Society for Light Treatment and Biological Rhythms

Program and Abstracts: Volume 23

23rd Annual Meeting, July 10th – 13rd, 2011
Montréal, Canada

Marc Hébert, SLTBR President
Program Committee: Marc Hébert, Marie Dumont, Konstantin Danilenko, Raymond Lam
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SLTBR 23RD ANNUAL MEETING PROGRAM

Sunday, July 10th, 2011

15:30-17:30 **SLTBR Board Meeting**

19:00-21:00 **Welcome Reception at the Centre Mont-Royal**
(2200 rue Mansfield, Montréal, H3A 3R8, Canada)

Monday, July 11th, 2011

8:00-9:00 Registration

9:00 - 9:15 **President's Welcome**
Marc Hébert, Laval University, Canada

9:15 – 11:15 **Symposium I: Aspects of non-visual photoreception**
Chair: Melanie Rueger, Harvard Medical School, USA
Claude Gronfier, University of Lyon, France

9:15–9:45 **Effects of spectral modulation on acute endocrine, molecular and behavioural responses to nocturnal light**
Shadab Rahman, Harvard Medical School, USA

9:45–10:15 **Phase response curve to a single 6.5-h light pulse of short-wavelength light**
Melanie Rueger, Harvard Medical School, USA

10:15–10:45 **Retinal circuits underlying impairment of learning and mood by aberrant light exposure**
Samer Hattar, John Hopkins University, USA

10:45–11:15 **What short duration light pulses can tell us about human circadian photoreception: results from modeling and experiments**
Melissa St. Hilaire, Harvard Medical School, USA

11:15-12:15 Coffee break

11:15 - 12:25 **Poster Session I**
Presenter with an even number will be asked to remain in front of their posters. Posters will be up on Monday and Tuesday.

12:25 - 14:00 Lunch (on your own)

14:00 - 15:20 **Oral Presentations I. Light and Rhythms: Clinical Aspects**
Chair: Namni Goel, University of Pennsylvania, USA

14:00–14:20 **The University of Vermont study of cognitive behavioral therapy Vs. light therapy for preventing SAD recurrence: design and methods**
Kelly J. Rohan, University of Vermont, USA

14:20–14:40 **Daylight exposure delay reduces hospitalization length in manic episodes: a multicentric experience**
Dario Delmonte, Vita-Salute San Raffaele University, Italia

14:40–15:00 **Light-associated perinatal imprinting of circadian clocks: consolidation and "white-box" epidemiological studies of latitude and instability hypotheses of mood disorders and cancer**
Thomas C. Erren, University of Cologne, Germany

15:00–15:20 **Diurnal variations in the acute response to exercise in the chronic obstructive pulmonary disease**
Emilie Chan-Thim, Concordia University, Canada

15:20-16:30 Coffee break

15:20 - 16:30 **Poster Session II**
Presenter with an odd number will be asked to remain in front of their posters. Posters will be up on Monday and Tuesday.

Tuesday, July 12th, 2011

8:00-9:00 Registration

9:00 - 11:00 **Symposium II: Influences of circadian clocks on cognitive functions and psychological well-being**
Chair: Julie Carrier, University of Montreal, Canada

9:00–9:30 **Bright light treatment for anxiety**
Shawn Youngstedt, University of South Carolina, USA

9:30–10:00 **Circadian rhythms in premenstrual syndrome: impacts for mood disorders**
Diane Boivin, McGill University, Canada

10:00–10:30 **Circadian and sleep-wake dependent influences on sleepiness and cognitive performance in young and older adults**

Jeanne Duffy, Harvard Medical School, USA

10:30–11:00 **Light sensitivity measured by pupillometry and brain imaging in young and older subjects**
Véronique Daneault, University of Montreal, Canada

11:00-11:20 Coffee break

11:20 – 12:20 **Invited Speaker: Modeling and remote sensing of light pollution in heterogeneous environments**
Martin Aubé : University of Sherbrooke, Canada

12:20-14:00 Lunch (on your own)

14:00 - 15:20 Oral Presentations II. Light and Rhythms: Regulation
Chair: Dr. Raymond Lam, University of British Columbia, Canada

14:00–14:20 **Preprohypocretin/prepro-orexin (HCRT) gene: role in mediating individual differences in daytime sleep propensity and nighttime homeostasis during sleep loss**
Namni Goel, University of Pennsylvania, USA

14:20–14:40 **Association between melanopsin gene polymorphism and pupillary light response in a Japanese young population**
Shigekazu Higuchi, Kyushu University, Japan

14:40–15:00 **Melanopsin gene variations interact with season to predict sleep timing and chronotype**
Kathryn A. Roecklein, University of Pittsburgh, USA

15:00–15:20 **A comparison of subjective and polysomnographic sleep onset latencies across circadian and menstrual phases**
Ari Shechter, McGill University, Canada

15:20 - 16:30 SLTBR Annual Business Meeting

19:00 Annual Banquet

Wednesday, July 13th, 2011

8:00-9:00 Registration

9:00 - 10:30 **Symposium III: Light at the Work Place**

Chair: Marijke Gordjin, University Medical Center Groningen, The Netherland
Ybe Meesters, University Medical Center Groningen, The Netherland

9:00–9:30 **Blue-enriched light and daylight - a heavy competition**
Celine Vetter, Ludwig-Maximilians-University, Germany

9:30–10:00 **Dynamic light in a fast forward rotating shift work environment**
Marijke Gordjin, University Medical Center Groningen, The Netherland

10:00–10:30 **First results of an innovative light device used at night by saw mills workers and patrol officers**
Marc Hébert, Laval University, Canada

10:30-11:00 Coffee break

11:00 - 12:40 **Oral Presentations III. Natural and Artificial Light Exposure at Work**

Chair: Marie Dumont, University of Montreal, Canada

11:00–11:20 **The relationship between chronotype, sleep, chronic fatigue and natural light exposure in young student workers**
Jeanne-Sophie Martin, Laval University, Canada

11:20–11:40 **Daily light exposure and feelings of alertness and vitality: intermediate results of a longitudinal study**
Karin Smolders, Eindhoven University of Technology, The Netherland

11:40–12:00 **Tests on solid state lighting for the international space station**
George C. Brainard, Thomas Jefferson University, USA

12:00–12:20 **Blue enriched room light in the morning enhances daytime alertness and night time sleep**
Claudia Stoll, Charité – University Medicine Berlin, Germany

12:20–12:40 **Exposure to daylight as well as to blue and red lights at night interact to affect nocturnal performance, subjective sleepiness and biomarker production**
Mariana G. Figueiro, Rensselaer Polytechnic Institute, USA

12:40 - 12:45 **President's Closing Remarks**
Marc Hébert, Laval University, Canada

SLTBR 23RD ANNUAL MEETING

POSTER PRESENTATIONS

1. **EXAMINING THE ACUTE SIDE EFFECTS OF BRIGHT LIGHT THERAPY IN A NON-DEPRESSED POPULATION**
   Y. Botanov, S.S. Ilardi, C.E. Brown, M.T. Beauchamp

2. **CIRCADIAN VARIATION OF HEART RATE DURING REM AND NON-REM SLEEP**
   P. Boudreau, G. Dumont, D.B. Boivin

3. **SEASONALITY IN MOOD DISORDERS: CLINICAL AND GENETIC ASPECTS**
   Brambilla C., Locatelli C., Gavinelli C., Cigala Fulgosi M., Lorenzi C., Pirovano A., Barbini B., Colombo C.

4. **MELATONIN AND SLEEP: ROLE OF MT1 RECEPTOR**
   S. Comai, R. Ochoa-Sanchez, G. Gobbi

5. **EFFECT OF BRIGHT LIGHT ON MESOCORTICOLIMBIC AND THALAMOCINGULATE ACTIVITY IN POSTPARTUM DEPRESSION: an FMRI PILOT STUDY**
   S. K. Crowley, R. D. Newman-Norlund, S. D. Youngstedt

6. **SELF REPORTED EVENINGNESS CHRONOTYPE AND EARLY SLEEP/WAKE CYCLE DURING BASIC COMBAT TRAINING**
   S. K. Crowley, S.D. Youngstedt, E. Burroughs, L. Wilkinson, S. Muraca, L. Wigfall, T. Louis-Nance, E. M. Williams, S. Glover

7. **PUPIL LIGHT REFLEX IN RESPONSE TO MONOCHROMATIC LIGHT STIMULI IN YOUNGER AND OLDER SUBJECTS**
   V. Daneault, G. Vandewalle, P. Teikari, L.S. Mure, M. Hébert, C. Gronfier, H.M. Cooper, M. Dumont, J. Carrier

8. **CIRCADIAN VARIATION OF QUANTITATIVE SLEEP EEG ACROSS THE MENSTRUAL CYCLE**
   J.L. de Zeeuw, A. Shechter, D.B. Boivin

9. **MONOAMINERGIC FIRING ACTIVITY IN THE VENTRAL TEGMENTAL AREA AND THE DORSAL RAPHE ACROSS THE LIGHT-DARK CYCLE**
   S. Domínguez-López, R. Howell, M.G. López-Canul, M. Leyton, G. Gobbi

10. **THE EFFECTS OF LOW INTENSITY MONOCHROMATIC BLUE LIGHT TREATMENT COMPARED TO STANDARD LIGHT TREATMENT IN SUB-SYNDROMAL SAD**
    W.B. Duijzer, Y. Meesters

11. **RAMELTEON FOR INSOMNIA RELATED TO ATTENTION-DEFICIT/HYPERACTIVITY DISORDER (ADHD)**
    R.E. Fargason, K.L. Gamble, R.C. Besing, K.T. Avis

12. POSSIBLE IMPLICATION OF MELANOPSIN BISTABILITY ON THE INCREASE OF HUMAN HEART RATE BY BICHROMATIC BLUE AND RED LIGHT
C.Fontaine, M.Hébert

13. CIRCADIAN RHYTHM OF MELANOPSIN-EXPRESSING RETINAL GANGLION CELLS IN THE HUMAN RETINA
Y. Fukuda, S. Tsujimura, S. Higuchi, A. Yasukouchi, T. Morita

14. ADHD CLINICAL SUBTYPE DIFFERENTIALLY PREDICTS SLEEP AND CIRCADIAN DISRUPTION IN ADULT ADHD PATIENTS WITH INSOMNIA
K.L. Gamble, R.C. Besing, K.T. Avis, R.S. May, R.E. Fargason

15. EFFECTS OF FLUORESCENT LIGHT CORRELATED COLOR TEMPERATURE ON MELATONIN REGULATION IN HEALTHY HUMANS
J. Hanifin, J. Kemp, M. Downes, B. Warfield, M. Ayers, K. Cecil, E. Gerner, H. Noguchi, M. Shimizu, G. Brainard

16. ANALYSIS OF THE HUMAN EYE'S ILLUMINATION CONDITIONS IN INTERNAL ENVIRONMENT
P. Hanuliak, E. Kucserová, M. Janák

17. EFFECTS OF RED VISOR CAP IN PREVENTING LIGHT-INDUCED MELATONIN SUPRESSION DURING SIMULATED NIGHT WORK
S Higuchi, T Fukuda, T Kozaki, M. Takahashi, N Miura

18. THE COMPREHNSIVE SEASONAL ASSESSMENT FORM (CSAF) FOR ASSESSING SEVERITY OF SEASONAL SYMPTOMATOLOGY
P.J. Hutman, M.A. Young, J.L. Enggasser, Y. Meesters, E. Roubal, R. Gabelman, P. Ogu

19. CIRCADIAN LOCOMOTOR ACTIVITY OF GSK3B KNOCKOUT MICE
J. Lavoie, J.M. Beaulieu, M. Hébert

20. SAD-SPECIFIC EMOTIONAL RESPONSES TO LIGHT AND SEASONAL STIMULI: SURFACE ELECTROMYOGRAPHY, SKIN CONDUCTANCE, AND MOOD
J.N. Mahon1, K.J. Rohan1, K. Tierney Lindsey2, K.A. Roecklein

21. THE EFFECTS OF LOW INTENSITY MONOCHROMATIC BLUE LIGHT TREATMENT COMPARED TO STANDARD LIGHT TREATMENT IN SAD
Y. Meesters, W.B. Duijzer

22. DO CANCER RELATED SYMPTOMS FOLLOW A SEASONAL PATTERN?
J. Mercier, V. Audet Croteau, A. Dorval, A. Avril, J. Savard

23. EFFECTS OF EXTENDED SLEEP OPPORTUNITIES AND ACUTE SLEEP DEPRIVATION ON PSYCHOMOTOR PERFORMANCE IN SHORT AND LONG SLEEPERS: EVIDENCE FOR INDIVIDUAL DIFFERENCES IN TOLERANCE TO SLEEP PRESSURE
M. A. Mograss, S. H. Wielinga, S. K. Baddam, D. Aeschbach

24. TIME-OF-DAY AND LIGHT MODIFY MARKERS OF HOMEOSTATIC SLEEP PRESSURE IN MICE
V. Mongrain, Y. Emmenegger, P. Franken

25. LIGHT EXPOSURE AND REST-ACTIVITY RHYTHMS IN OLDER PEOPLE: EFFECT OF LIGHT SUPPLEMENTATION IN COMMUNAL CARE HOME ROOMS
P.L. Morgan, S. Hopkins, B. Middleton, L.J.M. Schlangen, D.J. Skene

26. EFFECTS OF PRIOR DAYTIME LIGHT EXPOSURE ON COGNITIVE PERFORMANCE, SUBJECTIVE SLEEPINESS AND HORMONAL SECRETION IN THE EVENING
M. Münch, F. Linhart, A. Borisuit, S.M. Jaeggi, J.-L. Scartezzini

27. COMPLEXITY AND REGULARITY OF CIRCADIAN MOTORIC ACTIVITY IN INDIVIDUALS WITH DEMENTIA AND AGGRESSION
L.Nowak, A.Whall, V.Yeragani, et.al.

28. THE ROLE OF THE DEUBIQUITINASE USP2 IN CIRCADIAN RHYTHMS AND BEHAVIOUR
K. Stojkovic1, A. Rachalski1, D. Duguay1, S.S. Wing2, N. Cermakian

29. THE KINETICS OF THE BISTABLE MELANOPSIN SYSTEM – IMPLICATIONS FOR ARCHITECTURAL LIGHTING
P Teikari , L.S. Mure and H.M. Cooper

30. THE INFLUENCE OF FEVER AND INFLAMMATION ON PERIPHERAL CLOCK GENE EXPRESSION
S.Westfall; A.Aguilar-Valles; V.Mongrain; G.N.Luheshi; N.Cermakian

31. SEX DIFFERENCE IN THE CIRCADIAN VARIATION OF DISTAL-CORE TEMPERATURE GRADIENT
W.H. Yeh, A. Shechter, P. Boudreau, D.B. Boivin

32. CIRCADIAN VARIATION IN THE RESPONSE OF T CELL TO ANTIGEN
E. Fortier, J. Rooney, H. Dardente, MP. Hardy, SW. Liu, N. Labrecque, N. Cermakian

SOCIETY FOR LIGHT TREATMENT AND BIOLOGICAL RHYTHMS ABSTRACTS 2011

MODELING AND REMOTE SENSING OF LIGHT POLLUTION IN HETEROGENEOUS ENVIRONMENTS: AN ATTEMPT TO UNDERSTAND LIGHT POLLUTION

Aubé, M. [1, 2]

[1]CÉGEP de Sherbrooke, Québec, Canada, [2]Université de Sherbrooke, Québec, Canada

Light pollution is constantly growing all over the world as long as inhabited zones are growing with population. Real dark night may only be perceived in few places, mainly located on top of remote mountains like Mauna Kea (Hawai), La Palma (Canary islands) and some peaks in north Chile.

