are some indications of a different pattern of circadian changes in cortisol and melatonin levels when comparing patient and control groups. Light does not seem to affect this pattern in controls, however there is a trend towards a "normalization" in patients after regular exposure to the light source. However, at present none of these preliminary observations can be confirmed statistically, since so far only a very limited number of individuals has been included into this pilot study.

**Conclusions:** The results of our study confirm earlier findings of an altered circadian rhythm and evening preference in ADHD patients. Furthermore, we demonstrate that it is feasible to use simple systems to monitor and possibly alter the circadian rhythm in this group of psychiatric patients in an outpatient setting. At present, we are working on increasing case numbers and initiate similar studies with different patient populations including autism, affective and neurodegenerative disorders.

**INTERACTION OF METHAMPHETAMINE-INDUCED OSCILLATOR (MAO) AND THE SCN CIRCADIAN CLOCK**

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The human circadian system consists at least of two major oscillatory mechanisms; one regulating the circadian rhythms of body temperature and plasma melatonin and the other regulating sleep-wake cycles. The two mechanisms are highlighted by spontaneous internal desynchronization observed under temporal isolation experiments. However, the mechanism of internal desynchronization as well as the nature of sleep-wake cycle is a long lasting matter of discussion. To investigate the oscillatory mechanism of sleep-wake cycle, we developed the animal model in which a stimulant of central dopaminergic systems, methamphetamine (MAP), was chronically manipulated and demonstrated several important phenomenon thought to be specific to the human circadian system such as internal desynchronization and circabidian rhythm.

In the present study, we used transgenic rats carrying a bioluminescent reporter system of a clock gene product, PER2. The rats under light-dark cycles were treated chronically with MAP by three different ways; ip injection, ad lib drinking of MAP dissolved water and restricted MAP water supply (rMAP). Behavior rhythms were measured by thermal sensors and running-wheel. Circadian rhythms in PER2 were monitored in cultured brain slices of several areas of the dopaminergic system.

As a result, chronic MAP treatment by either way desynchronizes the behavior rhythms from the light-dark cycles. The circadian PER2 rhythm in the suprachiasmatic nucleus (SCN) was not affected by MAP treatment. On the other hand, circadian rhythms in the brain dopaminergic system showed significant phase-shifts in association with desynchronization of behavior rhythm. Interestingly, the extent and direction of phase-shift were different among areas examined. From these results, the brain dopaminergic system was strongly suggested as the site of MAP-induced oscillation (MAO) in rats and the multiple circadian oscillators in different brain areas were involved in the MAO. In addition, the circadian PER2 rhythms in the extra-SCN brain areas behaved differently by restricted daily feeding. MAO and food-entrainable oscillator (FEO) are unlikely to share the common oscillatory mechanism in the brain. The SCN circadian clock and MAO could be the bases of two oscillator hypothesis for the human circadian system.

**LONG-TERM DAILY BRIGHT LIGHT TREATMENT AS A STABILIZER OF MOOD AND SLEEP**

Martiny K, Refsgaard E, Lund V, Lunde M, Sørensen L, Thougaard B, Lindberg L, Bech P.

**Purpose:** to examine whether the initial 9-week antidepressant effect of wake therapy in combination with Bright Light Therapy (BLT) and Sleep Time Stabilisation (STS) could be maintained in a 20-week follow-up period.

**Method:** We have previously showed that 3 wake therapies (on alternate days) in combination with BLT and STS had a sustained antidepressant effect compared to exercise in a 9-week period with fixed medication (1). In the follow-up period from week 9 till week 29, duloxetine dosage could be increased or patients shifted to other antidepressants and daily BLT and STS were continued. Depression severity was assessed by the HAM-$D_{17}$ with remission defined as a score of less than 8. Analysis was done within a mixed model repeated measures model and estimated scores are presented. Patient made daily entries in sleep and light therapy logs.

**Results:** in the wake/exercise group 6/4 patients dropped out; dosage of duloxetine was increased in 26/27 patients and shift to other antidepressant was made in 4/7 patients. HAM-$D_{17}$ scores in the wake/exercise group were: week 9 a score of 9.0 (SE=0.9) / 11.5 (SE=0.8); week 29 a score of 7.6 (SE=0.9) / 10.1 (SE=0.9), (F=4.7; p = 0.03). Remission rates for wake/exercise group: week 9 a rate of 44.8 % (N=30) / 23.4 % (N=34), week 29 a rate of 61.9 % (N=24) / 37.9 % (N=30), (OR=2.7; CL 1.3-5.6, p=0.01). Mean sleep parameters in the wake/exercise groups from the whole follow-up period: sleep onset 23:11 (SD=1:28) / 23:46 (SD=1:38), (F=10.7;p=0.002), sleep offset 7:21 (SD=1:26) / 7:44 (SD=1:54), (F=2.3;p=0.14), sleep duration 8:09 (SD=1:30) / 7:58 (SD=1:47), (F=1.9;p=0.18) hour: minutes. Day-to-day variance of sleep offset was significantly lower in the wake group (F=0.56; p<0.0001).

**Conclusion:** the initially seen 9-week augmentation of antidepressant effect for the wake group was continued for 20 additional weeks despite the opportunity to increase dosage or shift antidepressant. We suggest that this was partly due to the stabilizing action of bright light therapy on mood and sleep. Dropout was moderate. Long-term light therapy should be considered as an augmenting treatment in major depression.

1. **Martiny K**, Refsgaard E, Lund V, Lunde M, Sørensen L, Thougaard B, Lindberg L, Bech P. A 9-Week Randomized Trial Comparing a Chronotherapeutic Intervention (Wake and Light Therapy) to Exercise in Major Depressive Disorder Patients Treated With Duloxetine. J Clin Psychiatry. 2012 Sep;73(9):1234-42.

**A NEW LOOK AT THE EYE**

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**Objective:** Until recently it seemed inconceivable to most vision researchers and ophthalmologists alike that there could be an unrecognised class of photoreceptor within the eye. Yet research starting in the early 1990's led to the discovery that the eye contains a sub-set of photosensitive retinal ganglion cells (pRGCs). The role and clinical importance of these photoreceptors is slowly being appreciated and this presentation will draw upon both published and unpublished data to illustrate this point.

**Methods:** Much of our understanding of this new photoreceptor system has arisen from studies on mice carrying genetic lesions of the rod and cone photoreceptors, most notably the rodless/coneless (*rd/rd cl*) mouse. More recently human subjects have been examined, including individuals who also lack functional rod and cone photoreceptors.

**Results:** In both mice and humans a small number of pRGCs contribute to a broad range of light detection tasks including the regulation of the circadian and sleep systems, pupil constriction and alertness. They respond maximally in the "blue" part of the spectrum ($\lambda_{max}$~480nm) and utilize melanopsin (Opn4) as the photopigment. Surprisingly, the Opn4 signaling pathway shares more in common with invertebrate rather than vertebrate phototransduction. Recent and unpublished findings in mice have shown that: (i) cone photoreceptors also play a critical role in regulating how clock cells within the suprachiasmatic nuclei respond to light; (ii) that different isoforms of the melanopsin gene regulate different responses to light; (iii) the effect of light on the molecular clock is restricted by a negative feedback mechanism that limits light-induced gene expression. In humans we are assessing sleep and circadian timing in large numbers of subjects with clinically well-defined ocular diseases.

**Conclusions:** Our increasing appreciation of the cellular and molecular mechanisms whereby pRGCs, rods and cones regulate non-image forming responses to light is redefining our understanding of the eye. Furthermore, this fundamental knowledge from animal models, combined with detailed studies in human subjects, is providing the substrate for the establishment of evidence-based guidelines in clinical ophthalmology. Ultimately this research will have a major impact upon the quality of life of millions of individuals world-wide.