In recent years, some attempts have been made to recover in part an access to darkness. Among them, the case of the Mont-Mégantic region (Québec) may be cited as example. In 2007, this region became the first international dark sky reserve. During this project, most of the badly designed light fixtures have been replaced by more efficient ones. This conversion resulted in the recovery of sky quality as it was in the 70's. The net result is a reduction of about 40% of the light pollution and a reduction of the energy demand of about 1.8 GWh per year (150 k$ per year, 5 years payback period). This project have also had the side effect of stimulating the touristic industry in that region, since it is more attractive for amateur astronomers and people interested to environmental integrity.

In this presentation, we will define in detail the concept of light pollution and its related issues. Then we will discuss of the way we have chosen to get a better understanding of that complex and nonlinear phenomenon. More specifically we will present our spectrometer dedicated to remote sensing of light pollution along with some sample data for different sites around the world. Then we will present our heterogeneous light pollution numerical model, designed to simulate light pollution in its geographical complexity. Some conclusions will then be drawn about the behavior of light pollution. We will more specifically discuss of the most common lighting devices and their possible interference with human health and their masking effect on the starry night.

Finally, we will summarize the results of two major field campaign and associated modeling experiments conducted on two very different sites: 1- the dark sky reserve of Mont-Megantic before and after the conversion, and 2- the case of the Northern European observatories in La Palma and Tenerife, Canary islands, Spain.

CIRCADIAN RHYTHMS IN PREMENSTRUAL SYNDROME: IMPACTS FOR MOOD DISORDERS

D.B. Boivin, A. Shechter

Centre for Study and Treatment of Circadian Rhythms, Douglas Mental Health University Institute, McGill University, Montreal, Quebec, Canada

Objectives: Altered circadian and/or homeostatic processes can modulate the expression of mood and sleep in major depressive, bipolar, seasonal affective, and premenstrual dysphoric (PMDD) disorders. An interaction between these processes and the menstrual cycle could contribute to the increased female vulnerability to mood and sleep disturbances. Our aim was to investigate sleep and circadian rhythms disturbances in women suffering from PMDD in order to further understand their role in mood disorders.

Methods: 8 healthy ovulating women (aged 18-30) underwent a 72-h ultradian sleep-wake cycle (USW) procedure (36 cycles of 60-min wake/60-min nap episodes) during their mid-follicular (MF) and mid-luteal (ML) phases. Measures included PSG sleep recordings, core body temperature (CBT), distal temperature (DT), a calculated distal-core temperature gradient (DCG), and salivary melatonin. Seven PMDD women and 5 controls (aged 18-35) underwent PSG sleep recordings every third night for a full menstrual cycle. Six PMDD women and 5 healthy controls underwent 24-hour blood sampling assessments during the follicular and luteal phases, under highly controlled environmental conditions in time isolation.

Results: Throughout the USW, TST, SE, SOL, REM onset latency (ROL), stage 2, SWS, REM and non-REM sleep showed a significant circadian variation (for all, $P < 0.001$). A trend for a menstrual phase difference was observed for ROL ($P = 0.08$) and REM sleep ($P = 0.12$). A series of Tukey pairwise comparisons on REM sleep data spanning times throughout the habitual nocturnal sleep episode, which were based on an a priori prediction of reduced nocturnal REM sleep during ML, confirmed significantly decreased REM sleep at ML compared to MF at circadian phase 0° and 30° ($P < 0.05$). The salivary melatonin rhythm was similar at both menstrual phases. A significantly increased CBT ($P = 0.03$) and decreased CBT amplitude occurred in ML ($P = 0.01$), although DT and DCGwere preserved. In the study of PSG sleep across the menstrual cycle, both PMDD and controls showed a significant menstrual phase variation for stage 2 sleep ($P = 0.04$), which was significantly increased during the mid-luteal phase compared to the early follicular phase. SWS was significantly increased in PMDD compared to controls across the menstrual cycle ($P = 0.004$). Plasma melatonin was significantly reduced in PMDD patients compared to controls at both menstrual phases, with a further reduction of area under the curve observed in PMDD during the luteal phase compared to the follicular phase ($P = 0.05$).

Conclusion: Our studies demonstrated a significant reduction of melatonin secretion and an increase in nocturnal SWS duration across the menstrual cycle in PMDD patients compared to controls. These results suggest disturbances in both circadian and homeostatic processes in PMDD women.

Keywords: Sleep, Menstrual Cycle, Circadian Rhythms, melatonin, PMDD

Funding Support: Study funded by the Canadian Institutes of Health Research (CIHR)

EXAMINING THE ACUTE SIDE EFFECTS OF BRIGHT LIGHT THERAPY IN A NON-DEPRESSED POPULATION

Y. Botanov[1], S.S. Ilardi[1], C.E. Brown[1], M.T. Beauchamp[1],

[1]Department of Psychology, University of Kansas, Lawrence, Kansas

Objectives: The integral role of light in physiological and psychological well-being is illustrated by the application of phototherapy, or bright light therapy (BLT), in treating mood disorders such as seasonal affective disorder and non-seasonal depression. More recently, BLT has been applied in treating jet lag due to transmeridian travel, complications from shift work, and disorders of sleeping and waking. Despite the numerous potential applications of BLT, deleterious side effects have not been fully explored in a non-clinical population. An extensive literature search did not reveal any controlled studies examining the tolerability of bright light, in a healthy population, at the currently accepted dosage and illumination. Thus, we examined the acute side effects of bright white light therapy in a young, non-depressed sample as compared to a dim red light.

Methods: One hundred and fifteen undergraduate students (56% female, mean age = 19.6) were randomly assigned to either 30 minutes of 10,000 lux white light or 500 lux red light via a light box. Participants with a history of depressive disorders, bipolar disorder, or retinal light sensitivity were excluded. Since previous findings demonstrate that most side effects appear after initial exposure and dissipate with repeated exposures (Kogan & Guilford, 1998), only one session of BLT was employed. Participants completed a self-report measure of the most commonly reported side effects of BLT (reviewed in Terman & Terman, 2005) - headache, eye strain, blurred vision, nausea, and restlessness – immediately before and after exposure.

Results: Repeated measures analysis of variance revealed no significant group (white vs. red)-by-time (pre vs. post) interactions for headache ($F = 1.406$, $p = .238$), blurred vision ($F = 3.126$, $p = .08$), eye strain ($F = 0.332$, $p = .566$), nausea ($F = 0.351$, $p = .555$), or restlessness ($F = 0.054$, $p = .816$). A main effect of time was found only for eye strain ($F = 24.785$, $p < .001$) and no main effects for condition emerged.

Conclusions: These results suggest that the prevalence of acute adverse side effects in the extant clinical literature may not apply to non-clinical populations. After one exposure of BLT, no symptoms of headache, blurred vision, nausea, or restlessness emerged in the present investigation. Only eye strain showed a significant increase from pre-exposure to post-exposure, but it was equivalent across the dim red light and the bright white light groups. This finding is consistent with previous research showing that eye strain is a potential concern of light therapy, but we demonstrate that it is not a consequence of the luminosity or color of light. Bright white light therapy may be more tolerable with fewer side effects, when employed with non-depressed, as opposed to clinical, populations.

Keywords: Phototherapy, Illumination, Side Effects (Treatment), Safety

CIRCADIAN VARIATION OF HEART RATE DURING REM AND NON-REM SLEEP

P. Boudreau [1,2], G. Dumont [3], D.B. Boivin [1,2]

[1]Centre for Study and Treatment of Circadian Rhythms, Douglas Mental Health University Institute, Department of Psychiatry, McGill University, Montreal, Quebec, Canada; [2]Integrated Program in Neuroscience, McGill University, Montreal, Quebec, Canada; [3]Department of Electrical and Computer Engineering, University of British Colombia, Vancouver, BC, Canada.

Objectives: Using forced desynchrony and constant routine protocols, heart rate (HR) has been shown to be influenced by the circadian system during wakefulness. Whereas it is often favorable to exclude sleep as a masking variable while studying circadian rhythms, the circadian variation of HR during sleep is an important process to understand. Therefore, we utilized a 72-hour ultradian sleep-wake cycle (USW) procedure to determine if HR maintains a measurable circadian rhythm during sleep.

Methods: Nine healthy participants (7 men, 2 women; mean age ± SD: 26.5 ± 4.8 years) entered a time isolation suite to undergo a 72-hour USW consisting of 36 cycles of alternating 60-minute wake and 60-minute nap episodes. The USW procedure required that participants maintain a semi-recumbent position with low activity levels in dim light (<10 lux) during wake episodes or in total darkness during nap opportunities. Participants received iso-caloric snacks every 2 hours. HR (200 Hz) and core body temperature (CBT; 4x/min) were recorded. Sleep was polysomnographically recorded, and scored according to standard criteria. HR data were binned according to circadian phase (30° bins relative to CBT minimum) and sleep stage.

Results: RR intervals were progressively longer with deeper non-REM sleep stages. A significant circadian rhythm was observed for RR intervals during wake after lights out (WALO), stage 1, stage 2, slow wave sleep (SWS) and REM sleep ($p \leq 0.035$). Circadian amplitude of RR intervals was significantly increased during WALO compared to other sleep stages. The circadian rhythm of RR intervals peaked in the early afternoon during REM whereas it peaked at night during the other sleep stages. Circadian phase of RR interval during stage 1, stage 2 and SWS were significantly advanced (~ 2.5 hours) compared to WALO ($p \leq 0.013$).

Conclusion: The circadian variation of HR is preserved and measurable during sleep. Surprisingly, circadian phase was almost inverted when RR intervals were measured during REM sleep compared to non-REM sleep. This observation suggests an interaction between the circadian and sleep systems.

Keywords: Heart rate**,** Circadian Rhythms, Sleep, REM sleep

Funding Support: Research was supported by the Canadian Institutes of Health Research (CIHR). P. Boudreau and D.B. Boivin were supported by Institut de recherche Robert-Sauvé en santé et en sécurité du travail (IRSST) and Fond de la Recherche en Santé du Québec (FRSQ), respectively.

TESTS ON SOLID STATE LIGHTING FOR THE INTERNATIONAL SPACE STATION

G. Brainard[1], M. Downes[1], J. Kemp[1], M. Ayers[1], K. West[1], B. Warfield[1], M. Jablonski[1], K. Cecil[1], C. Bowen[2], J. Maida[2], J. Hanifin[1]

[1]Department of Neurology, Thomas Jefferson University, Philadelphia, PA;
[2]Habitability and Human Factors Branch, Johnson Space Center, Houston, TX

Objectives: Onboard lighting for the International Space Station (ISS) is currently provided by General Luminaire Assemblies (GLAs) that house fluorescent lamps for illuminating the astronauts' working and living environments. Arrays of solid-state light emitting diodes (LEDs) are attractive candidates for replacing the GLAs on the ISS. The advantages of LEDs over conventional fluorescent light sources include lower up-mass, power consumption and heat generation, as well as fewer toxic materials, greater resistance to damage and longer lamp life. A prototype Solid-State Lighting Assembly (SSLA) was developed at Kennedy Space Center and successfully installed on the ISS. The broad goal of this work is to meet NASA's requirements for development, testing and installation of SSLAs on the ISS that will support astronaut vision and as well as provide optimum circadian, neuroendocrine, neurobehavioral and sleep regulation. The study reported here assesses the efficacy of light emitted by white LEDs with a correlated color temperature of 6500 K for melatonin suppression. This white LED is one of the four LED types being proposed for use in new ISS lighting system.

Methods: Eight healthy females (N=4) and males with normal color vision participated in this study (mean age 25.3 ± 1.2 years). The 6500 K white LED light exposure system consisted of a 119 x 120 cm flat panel which subjects viewed face-on at a distance of 30 cm to achieve a full visual field exposure. The volunteers' pupils were freely reactive during the polychromatic light exposures between 2:00 and 3:30 AM. Each volunteer was exposed to nine irradiances of this light (1 to 600 $\mu W/cm^2$) and a dark control exposure with at least one week between each experiment. Blood samples were quantified for melatonin by radioimmunoassay.

Results: A preliminary one-way ANOVA was used to compare both plasma melatonin percent change scores and control-adjusted percent change scores. The data show a significant intensity-related suppression of melatonin ($p<0.001$). A preliminary plot of the mean and SEM melatonin control-adjusted percent change data against a four parameter sigmoidal fluence-response curve has a high coefficient of correlation ($R^2=0.84$).

Conclusions: The data from this study quantify the neuroendocrine potency of light emitted by 6500 K white LEDs. This white LED is one of the four LED types being proposed for use in new ISS lighting system. Risk factors for the health and safety of astronauts include disturbed circadian rhythms and altered sleep-wake patterns (1,2). The data presented here, along with other emergent data (3-5) will help determine if SSLA lighting can be used both to support astronaut vision and serve as an in-flight countermeasure for circadian disruption, sleep disturbances and performance deficits on the ISS.

Keywords: Melatonin, LEDs, Lighting

Funding Support: National Space Biomedical Research Institute through NASA NCC 9-58, NASA #NNX09AM68G.

References:

1) D. Longnecker and R. Molins, Bioastronautics Roadmap (http://criticalpath.jsc.nasa.gov/), 2005.
2) National Aeronautics and Space Administration. *Human Research Program Integrated Research Plan*. HRP- 47065, January, 2009.
3) West, K. et al., Blue light from light-emitting diodes (LEDs) elicits a dose-dependent suppression of melatonin in humans. *Journal of Applied Physiology* 110: 619-626, 2011.
4) Hanifin J et al., Effects of blue solid-state lighting on melatonin suppression and alertness. *Society for Research on Biological Rhythms, Program and Abstracts, May 2010.* Society for Research on Biological Rhythms, Destin, Florida, May 22-26, 2010.
5) G. Brainard et al., Solid-state lighting for the International Space Station: Tests of visual performance and melatonin regulation. 18th IAA Humans in Space Symposium, April, 2011.

SEASONALITY IN MOOD DISORDERS: CLINICAL AND GENETIC ASPECT

Brambilla C., Locatelli C., Gavinelli C., Cigala Fulgosi M., Lorenzi C., Pirovano A., Barbini B., Colombo C.

Department of Clinical Neurosciences, University Vita-Salute San Raffaele, Milan (Italy)

Objectives: The periodical pattern of recurrence is an intrinsic feature of Mood Disorders: the recovery from the first episode of illness is followed by a subsequent recurrence in about 90% of affected patients during their lifetime (Keller et al., Arch. Gen. Psych. 37: 299-308, 1982): this pattern of ciclicity is due to biological, chronobiological, environmental, genetic and drug-related features of the illness.
The recurrence pattern follows interindividual rules since each patient presents his own specific pattern with pharmacological treatments, which shorten the subsequent cycle of illness, and maintenance treatments, which are expected to decrease the episode rates (Serretti et al., Chronobiol Int. 27: 706-721, 2010). The purpose of this study was to evaluate the seasonal profile of each patient, to correlate the clinical characteristics with seasonality and to assess how CLOCK gene polymorphisms correlate with clinical and chronobiological variables.

Method: We recruited a sample of 224 euthymic outpatients affected by Mood Disorders: 101 with Major Depression and 123 with Bipolar Disorder. A subgroup of 100 patients underwent a genetic analysis of the CLOCK gene T3111C polymorphism (75 bipolars and 22 unipolars). All patients underwent a clinical interview for the collection of clinical, sociodemographic information, and for the collection of data regarding the seasons of onset and the seasons of past episodes. Patients completed the following questionnaires: the Seasonal Pattern Assessment Questionnaire (SPAQ) to assess seasonality, Morningness-Eveningness Questionnaire (MEQ) to evaluate differences among chronotypes, and the Medical Outcomes Study (MOS) Sleep Scale to assess their quality of sleep. The subgroup of 100 subjects underwent a venous blood test to analyse the T3111C polymorphism of the CLOCK gene. We used t-test analysis for groups to investigate the relationships between socio-demographic and clinical variables and the differences between the scales of assessment and t-test analysis, ANOVA and Chi Square to assess the correlations with the CLOCK polymorphism.

Results: We found a pattern of recurrence of episodes of illness always in the same season in more than 61% of cases. The higher incidence of Depressive Episodes is in spring among unipolar patients (49%) and in the fall (31%) and spring (33%) for bipolar subjects, which in turn have a high reccurrence of manic episodes in summer (50%). Seasonality also appears to be linked to the family history of psychiatric disorders in patients with Bipolar Disorder ($p=0.026$). For the sleep variable, unipolar patients are the diagnostic group with the most disturbed sleep and the most affected patients by higher seasonality fluctuatins. In bipolar patients undergoing a stabilizing treatment with Lithium Salts, we found decreased sleep disturbances and a lower GSS score.
Genetic studies of the T3111C CLOCK polymorphism showed an association between the genotype C carriers and the morningness chronotype (MEQ score> 51) in bipolar patients. C carrier bipolars without a maintenance therapy (which probably represent a naturalistic example of the cyclinc illness) have a MEQ score significantly higher ($p=0.016$) and more sleep problems in line with our clinical results. The CC genotype in patients with Major Depression have a trend of greater illness severity , of higher recurrency, but they have lower seasonal fluctuations.

Conclusions: Seasonality, chronotype, genetic asset and sleep are interdependent characteristic that lie at the basis of chronobiology. A thorough understanding of these components and their genetic susceptibility would allow a better diagnostic –therapeutic approach of Mood Disorders. An in-depth knowledge of these elements could help psychiatrists in treating patients based on their genetic/symtomatological asset and to be able to use more specific non-pharmacological therapies such as chronobiological therapies aimed at resettig the chronobiological clock with Total Sleep Deprivation and Light Therapy .

Key Words: Seasonality, Mood Disorders, Chronobiology, Sleep, Clock Gene

DIURNAL VARIATIONS IN THE ACUTE RESPONSE TO EXERCISE IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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Objective: Pulmonary function has been shown to vary depending on the time of day in healthy populations and in respiratory conditions like in asthma (Medarov et al., Int. J. Clin. Exp. Med. 1: 267-73, 2008). Yet, research remains limited in other chronic conditions such as with chronic obstructive pulmonary disease (COPD), which is the fourth leading cause of death worldwide (O'Donnell et al., Can. Respir. J. 15: 1A-8A, 2008). Diurnal variations in a COPD patient population may have important clinical repercussions and need to be further investigated. Therefore, this study aims to determine the impact of time of day under resting and exercising conditions in individuals with COPD.

Methods: Baseline evaluations were conducted at Hôpital du Sacré-Coeur de Montréal including a pulmonary function test, questionnaires on chronotype, sleep and eating habits, measurements of physical activity (Actigraph), and a familiarization session was given on the testing procedure. The study used a counterbalanced research design where each participant served as his or her own control. Participants completed a pulmonary function test and a symptom-limited incremental cycling exercise test in a randomized order at three different times of day (08:00, 12:00, and 16:00). Each test is separated by at least 36 hours. Testing times were selected to cover the range of hours when exercise tests are conducted in clinical practice. Peak exercise capacity is defined as the highest work rate maintained for a minimum of 30 seconds. So as to limit the effect of medications, participants who were prescribed a long-acting anticholinergic were switched to a short acting anticholinergic two weeks prior to the evaluations and all COPD medications were withdrawn 6-24 hours preceding each exercise test. The cardiorespiratory parameters were measured at rest and during exercise on a breath-by-breath basis with a metabolic cart. Symptoms were measured at rest and during exercise with a modified 10-point Borg scale. A general linear model was conducted to evaluate the effect of testing times on outcome measures. Post hoc analyses were conducted using multiple paired sample t-test with Bonferroni correction.

Results: To date, nine participants (5 men, 4 women) aged 71 ±8 years with moderate airflow obstruction (FEV_1: 59 ± 8% predicted values) completed all evaluations. No significant time effect was found for peak exercise capacity ($p= 0.24$). Yet, outcomes for resting lung function approached statistical significance ($p = 0.052$) where inspiratory capacity was lowest in the morning. Furthermore, the respiratory exchange ratio, the ratio between carbon dioxide consumption and oxygen consumption, was found to be greatest in the morning and lowest in the late afternoon ($p = 0.01$).

Conclusion: Preliminary results suggest that time of day may affect pulmonary function, with no variation in peak exercise capacity. This may be important for the clinical follow-up of these patients.

Keywords: COPD, Diurnal Variations, Pulmonary Function, Exercise Capacity.

MELATONIN AND SLEEP: ROLE OF MT1 RECEPTOR.

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Objectives: Insomnia is a common public health problem, with a prevalence ranging from 11% to 16%. The neuro-hormone melatonin (MLT) is well known for its involvement in circadian rhythm regulation and in the control of the sleep wake cycle. Although many years of research since its discovery, the role of MLT and its receptors, namely MT1 and MT2, in sleep regulation is still debated and not completely elucidated. By using knockout (KO) mice for the MT1 receptor we investigated the role of this MLT receptor subtype in the control of the sleep-wake cycle.

Methods: EEG and EMG recordings were performed across 24 hrs in MT1KO mice and their wild-type (WT) littermates. The animals were kept under 12:12 light/dark cycle with access to water and food ad libitum in a temperature controlled room (21-22 °C). For EEG monitoring, three stainless-steel epidural electrodes were positioned through 1.5 mm burr holes: one over the parietal cortex on each side, and the third –as a reference- in the right parietal cortex. To monitor EMG, three flexible stainless-steel wire electrodes, isolated except for the last 3-4 mm, were implanted into the neck muscles (two bilaterally and one in the middle). EEG and EMG signals were digitized using a CED 1401 Plus interface and analyzed manually using Spike2 software (CED, Cambridge, UK) according to the three classical vigilance states: Non Rapid Eye Movement Sleep (NREMS), Rapid Eye Movement Sleep (REMS), and wakefulness.

Results: MT1KO mice showed a modified sleep-wake cycle compared to WT with increased NREMS (+40.2%; two-way ANOVA; $P=0.001$) and decreased wakefulness total time during the active/dark phase (+24.5%; $P=0.001$). Moreover, MT1KO mice spent equal time in REMS during the light and dark phases ($P=0.69$) in contrast to WT mice in which REMS lasted longer during the inactive/light phase (+50%; $P<0.001$). Power spectra analyses during the light and the dark phases indicated a modified spectral power in MT1KO mice for both NREMS and REMS.

Conclusions: These results confirm that MLT and its receptors are necessary for the control of the sleep-wake cycle since the lack of MT1 receptor significantly affects both NREMS and REMS parameters. These findings add new insights into how melatonin, acting through MT1 receptor, affects the sleep-wake cycle.

Keywords: Sleep, Melatonin, MT1 receptor, Mice

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EFFECT OF BRIGHT LIGHT ON MESOCORTICOLIMBIC AND THALAMOCINGULATE ACTIVITY IN POSTPARTUM DEPRESSION: AN FMRI PILOT STUDY

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Introduction: Postpartum Depression (PPD) is a major public health problem affecting between 12-15% of childbearing women. Previous studies have correlated PPD with low levels of serotonin, a neurotransmitter involved in mood, sleep, and cognition. Serotonergic pathways are involved in the same mesocorticolimbic and thalamocingulate neural circuits found to be involved in maternal emotional attachment, reward processing, and care and planning involved in response to infant stimuli in mother-infant interactions. Several studies have shown that activity in these neural circuits is negatively affected by PPD. Because the serotonergic pathways involve the mesocorticolimbic and thalamocingulate circuits in the brain, it may be possible to correlate positive effects on these areas with bright light treatment.

Methods: Five participants (mean age 35.8yrs) who were within 12 months post-partum have participated in this ongoing study. All participants were experiencing symptoms of postpartum depression. Participants were screened for MRI safety, and for exclusionary criteria including suicidal ideation and history of psychosis. At baseline, participants were assessed for probable PPD using the Edinburgh Postpartum Depression Scale (EPDS). Sleep quality (Pittsburgh Sleep Quality Index), mood (Profile of Mood States), and anxiety (Speilberger State-Trait Anxiety Inventory) were also assessed. A baseline fMRI exam was administered using the subject's own infant cry as a stimulus for emotional response measured during the scan. Following baseline, participants were randomized to 2 weeks of daily self-administered bright light therapy (10,000 lux for 30 min) or placebo (sham negative ion generator). The treatments were completed within an hour of waking each morning. Following the two-week treatment phase, participants were re-assessed using the same protocol as for baseline.

Results: Preliminary results show increased activity (vs. placebo), in mesocorticolimbic and thalamocingulate circuits following bright light treatment. Increased activation was observed in the orbital frontal cortex, anterior cingulate, thalamus, and hippocampus. In addition, we observed decreased activation of the insula post bright light treatment vs. placebo. Minimal differences were observed in self-reported measures of depression, anxiety, mood, and sleep quality between bright light therapy and placebo.

Conclusion: This ongoing study is investigating the effect of bright light therapy on neural correlates of mother-infant interactions in women with postpartum depression. The therapeutic effects of bright light therapy might be modulated by an increase in serotonin activity in the mesocorticolimbic and thalamocingulate circuits of the brain. These neural circuits have been shown to be involved in parenting behavior including attachment, empathy, and care and vigilance in response to infant stimuli, and have been shown to be negatively affected in individuals with depression. Preliminary results indicate that emotional information processing in response to newborn cry may be substantially modified following bright light therapy. The observed positive changes in these neural activity patterns may shed light on the neurobiological mechanisms of bright light therapy for postpartum depression.

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SELF REPORTED EVENINGNESS CHRONOTYPE AND EARLY SLEEP/WAKE CYCLE DURING BASIC COMBAT TRAINING

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Introduction: Abrupt schedule changes which require early morning awakening can be detrimental to performance and well-being of individuals with an eveningness chronotype. The aim of this qualitative focus group study was to investigate Soldier self-reported performance and sleep quality during the regimented early sleep/wake schedule imposed during Army Basic Combat Training at Fort Jackson, Columbia, SC, U.S.A.

Methods: Six focus groups of Soldiers (ages 18-24) undergoing Army Basic Combat Training (BCT) at Fort Jackson, Columbia, SC, U.S.A. were assembled. Three focus groups consisted of female Soldiers, and three consisted of male Soldiers. Focus groups were conducted by gender-matched, trained facilitators and note-takers from the University of South Carolina. Focus group discussions lasted 45-60 minutes and consisted of nine questions regarding the sleep environment during Basic Combat Training. Questions about changes in sleep schedule, sleep quality, barriers to sleep, and adaptations to the sleeping environment at BCT were addressed, and Soldiers were also encouraged to write any comments on a notepad if they ran out of time or preferred to submit comments privately.

Results: Out of the 32 male and 28 female Soldiers who participated in the focus groups, only 3 males and 6 females classified themselves as 'morning types' prior to starting BCT, with the majority of Soldiers reporting that they had been "night owls" prior to entering BCT. Almost all Soldiers reported difficulty falling asleep at least in the beginning of BCT due to the earlier bed time imposed by the BCT schedule. This resulted in getting less sleep than they typically got at home. Moreover, sleep was commonly interrupted during the night for various reasons, including noise, off-hour work duties, etc. Soldiers reported that their performance in class or in physical training has been adversely affected by the change in sleep/wake cycle, and the resultant decrease in sleep. Several Soldiers reported falling asleep in class, experiencing slower reflexes, and having problems with retention of information. Soldiers also reported greater irritability and decreased well being associated with the change in sleep/wake cycle imposed by the BCT schedule.

Conclusions: Consistent with many young adults, the Soldiers had a propensity towards 'eveningness.' The rigid early morning schedule of Basic Combat Training contrasts to optimal times for performance and well-being of "evening type" individuals. Previous studies have shown adverse effects of forced early morning awakening on performance, cognition, sleep quality, and well-being of young adults, assessed as being 'evening types.' Soldier self-report of these factors from this focus group discussion have paralleled these findings, and may suggest a need for young adults entering Basic Combat Training to adjust their sleep/wake schedule in advance of BCT in order to entrain their circadian system to the earlier sleep/wake cycle.

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LIGHT SENSITIVITY MEASURED BY PUPILLOMETRY AND BRAIN IMAGING IN YOUNG AND OLDER SUBJECTS

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Objectives: Light is the main synchronizer of circadian rhythmicity and is known to directly affect sleep and other non-visual functions, with a maximal sensitivity to blue light. Age-related modifications in the circadian timing system may be associated with the effect of light on non-visual functions..

Methods: Here, we investigated the acute effect of blue monochromatic light exposure, presented at low ($7x10^{12}$ ph/cm^2/s), medium ($3x10^{13}$ph/cm^2/s), and high (10^{14}ph/cm^2/s) irradiance levels, on pupil light reflex (PLR) and non-visual cognitive brain activity as a function of age. Thirty subjects (16 young: mean±SD 23 y.o±3.9; 14 older: mean 61 y.o±4.4) complete PLR measures with undilated pupils and fMRI study consisting of performing an auditory working memory 2-back task while alternatively maintained in complete darkness and exposed to short (45s) monochromatic blue light.

Results: PLR analysis of absolute pupil size showed that young subjects had larger pupils than older subjects both in darkness (young: 0.39±0.01, arbitrary unit, mean±SEM, older: 0.33±0.02; p=0.008) and during light exposure (young: 0.23±0.01, older: 0.19±0.01; p=0.002). Analysis of normalized sustained pupil constriction revealed greater constriction with higher irradiances of blue light (low: 35.07±1.69%; medium: 42.18±1.54%; high: 47.06±1.57%; p<0.01) without significant effect of age or interaction with age. fMRI analyses revealed that blue light exposure induced higher brain activation in the amygdale, thalamus and cerebellum in older subjects compared to younger subjects (p corrected<0.05). Compared to younger subjects, older individuals also showed enhanced brain responses to increasing light irradiance (p corrected<0.05). These age-related differences in the impact of light irradiance on brain responses to the task were found in the prefrontal cortex, occipital cortex, and cerebellum.