**THE CIRCADIAN CLOCK AND MOOD RELATED BEHAVIORS**

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**Objectives:** The circadian timing system provides a temporal structure across an organism to modulate and synchronize biological function. Individual cells contain the molecular set up to drive a circadian clock. Cellular clocks are directly or indirectly synchronized by a light sensitive pacemaker, which is located in the suprachiasmatic nuclei (SCN). How does light affect the circadian clock in the SCN and other brain clocks and how does this impinge on mood related behaviors?

**Methods:** Wild type and mice mutant in clock genes were used to study the behavioral response to a nocturnal light pulse and their behavior was assessed using the forced swim test paradigm. Transfection experiments were performed to study the involvement of clock genes in the regulation of genes important for mood regulation .

**Results:** We found that light pulses can influence mouse behavior in the forced swim test. We also found a mechanistic relationship between the circadian clock and mood related behaviors. Monoamine oxidase A (MAOA), a mitochondrial enzyme degrading catecholamines including dopamine, is transcriptionally regulated by components of the circadian clock in a cell type specific manner.

**Conclusions**: The results suggest that clock components can modulate mood-related behaviors in mice and that this regulation may be affected by light.

**Keywords:** signal transduction, neurotransmitters, light, dopamine

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**A SYSTEM FOR DELIVERING PRESCRIBED DOSES OF CIRCADIAN LIGHT**

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**Background**: The science of circadian phototransduction has progressed considerably in the last decade. The neural mechanisms responsible for conveying optical radiation on the retina to the circadian pacemaker are understood well enough to support a computational model encompassing the spectral and absolute sensitivities of the system. In addition, mathematical models of the circadian pacemaker have been developed to predict changes in circadian phase with light exposure.

**Methods**: A practical field system was developed and used to continuously measure personal circadian light exposures and activity over several weeks. The system is composed of a small, calibrated light and activity measuring device; the photosensors are calibrated in terms of optical radiation incident on the human retina as it suppresses nocturnal melatonin. The device is designed to be worn near the eye to continuously acquire and store light exposure and activity data. The photometric data are downloaded daily onto a computer, and used to estimate circadian phase. These data are processed using a van der Pol oscillator model of the circadian pacemaker. Based upon model predictions, a light prescription (when to add or remove circadian light) for maintaining or reaching a new circadian phase can be prescribed. For the study presented here, changes in circadian phase were predicted using the system and measured for 21 subjects from weekly assessments of their dim light melatonin onset (DLMO).

**Results:** By systematically exposing and limiting retinal light exposures it was possible to predict the directions of change in circadian phase. Predictions of the magnitudes of those changes were not accurate unless the entire daily light exposure data were incorporated into the circadian pacemaker model. Mean $\pm$ standard error of the mean (SEM) phase advance, as measured by DLMO was 132 $\pm$19 (n=10) and mean $\pm$ SEM phase delay was 59 $\pm$ 7.9 minutes (n = 11). The correlation between the modeled and the measured (delta DLMO) circadian phase angle changes was statistically significant ($R^2$ = 0.81, $p<0.0001$).

**Conclusions**: Models of circadian entrainment by light appear to be accurate to within 1.5 hours given current uncertainties in measurements necessary to estimate circadian phase. Within that uncertainty, it now seems possible to have a practical field device for maintaining and adjusting circadian phase. Clinical trials need to be undertaken to assess the efficacy and the acceptability of the entire system among individuals with circadian phase alignment problems.

**COMPARISON OF NON-VISUAL, LIGHT DEPENDENT FUNCTIONS IN HEALTHY SUBJECTS AND PATIENTS WITH HEREDITARY OPTIC NEUROPATHY**

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**Objective:** Non-visual, light dependent functions of the eye are signaled by intrinsically photosensitive retinal ganglion cells (ipRGC). These cells are the origin of the retinohypothalamic tract which enables photo- entrainment of circadian rhythms and the retinotectal tract which initiates the pupillary light reflex. We aimed to compare the functional integrity of these two monosynaptic pathways in patients with hereditary optic nerve disease and healthy controls by measuring pupil responses and melatonin suppression by light.

**Methods:** 8 patients with hereditary optic neuropathy (HON) and 8 healthy age-matched controls underwent ophthalmologic examination [acuity, octopus visual field, and optical coherence tomography (OCT) for peripapillary nerve fiber layer]. All study participants (HON: 36±15 years, CON 35±14 years; mean age ± SD) spent 10 hours in the laboratory under controlled lighting conditions (<6 lx, except during light exposure). The study started 10 hours after habitual wake time. At three occasions, post-stimulus pupil responses were recorded following a 1s and a 30s narrow-bandwidth red and blue light stimulus (both at 200cd/m2). Suppression of salivary melatonin was tested during two hours of polychromatic white light exposure (5000 lx at the corneal level), and salivary samples for hormonal analyses were obtained in hourly intervals throughout the study.

**Results:** HON patients had significantly reduced visual function and thinner nerve fiber layer, when compared to controls (HON: acuity=0.4; mean deviation on visual field=6.6, OCT=64µm; controls: acuity=1.0, mean deviation on visual field= -0.6, OCT=105µm). Pupillary re-dilatation following blue light stimulation was slower to return to baseline compared to red light stimulation, indicating a greater melanopsin contribution to the blue light pupil response ($p<0.05$). In both subject groups, prior exposure to a constant bright light decreased the delayed re-dilation after 1s of blue light when compared to pre-light exposure recordings ($p<0.05$). This may indicate potential desensitization of ipRGCs by prior bright light exposure. Salivary melatonin suppression was similar in both groups: HON patients=54% ± 18% and, controls=52% ± 16% ($p>0.8$; mean ± SD; in % of the pre-light exposure melatonin concentration). The smaller post-stimulus pupil size (due to prolonged pupillary re-dilation) following 1s of blue, but not red, light stimulation was significantly correlated with greater salivary melatonin suppression in response to bright light ($n=16$; $r=0.62$; $p<0.05$; red light stimulus $r=0.12$; $p>0.6$).

**Conclusion**: Despite striking visual decrements in patients with hereditary optic nerve disease, post-illuminatory pupil light responses and the ability to acutely suppress melatonin during bright light exposure were equally preserved in these patients, when compared to healthy controls. Our findings corroborate other studies in which either melatonin secretion or pupil responses were shown to be spared, indicating the intact function of ipRGC in this patient group. In addition, we have shown that there is an association in the magnitude of inter-individual ipRGC responses between two non-visual light dependent functions, the post-stimulus pupil size and salivary melatonin suppression.

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**SEASONAL SYMPTOMATOLOGY AND THE APPRAISAL OF VEGETATIVE SYMPTOMS**

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**Purpose**: Criteria for seasonal affective disorder (SAD) require the usual combination of vegetative, cognitive, and affective symptoms included in DSM criteria for major depressive episode. According to the dual vulnerability model of seasonal symptomatology (Young, et al, 1991, 2008), seasonal vegetative symptoms are due to seasonal environmental changes, but cognitive and affective symptoms are the result of the tendency to negatively appraise the vegetative changes that occur in the wintertime. These processes are proposed to occur across the full range of diagnosable and subsyndromal symptomatology with the severity of cognitive/affective symptoms depending on the interaction of the severity of vegetative symptoms and the tendency to make negative appraisals of them.

Rumination (thinking repetitively and passively about one's symptoms and their possible causes and consequences) is a well-documented vulnerability factor for unipolar depression (Nolen-Hoeksema, Wisco, & Lyubomirsky, 2008). Research has also found that rumination interacts with the severity of winter vegetative symptoms to predict the severity of winter cognitive/affective symptoms (Young, et al., 2008). Through repetition, rumination may make negative cognitions about vegetative symptoms more easily accessible, and should therefore be associated with negative appraisal of fatigue.

Based on these two lines of research we hypothesized (1) that negative illness attitudes about fatigue (a common seasonal vegetative symptom) moderate the relationship between the severity of winter vegetative symptoms and the severity of winter cognitive/affective symptoms and (2) that the illness attitudes about fatigue are associated with a more ruminative response style. Illness attitudes were assessed with a new implicit measure. Implicit measures are less prone to the effects of limited insight, bias, and social desirability than are more typical self-report measures.