Summary and conclusion: Compared to young subjects, older individual showed smaller absolute pupil but similar light-induced pupil constriction. Importantly, older subjects showed lower light induced modulation of brain response in subcortical and cortical regions engaged in alertness regulation and in the ongoing task. Thus, aging affects differently two non-visual responses to light. These results support the notion that light sensitivity may differ between non-visual functions as suggested by animal studies. Further analyses will assess how age-related difference in absolute pupil size may affect the impact of light on non-visual cerebral responses.

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PUPIL LIGHT REFLEX IN RESPONSE TO MONOCHROMATIC LIGHT STIMULI IN YOUNGER AND OLDER SUBJECTS

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Objectives: Aging induces changes in the circadian regulatory process which may be associated with impaired photic input. Changes in pupil light reflex (PLR) during aging may alter retinal photic input and consequently affect the impact of light on non-visual functions. Circadian entrainment and other non-visual functions are regulated by a non-visual photoreceptive system that shows peak sensitivity to blue light, in contrast to the photopic visual system, maximally sensitive to green light. Here, we assessed whether PLR to green and blue light of different irradiance levels changes with aging.

Methods: PLR was measured in 16 young (23±3.9y) and 14 older (61.1±4.4y) healthy subjects with undilated pupils, in response to blue (480nm, hbw=10nm) and green (550nm, hbw=10nm) monochromatic light presented at low ($7x10^{12}$ ph/cm^2/s), medium ($3x10^{13}$ph/cm^2/s), and high (10^{14}ph/cm^2/s) irradiance levels. Subjects were first dark adapted before light exposure. Light exposures lasted 45s and were separated by 60s of darkness. Pupil constriction was normalized according to pupil size at the end of dark adaptation.

Results: Analysis of raw data showed that young subjects had larger pupils than older subjects at the end of dark adaptation (young: 0.39±0.01, arbitrary unit, mean±SEM, older: 0.33±0.02; p=0.008) and during light exposure (young: 0.23±0.01, older: 0.19±0.01; p=0.002). Analysis of normalized sustained pupil constriction (6-45s) revealed that blue light induced more constriction than green light (blue: 42.26±1.64%, mean±SEM; green: 40.61±1.68%; $p<0.05$), and constriction was greater with higher irradiances (low: 35.07±1.69%; medium: 42.18±1.54%; high: 47.06±1.57%; $p<0.01$).

Conclusions: Pupillary constriction is greater with blue than green light and varies with irradiance level. Although the degree of pupil constriction is not significantly affected by age, absolute pupil size is smaller in older individuals both in darkness and during light exposure. This may reduce retinal illumination and affect other non-visual responses to light such as circadian entrainment.

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DAYLIGHT EXPOSURE DELAY REDUCES HOSPITALIZATION LENGHT IN MANIC EPISODES: A MULTICENTRIC EXPERIENCE

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Objectives. Several studies linked wake–sleep and light–dark rhythms and psychopathological status in patients affected by Bipolar Disorder (BD). Patients affected by BD are more sensitive to the biological effects of light: the exposure to light can exert antidepressant effects and trigger rapid mood swings. A relationships were detected between mood, hours of sunlight, and solar exposure in affective patients, with admissions rates for mania correlating with length of day and levels of sunshine. A strict control of the wake–sleep and light–dark rhythms could act as a mood stabilizer. Some studies showed that extended bed rest and darkness could stabilize timing and duration of sleep, and rapidly improve mood swings in rapid cycling patients. The orientation of rooms in a Canadian ward provided a 'natural experiment' on the relationship between sunlight and length of hospitalization for depression (Beauchemin, 1996). In 1999 at San Raffaele-Turro Hospital in Milan this result was replicated. In a corridor with rooms on either side, windows are oriented towards the East (E) or the West (W). Ambient light intensity in the two conditions showed wide differences. Inpatients in E rooms had a shorter hospital stay than patients in W rooms. The aim of the present work was to investigate if inpatients affected by BD during Manic Episode show a similar sensibility to light exposure and therefore a therapeutic effect due to an extended dark period, with an inverse relationship with respect to depressed patients.

Methods. We reviewed charts for all admissions for Manic Episode (DSM IV criteria), with a diagnosis of Bipolar Disorder, over a 3-year period (2008-2010) at San Raffaele-Turro Hospital of Milan (Italy) and at Santa Croce Clinic of Locarno (Swiss), with the same rooms orientation. Rooms (E or W) had been randomly assigned based on first available free space. Young Mania Rating Scale (YMRS) was repeatedly administered to assess the basal level and the disease course. Medications were administered upon clinical need. According to daytime clinical activities, patients stayed in rooms in morning and evening hours. No exact recording of time spent in rooms is available. Length of hospitalization, based on room orientation, was calculated and compared for a sample of 111 (41 males, 70 females) Bipolar Manic inpatients.

Results. Patients hospitalized in E rooms and in W rooms didn't show differences for clinic and demographic characteristics for both the locations: two groups were overlapped for gender distribution, age, diagnosis and YMRS basal scores. Hospitalization was significantly shorter for W rooms, with a concordance of both the locations, than E rooms. In particular for the Milan sample (92 patients) we observed a length of hospitalization of 23.88 days for patients in E rooms (N° 76) and of 17.56 days for those (N° 16) in W rooms (T-test: 2.17; p=0.03). For the Locarno sample (19 patients) the length of hospitalization was of 48.31 days for patients in E rooms (N° 13) and of 33.33 days for those (N° 6) in W rooms (T-test: 1.95; p=0.06).

Conclusions. Bipolar patients showed an increased sensitivity to the biological effects of light. Our results support the hypothesis that reduction of light exposure and the dark period expansion can have a therapeutic effect during Manic Episodes, and are consistent with studies stressing the role of photoperiodic mechanisms in the course of BD. Aware of the methodological issues raised by a retrospective 'natural experiment', we expect our results to be confirmed by prospective studies. If confirmed, our results suggest the clinical usefulness of chronobiological interventions and control of environmental stimuli in the treatment of acute mania.

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Keywords: Circadian Rhythm, Bipolar Disorder, Manic Episode, Light Exposure, Dark Therapy

CIRCADIAN VARIATION OF QUANTITATIVE SLEEP EEG ACROSS THE MENSTRUAL CYCLE

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Objectives: Complaints from women indicating that their sleep is negatively affected during the mid-luteal (ML) phase compared to the mid-follicular (MF) phase have drawn interest to the relationship between the menstrual cycle and sleep. The causes underlying these effects remain unclear. The increased sleep problems in ML may be linked to the increased concentration of sex hormones and elevated body temperature. These cyclic changes might result in sleep structure changes seen in EEG recordings. Indeed, Driver et al. (Driver et al., J Clin Endocrinol Metab 81: 728-735, 1996) found significant changes in the high sleep spindle range (14.25-15.0 Hz band), with a maximum observed in the luteal phase. They found no effect on slow wave activity (SWA). Therefore we aim to document changes in quantitative sleep EEG across the menstrual cycle, with particular interest in spindle frequency activity (SFA).

Methods: We had 6 women with regular menstrual cycles come in at two phases of their menstrual cycle, namely during the MF and ML phase. During each visit, participants underwent an 8-hour baseline nocturnal sleep episode in the laboratory. The EEG, EOG and EMG were recorded in 30-second epochs and scored according to standard criteria. Sleep was recorded with a sampling frequency rate of 250 Hz. The C3-A2 channel was subjected to spectral analysis via fast Fourier transform. The power spectra were computed for 4.096-second epochs resulting in power density values per 0.244 Hz bins. Spectral analysis was done for the 0-25 Hz range. Data were combined into frequency ranges including SWA (0.732 to 4.880 Hz), theta activity (4.636 to 7.564 Hz), alpha activity (7.808 to 12.200 Hz), low SFA (LSFA; 12.200 to 13.908 Hz), high SFA (HSFA; 13.908 to 15.616 Hz), and beta activity (15.616 Hz to 24.644 Hz). The raw data were analysed with paired samples t-tests. In addition, the raw data were analysed by a two-way within subjects ANOVA for repeated measures (factors: menstrual phase x frequency bins).

Results: The t-test showed no significant difference in SWA ($t_5 = 0.42$, $p = 0.69$), theta activity ($t_5 = 0.45$, $p = 0.67$), alpha activity ($t_5 = 0.27$, $p = 0.79$) and beta activity ($t_5 = -1.8$, $p = 0.13$) between MF and ML. In SFA (12.200 to 15.616 Hz), a two-tailed paired sample t-test showed a trend for significance ($t_5 = -2.22$, $p = 0.078$). Based on an a priori prediction that SFA is increased in the ML compared to MF, a one tailed paired sample t-test was performed. This showed a significant increase in the ML compared to MF ($t_5 = -2.22$, $p = 0.038$). Furthermore a two-way ANOVA was performed for LSFA and HSFA separately. This revealed a significant interaction ($p = 0.0075$) for HSFA. In the ML phase, HSFA was increased compared to the MF phase. In the LSFA, we did not find any variation between the two menstrual phases. We also found a significant interaction ($p = <0.0001$) in the Beta activity range. The beta activity was increased in the ML phase compared to the MF phase. For the SWA, the theta activity and alpha activity we found no variation between the two menstrual phases.

Conclusions: This study confirms the results found by Driver et al. There was a significant increase in HSFA during the ML phase while there was no significant difference in LSFA. Also there was an increase in beta activity in the ML phase compared to the MF phase. Since beta activity is known to be increased in disturbed sleep, this indicates that sleep was more disturbed by the influence of the menstrual cycle during the ML phase. Spindles arise from cyclic inhibition of the thalamo-cortical neurons. They are thought to have a protective effect on sleep. Therefore, an increased occurrence of spindles in the ML phase could potentially have a protective function against the negative effects of menstrual cycle on sleep. Both LSFA and HSFA show a strong circadian rhythm (D.J. Dijk & C.A. Czeisler. J. Neurosci 15: 3526-3538, 1995). In future research we will investigate effects of menstrual phase on the circadian rhythm of LSFA, HSFA and other frequency ranges.

Keywords: Sleep, Menstrual Cycle, Spectral Analysis, Spindles

MONOAMINERGIC FIRING ACTIVITY IN THE VENTRAL TEGMENTAL AREA AND THE DORSAL RAPHE ACROSS THE LIGHT-DARK CYCLE

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Objectives: In this work we characterized the firing activity of dopaminergic (DA) and serotonergic (5-HT) neuronal populations in the ventral tegmental area (VTA) and the dorsal raphe (DR) nuclei, respectively, across the light-dark cycle.

Methods: Rats kept under a constant 12/12h light-dark cycle (lights on at 7h) were used to perform in vivo single-unit extracellular recordings under chloral hydrate anaesthesia at 6 different time intervals of 4 hours (7-11h, 11-15h, 15-19h, 19-23h, 23-3h and 3-7h).

Results: In the VTA, DA firing rate oscillates between intervals but not in a significant manner (7-11h: 3.5±0.4 Hz; 11-15h: 2.7±0.2 Hz; 15-19h: 2.8±0.3 Hz; 19-23h: 3.6±0.3 Hz; 23-3h: 2.9±0.3 Hz; 3-7h: 2.8±0.4 Hz; $F_{(5,203)}$=0.792, p=0.556). However, at 15-19h and at 19-23h, a significant decrease in the number of spontaneously active DA neurons was observed ($p<0.05$ in both cases), compared with the peak of activity observed at 23-3h (7-11h: 2.2±0.3 neurons/track; 11-15h: 2.4±0.4 neurons/track; 15-19h: 1.6±0.1 neurons/track; 19-23h: 1.5±0.2 neurons/track; 23-3h: 2.9±0.2 neurons/track; 3-7h: 2.2±0.3 neurons/track; $F_{(5,96)}$=3.065, p=0.013).

In the DR, the 5-HT neuronal activity decreases during intervals corresponding to the dark phase. In particular, 5-HT firing rate significantly decreases at 3-7h (7-11h: 0.9±0.1 Hz; 11-15h: 0.85±0.1 Hz; 15-19h: 0.98±0.09 Hz; 19-23h: 0.75±0.1 Hz; 23-3h: 0.65±0.06 Hz; 3-7h: 0.53±0.09 Hz; $F_{(5,253)}$=2.841, p=0.016) and the number of spontaneously active DA neurons decreases at 19-23h and at 23-3h (7-11h: 3.0±0.6 neurons/track; 11-15h: 3.7±0.2 neurons/track; 15-19h: 3.8±0.3 neurons/track; 19-23h: 2.6±0.3 neurons/track; 23-3h: 2.4±0.2 neurons/track; 3-7h: 2.6±0.3 neurons/track; $F_{(5,79)}$=3.331, p=0.009), compared with the peak of activity detected at 15-19h in both parameters ($p<0.05$, in all cases).

Conclusion: These data suggest that DA and 5-HT neuronal populations have distinct diurnal rhythms of firing activity. Implications of these findings in the physiopathology of psychiatric disorders remain to be explored.

Keywords: Serotonin, Dopamine, Neuronal Activity, Diurnal Rhythm.

Funding Support: SDL was supported by a scholarship from the Mexican National Council for Science and Technology (CONACYT, Reg. 193202/302017).

CIRCADIAN AND SLEEP-WAKE DEPENDENT INFLUENCES ON SLEEPINESS AND COGNITIVE PERFORMANCE IN YOUNG AND OLDER ADULTS

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Objectives: Aging is associated with a decline in sleep depth, continuity, and duration. These changes occur in otherwise healthy individuals, even in the absence of clinical sleep disorders. Because of this deterioration of sleep, a similar deterioration in waking alertness and performance is often accepted as a parallel consequence of aging. To explore whether increased sleepiness and an inability to cope with sleep loss are indeed consequences of aging, we conducted 2 studies to assess circadian and sleep-wake homeostatic influences on sleepiness and performance during acute sleep deprivation and when sleep and wake were scheduled at different times of day (thereby inducing chronic circadian misalignment).

Methods: In the first study, a group of healthy older (n=11; 3 women, 8 men; mean age 68.1 ± 3.6 years) and healthy young (n=26; 7 women, 19 men; mean age 21.9 ± 3.3 years) adults without medical, psychological, or sleep disorders took part in an extended 26-hour wake episode in constant conditions. We collected continuous EEG recordings to assess inadvertent sleep and slow eye movements, 10-minute Psychomotor Vigilance Task (PVT) performance (every 2h) to assess sustained attention, and Karolinska Sleepiness Scale (KSS) results (every ½ hr) to assess subjective sleepiness. In the second study, a group of healthy older (n=10; 5 women, 5 men; mean age 64.0 ± 5.98 years) and healthy young (n=10; 5 women, 5 men; mean age 24.5 ± 3.54 years) adults without medical, psychological, or sleep disorders took part in a study in which their sleep and wake were scheduled on a 20-h day for ~2 weeks. There were 18 such "days," consisting of 13.3 h of scheduled wakefulness and 6.7 h of scheduled sleep opportunity, allowing for data collection at a full range of circadian phases. During each wake episode, we measured sustained attention using the PVT every 2 h, cognitive throughput (using an addition task every 2h), and subjective sleepiness using the KSS every ½ h.