**Methods**: This study developed a performance-based implicit method to assess the appraisal of fatigue as indicating illness using the Go/No Go Association Task (GNAT; Nosek & Banaji, 2001). Participants consisted of 32 undergraduate students who completed the GNAT, as well as measures of typical seasonal symptoms (Seasonality Assessment Form; Hutman, Young, Enggasser, Meesters, et al., 2011), and ruminative response style (Ruminative Response Scale; Nolen-Hoeksema & Morrow, 1991).

**Results**: Results of regression analyses supported both hypotheses. Illness attitudes toward fatigue moderated the relationship between vegetative symptoms and cognitive/affective symptoms (interaction $p = .032$). In addition, ruminative response style was positively associated with implicit illness attitudes towards fatigue ($r = .39$, $p = .01$).

**Conclusions**: The study provides support for the role of negative appraisals of vegetative symptoms in the development of cognitive/affective symptoms in seasonal psychopathology. Results are also consistent with the idea that rumination might contribute to the strength of these negative appraisals. These findings have implications for the etiology and the treatment of SAD and subsyndromal seasonal symptoms. Finally, the study demonstrated the potential utility of an implicit measure of attitudes in the study of seasonal depressive symptomatology.

**ACTIVITY FORECAST BY SEASON AND WEATHER? TWO YEARS ACTIGRAPHY IN A WOMAN WITH ALZHEIMER´S DISEASE**

Wahnschaffe, Amely, Stoll, Claudia, Rath, Andreas, Kunz, Dieter

**Objectives:** With age the linkage between internal and external clock tends to become weaker and the amplitudes of circadian rhythms flatten. In dementia the decline of circadian power seems to be even more severe and culminates in the clinical problem of nighttime agitation often referred to as the main reason for admission to nursing homes. A positive influence of light interventions on nighttime agitation as reflected in short term actigraphy rhythms was shown in several studies. The current single case report describes two years of actigraphy in an 82 year old woman with Alzheimer´s Disease (AD) focusing the impact of season and weather.

**Methods:** Starting in december 2009 the activity of an 82 year old woman with AD living in a nursing home is continuously monitored by a wrist actigraph. The current case report analyzes the activity data from two consecutive years using the Actiwatch and Sleep Analysis software version 7.3. For explorative analysis the Nonparametric Circadian Rhythm Analysis (NPCRA) as suggested by van Someren et al. (1999) was performed in terms of a rolling 7day analysis. Day by day plots of raw data and sequence charts of NPCRA data were visually inspected. Furthermore the NPCRA data was correlated (Pearson) with paralleled regional daily weather data from German Meterological Service (DWD: Deutscher Wetterdienst).

**Results:** Visual inspection of plotted raw data shows fluctuations in the day-night-relation of rest and activity. Relative amplitude of activity fluctuates in a seasonal manner recurring in both years. There is a high peak in spring and troughs in midsummer and winter. Degree of cloudiness, sunshine duration and air temperature correlate significantly with interdaily stability and intradaily variability of acitivity data.

**Conclusions:** The observation of seasonal fluctuation in long term activity data and their association with weather variables in this case should be tested in a bigger sample. An “activity forecast” in AD patients by seasonal and meteriological variables could provide compensation techniques for negative influences by artificial lighting and climitisation in the living environment.

**Funding Support:** German ministery of economy FKZ 0319057L

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**MODELLING PHOTORECEPTOR INPUT TO NON-IMAGE FORMING RESPONSES TO LIGHT**

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In addition to the rods and cones of the retina, the last decade has seen the identification of a novel retinal photoreceptor, the melanopsin-expressing photosensitive retinal ganglion cell (pRGC). These cells are critically involved in mediating many non-image forming (NIF) responses to light. However, it is unclear how advances in our understanding of this system can inform the design and regulation of environmental lighting. Whilst there would be great utility in being able to predict NIF activity based upon the intensity and spectral composition of light, this is not straightforward. Melanopsin pRGCs receive input from rods and cones in the outer retina, and as such, output from pRGCs reflects a complex integration of photoreceptor channels, each with distinct spectral sensitivities and temporal properties. The contribution of these photoreceptor channels is weighted differently in different types of ipRGCs and the NIF responses they mediate. Moreover, the contribution of these channels may depend on the intensity and duration of the light, prior lighting history, and the time of day. As a result, it is not possible to provide a single spectral response function that is predictive of all NIF responses to light. As such, it is recommended that researchers use empirically determined spectral power distributions (SPDs) to calculate the effective irradiance for each type of photoreceptor found in the mammalian retina. This enables the relative stimulation of the 5 photoreceptor channels to be reported, including rods, melanopsin, S-, M- and L-cones. Here we describe a freely-available tool for this purpose. This approach has several advantages. Firstly, it allows future studies to reproduce the effective light exposure for all 5 photoreceptor classes. Secondly, it allows the predicted activity of individual photoreceptor inputs to be compared across studies and related to conditions in the field. Finally, adoption of this approach will enable meta-analyses of the literature to determine the ability of the 5 channels alone or in combination to predict NIF responses under diverse conditions.

**EFFECTS OF LIGHT WAVELENGTHS ON EVENT-RELATED DESYNCHRONIZATION/SYNCHRONIZATION DURING A WORKING MEMORY TASK**

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**Purpose:** Light exposure affects not only human alertness but also cognitive function. A study using functional magnetic resonance imaging (fMRI) has shown that daytime exposure to bright white light enhances brain responses during a cognitive task. Moreover, fMRI studies during the daytime have shown that brain activity related to cognitive tasks is increased by exposure to short-wavelength light. This study, using magnetoencephalography (MEG), aimed to investigate the effects of light wavelengths on brain oscillatory responses correlate with cognitive processing.

**Methods:** This study consisted of two sessions, each conducted between 14:00 and 16:00. After a10-min period of darkness, a monochromatic light with short (460 nm) or medium (530 nm) wavelength was presented for 30 min. MEG responses were measured while performing an auditory working memory task (the Sternberg memory search paradigm) under exposures to these lights. Each trial of the paradigm consisted of four Japanese words as a memory set and a Japanese word as a probe, which were presented auditorily. Participants were instructed to indicate whether a probe item was or was not presented within the memory set. A total of 90 trials were conducted after the start of light exposure. Event-related desynchronization (ERD) and event-related synchronization (ERS) of MEG signals during a task were analyzed.

**Results:** ERS responses in the alpha frequency range during memory encoding were significantly larger under the short-wavelength light condition than under the medium-wavelength light condition. No significant effect of light wavelength was observed during memory retrieval.

**Conclusions:** It has been suggested that alpha ERS during memory encoding most probably reflect active memory maintenance and/or attentional processes. Therefore, the present results suggest that daytime exposure to short-wavelength light may enhance active memory maintenance and/or attention to auditory stimuli.
**Keywords:** Monochromatic light; Daytime exposure; Working memory; Event-related desynchronization/ synchronization

**SPECTRAL DEPENDENCY OF LIGHT-INDUCED RETINAL DEGENERATION**

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All action spectra of light damage analyzed thus far have their peak in the short wavelength range of the visible spectrum, i.e., the violet-blue region (van Norren and Gorgels, 2011). The action spectrum of light input to the circadian system via melanopsin containing retinal ganglion cells has its peaks around 420 nm, 460 nm or 480 nm, respectively,(e.g.Brainard, Sliney et al., 2008).