Results: In study 1, across the first 16 hours corresponding to the usual waking day, both groups rated themselves as alert, had similar levels of vigilance, and little evidence of sleepiness. As the wake episode continued from hours 17-26, the older subjects were less impaired, showing faster reaction times, fewer performance lapses and attentional failures (slow eye movements), and less frequent unintentional sleep episodes. In study 2, we could separate and quantify the performance outcomes with respect to time awake (across the 13.3h wake episodes), circadian phase, and duration into the study. We observed significant main effects of time awake, circadian phase, and duration into the study, such that performance and alertness were worse with longer time awake and further into the study, and worse during the biological nighttime. There were significant interactions between age and the main effects, such that older subjects were less subjectively sleepy and performed significantly better on reaction time measures than young subjects. Performance decrements were greater in the young subjects as the experiment progressed, while the performance of older subjects remained stable.

Conclusions: These findings demonstrate that performance and alertness of healthy older subjects are less impacted by acute sleep deprivation or by the cumulative effects of repeated exposure to circadian misalignment than that of young adults, findings that are consistent with several prior studies. These findings in healthy older adults are in contrast with most field studies of older shift workers, who report greater difficulty coping with a shift work schedules than do younger workers. Whether our findings indicate age-related changes in the circadian rhythm of sleep-wake propensity, in the homeostatic regulation of sleep and wakefulness, and/or in how these two regulatory systems interact in healthy aging is not clear. However, while our findings indicate that healthy older adults are better able to sustain performance and alertness in response to acute sleep deprivation and to chronic circadian misalignment (and the associated sleep loss) than young adults, they did in fact show performance and alertness impairments, and it is unclear whether they experienced adverse metabolic, immune, or cardiovascular impacts from their disrupted schedules. Finally, our findings indicate that excessive sleepiness is not normal in healthy older adults, and symptoms of excessive sleepiness in this population, including reliance on caffeine to maintain alertness, should be evaluated and treated.

Keywords: Aging, Circadian Rhythm, Performance, Sleepiness

Funding Support: The studies were supported by National Institutes of Health (NIH) grants AG06072, AG09975, AG12642, MH45130; and NASA grant NAS9-1435. The studies were conducted in the Brigham and Women's Hospital General Clinical Research Center, supported by NIH grant RR02635.

THE EFFECTS OF LOW INTENSITY MONOCHROMATIC BLUE LIGHT TREATMENT COMPARED TO STANDARD LIGHT TREATMENT IN SUB-SYNDROMAL SAD

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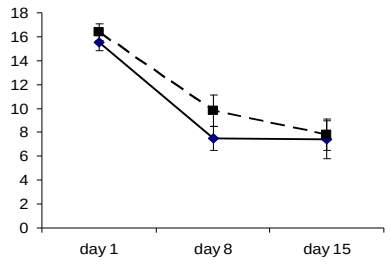
Objectives: Non-image forming (NIF) photoreceptors play a role in the phase-shifting effects of short-wavelength light. In previous studies, we compared standard full spectrum light treatment (SLT) with a treatment that used short-wavelength blue-enriched white light in different intensities (Gordijn et. al, 2006, Meesters et al., 2011) in treating Seasonal Affective Disorder (SAD). All treatments were highly, and equally, effective despite a difference in intensity. In a study comparing the effects of low intensity monochromatic blue light (mBLT) against the effects of high intensity SLT, we did not find differences in therapeutic outcome (Meesters and Duijzer, 2011). Although the effects of light treatment and especially the effects of blue- or blue-enriched light are studied quite well in SAD population, only few studies of the effects of light treatment in sub-syndromal SAD (sub-SAD) are available. People suffering from sub-SAD have seasonal related complaints (hypersomnia, loss of energy, a.o.), but no mood disorder. This study compares the effects of low intensity mBLT against the effects of high intensity SLT in patients suffering from sub-SAD.

Methods: In a 15 days design, 34 patients (41.9 y, sd 11.0) suffering from sub- SAD (without a mood disorder according to the DSM-IV), a Global Seasonality Score of $\geq$8 on the SPAQ and a score of $\geq$12 on the SIGH-SAD (24 items) were offered light treatment at home for five days, on workdays before 8.20 a.m., in the winter of 2010/2011. Light treatment either consisted of 20 minutes SLT (5000ºK) with the EnergyLight (Philips, Consumer Lifestyle) with a vertical illuminance of 10 000 lux at eye position or monochromatic blue light (mBLT) with the goLite (Philips, Consumer Lifestyle) with a vertical illuminance of approx. 100 lux. All participants completed questionnaires concerning mood, sleepiness and sleep qualitiy on a daily basis starting at day 1 (3 days before treatment). SIGH-SAD ratings were obtained 3 times (on days 1, 8, and 15).

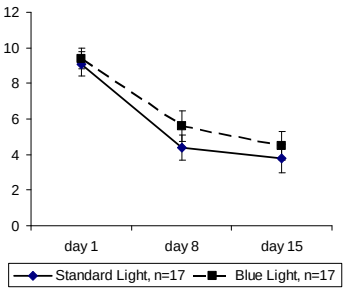
Results: On day 15, SIGH-SAD ratings were significantly reduced compared to day 1 (SLT 52.7% and mBLT 51.9%). Between the conditions, no statistically significant differences were found. In both conditions atypical symptoms (energy, hypersomnia, etc.) improved (SLT 59.3 % and mBLT 51.3 %) in a statistically identical way. There were 59 % responders (SIGH-SAD reduction $\geq$ 50%) in the SLT condition, and 71% in the mBLT condition. The differences were not statistically significant.

Conclusions: This is an ongoing study, so the results can only be preliminary. The two treatment conditions were highly effective. The therapeutic effects of low intensity monochromatic blue light were comparable to those of the standard light treatment.

SIGH-SAD



ATYPICAL SYMPTOMS



Key Words: sub-SAD, light treatment, monochromatic blue light

Funding Support: Philips Consumer Lifestyle, Amsterdam, The Netherlands

References: Gordijn et al. (2006): SLTBR abstracts 18: 6; Meesters et al. (2011): BMC Psychiatry 11:17; Meesters and Duijzer (2011): SLTBR abstracts 23: …

LIGHT-ASSOCIATED PERINATAL IMPRINTING OF CIRCADIAN CLOCKS: CONSOLIDATION AND "WHITE-BOX" EPIDEMIOLOGICAL STUDIES OF LATITUDE AND INSTABILITY HYPOTHESES OF MOOD DISORDERS AND CANCER

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Objectives: A recent report in *Nature Neuroscience* (Ciarleglio et al., 14: 25-7**,** 2010) suggested that perinatal exposure to seasonal photoperiods may imprint circadian clocks with lasting effects on the alignment and the stability of circadian rhythms in relation to light exposures later in life. Assuming these developmental findings in mice can be replicated and substantiated for longer observation periods, we considered the consequence of this premise with regard to the aetiologies of mood disorders and internal cancers in humans (Erren et al., *Psychopharmacology* 2011 Feb 19; Erren et al., *Chronobiol. Int.* 28(5), 2011).

Methods: We identified four hypotheses for the development of mood disorders and internal cancers in the peer reviewed literature for which the insights reported by Ciarleglio and colleagues could be relevant: (i) the 1986 latitude hypothesis of an association between latitude and seasonal affective disorders (SAD); (ii) the 1990 instability hypothesis of bipolar disorder; (iii) the 1999 latitude hypothesis of an association between latitude and internal cancers; (iv) the 2008 chronodisruption-cancer theory. We then investigated how these hypotheses of a causal link between light and mood disorders as well as the development of cancer could be consolidated by incorporating the novel experimental insights and how this new approach could contribute to targeted "white-box" epidemiological studies.

Results: The suggested perinatal imprinting of circadian clocks and systems by seasonal light/darkness cues can form the basis for refined tests related to all four hypotheses. Indeed, our synthesis evinces that "latitude hypotheses" and "instability hypotheses" for the development of mood disorders and internal cancers represent different facets of the same underlying phenomenon. The cornerstone of the consolidated rationale is the interaction of light with circadian rhythmicity at two levels and in different time windows. Early in life, light exposures could imprint and determine the susceptibility of an individual's circadian system to *Zeitgeber* information later in life. Exposure to light at unusual times later in life could then provide confusing timing information and derange the body's circadian rhythms. Overall, instable circadian systems – primed more or less by time and location of birth (i.e., season and latitude) and thus differential light/darkness exposure patterns in early life – may be a key determinant of a human being's susceptibility to developing mood disorders, such as SAD, and internal cancers.

Conclusions: Our results lead to research questions which can and should be rigorously tested either through re-examining published data or through newly designed epidemiological investigations: (a) Are SAD rates in cohorts of individuals born in winter months at extreme latitudes higher than in cohorts born there at other times of the year and/or in locations closer to the equator? (b) Is the likelihood of having been born in winter months and/or at extreme latitudes higher in cases with SAD than in controls without the disease? (c) Are internal cancers more frequent in cohorts of individuals born in winter months at extreme latitudes than in cohorts born there at other times of the year and/or in locations closer to the equator? (d) Is the likelihood of having been born in winter months and/or at extreme latitudes higher in cancer cases than in controls without the disease? Remarkably, when and where people are born might critically determine a predisposition to both mood disorders and internal cancers and affect their onsets and courses.

Keywords: Light-associated Perinatal Imprinting of Circadian Clocks, Mood Disorders, Internal Cancers, Consolidation and Tests of Latitude and Instability Hypotheses

RAMELTEON FOR INSOMNIA RELATED TO ATTENTION-DEFICIT/HYPERACTIVITY DISORDER (ADHD)

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Objectives: This study evaluated the efficacy of ramelteon for insomnia in adult subjects with ADHD.

Methods: For this randomized, double-blind, placebo-controlled crossover trial, 8 mg of ramelteon was given nightly, within three hours of bedtime, to ADHD-insomnia subjects confirmed by DSM-IV-TR, ADHD-RS, MINI, and clinical interview. All subjects underwent two weeks each of ramelteon and placebo. Objective sleep measures were obtained by actigraphy. Subjective measures included: the Epworth Sleepiness Scale (ESS) and ADHD-RS.

Results: Of 36 subjects entering the study, 58% met criteria for circadian rhythm sleep disorder (CRSD), delayed sleep phase type. During ramelteon period, mid-sleep time, an indicator of circadian phase, occurred significantly earlier, by ~45 minutes compared to placebo period. An association was noted between the magnitude of the sleep phase advance and the timing of ramelteon administration in relationship to sleep start time, but did not reach statistical significance; maximal efficacy was noted 1.5 hours before bedtime. Paradoxically, ramelteon marginally, but significantly increased sleep fragmentation and ESS scores compared to the placebo state.

Conclusions: Ramelteon is efficacious in maintaining an earlier sleep/wake cycle in adults with ADHD and CRSD but can have paradoxical fragmenting effects on sleep and exacerbate daytime sleepiness. In the presence of a circadian rhythm disorder, the usual dosing and timing parameters for ramelteon need to be carefully considered.

Key Words: Melatonin agonists, Circadian rhythm sleep disorder, delayed sleep phase type, Attention disorders, Chronobiologic treatments

Takeda Pharmaceuticals North America, Inc. funded this study as an investigator-initiated trial.

EXPOSURE TO DAYLIGHT AS WELL AS TO BLUE AND RED LIGHTS AT NIGHT INTERACT TO AFFECT NOCTURNAL PERFORMANCE, SUBJECTIVE SLEEPINESS AND BIOMARKER PRODUCTION

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Objectives: Light affects visual as well as non-visual pathways in ways not fully understood. Natural daylight is considered a desirable source of illumination in buildings and daytime light exposure has been shown to activate brain regions associated with alertness. Observations in our laboratory suggest that deprivation of daylight or of sufficient electric light during the day (i.e., remaining in a dark room all day) might affect performance and alertness at night. At night, short-wavelength (blue) light (40 lux at the cornea) will suppress melatonin production, increase performance, increase EEG power in the beta region, decrease EEG power in the alpha region, and reduce subjective sleepiness. It is believed that the suppression of melatonin by light at night mediates these effects of light on performance, alertness and biomarkers. Suppression of melatonin by light at night has been shown, however, to be associated with increased cancer risks. Recent work by our laboratory suggests that long-wavelength (red) light, which does not suppress melatonin, positively impacts alertness and performance at night. Here we examined the interactive effects of daylight and narrow-band (red and blue) light on performance, subjective sleepiness, and on melatonin, cortisol and alpha amylase production over the course of 26 hours without sleep.

Methods: 13 subjects, (2 females) participated in a 4-session, within-subjects study. Each session was separated by at least 1 week. Each 26-hour session began at 07:00 and concluded at 09:00 the following day. The four experimental conditions were: daylight or dim light (< 3 lux) interspersed every 4 hrs with 40 lux of 630-nm (red) or with 470-nm (blue) light for one hour starting at 08:00. Eight of the subjects who participated in the within-subjects study agreed to participate in a 5th session, where they remained in continuous dim light for 26-hours, again without sleep. During every session subjects were seated at desks facing a window, either open to the natural daylight or covered with opaque, black-our shades. During the red-light or blue-light exposure periods performance was measured on the Multi-Attribute Task Battery (MAT) for Human Operator Workload and Strategic Behavior Research software program (NASA COSMIC collection, Open Channel Foundation); the MAT Battery was comprised of (i) a monitoring task, (ii) a tracking task, (iii) a communication task, and (iv) a resource management task. At the end of the 54-minute MAT Battery, subjects provided saliva samples for assaying melatonin, cortisol and alpha amylase. Subjects were also asked to fill out the Karolinska Sleepiness Scale to assess their subjective sleepiness.

Results: Both blue and red lights improved nighttime performance and increased cortisol production at night compared to dim light. Only blue light suppressed melatonin at night. Light did not have a significant impact on alpha amylase levels. Subjective sleepiness at night was highest when subjects remained in dim light for 26 hours. Blue light in combination with daylight had the greatest positive impact on nighttime performance, while red light in combination with daytime darkness had the least positive impact. The red light/daylight condition improved performance just as much as the blue light /dim light condition. Daylight exposure did not improve daytime performance or affect biomarker production, but positively impacted nighttime performance compared to daytime dim light exposure.

Conclusions: As shown before, light can impact performance and alertness via pathways other than melatonin suppression. Light exposures during the day and at night interact to affect human behavior and physiology. Understanding these interactions has important implications for human performance, particularly in shift work applications. This understanding can aid in the development of 24-hr lighting schemes to increase alertness and improve performance at night without impacting health and well-being of shift workers.

Keywords: light, performance, melatonin, cortisol, alertness

POSSIBLE IMPLICATION OF MELANOPSIN BISTABILITY ON THE INCREASE OF HUMAN HEART RATE BY BICHROMATIC BLUE AND RED LIGHT.

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Objectives: It is now well known that within the visible spectrum, blue light is more efficient to improve arousals and activate biological clock during the night. This characteristic comes from the sensibility to short wavelengths of the photopigment melanopsin contained in intrinsically photosensitive retinal ganglion cells (ipRGCs). Knowing this, it could be possible to reduce the hypovigilance related accident risk of night workers with adequate light management. However, since melanopsin photopigment does not regenerate in presence of blue light, it could resulte in the loss of efficiency over a long exposures time in this industrial context for instance. Nevertheless, melanopsin photopigment appears to regenerate when exposed to red light. Therefore, to prevent this lost of efficiency, we tested the impact on arousal of bichromatic stimuli composed of blue (λ_{max} 460 ± 10 nm) and red wavelengths (λ_{max} 620 ± 10 nm). Moreover, we also tested the impact of a pulsatory versus a continous light emission mode.