Thus we are faced with a conflict:
From the viewpoint of ophthalmology it is advisable to reduce violet-blue input to the eye. This is of special concerns for individuals with a genetic predisposition for retinal degeneration, such as certain rhodopsin mutations of retinitis pigmentosa or mutations in the complement system that significantly increase the risk of age-related macular degeneration. On the other hand, the suppression of melatonin production at night, and the accompanying circadian phase shifts, is intimately involved with sleep timing and its manipulation by light therapy. Blue light, including the blue component of white light, provides the most efficient input signal.
Lenses implanted after cataract surgery, often erroneously called “blue blockers,” moderately reduce violet-blue transmission, with benefit for the aging retina. Considering the slow development of cataract and yellow lens pigments, such lenses protect against overdose of short wavelength light exposure before cataract extraction.
The retina and pigment epithelium contain several chromophores that predispose for blue light damage, as has been demonstrated in numerous of experimental studies. Obviously, studies in humans are much harder to unequivocally demonstrate blue light damage, but several epidemiological studies and case reports clearly point in this direction.

We need to balance protection against the harmful effects of blue light and efficient suppression of melatonin in the context of circadian rhythm regulation. Studies of “blue-blocking” intraocular lenses on the entrainment of circadian rhythms and visual sensory function show no significant negative effects (Hayahsi et al., 2006; Henderson et al., 2010; Bronsted et al., 2013).

**IMPACT OF SLEEP RESTRICTION ON ENERGY BALANCE**

Marie-Pierre St-Onge, Ph.D, FAHA

**Purpose**: There is much epidemiological evidence pointing to a relationship between sleep duration and obesity. In fact, in both adults and children, short sleep duration is linked to a higher body mass index (BMI), prevalence of obesity, and risk of weight gain. However, epidemiological studies, whether cross-sectional or longitudinal, do not indicate causal relationships. Nonetheless, there is a model by which short sleep duration could be a causal factor in the development of obesity: short sleepers have lower physical activity level, greater fatigue, lower leptin and higher ghrelin than longer sleepers. Moreover, restricting sleep increases feelings of appetite and reduces satiety.

**Methods**: We conducted a clinical intervention study in which participants were studied under 2 separate conditions: habitual sleep (9 h/night in bed) or restricted sleep (4 h/night in bed). Each test period lasted 5 nights and 6 days. Participants were normal weight, normal sleepers, as determined over a 2-wk screening period with actigraphy. The study was conducted under controlled feeding conditions over the first 4 d, after which participants self-selected their food intake. Hormones were assessed from samples obtained at frequent intervals during day 4. Resting metabolic rate was assessed in the fasting conditions on day 5. Self-selected food intake was assessed on day 5 and neuronal responses to food stimuli were measured using functional magnetic resonance imaging in the fasted state on day 6. Total energy expenditure was assessed by doubly-labeled water over each 6-d test period.

**Results**: Participants consumed more energy during restricted sleep than habitual sleep (295.6 ± 123.6 kcal, P = 0.03), mostly due to increased consumption of fat (20.7 ± 7.5 g, P = 0.01), notably saturated fat (8.7 ± 4.0 g, P = 0.04). Although there was no significant sleep duration by sex interaction, the difference between restricted and habitual sleep tended to be more pronounced in women (328.6 ± 174.5 kcal, P = 0.07) compared to men (262.7 ± 176.7 kcal, P = 0.15). There was no effect of sleep duration on energy expenditure. There was no effect of sleep duration on glucose, insulin, and leptin profiles (all $P > 0.05$). Ghrelin and GLP-1 responses differed by sex. Short sleep increased fasting ($P = 0.054$) and 0800-1200 h ($P = 0.042$) total ghrelin in men but not women. The reverse was observed for GLP-1: afternoon levels (1230-1900 h) were lower ($P = 0.016$) after short sleep compared to habitual sleep in women but not men. Overall neuronal activity in response to food stimuli was greater after restricted sleep compared to habitual sleep, and a relative increase in brain activity in areas associated with reward, including the putamen, nucleus accumbens, thalamus, insula and prefrontal cortex in response to food stimuli was observed.

**Conclusions**: Our study provides evidence that restricting sleep is a plausible causal factor in the development of obesity, mostly via increases in food intake. However, unlike others, we did not find overwhelming evidence for a role of appetite-regulating hormones in this pathway. Rather, reward pathways may be more active in response to food stimuli, leading to increased susceptibility to overeat. This observation warrants further study.

**LIGHT AND DARK FOR PHASE SHIFTING CIRCADIAN RHYTHMS: HOW TO MAXIMIZE THE EFFECTIVENESS OF A LIGHT TREATMENT WITH BLUE-BLOCKING LENSES**

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Circadian rhythms, including the sleep/wake cycle, are governed by the master clock located in the suprachiasmatic nuclei (SCN) in the brain. In the absence of external stimuli, the SCN will free-run with a period slightly greater than 24 hours in humans. Light/dark patterns reaching the retina affect the phase relationship between the external environment and the master clock. The phase response curve (PRC) can be used to characterize the magnitude and direction of the phase adjustment that occur in the SCN resulting from retinal light exposures. Because light is the most potent synchronizer of circadian rhythms to the 24-hour solar day, it has been used as therapy to correct circadian sleep disorders, such as delayed sleep phase disorder (DSPD). Light treatment specifications commonly recommended by clinicians include the use of high levels (at least 2500 lux at the cornea) of a polychromatic light source (usually a 4100 K lamp). The spectral sensitivity of the circadian system, as measured by acute melatonin suppression and phase shifting of the dim light melatonin onset (DLMO), a circadian phase marker, peaks at short wavelengths. Therefore, light sources with high short-wavelength content will be more effective at phase shifting the master clock than light sources with low short-wavelength content at the same photopic light (lux). In theory then, clinicians could specify lower photopic levels of light from sources that contain more short wavelengths to obtain the same therapy benefit as what is currently being specified. This knowledge led to a series of studies investigating the effectiveness of low levels of “blue” light or “blue-enriched” light on treating circadian sleep disorders. Some published studies, however, failed to show the benefit of “blue” or “blue--enriched” light treatment. These negative results casted some doubt on the benefits of exposing people to “blue” or “blue-enriched” light sources. Data from our laboratory showed, however, that measuring and controlling the total light exposure over the waking day was needed for phase shifting DLMO in the desired direction. For example, we showed how important morning light exposures were to maintain entrainment in adolescents, by demonstrating that removal of morning short-wavelength light using blue-blocking lenses for 5 consecutive days delayed DLMO by about 30 minutes. In another study, morning blue light exposure in combination with evening blue-blocking lenses significantly advanced DLMO while a combination of morning blue- blocking lenses and evening blue light exposure significantly delayed DLMO. Therefore, blue-blocking lenses in combination with bright/blue light treatment is a more effective treatment for correcting circadian sleep disorders than light treatment alone. For clinical purposes, then, as suggested by Rea et al., the use of a personal light delivery system that provides prescription as to when to give (i.e., deliver circadian light) and when to remove (i.e., use blue-blocking lenses) light is recommended to maximize the effectiveness of the light treatment for phase shifting circadian rhythms.

**BLUE LIGHT THERAPY IN THE MORNING SUPPORTS A SLEEP ADVANCING PROTOCOL**

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**Objectives**: Light in the morning is able to induce phase advances of the endogenous clock. It is therefore often proposed as the most effective method to treat a delayed circadian rhythm and sleep phase. However, the optimal parameters which should be used to treat a delayed sleep phase are still unknown. It was recently found that properly timed high intensity white or blue morning-light pulses of ≤30 minutes are capable of inducing phase advances of the melatonin rhythm (Geerdink et al. 2011, Chang et al. 2012). In our present placebo controlled home- study we examined whether properly timed short blue light pulses in the morning could also be used as a therapy to treat a delayed sleep phase and by doing so improve daytime performance.

**Methods:** We included 42 participants (mean age 21.4y SEM +- 6.5, 23f/19m) who suffered from a 'social jetlag' (Roenneberg et al. 2006) on workdays (mean 2.33h SEM +- 0.7). Participants were randomly assigned to either a high intensity blue light (Philips GoLite BLU HF3330, peak transmission at 470 nm, intensity at the cornea +/-14000 m-lux, 300 lux), or an amber light with similar illuminance/lux (placebo) advancing therapy protocol (adapted GoLite HF3320, peak transmission at 590 nm, Philips Consumer Lifestyle B.V. Drachten, The Netherlands, intensity at the cornea +/-350 m-lux, 250 lux). The protocol consisted of 14 baseline days without sleep restrictions, 9 treatment days with either 30-min blue light pulses or 30-min amber light pulses in the morning along with a sleep advancing scheme and 7 post-treatment days without sleep restrictions. Melatonin samples were taken at days 1,7,14 (baseline), day 23 (effect treatment), day 30 (post-treatment). Sleep was monitored with the Actiwatch Spectrum (Philips Respironics Inc., Murrysville, USA) during the whole protocol. Performance was measured with a reaction time task on a handheld minicomputer (HP Ipaq114) on four time points each day.

**Results:** As expected, the phase advance in the melatonin rhythm from day 14 to day 23 was significantly ($t_{38}$=2.14, P<0.05) larger in the blue light therapy group (81min. SEM +- 12), compared to the amber light therapy group (47min. SEM +- 10). Wake-up time during the post-treatment days was slightly earlier compared to baseline in the blue light group (-16min. SEM +-9) compared to slightly later (+10min SEM +-10) in the amber light group ($t_{34}$=1.99; P=0.055). Sleep quality as measured by the number of sleep bouts was significantly worse in the amber light group during treatment ($t_{16}$=2.6, P<0.05) compared to baseline, while there were no differences in sleep quality for the blue light group. Performance was significantly worse around noon during treatment (noon $F_{1,32}$=6.24, P<0.05) and noon as well as evening during post-treatment (noon $F_{1,32}$=11.4, P<0.01; evening $F_{1,28}$=6.86, P<0.05) in the amber light group while not different compared to baseline in the blue light group.

**Conclusion:** Blue light was able to compensate both for the sleep quality reduction and the performance decrement that was observed in the amber light condition, probably as a consequence of the advancing sleep schedule. This study shows that blue light therapy in the morning supports a sleep advancing protocol by phase advancing circadian rhythms including sleep timing.

**References**: Geerdink et al. 2011; Abstracts EBRS; p141 Chang et al. 2012; J Physiol; 590.13; p3103–p3112
Roenneberg et al. 2006; Chr.Biol.Int.; 23; 497-509

**PHASE-DELAYED EATING PATTERNS IN NIGHT EATING SYNDROME PATIENTS AND IN HEALTHY SLEEP-DEPRIVED ADULTS**

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**Purpose**: Night eating syndrome (NES) is characterized by evening hyperphagia and frequent awakenings accompanied by food intake. Patients with NES display a delayed circadian pattern of food intake but retain a normal sleep-wake cycle. In addition, patients with NES are at greater risk for obesity and weight gain. These characteristics initiated a controlled laboratory study in which the phase and amplitude of behavioral (caloric intake) and neuroendocrine circadian rhythms in patients with NES and control subjects was evaluated (Study 1). Relatedly, experimental studies indicate that meal timing may be an important contributor to weight gain and indicate that sleep loss is associated with increased caloric intake, possibly explaining the relationship between sleep duration and weight gain found in epidemiological studies. These findings initiated a study examining the effect of sleep restriction on weight gain, daily caloric intake and meal timing in healthy adults (Study 2).

**Methods**: Study 1: Fifteen women with NES (mean age ± SD, 40.8 ± 8.7 y) and 14 control subjects (38.6 ± 9.5 y) were studied in the laboratory, with ad libitum food access, for 3 days. Daily food intake was measured. Blood was collected for 25 h (every 2 h from 0800 h to 2000 h, and then hourly from 2100 h to 0900 h) and assayed for glucose and 7 hormones [insulin, ghrelin, leptin, melatonin, cortisol, thyroid stimulating hormone (TSH) and prolactin]. Study 2: Subjects were 225 healthy adults aged 22-50 y (n=198 sleep-restricted subjects and n=27 control subjects). They participated in a controlled lab experiment, with ad lib food access, assessing body weight at admittance and discharge in all subjects (N=225) and caloric intake and meal timing across days following two baseline nights, five sleep restriction nights (4 h time in bed [TIB]/night, 0400 h-0800 h) and two recovery nights or across days following control condition nights (all nights 10 h TIB/night, 2200 h-0800 h) in a subset of subjects (n=37).

**Results**: Study 1: Control subjects displayed normal phases and amplitudes for all circadian rhythms. In contrast, NES patients showed a phase delay in the timing of meals, and delayed circadian rhythms for total caloric, fat and carbohydrate intake. In addition, phase delays of 1.0 h to 2.8 h were found in two food-regulatory rhythms — leptin and insulin — and in the circadian melatonin rhythm (with a trend for a delay in the circadian cortisol rhythm). In contrast, circulating levels of ghrelin, the primary hormone that stimulates food intake, were phase advanced by 5.2 h. The glucose rhythm showed an inverted circadian pattern. Patients with NES also showed dampened amplitudes in the circadian rhythms of food intake, cortisol, ghrelin and insulin, but showed heightened TSH amplitude. Study 2: Sleep-restricted subjects gained more weight than control subjects. Among sleep-restricted subjects, African Americans gained more weight than Caucasians and males gained more weight than females. Sleep-restricted subjects consumed excessive calories during days with a delayed bedtime (0400h) compared with control subjects who consumed adequate calories during corresponding days. In sleep-restricted subjects, increased daily caloric intake was due to more meals and the consumption of an average of 553 additional calories between 2200 h-0359 h. The percentage of calories derived from fat was greater during late-night hours (2200 h-0359 h) compared to daytime (0800 h-1459 h) and evening hours (1500 h-2159 h).

**Conclusions**: NES patients demonstrate significant changes in the timing and amplitude of various behavioral (caloric intake) and physiological circadian markers involved in appetite and neuroendocrine regulation, including phase delays in meal timing, and delayed circadian rhythms for total caloric, fat and carbohydrate intake. Such delayed intake may relate to higher body weights in these patients. In the largest, most diverse healthy sample studied to date under controlled laboratory conditions, sleep restriction promoted weight gain and delayed caloric intake. Thus, NES patients and chronically sleep-restricted adults with late bedtimes may be more susceptible to weight gain due to greater daily caloric intake and the consumption of calories during late-night hours.

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**A PILOT RANDOMIZED CONTROLLED STUDY OF LIGHT THERAPY FOR SLEEP-WAKE DISTURBANCES IN RENAL TRANSPLANT RECIPIENTS**

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**Objectives:** Sleep-wake disturbances among renal transplant (RTx) recipients are a common condition requiring careful judgment to treat the disturbance while minimizing the risk to the transplanted kidney. We hypothesized that morning light therapy could be an effective treatment to improve sleep-wake disturbances, performance, as well as depressive symptomatology.

**Methods:** This was a non-blinded, randomized controlled pilot trial to study the efficacy of light therapy. Thirty home dwelling RTx recipients aged 56.9±13.5y, previously screened for sleep-wake disturbances, were randomly assigned either to immediate or delayed (intervention at end of study) light therapy. Morning light (10'000 lux) was scheduled according to chronotype daily for 30 min during 3 weeks.

**Measures:** The rest-activity cycle was monitored throughout the 3 periods lasting each 3 weeks (Baseline, intervention, follow-up) with a wrist actimeter (DaQtix) and analyzed for circadian rhythm and sleep parameters. Depressive symptomatology was assessed (Depression, Anxiety and Stress scale (DASS)) once every three weeks (scoring 0-21; >4 depressive symptomatology). We used a random-intercept regression model to test group*time interaction. Effect sizes reflect the interaction estimate on standardized outcome variables.

**Results:** Morning bright light therapy induced a small phase advance for bedtime (mean±SD: from 22:58±106 min to 22:53±122 min; ES: -0.12; 95%CI -0.28 - 0.04) and get up time (from 7:26±101 min to 7:01±107 min; ES: -0.23; 95%CI -0.42 -
-0.03). Sleep latency decreased slightly during the therapy (from 45.3±0.8 min to 38.4±0.2 min; ES: -0.18; 95%CI -0.40 - 0.04) but lengthened again in the follow-up period. Depressive symptomatology showed improvement at all measurement times (DASS-D score from 5.9±3.4 to 5.7±3.8 to 4.1±3.1; ES: -0.24 - -0.52).