Methods: Twelve healthy men came four times in laboratory (once a week) between 07h00 PM and midnight. The first night in laboratory served a baseline where participants were kept in no light. Throughout the other three nights, participants were randomly exposed during 120 minutes to one of the light conditions between 09h00 PM and 11h00 PM:

1. Monochromatic blue light at an intensity of 21 ± 1 $\mu W/cm^2$ with a pulsatory emission mode at 70 Hz, alterning 3 ms of blue light and 11 ms without light.
2. Bichromatic blue and red light at an intensity of 21 ± 1 $\mu W/cm^2$ and 9 ± 1 $\mu W/cm^2$ respectively with a pulsatory emission mode at 70 Hz, alterning 3 ms of blue light and 11 ms of red light.
3. Bichromatic blue and red light at an intensity of 21 ± 1 $\mu W/cm^2$ and 10 ± 1 $\mu W/cm^2$ respectively with a continuous emission mode.

During each visits, we measured subjective alertness, performance, temperature, salivary melatonin and electrocardiography.

Results: Here, we are reporting the results of heart rate (HR) derived from ECG signals. In the two bichromatic conditions, independently of the emission mode, heart rate significantly increases nearly two beats per minutes ($p < 0.05$) when compared to monochromatic blue light and baseline conditions.

Conclusions: Results are suggesting that dim red light enhance arousals thought cone inputs into the ipRGCs and/or by regenerating the melanopsin photopigment as well as maintaining his responsiveness. Bichromatic lighting design, containing short and long wavelengths, might be superior to monochromatic lighting to improve arousals of night workers.

Keywords: wavelenghts of light, night workers, heart rate, biological clock, melanopsin

Funding Support: MH was supported by the « Fonds de la Recherche en Santé du Québec (FRSQ) » and « Institut de la recherche en santé du Canada (IRSC) ». CF was supported by doctoral awards from « Institut de Recherche en Santé Sécurité au Travail (IRSST) » and « Centre de recherche sur le cerveau, le comportement et la neuropsychiatrie" (CRCN) ».

CIRCADIAN RHYTHM OF MELANOPSIN-EXPRESSING RETINAL GANGLION CELLS IN THE HUMAN RETINA

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Objectives: The mechanisms by which melanopsin-expressing retinal ganglion cells (mRGCs) regulate circadian rhythms in humans have not been established. To understand mRGC characteristics and their role, mRGC responses should be induced or measured independent of cone and rod responses. Even though researchers in the fields of medicine, architecture and illumination engineering are trying to produce standards for environmental lighting and to promote light therapy for the regulation of human circadian rhythms, it is important to note that the light stimuli used in these studies also affect the other photoreceptors, rods and cones, as well as the mRGCs. In a prior study (Fukuda et al., Neurosci. Lett. 479: 282-286, 2010), we successfully investigated mRGC responses independent of rods and cones by using our innovative method with the receptor-silent substitution technique, which induces responses in only the mRGCs as measured by the electroretinogram (ERG). In the present study, we have attempted to use the ERG to measure changed responses of the mRGCs over the course of the day.

Methods: Two healthy female Japanese subjects (22 years old) had their sleep-wake cycles recorded at home for one week prior to the two experimental days; they were asked to go to bed between 11 pm and midnight and to get up at between 6 and 7 am. During this week and the following two experimental days, they wore an Actiwatch-L (Mini Mitter Co. Inc., USA) on their non-dominant hand, which recording their sleep-wake cycle, and kept a sleep diary. On the two experimental days, the subjects stayed in a room where the light was regulated at approximately 50 lx and room temperature and humidity were maintained constant (approximately 21°C, 50% RH). They undertook test sessions - to investigate changes in mRGC responses to light stimuli which induced only mRGC responses as measured by the ERG - at 9 pm on the first day and 9 am and 3 pm on the second. The subjects' salivary melatonin and tympanic temperature were also measured every two hours as markers of their biological rhythms. For each test session, a mydriatic agent was dropped into the subject's left eye (to cause pupil dilation) and subjects wore an ERG electrode while they rested their head on a chin rest and gazed at a fixation point at the center of circular light stimulus (100 mm in diameter) on a diffuser in front of them. The diffuser was at a distance of 300 mm from the subject and the circle subtended an angle 18.9 degrees at the eyes. After 5-min adaptation, in order to saturate rod responses, the light stimuli were given for 250 msec and repeated 30 times at intervals of 5 sec. The study was approved by the Ethics Committee at Fukuoka Women's University and subjects gave written informed consent prior to study.

Results: The hormone (salivary melatonin) and body temperature (tympanic temperature) rhythms were normal in both subjects. Amplitudes of the mRGC responses in the ERG were higher in the evening (9 pm) than in the morning (9 am) and afternoon (3 pm). Also, it was found that the overall amplitude of the ERG increased from morning to evening, indicating the possibility that the sensitivity of the cones as well as of the mRGCs would be heightened in the evening.

Conclusions: The results in this study indicate a strong possibility that the sensitivity of photoreceptors is higher in the evening than the daytime. One explanation of this phenomenon is that human eyes have adapted in order to respond to more feeble lights in a dark environment in the evening. Therefore, in a modern society, people should take more care with exposure to bright light in the evening, since their light sensitivity might be higher at this time. The results also suggest that light might more easily disrupt human circadian rhythms in the evening.

Keywords: Melanopsin-Expressing Retinal Ganglion Cells, Circadian Rhythms, Receptor-Silent Substitution Technique, Electroretinogram

Funding Support: This work was funded by the Sasakawa Scientific Research Grant from the Japan Science Society, and JSPS (22770245).

ADHD CLINICAL SUBTYPE DIFFERENTIALLY PREDICTS SLEEP AND CIRCADIAN DISRUPTION IN ADULT ADHD PATIENTS WITH INSOMNIA

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Objectives: Patients with Attention-Deficit/Hyperactivity Disorder (ADHD) often exhibit disrupted sleep and circadian rhythms, and a large percentage show signs of sleep onset insomnia (SOI) and/or delayed sleep phase syndrome. Recently, a study found that in adult ADHD patients with SOI (77.5% of total ADHD patients sampled), dim light melatonin onset and sleep onset/offset were significantly delayed compared to ADHD patients without SOI (VanVeen, et al, Biol Psychiatry 67: 1091-1096, 2010). Here, we sought to address whether sleep and circadian parameters are differentially disrupted in adult ADHD clinical sub-types, and whether sleep and circadian disruption is associated with ADHD symptoms using two weeks of baseline data from an ongoing clinical trial.

Methods: Measures from 24 subjects included a daily sleep diary, actigraphy (via Actigraph wrist devices), Epworth Sleepiness Scale (ESS), ADHD Rating Scale, Clinical Global Impression Scale, Pittsburgh Sleep Quality Index (PSQI), and an insomnia questionnaire. Clinical subtypes (Inattentive, Hyperactive-Impulsive, and Combined) were defined as scoring 12 or greater on the ADHD-RS Inattentive and Hyperactive-Impulsive dimensions and compared to patients with controlled symptoms (scoring less than 12). In addition, principal components analysis was used to identify correlated circadian- and sleep-related variables. The identified components were then entered into a backwards step-wise linear regression analysis in order to identify which components significantly predicted ADHD-RS Inattentive, Hyperactive-Impulsive, and Total dimensions.

Results: ADHD sub-types differed in Epworth Sleepiness Scale (ESS) scores, times of mid-sleep, and wake-up times (ANOVA, $p < 0.05$). Specifically, ESS scores of Combined subtypes were significantly greater than Inattentive subtypes and ADHD patients whose symptoms were controlled. Inattentive and Combine subtypes had significantly later mid-sleep and wake-up times compared to patients whose symptoms were controlled (ANOVA, $p < 0.05$). There was a trend for higher PSQI scores for Combined subtypes (ANOVA, $p = 0.056$). In addition, factors explaining 87% of the variance predicted Total ADHD Score, as well as ADHD-RS Inattentive and Hyperactive-Impulsive dimensions. Results of the Principal Components regression indicated that delayed sleep timing and increased sleepiness (ESS) significantly predicted higher ADHD total scores (greater severity), hyperactive-impulsive, and inattentive ADHD symptoms (linear regression, $p < 0.01$). These same factors as well as increased wake difficulty were associated with greater hyperactive-impulsive symptoms.

Conclusions: In summary, these results suggest that circadian rhythm and sleep disruptions are associated with more severe ADHD symptoms in ADHD-SOI patients, and these disruptions contribute to inattentive and hyperactive-impulsive symptoms.

Keywords: delayed sleep phase, attention deficit hyperactivity disorder, circadian, sleep, actigraphy

Funding Support: Supported by Takeda Pharmaceuticals North America, Inc (REF) and NIH Grant GM086683 (KLG).

PREPROHYPOCRETIN/PREPRO-OREXIN (HCRT) GENE: ROLE IN MEDIATING INDIVIDUAL DIFFERENCES IN DAYTIME SLEEP PROPENSITY AND NIGHTTIME HOMEOSTASIS DURING SLEEP LOSS

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Objectives: The orexin-hypocretin system is involved in normal regulation of sleep and wakefulness and is disturbed in the sleep disorder narcolepsy. The -909 C/T polymorphism of the prepro-hypocretin/prepro-orexin (*HCRT*) gene is associated with an increased risk of sudden onset of sleep (SOS)/sleep attacks in Parkinson's patients, though it has not been directly associated with narcolepsy. We evaluated the role of this polymorphism in mediating sleep and wake responses, as well as cognitive, sleepiness and mood responses, during baseline and chronic sleep restriction—the latter is commonly experienced by millions of people on a daily and persistent basis and is associated with serious health consequences.

Methods: 16 *C/C*, 59 *C/T* and 54 *T/T* healthy adults (29.9±6.9y;63 females) completed 2 baseline 10h time in bed nights, followed by 5 consecutive sleep restriction nights (4h time in bed) in a controlled laboratory experiment assessing physiological sleep responses (including NREM slow-wave energy [SWE]) and neurobehavioral outcomes (i.e., mood, cognitive tests, subjective sleepiness and fatigue, and sleep propensity as measured by the Maintenance of Wakefulness Test [MWT]). Comparisons were made across the 3 genotypes. *T/T* genotypic and *T* allelic frequencies were significantly higher in Caucasians than African Americans; thus, analyses statistically controlled for ethnicity.

Results: At baseline, during fully-rested conditions, the *C/C* group showed decreased sleep homeostatic pressure (SWE) during the night ($p<0.05$); this group, however, showed comparable SWE elevation responses to sleep restriction. Relative to *T* allele carriers, *C/C* subjects also had more stage 2 sleep and less slow-wave sleep during both baseline (p's<0.05) and sleep restriction (p's<0.05), and greater REM sleep latency reductions ($p<0.05$) during sleep restriction. *C/C* subjects showed longer MWT sleep onset latencies, indicating lower sleep propensity, during sleep restriction ($p<0.05$) but not during baseline conditions. No group differences were found for circadian phase typology (morningness-eveningness or sleep midpoint), habitual sleep, demographic characteristics, mood, subjective sleepiness, or cognitive performance. All genotypes demonstrated similar cumulative cognitive performance decreases, and comparable cumulative increases in subjective sleepiness in response to sleep restriction.

Conclusions: The *HCRT* -909 C/T polymorphism is associated with differences in sleep homeostasis during fully-rested conditions, as well as with differences in physiological sleepiness and sleep structure during sleep restriction, and thus may be a biomarker for predicting such responses to sleep loss. The rarer *C/C* genotype is particularly buffered from the physiological— but not the cognitive performance—effects of sleep restriction.

Keywords: Sleep Deprivation, Cognitive Functioning, Sleep Homeostasis, *HCRT* Gene, Individual Differences

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DYNAMIC LIGHT IN A FAST FORWARD ROTATING SHIFT WORK ENVIRONMENT

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Objectives: Light, especially the short wavelengths of the spectrum, elicits robust non-image forming effects on human physiology and behavior, including improving alertness and performance, irrespective time of day. Making use of this knowledge to optimize artificial lighting at the workplace seems a logical step. However the decision of what to do with light exposure in a fast forward rotating shift work environment is not simple. On the one hand increasing light intensity, especially the short wavelengths of light, at night may improve alertness and performance and reduces risks. On the other hand the so called "light-at-night" hypothesis suggests that the increased risk for cancer is due to the suppression of melatonin by (blue) light exposure at night, and light-at-night may induce unwanted shifts of the biological clock. We recently conducted two types of studies to investigate the effects of light at the working place.

Results: The first study was performed in the lab. In a simulated night shift work paradigm 17 subjects were either exposed to dim light, to regular white light (3000K, 150-600 lux at the eye), or to blue reduced ("yellow") light (same tubes but with wavelength below 530nm filtered out, 150-450 lux at the eye) between 11 p.m. and 7 a.m. On average melatonin was significantly suppressed by white light to an amount of 53%, but not by "yellow" light (4%). While melatonin was not suppressed in the "yellow" light condition, this had no repercussion on performance: performance in an addition task was better in both the white light and the "yellow" light condition compared to dim light, with no difference between lighting conditions.

In a real-life shift work environment it seems not optimal to permanently shift to blue reduced light. A dynamic light system that is able to change both light intensity and light color (spectrum) relative to the time of day could be the solution. Although the most optimal choice for a lighting scheme over the 24h day is yet unknown, we recently evaluated dynamic light patterns in two control rooms with a fast forward rotating shift work schedule. We tested two types of lighting schedules with a pattern of higher intensities and more short wavelengths during the day and with lower intensities and lower amount of short wavelengths during the evening and night. Data show that both an increase and a reduction in sleepiness can be obtained by changing the spectral characteristics of light at the working place. Higher levels of alertness have been observed in both control rooms consistently in the late shift, and at some instances also in the night shift and during the early shift as a result of our latest lighting scheme.

Conclusion: As long as it is unclear whether light-at-night is responsible for detrimental health effects in shift workers we have to search for lighting patterns at the workplace that reduce sleepiness without inducing phase shifts of the clock and/or complete suppression of melatonin. Future studies, both in the lab and in the field, are necessary to disentangle the contribution of the different photoreceptors to the non-image forming effects of dynamically changing light patterns and to find the optimal characteristics of the dynamic light scheme to improve short term alertness and performance without increasing long term health risks.

Keywords: Light exposure, spectral composition, shift work, alertness, health

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EFFECTS OF FLUORESCENT LIGHT CORRELATED COLOR TEMPERATURE ON MELATONIN REGULATION IN HEALTHY HUMANS

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Objectives: The discovery of melanopsin, the photopigment in intrinsically photosensitive retinal ganglion cells, significantly advanced our understanding of human circadian phototransduction. Ten separate analytic action spectra in rodents, nonhuman primates and humans show that the peak wavelength sensitivity for this sensory system is in the blue-appearing short wavelength portion of the visible spectrum, fundamentally different from that of the classical visual system (1-3). Correlated color temperature (CCT) is a standard measure to describe lamp light and is based on the relative balance of wavelength emissions from a specific light source. Multiple studies have documented how different color temperature lamps can influence circadian, neuroendocrine and neurobehavioral responses. Earlier studies compared 6500 K versus 3000 K and 6480 K versus 3150 K fluorescent lamp light for melatonin suppression (4, 5). Both studies showed that higher color temperature lamp light evokes a stronger melatonin suppression than lower correlated color temperature lamp light Our aim was to test the hypothesis that fluorescent light enriched in the blue-appearing portion of the spectrum with a CCT of 12,000 K will have increased efficacy for melatonin suppression when compared to low CCT light of 2,300 K.

Methods: Subjects included healthy females and males (N=8), with a mean age of 24.5 ± 0.5 and normal color vision (FM-100 score: 93.8 ± 14.2). The light exposure system consisted wall-mounted, 127 cm^2 light panel containing the prototype lamps which subjects viewed face-on at a distance of 30 cm to achieve a full visual field exposure. The volunteers' pupils were freely reactive during the polychromatic 90 minute light exposures between 2:00 and 3:30 AM. All volunteers were exposed to five equivalent photon densities each of low CCT white 2,300 K fluorescent light and high CCT 12,000 K fluorescent light as well as two equivalent photon densities of medium CCT 5,000 K fluorescent light. Blood samples collected before and after light exposures were quantified for melatonin by radioimmunoassay.

Results: A comparison of the pre-light exposure values for all subjects across all conditions showed no statistically significant variation ($p=0.12$). Repeated measures ANOVA was used to compare both plasma melatonin % change scores and control-adjusted % change scores and showed a significant intensity-related suppression of melatonin ($p<0.0001$). Comparison of pre- vs. post-exposure melatonin values by paired, two-tailed t-tests showed that two intensities of high CCT 12,000 K fluorescent light induced a significant reduction of melatonin ($p< 0.05$ to 0.01) while only the highest intensity of low CCT 2,300 K fluorescent light induced a significant reduction of melatonin ($p< 0.05$).

Conclusions: The data provided support the hypothesis that light enriched in the blue-appearing portion of the spectrum with a higher CCT has an increased efficacy for melatonin suppression when compared to low CCT light. These data have value in considering the use of fluorescent light in future architectural applications. In addition, the data may help in characterizing the photoreceptor system(s) that mediate the circadian, neuroendocrine, and neurobehavioral responses to polychromatic light stimuli.

Keywords: Circadian Phototransduction, Light, Melatonin, Correlated Color Temperature

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ANALYSIS OF THE HUMAN EYE'S ILLUMINATION CONDITIONS IN INTERNAL ENVIRONMENT

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Objectives: The objective of this paper is to describe a simulation procedure of the daylight conditions, which may promote human health and wellbeing through the proper circadian rhythms entrainment. Based on the actual biological findings, it is necessary to provide proper light quality and sufficient quantity directly to the human's eye. In the architectural praxis, the current standards rely solely on the horizontal plane illuminance. But in the terms of circadian efficacy, we have to analyze the light conditions further than this. Analysis of the light spectral composition directly at the human's eye is a necessary procedure. There are many variation factors that influence light entering the eye. Among the spectral properties of the light source (SPD) there are spectral transmittance of the glazing systems and the spectral reflectivity of the surrounding surfaces that influence the quality, or the light's spectral composition. In the terms of light quantity, the geometry of the internal space is the key factor, but we focused additionally on the presence and the properties of the human's body model.

Methods: A model of a typical office room (fig.1) was constructed and used in DAYSIM simulation software for an annual interior illumination estimation, which was further verified using the native RADIANCE algorithms. Typical illumination levels were calculated and compared in situations with and without the presence of a human's body model. Two control points were located directly in the position of the each pupil to assess the influence of the human's facial geometry and compared to those in the horizontal plane.

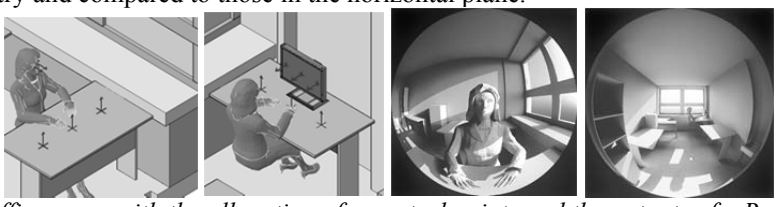

Fig. 1 Modeled office room with the allocation of a control points and the outputs of a Radiance simulation

Results: These model simulations show the need for a human body modeling in the process of daylight analysis and are prepared to be tested in real-life conditions. These initial findings demonstrate that pupil illuminance levels can be influenced with a presence of a human body, also as the facial geometry significantly influenced the light levels at each particular pupil (fig.2).

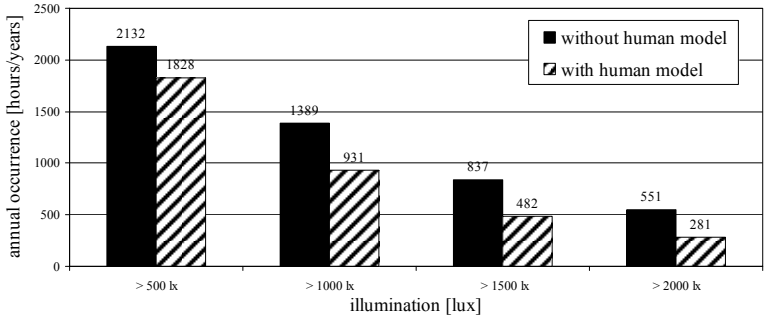

Fig. 2 Typical simulation output. Annual occurrence of designated light levels at subject's eye

Conclusions: This paper demonstrated how detailed simulation method may be utilized in prediction of the light as received by the human eye. Presented model is prepared to incorporate the spectral analysis of the light and to be assessed with prospective limits for proper circadian entrainment. That would help the light engineers and architects to design better and healthier internal environments it the term of light climate in the buildings.

Keywords: Circadian Rhythms, Light Environment, Annual Daylight Simulation

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RETINAL CIRCUITS UNDERLYING IMPAIRMENT OF LEARNING AND MOOD BY ABERANT LIGHT EXPOSURE

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Seasonal changes in day length, shift-work, and transmeridian travel cause sleep and circadian rhythm disruptions and also influence mood and cognitive functions. A common feature of these various conditions is a change in the timing or duration of light input. It was thought that mood and cognitive deficits in aberrant light conditions result from sleep and circadian rhythm disruptions, which are directly regulated by light. Here, we reveal a direct role for light in regulating mood-related behaviors and cognitive functions in mice, by using an aberrant light cycle that does not change sleep amount or abolish circadian rhythmicity. We show that this aberrant light cycle increases depression-like behaviors, elevates serum corticosterone levels, reduces hippocampal long-term potentiation, and impairs spatial and recognition learning. Administering antidepressant drugs reduces depression-like behavior and restores learning in mice exposed to this aberrant light cycle. Furthermore, animals lacking melanopsin-expressing retinal ganglion cells (RGCs), which show no circadian photoentrainment but maintain image formation, do not show mood and learning deficits under aberrant light conditions. These results reveal that aberrant light conditions, through melanopsin-expressing RGCs, directly influence mood and learning.

FIRST RESULTS OF AN INNOVATIVE LIGHT DEVICE USED AT NIGHT BY SAW MILLS WORKERS AND PATROL OFFICERS

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Objectives: For most night shift workers, light level in the workplace is insufficient to synchronize the biological clock which may further contribute to the decrease in vigilance commonly observed at night. In addition, morning light after the night shift tends to maintain the biological clock to a daytime schedule. It has been demonstrated that bright light (>1000 lux) at night combined with wearing dark goggles in the morning could represent an effective strategy to resynchronized the biological clock. This strategy is however hardly applicable in natural settings. Moreover, there are situations where bright light is not possible such as in the case of patrol officers on the night shift.

Methods: Considering that the biological clock appears more sensitive to the blue-green portion of the light spectrum (446 to 483 nm), in a first study we therefore investigated if the use of a commercial dim green light (Sunnex technologies) at night combined with wearing orange lens glasses (Chron-optic glasses) could help synchronize the biological clock of saw mills shift workers (N=4). Vigilance (VAS) was assessed at the beginning, middle and the end of the 8-hour shift. These evaluations were made while workers were on: 1) a daytime schedule, 2) a night schedule (baseline), 3) and a night schedule with experimental conditions (green light and orange lens glasses). During the experimental week, workers were exposed from Monday to Thursday to 200 lux of green light during a part of their night shift (00h00-05h00). In a second study, police officers (N=10) were all submitted to three conditions (no light called baseline, dim red light and dim blue light) while in a police car on the night shift. In the two light conditions (red and blue), officers had to wear the orange lens glasses starting at 5 AM or at sunrise. Light level in the car was about 1 lux. Vigilance was also assessed at night every two hours (KSS). In both studies, melatonin assessment was obtained on the night before and after 4 consecutive night shifts and all workers wore an actiwatch for sleep assessment.

Results: Saw mills workers saw their vigilance increased up to the daytime level at the end of the night shift week. A melatonin phase shift of 2 hours was observed and sleep during the daytime improved by 40 min in duration. For the police officers, preliminary analysis revealed that sleep during dayshifts (mean 5h50) was significantly shorter than during the night shifts (mean of 6h24) when taking into account naps, but not different when taking account only the main daytime sleep episode except for the blue light condition where officers tended to sleep 27 min longer. Mean phase shifts were 2h42±1h35 in baseline, 2h40± 1h50 in blue light, 2h01±0h17 in red light.

Conclusions: In saw mill workers, the strategy revealed to yield to some significant improvement in vigilance at night and daytime sleep. With the police officer, blue light appears to yield to more daytime sleep and to similar phase shift to those observed in baseline when workers are exposed to natural sunrise. Although preliminary, it would appear that dim light exposure at night, even in a car, could yield to some benefit to night workers, especially for day time sleep.

EFFECTS OF RED VISOR CAP IN PREVENTING LIGHT-INDUCED MELATONIN SUPRESSION DURING SIMULATED NIGHT WORK

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Objectives: Bright light at night improves alertness of night workers. Melatonin suppression induced by light at night is, however, reported to be a possible risk factor of breast cancer. Short-wavelength light has a strong impact on melatonin suppression. A red visor cap can cut the short-wavelength light from the upper visual field selectively with no adverse effects on visibility. The purpose of this study was to investigate the effects of a red visor cap on light-induced melatonin suppression, performance, and sleepiness during simulated night work.

Methods: Eleven healthy young male adults (mean age: 21.2 ± 0.9 yr) volunteered to participate in this study. On the first day, the subjects spent time in dim light (<15 lux) from 20:00 to 3:00 to measure baseline data of nocturnal salivary melatonin concentration. On the second day, the subjects were exposed to light for four hours from 23:00 to 3:00 with a non-visor cap (500 lx) and red visor cap (150~170 lx). Subjective sleepiness and performance of a psychomotor vigilance task (PVT) were also measured on the second day. To determine the effect of spectrum change by the red visor, a blue visor cap (blue visor) was also used. The illuminance level of the blue visor was the same as that of the red visor.

Results: Compared to salivary melatonin concentration under dim light, the decrease in melatonin concentration was significant in a non-visor cap condition but was not significant in a red visor condition. The percentages of melatonin suppression in the non-visor cap and red visor cap conditions at 4 hours after exposure to light were 52.6 ± 22.4% and 7.7 ± 3.3%, respectively. No significant melatonin suppression by light exposure was found in the red visor and blue visor conditions. The red visor cap had no adverse effect on performance of the PVT, brightness and visual comfort.

Conclusions: The use of a red visor cap is a potential countermeasure for preventing melatonin suppression by light with no adverse effect on performance and visibility of night workers.

Keywords: melatonin, spectrum of light, shift work, performance

ASSOCIATION BETWEEN MELANOPSIN GENE POLYMORPHISM AND PUPILLARY LIGHT RESPONSE IN A JAPANESE YOUNG POPULATION

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Objectives: Melanopsin-containing retinal ganglion cells (mRGCs) play an important role in non-image forming processing, such as circadian photoentrainment and pupillary light reflex. There are large inter-individual variations in light-induced melatonin suppression and pupillary light reflex (Higuchi et al., 2008). The melanopsin gene (OPN4) polymorphism may be a cause of the inter-individual variation in non-image forming effects of light. It has been reported that a missense variant (P10L) of the melanopsin gene is associated with prevalence of seasonal affective disorder (Roecklein et al., 2009). In the present study, the association between melanopsin gene polymorphism and pupillary light response was investigated in a Japanese population.

Methods: One hundred ninety-three healthy Japanese university students (mean age: 21.1 ± 1.8 yr) with normal color vision participated in this study. All participants gave written informed consent and the study was approved by the local research ethics committee. Genomic DNA was extracted from hair follicle cells. The target regions of OPN4 were rs2675703 (P10L) and rs1079610 (I394T). Pupil size was measured under dim light (15 lx) and bright light (1000 lx) conditions. Relative constriction rate of pupil size was calculated.

Results: Significant differences in pupil size under 15 lx light and relative constriction rate were found among the genotype at rs1079610 (I394T). Pupil size under dim light (15 lx) in subjects with the homozygous minor genotype (C/C, n=9) was significantly larger than that in subjects with the homozygous major genotype (T/T, n=130). Constriction rate of pupil size in subjects with C/C genotype was significantly larger than that in subjects with T/T genotype. There were no significant differences in pupillary light response among the genotype at rs2675703 (P10L).

Conclusions: The results suggest that melanopsin gene polymorphism is significantly associated with non-image forming effects of light.

Keywords: melanopsin gene polymorphism, Pupilally light response

THE COMPREHNSIVE SEASONAL ASSESSMENT FORM (CSAF) FOR ASSESSING SEVERITY OF SEASONAL SYMPTOMATOLOGY

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Objectives. Most self-report scales designed specifically for diagnosable and sub-threshold Seasonal Affective Disorder (SAD) focus on making a classification (for screening or diagnosis) rather than assessing symptom severity. In addition, commonly used SAD-specific scales of symptom severity (e.g., the Global Symptom Severity scale of the Seasonal Pattern Assessment Questionnaire) assess a narrow range of depressive symptomatology. The CSAF was developed to be a concise and comprehensive self-report assessment of the severity of SAD-specific depressive symptoms. In this poster, we describe the CSAF, report its reliability, and establish its factor structure.

Method. The CSAF consists of 14 items. The primary 12 symptom items scored on a 0-4 scale of intensity and two additional items that assess the level of distress and the impairment caused by seasonal symptoms. The version of the CSAF used in this poster assessed how participants "typically feel during the winter." However, instructions can be varied to assess seasonal symptoms in the past winter or past few weeks. Based on theoretical considerations (Young, et al., 2008), vegetative (6 items) and cognitive/affective (6 items) subscales, as well as overall severity (12-items), are scored. The validity of this scoring system was addressed in the factor analyses.

596 participants were recruited from three different populations: a) incoming undergraduate and graduate students at a Chicago university recruited for a student adjustment study (n = 181), b) residents of Chicago recruited for a of study people who experience seasonal vegetative changes (n = 285), and c) Dutch psychiatric patients being assessed and treated for SAD (n = 130). Together, participants represented a wide range of seasonal symptom severity, from none to diagnosable SAD. Internal consistency reliabilities were calculated for each factor for the entire sample and for each sample (a, b, and c) separately. Additionally, Confirmatory Factor Analysis (CFA) was used to test three possible factor structures.