**Conclusion:** The findings of this pilot study indicate that light therapy in RTx recipients with sleep-wake disturbances can improve sleep latency and depressive symptoms. No adverse events and no side effects were noted.

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**Keywords:** renal transplantation, bright light
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**MODELING DYNAMIC ASPECTS OF HUMAN NONVISUAL RESPONSES TO LIGHT**

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**Purpose**: Since 2002, when the first reports on the discovery of a novel type of mammalian ocular photoreceptor were published, a new field of study at the intersection of photobiology and architecture started to emerge. These novel non-rod, non-cone photoreceptors in the retinal ganglion cell layer are the primary mediators of nonvisual responses to light in humans, including synchronizing circadian rhythms and directly alerting the brain. This study aims to understand how these nonvisual responses evolve over time with respect to changes in the intensity, spectral composition and exposure duration of light stimuli. The ultimate goal is to incorporate these effects of light into building design.

**Methods**: Recent studies in the field of photobiology provide us with information about the human nonvisual responses to light. Researchers have identified intensity, spectrum, duration, history and timing of light exposure as important parameters that influence the responsiveness of the nonvisual system. Experimental research quickly reaches its limitations, because it is infeasible to carry out a complete experiment with respect to all parameter combinations. Mathematical models are the method of choice to enable such analysis. A block-structured model is proposed that combines linear filters, a nonlinear term and a feedback mechanism. The linear filters reflect the temporal processing between the light stimulus and the output response. The nonlinear term is the sigmoid-shaped intensity-response curve that receives input from the feedback mechanism to regulate the system's response with changes in prior light history and timing of circadian phase. Moreover, the spectral sensitivity of the nonvisual system is modeled as a time-varying function.

**Results**: Based on this model, which takes the intensity, spectrum and duration of light exposure into account, it is possible to compare the nonvisual efficiency of different spectra as a function of duration. Results demonstrate that duration is an important parameter in addition to spectral sensitivity when comparing nonvisual effects of different light sources at low light intensities.

**Conclusions**: This model provides a framework that can inform designers about the effects of lighting on human health and wellbeing in real-life settings. The ultimate goal of this work is not to reveal the underlying functionality of the retina, but rather to predict human nonvisual responses to light using mathematical models and test the predictions experimentally. Modeling dynamic aspects of nonvisual responses to light is important to understand the dynamic relationship between light and human nonvisual responses that occurs in real-world settings.

**INFLUENCE OF ARTIFICIAL DUSK ON SLEEP**

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**Objectives:** Dawn/dusk simulation is used as a therapeutic intervention since 1989 [1]. It can influence circadian rhythms, sleep, cortisol secretion, and alertness. While physiological importance of the artificial dawn signal for humans appears to be proven and it is often used in a single, little is known about the effects of the dusk signal on sleep of healthy humans. Aim of the study was to elucidate an influence of artificial dusk on sleep, mainly sleep latency.

**Methods:** The participants were healthy subjects with normal sleep habits, sleep latency up to 20 minutes, 5- or 6-workdays per week, a necessity to wake up in the morning, and sleeping single in bedroom. They were informed that the aim of the study is to investigate an influence of artificial dusk and dawn on 24-h biorhythms; the focus on sleep was hidden. For each participant, the study began on Sunday, lasted for 2 months, and comprised two arms, without a break. Each arm lasted for 4 weeks and consisted of 7 days baseline, 13 days intervention, and 8 days follow-up. The subjects had to adhere to their habitual bedtime. Testing intervention was dusk/dawn simulation; the comparator was the same device but with a rectangular light pulse replacing the dusk simulation (non-dusk). Dusk/dawn simulator (DDS; Philips Consumer Lifestyle, the Netherlands) comprised a LED light source and alarm clock. The subjects had to plan to turn on the bed-sided DDS 10-20 min prior to the intended sleep time. Dusk lasted for 30 minutes but was additionally preceded by a 10-min pre-pulse of constant light (intensity 140 lux at a distance of 45 cm). Non-dusk lasted for 17 min (similar light dose of ~2540 lux·min). Morning dawn lasted for 30 minutes and followed by an alarm sound and was equal in both arms. Times of artificial dusk and dawn were automatically registered in the DDS memory for compliance control (hidden from the test subjects). Subjects filled in a sleep diary before and after sleep. A wrist monitor of activity and illumination Actiwatch 2 (Phillips Respironics, the Netherlands) was worn throughout the 8-weeks study; additionally, subject had to press a monitor time button at sleep intention time (eyes closure) and sleep offset. Saliva for melatonin ELISA (Bühlmann biochemical kits) was sampled half-hourly prior to bedtime on days 7 or 8, 13 or 14, and 20. In total, 13 variables were analyzed: sleep intention time, offset time and duration, number of minutes with movements during the first and the last 40 minutes of sleep episode and in-between, total sleep efficiency (all – using actimetry), subjective sleep latency, sleepiness before and after sleep (by Karolinska sleepiness scale), and dim light melatonin onset (DLMO, using the hockey-stick method [2])

**Results:** Of the 47 participants, 26 successfully completed the study, all but 2, women, age ranged from 18 to 53 y. Only one variable showed a difference between dusk and non-dusk session: number of minutes with movements during the first 40 min of sleep episode was lower at dusk presentation ($p=0.049$, effect size = 0.53, Wilcoxon test; mean median values ±SD 5.4 ±3.4 min vs. 6.9 ±5.5 min). The difference was obvious during the first week, partly, as ancillary analysis showed, due to a later/shorter sleep at the initial dusk presentation. The effect did not depend on the sequence (1st vs. 2nd session) or photoperiod (session at shorter vs. longer days), nor there was a relationship with the DLMO circadian phase (which did not shift). When commenting on dusk signal, 11 subjects wrote that dusk helped them to fall asleep, 12 did not mention falling asleep or were neutral, and 3 wrote that dusk hindered the falling asleep ($p=0.057$, one-sample sign test). If add to the sample 7 withdrawn subjects explored both dusk and non-dusk, the distribution was as follows: 15–13–5 ($p=0.041$).

**Conclusions:** The results, based on both objective and subjective estimations, indicate that artificial dusk helps people to fall asleep more peacefully. Whether the effect is persistent, needs a further confirmation.

**Keywords:** Artificial Dusk, Sleep, Melatonin Rhythm

**References:** 1. Terman M, Terman JS (2005). Light therapy. In: Kryger MH, Roth T, Dement WC, eds. Principles and Practice of Sleep Medicine, 4th edn. Philadelphia: Elsevier, pp. 1424-1442.2. Danilenko KV, Antyufeev VS, Verevkin EG, Cajochen C, Wirz-Justice A. Hockey-stick method to estimate evening dim light melatonin onset (DLMO). Chronobiol Int, submitted.

**RAPID TREATMENT OF SUICIDAL SYMPTOMS IN DRUG-RESISTANT BIPOLAR DEPRESSION WITH LITHIUM AND CHRONOTHERAPEUTICS (LIGHT AND WAKE)**

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**Purpose.** One-third of patients with bipolar disorder (BD) attempt suicide. Depression in BD is associated with drug-resistance. The efficacy of antidepressants on suicidality has been questioned. Total sleep deprivation (TSD) and light therapy (LT) prompt a rapid and stable antidepressant response in BD. The aim of the present study is to assess the efficacy of chronotherapeutics on depressive suicidality in BD.

**Methods.** We studied 143 consecutively admitted inpatients with a major depressive episode in course of BD, among whom 23% had a positive history of attempted suicide, and 83% had a positive history of drug resistance. During one week, patients were administered three consecutive TSD cycles (composed by a period of 36 hours awake followed by recovery sleep) combined with bright LT in the morning, which was then prolonged for a second week. Patients were either taking lithium at admission and continued it, or started it. Severity of depression was rated on the Hamilton depression rating scale (HDRS) and Beck depression inventory (BDI).

**Results.** Two patients switched polarity. Among the 141 who completed the treatment, 70% achieved a HDRS score 50% reduction in one week. The amelioration involved an immediate decrease of suicide scores soon after the first TSD. A positive history of suicide associated with worse early life stress and with worse suicide scores at baseline, but did not influence response. Patients with current suicidal thinking or planning responded equally well. Remarkably, non-responders achieved however a benefit, with significantly decreased final scores also including suicidality ratings. Self-ratings showed the same pattern of change. Previous history of drug resistance did not hamper response. During the following month 78/99 responders continued to stay well and were discharged from the hospital on lithium alone.

**Conclusions.** The combination of TSD, LT, and lithium is able to rapidly decrease depressive suicidality and prompt antidepressant response in drug-resistant major depression in course of BD.

**A NEW LOOK AT THE EYE**

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**Objective:** Until recently it seemed inconceivable to most vision researchers and ophthalmologists alike that there could be an unrecognised class of photoreceptor within the eye. Yet research starting in the early 1990's led to the discovery that the eye contains a sub-set of photosensitive retinal ganglion cells (pRGCs). The role and clinical importance of these photoreceptors is slowly being appreciated and this presentation will draw upon both published and unpublished data to illustrate this point.

**Methods:** Much of our understanding of this new photoreceptor system has arisen from studies on mice carrying genetic lesions of the rod and cone photoreceptors, most notably the rodless/coneless (*rd/rd cl*) mouse. More recently human subjects have been examined, including individuals who also lack functional rod and cone photoreceptors.

**Results:** In both mice and humans a small number of pRGCs contribute to a broad range of light detection tasks including the regulation of the circadian and sleep systems, pupil constriction and alertness. They respond maximally in the "blue" part of the spectrum ($\lambda_{max}$~480nm) and utilize melanopsin (Opn4) as the photopigment. Surprisingly, the Opn4 signaling pathway shares more in common with invertebrate rather than vertebrate phototransduction. Recent and unpublished findings in mice have shown that: (i) cone photoreceptors also play a critical role in regulating how clock cells within the suprachiasmatic nuclei respond to light; (ii) that different isoforms of the melanopsin gene regulate different responses to light; (iii) the effect of light on the molecular clock is restricted by a negative feedback mechanism that limits light-induced gene expression. In humans we are assessing sleep and circadian timing in large numbers of subjects with clinically well-defined ocular diseases.

**Conclusions:** Our increasing appreciation of the cellular and molecular mechanisms whereby pRGCs, rods and cones regulate non-image forming responses to light is redefining our understanding of the eye. Furthermore, this fundamental knowledge from animal models, combined with detailed studies in human subjects, is providing the substrate for the establishment of evidence-based guidelines in clinical ophthalmology. Ultimately this research will have a major impact upon the quality of life of millions of individuals world-wide.

**PRO'S AND CON'S OF BLUE FILTERING LENSES**

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**Objective:** To present the advantages and disadvantages of blue filtering (yellow) intraocular lenses compared to UV blocking (clear lenses).

**Methods:** The impact of using a blue filtering intraocular lens on visual acuity, colour vision contrast sensitivity, and scotopic vision has been investigated by several groups. A review of this literature, and presentation of our preliminary data regarding the impact of implantation of blue filtering (yellow) or UV (clear) intraocular lenses after cataract removal on sleep wake cycle is also presented.

**Results:** No significant persistent impact has been described when looking at colour vision, contrast sensitivity, and scotopic vision, and the sleep wake cycle when using a blue filtering lens. There is some evidence for improved vision in conditions of glare when using a blue filtering lens, and experimental evidence to show reduced risk of short wavelength light damage.

**Conclusions:** Implanting blue filtering lenses does not appear to have any major disadvantage, and by filtering out short wavelength light may confer improved vision under certain conditions, and provide protection against damage at the level of the retina and retinal pigment epithelium.

**LONG-TERM EFFECTS OF REDUCING BLUE LIGHT INPUT ON MELATONIN AND SLEEP**

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**Objectives:** Light, especially in the short wavelength range, plays a key role in non-image-forming responses such as sleep timing, alertness and performance. How environmental changes in light impact our daily lives is less understood. We set out to investigate the effects of changes in the spectral composition of light (increased/reduced short wavelengths) on melatonin and sleep rhythms. Two studies were conducted for this purpose. Both studies were designed to investigate the effects of changes in spectral composition in a natural scenario (i.e., no restrictions were imposed upon the behavior of the participants) and our observations were not limited to acute effects but rather focused on the relatively long-term effects of changes in light spectral composition (days to weeks).

**Methods:** For the first study we took advantage of cataract surgery. Measurements took place before (reduced short wavelength input due to reduced lens transmission) and after cataract surgery. Measurements consisted of 3 weeks actigraphy and sleep diaries, and one visit to the laboratory for assessments of dim light melatonin profiles and the transmittance of the ocular lens. A similar but inverted scenario, simulated this time, was performed in young healthy participants. A *reduction* in short wavelengths was achieved by means of soft orange contact lenses that were worn 24 h/day during 2 consecutive weeks. Further, we not only measured actigraphy-sleep diaries (2 weeks) and melatonin profiles, but also the suppression of melatonin in response to a 2 h white light pulse (24:00 h to 2:00 h, 600 lux, Osram tubes).

**Results:** In study 1 we observed, on average, a significant delay of the sleep-wake and melatonin rhythms in the elderly after surgery. Not all individuals responded similarly. The magnitude of the shift correlated positively with chronotype. A different picture was revealed in study 2 in young subjects. No differences between conditions were observed in the rhythms of sleep and melatonin after two weeks. Data confirmed that melatonin suppression was reduced in response to an acute light stimulus with reduced short wavelengths compared to a full spectrum light pulse. However, these changes in melatonin suppression disappeared after two weeks of continued reduced short wavelength light input. The system in these young subjects adapted, restoring the melatonin suppression response to the levels of the control condition in spite of the fact that the suppression of short wavelengths was still present.

**Conclusions:** While we observed that healthy young subjects adapted during a 2-week exposure of reduced short wavelength input, the elderly did show a systematic response to the inverse situation of increased short wavelengths: after replacement of the cataractous lens with a clear one they showed a delay in the rhythms of sleep and melatonin. This suggests that age might play a role in the capacity of the circadian system to adapt to environmental changes. Moreover, the delay that we observed shows that small changes in light exposure can have a relatively large impact. We speculate that these effects are especially important in the evening hours of the day in the absence of natural day light.

**EXTRAOCULAR BRIGHT LIGHT EXPOSURE IN THE EVENING VIA THE EAR CANALS DOES NOT AFFECT MELATONIN, SLEEPINESS OR PSYCHOMOTOR VIGILANCE**

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**Background**
Evening and nocturnal exposure to bright light via the eyes acutely suppresses melatonin and sleepiness in humans. Recently, a new device has appeared on the market, which administers bright light via the ear canals. The aim of the study was to investigate whether extraocular light via the ear canals impacts on evening melatonin levels, sleepiness and psychomotor vigilance performance.

**Methods**
Sixteen healthy young men and women (8/8, 24.2±3.5 y) were asked to keep a regular sleep-wake cycle (±1h) during the 2-week study (compliance checked by actimetry). The volunteers reported to the laboratory on three evenings, 2h15min before usual bedtime. They were exposed to 3 different light conditions, each lasting for 12min: extraocular light (Valkee light therapy device NPT®1100), ocular light as an active control condition (Daylight® therapy device, Uplift Technologies Inc.), and a control condition (Valkee light therapy device with a completely blocked light ray, sham light). The timing of exposure was from 72 to 60min before usual bedtime. During the entire protocol, saliva samples were collected in 15min intervals for melatonin assays along with subjective sleepiness ratings. In addition, the volunteers performed a 10-min visual psychomotor vigilance task (PVT) prior to and after each light condition.

**Results**
Endogenous melatonin levels in all volunteers began to increase during the 2 hours before usual bedtime in all 3 evenings. However, this increase was significantly attenuated after the 12min ocular bright light exposure while no significant changes in melatonin levels were observed after the 12min of extraocular bright light via the ear canals or after the control ear light condition (condition x time $p<0.03$). Subjective sleepiness decreased immediately after ocular light exposure for 15min, but not after extraocular light or the control condition ($p<0.005$). No significant difference was found in mean reaction times and the number of lapses for the PVT between the three light conditions.

**Conclusion**
We do not have evidence that 12min extraocular bright light via the ear canal acutely affects evening melatonin secretion and sleepiness, when compared to an active control (ocular light exposure) and a sham light (i.e. no light) condition. Thus, it is likely that the internal clock, which regulates the circadian secretion of melatonin and modulates sleepiness, is not affected by extraocular bright light applied via the ear canals. Based on our results, the Valkee light therapy device may not be appropriate for the treatment of circadian rhythm sleep disorders.

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**IMPORTANCE OF CHRONOTYPE PREFERENCES IN EATING BEHAVIOR. LESSONS LEARNED FROM THE SLEEP EXTENSION STUDY, A RANDOMIZED, CONTROLLED STUDY OF SLEEP EXTENSION IN OBESE, CHRONICALLY SLEEP DEPRIVED INDIVIDUALS**

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*Sleep Extension Study Group*

**Background:** Short sleep duration and decreased sleep quality are emerging risk factors for obesity and its associated morbidities. Chronotype, an attribute that reflects individual preferences in the timing of sleep and other behaviors, is a continuum from morningness to eveningness. The importance of chronotype in relation to obesity is mostly unknown. Evening types tend to have unhealthy eating habits and suffer from psychological problems more frequently than Morning types, thus we hypothesized that eveningness may affect health parameters in a cohort of obese individuals reporting sleeping less than 6.5 hours per night.

**Methodology and Principal Findings:** Baseline data from obese (BMI: 38.5 ± 6.4kg/$m^2$) and short sleeping (5.8 ± 0.8h/night by actigraphy) participants (*n*=119) of the *Sleep Extension Study* were analyzed (www.ClinicalTrials.gov, identifier NCT00261898). Assessments included the Horne and Ostberg Morningness-Eveningness questionnaire, a three-day dietary intake diary, a 14-day sleep diary, 14 days of actigraphy, and measurements of sleep apnea. Twenty-four hour urinary free cortisol, 24h urinary norepinephrine and epinephrine levels, morning plasma ACTH and serum cortisol, fasting glucose and insulin, and lipid parameters were determined.

Eveningness was associated with eating later in the day on both working and non-working days. Progression towards eveningness was associated with an increase in BMI, resting heart rate, food portion size, and a decrease in the number of eating occasions and HDL-cholesterol. Evening types had overtly higher 24h urinary epinephrine and morning plasma ACTH levels, and higher morning resting heart rate than Morning types. In addition, Evening types more often had sleep apnea, independent of BMI or neck circumference.

**Conclusions:** Eveningness was associated with eating later and a tendency towards fewer and larger meals and lower HDL-cholesterol levels. In addition, evening types had more sleep apnea and higher stress hormones. Thus, eveningness in obese, chronically sleep-deprived individuals compounds the cardiovascular risk associated with obesity.

**THE RELATIONSHIP BETWEEN OVERWEIGHT STATUS AND SLEEP PROBLEMS IN PRE-SCHOOLERS**

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**Background**: Several lines of evidence point to an important relationship between disrupted sleep and obesity. However, understanding the directionality and mechanistic basis for this overlap has proven challenging in adult populations. The current study addresses this challenge by studying longitudinal weight gain and sleep problems in a cohort of developing children.

**Methods:** The current sample consisted of 225 pre-school children taking part in a longitudinal study of early brain development (Maternal Adversity, Vulnerability and Neurodevelopment-the MAVAN project). We examined whether overweight status at 36, 48 and 60 months was associated with sleep difficulties assessed at 48 and/or 60 months of age using the Children's Sleep Habits Questionnaire (CSHQ) administered to mothers.

**Results:** Both longitudinal and concurrent links between weight measures and sleep were found. The most notable longitudinal finding was a link between overweight status at age 36 months and greater sleep-onset delay at age 60 months (60-month sleep onset delay scores = 1.74 +/- .76 vs. 1.43 +/- .69 in age 36-month overweight vs. normal weight groups respectively, p=.039). The strongest concurrent associations were found at age 48 months, whereby overweight children had more sleep-disordered breathing and a longer sleep duration than did their normal weight peers (sleep-disordered breathing 3.46 +/- 1.02 vs. 3.22 +/- .60, p=.033; sleep duration 4.28 +/- 1.26 vs. 3.81 +/- 1.23; p=.017; overweight vs. normal weight respectively). There was no association between sleep problems at age 48 months and overweight status at age 60 months.

**Conclusions:** Several notable links between overweight status and sleep difficulties were identified in these pre-school children. While the current data suggest that weight problems may precede sleep problems more often than not, more work is needed to confirm these initial findings and to establish their neurodevelopmental basis.

**SEASONALITY IN SUICIDE RESEARCH: WHAT HAVE WE LEARNED IN 100 YEARS?**

**Nestor D. KAPUSTA**

Starting with Emile Durkheim in 1897, suicide research unveiled a peak of suicides in early summer and a through during winter months. In the meanwhile, the seasonality of suicide incidence is well replicated and the patterns are complementary on both hemispheres. Even more, seasonality of suicides seems to decline with proximity to the aequator. Besides social theories, such as the protective effects of religion and cohesion, especially around Christmas, increasing evidence supports a biological link through the association with meterological data such as temperature or fluctuant insolation. Thus, during recent years, findings on seasonality of suicide converge with neuroimaging and neurobiological findings on the effects of sunshine on serotonin transmission and affective disorders, which pose one of the most recognized risk factors for completed suicide. A review of the most current hypotheses and results of suicidology and seasonality is given in this presentation.

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**A REVIEW OF CIRCADIAN AND SEASONAL CHANGES IN BRAIN MONOAMINE FUNCTION**

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Several behaviours known to be regulated in part by brain monoamine neurotransmission display clear circadian and seasonal rhythms and many of these behaviours are altered in psychiatric disorders. These include eating, sleeping, motor activity, mood and energy regulation, and many others. Expression and function of monoaminergic molecules, such as dopamine, serotonin, norepinephrine, monoamine oxidase, tryptophan hydroxylase or monoamine transporters and receptors show circadian and seasonal changes in expression and function. There is increasing knowledge on the interplay between cellular clock components and many monoaminergic key structures in animals. Despite the fact that a variety of psychiatric disorders show chronobiological alterations and a clear seasonal distribution in frequency and severity, evidence on the molecular background of circadian and seasonal changes in human monoamine transmission is still limited. This is mainly due to the difficulties in assessing neurochemical changes in the living brain. However, peripheral indicators of central nervous monoamine function and peripheral models like monoaminergic enzymes and transporter molecules in blood platelets have provided evidence for circadian and seasonal rhythms in human central nervous monoamine function. Moreover, a growing body of neuro-imaging studies using single photon emission computer tomography (SPECT) or positron emission tomography (PET) suggests a seasonal rhythm and sunlight-induced changes in expression and function of several serotonergic and dopaminergic imaging targets. These include therapeutically important molecules such as the dopamine $D_{2/3}$ receptor or the serotonin transporter. Although far from giving a consistent overall picture, these findings help our understanding of rhythmical changes in monoamine function and their relevance for physiology and pathological states. Moreover, they show that research needs to integrate chronobiological knowledge when investigating monoaminergic alterations in psychiatric and other disorders.