Results. Across all participants, the internal consistency reliabilities for the total and two subscales were very high (α = .91 - .96). Internal consistency reliabilities for all factors, in each sample separately were also high (α = .74 - .93). The CFA tested three possible factor structures for the CSAF; a) a single factor, b) correlated vegetative and cognitive/affective factors, and c) a bi-factor structure with orthogonal cognitive/affective and vegetative factors as well as a general factor on which all items loaded. The factor structure that best fit the data was the bi-factor structure. Both absolute and comparative fit indices of the bi-factor model demonstrated incremental validity over the other two models.

Conclusions. The CSAF is a versatile, quickly administered, and easily scored measure of seasonal symptom severity. Results indicate that it has excellent reliability and its bi-factor structure supports the two symptom clusters proposed by the Dual Vulnerability Model (Young et al., 2008). The broad range of depressive symptomology assessed, the excellent psychometric properties, and the practicality of the CSAF make it a useful tool in assessing seasonal symptom severity in both clinical and non-clinical samples.

Keywords. Seasonal Affect Disorder, Psychometrics, Bi-factor Model, Dual Vulnerability Model, Scale Development

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CIRCADIAN LOCOMOTOR ACTIVITY OF GSK3β KNOCKOUT MICE

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Objectives : Glycogen synthase kinase-3 beta (GSK3β) is known to be a key component of multiple signalling pathways. In circadian physiology, GSK3β phosphorylates PER2 to promote is nuclear translocation. The inactivation of GSK3β induces a phase delay because of the late transfer of PER2 in the nucleus. Recent studies demonstrated that *Drosophila* circadian locomotor activity period was shortened by mammalian GSK3 and that lithium treated animals show an increased length of the circadian locomotor activity period. The aim of this experiment was to study the circadian locomotor activity of GSK3β knockout mice during a free-running period.

Methods: GSK3β knockout mice (wildtype (WT), n = 6; heterozygous (Het), n = 6) were housed individually to record their circadian wheel running activity. Mice were entrained to a 12h light/12h dark cycle (LD) for 14 days and then placed under constant darkness (DD) for 14 days to allow free-running.

Results: During the free-running period, circadian locomotor activity period of GSK3β Het mice was lengthened compared to WT mice (WT = 23.59 ± 0.16 h, Het = 23.91 ± 0.07 h; P = 0.0286). There was no significant difference between locomotor activity of WT and Het mice.

Conclusion: The present data suggest that GSK3β acts as a component of the mammalian circadian clock and plays an important role in regulating its period. Further investigations must be done to study the implication of GSK3α, the other isoform of GSK3 in the regulation of circadian locomotor activity.

Keywords: Circadian locomotor activity, GSK3β, mice, free-running

SAD-SPECIFIC EMOTIONAL RESPONSES TO LIGHT AND SEASONAL STIMULI: SURFACE ELECTROMYOGRAPHY, SKIN CONDUCTANCE, AND MOOD

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Objectives: Given the annual recurrence of seasonal affective disorder (SAD) in the fall or winter months, learned associations between depressive behavior and environmental stimuli (e.g. low light or winter weather) may play a role in SAD. The purpose of this study was to test whether light and season environmental cues elicit emotional responses that are distinct in SAD patients compared to never-depressed controls.

Methods: Participants were 24 currently depressed SAD patients, as determined by the Structured Clinical Interview for DSM-IV Axis I Disorders and the Structured Interview Guide for the Hamilton Depression Rating Scale-SAD Version, and 24 demographically-matched controls with no depression history and minimal seasonality, as assessed by the SCID and the Seasonal Pattern Assessment Questionnaire. Patients and controls were compared on emotional responses when viewing slides of six variations of the same five outdoor scenes, with each scene digitally photographed under two light intensity (i.e., clear, sunny vs. overcast sky) and three season (i.e., summer with green leaves, fall with autumn foliage, and winter with bare trees) conditions. Emotion measures included self-reported mood on the Profile of Mood States Depression-Dejection Subscale, surface facial electromyography (EMG) activity in the corrugator supercilii (brow-purse) and zygomaticus major (smile) muscle regions, and skin conductance. Data were analyzed using a series of 2 (Group: SAD, control) × 2 (Light: sunny, overcast) × 3 (Season: summer, fall, winter) mixed-design ANOVAs.

Results: In general, ANOVAs revealed significant Group × Light interactions. Relative to controls, SAD participants displayed more corrugator activity (p = .009), more self-reported depressed mood (p = .005), more frequent significant skin conductance responses (p = .047), and greater skin conductance response magnitude (p = .045) in response to overcast stimuli, regardless of the season represented. Conversely, SAD patients demonstrated less corrugator activity (p = .010), less self-reported depressed mood (p = .005), and lower skin conductance response magnitude (p = .047) in response to sunny scenes compared to controls, regardless of the season displayed.

Conclusions: Light intensity was a more salient cue than season in determining emotional reactions that distinguished SAD from control participants across measures of emotional valence (facial muscle patterning), emotional arousal (skin conductance), and self-reported affect. In general, SAD patients had more negative emotional reactions to overcast stimuli and less negative emotional reactions to sunny stimuli relative to controls. Extreme emotional responses to outdoor visual stimuli that vary in light intensity may be a correlate of winter depression. Future work should examine the potential onset or maintenance significance of extreme emotional reactivity to light-relevant stimuli in SAD. Future work should examine the additive effects of emotional associations and biological responses to low-light conditions.

Keywords: Seasonal affective disorder, Depression, Psychophysiology

THE RELATIONSHIP BETWEEN CHRONOTYPE, SLEEP, CHRONIC FATIGUE AND NATURAL LIGHT EXPOSURE IN YOUNG STUDENT WORKERS

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Objectives: Sleeping difficulties and chronic fatigue are predictors of occupational accidents in workers. Also, young adults are a population at increased risk of occupational accidents. Considering the sleep phase delay characteristic of adolescents and young adults and the putative effects of light exposure on circadian rhythm synchronization, it is relevant to assess the relationship between chronotype, sleep complaints, chronic fatigue, and environmental light exposure in students who work during school year.

Methods: Eighty-eight subjects (39 males), aged 19-21 years (7 high school, 49 college, 35 university) completed a morningness-eveningness questionnaire, the Pittsburgh Sleep Quality Index (PSQI), and the Occupational Fatigue Exhaustion/Recovery Scale (OFER-15). Subjects' light and sleep were monitored with an actigraph (Actiwatch-L, Minimitter) for two consecutive weeks during school year. Recorded light data were standardized in patterns of light exposure after wake time. ANOVAs and Chi-square were used for statistical comparisons.

Results: Evening-types (E-types, n=19) more often reported sleep complaints (PSQI>4) than intermediate-types (I-types, n=56), and I-types more often than morning-types (M-types, n=16) (83.3% vs 45.5% vs 18.8%, $p<0.001$). Also, chronotype differed with OFER chronic fatigue scores (41.2 vs 29.4 vs 26.0, $p<0.05$) but not with OFER acute fatigue scores. In addition, E-types were exposed to lower levels of light in terms of lux levels during the first half of the day, as compared to I-types and M-types ($p<0.05$).

Conclusions: Sleep complaints and fatigue were observed in E-types who also received a lower light exposure. Sleep parameters analysis are needed before establishing a link between light and sleep difficulties.

Keywords: Chronotype, sleep, student workers, chronic fatigue, natural light exposure

THE EFFECTS OF LOW INTENSITY MONOCHROMATIC BLUE LIGHT TREATMENT COMPARED TO STANDARD LIGHT TREATMENT IN SAD

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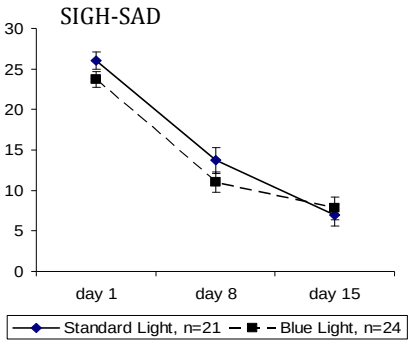
Objectives: Melanopsin expressing retinal ganglion cells (i-RGC), intrinsically sensitive to blue light, are directly connected to many central brain areas. Besides the suprachiasmatic nucleus (SCN), intrageniculate leaflet (IGL), and olivary pretectal nucleus (OPN) which are responsible for regulation of circadian rhythms and for light pupillary reflex, projections to lateral habenula (LHb), medial amygdaloid nucleus (MA), and ventrolateral preoptic area (VLPO), involved in regulation of mood, emotions, and sleep have been reported in rodents (Hattar et al. 2006). In humans it has been reported that SAD patients have different emotional processing than the healthy controls, and SAD patients presented increased activation of hypothalamic region under blue light exposure under emotional stimuli, the same region being less active under green light (Vanderwalle et al. 2010). In our previous studies, we compared the Seasonal Affective Disorder (SAD) treatment by standard 10000 lx full spectrum light treatment (SLT) with a treatment that used short-wavelength blue-enriched white light of same luminous intensity (10000lx) and of same melanopsin weighted photon density (750 lx) (Gordijn et. al, 2006, Meesters et al., 2011). All treatments were highly, and equally, effective despite spectral and intensity differences. First explanation for this lack of a difference is that the i-RGC receptors do not play a major role in the therapeutic effects of light. Alternatively, the effects may be (at least partly) mediated by the ganglion cells, which may already be saturated by the high illuminances used. The role of the i-RGC in the effects of light treatment of SAD has been further explored in a new randomised controlled study. The study compares the effects of low intensity monochromatic blue light (mBLT) against the effects of high intensity SLT.

Methods: In a 15 days design, 45 patients (36.7 y, sd 12.6) with major depression with a seasonal pattern (SAD) and a score of ≥ 18 on the SIGH-SAD (24 items) were offered light treatment for five days, on workdays between 7.30 and 8.30 a.m., in the winter of 2010/2011. Light treatment either consisted of 30 minutes SLT (5000ºK) with the EnergyLight (Philips, Consumer Lifestyle) with a vertical illuminance of 10 000 lux at eye position or monochromatic blue light (mBLT) with the goLite (Philips, Consumer Lifestyle) with a vertical illuminance of approx. 100 lux. All participants completed questionnaires concerning mood, sleepiness and sleep qualitiy on a daily basis starting at day 1 (3 days before treatment). SIGH-SAD ratings were obtained 3 times (on days 1, 8, and 15).

Results: On day 15, SIGH-SAD ratings were significantly reduced compared to day 1 (SLT 73.8% and Mblt 68.0%). Between the conditions, no statistically significant differences were found. In the SLT condition were 86 % responders (SIGH-SAD reduction ≥ 50%), in the mBLT condition 67%. In the SLT condition 67 % recovered (SIGH-SAD ≥50% and final score ≤ 8) and in the mBLT condition 63 %. These differences were not statistically significant.



Conclusion: The two treatment conditions were highly effective. The therapeutic effects of low intensity monochromatic blue light were comparable to those of the standard light treatment. Even with an intensity of 100 lux monochromatic blue light, it is still possible that saturation effects play a role. Further research is necessary to find the optimal intensity of blue light in treating SAD.

Key Words: SAD, Light treatment, monochromatic blue light,

Funding Support: Philips Consumer Lifestyle, Amsterdam, The Netherlands

References: Gordijn et al. (2006): SLTBR abstracts 18: 6; Meesters et al. (2011): BMC Psychiatry 11:17; Hattar et al. (2006) J. Comp. Neurol. 497:326-349; Vandewalle et al. (2010) Abstracts of ESRS congress.

DO CANCER RELATED SYMPTOMS FOLLOW A SEASONAL PATTERN?

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Objectives: Symptoms of fatigue, insomnia, and depression are frequently encountered in patients with cancer. There are some indications that these symptoms could be related, at least in part, to disruption of circadian rhythms and their determinants. For instance, some authors showed a link between fatigue and a lower exposure to natural day light (Liu et al., Support Care Cancer. 13: 1010-1017, 2005). It would therefore appear that the severity of symptoms experienced by cancer patients are influenced by their degree of exposure to light although this hypothesis needs further investigation. The first objective of this study conducted in a large sample of patients with cancer was to: (1) evaluate the relationship between seasons and symptoms of fatigue, insomnia and depression. It was expected that patients would experience significantly greater symptoms of fatigue, insomnia, and depression during the winter period as compared to the summer period, and that these symptoms would be at an intermediate level in fall and spring. The second objective was: (2) to evaluate the relationship between illumination (number of hours between sunrise and sunset) and symptoms of fatigue, insomnia, and depression. A significant relationship was expected between a lower average number of hours of illumination and an increased severity of symptoms of fatigue, insomnia and depression. Finally, the third objective of this study was: (3) to evaluate the moderating effect of cancer treatments in the relationship between the seasons and symptoms, and between the hours of illumination and these symptoms.

Methods: As part of a larger population-based longitudinal study, 991 cancer patients completed various self-report scales on six occasions throughout 18 months following the initial evaluation. These evaluations included validated measures of insomnia (*Insomnia Severity Index*), depressive symptoms (depressive subscale of the *Hospital Anxiety and Depression Scale*), and of fatigue (*Multidimensional Fatigue Inventory*).The average number of hours of illumination of the 14 days preceding completion of questionnaires was also used. To evaluate the effect of seasons, the participants were divided into four groups for each measurement time according to the season during which they completed the questionnaires.

Results: The ANOVAs performed showed no significant difference across seasons on fatigue, F (3.950) = 1.45, p = .23, η^2 = .005, insomnia, F (3.949) = 1.27, p = .28, η^2 = .004, and depression, F (3.950) = 2.1, p = .10, η^2 = .007. No significant correlation was observed between hours of illumination and fatigue, r (954) = -. 02, p = .59, insomnia, r (953) = .02, p = .56, and depression scores, r (954) = -. 01, p = .70. Finally, none of the three performed ANCOVAs revealed a significant interaction between season and cancer treatments. Moreover, the results obtained on the multivariate linear regression (performed to evaluate treatment effect on the relationship between hours of illumination and symptoms) were not significant.

Conclusions: This study represents an initial exploration of the effect of seasons and sunlight on fatigue, insomnia and depression symptoms in the context of cancer. The absence of significant effect for the three objectives of the study suggests that cancer-related symptoms are not influenced by seasons and natural daylight. However, future research will be needed to investigate these questions by measuring patients' actual exposure to natural daylight.

Keywords: Cancer, Insomnia, Depression, Fatigue, Light

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EFFECTS OF EXTENDED SLEEP OPPORTUNITIES AND ACUTE SLEEP DEPRIVATION ON PSYCHOMOTOR PERFORMANCE IN SHORT AND LONG SLEEPERS: EVIDENCE FOR INDIVIDUAL DIFFERENCES IN TOLERANCE TO SLEEP PRESSURE

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Objectives: Habitual short sleepers live under and appear to tolerate higher homeostatic sleep pressure than long sleepers. It is unknown whether this is reflected in measures of performance. This study investigated whether there are trait-like differences in cognitive performance between short sleepers and long sleepers when exposed to different levels of homeostatic sleep pressure.

Methods: Participants consisted of young (18-30 y) healthy short sleepers (n = 7, habitual bedrest < 6.5 h) and long sleepers (n = 11, habitual bedrest > 9 h) who completed a 28-day inpatient protocol. After four days on their habitual sleep (HS), subjects were given extended (12-h) sleep (ES) opportunities for 20 days, a 36-h sleep deprivation (SD) interval and two recovery nights. The Psychomotor Vigilance Test (PVT) was administrated several times throughout their wake episodes. PVT lapses (reaction times, RT > 500 ms), median speed (1/RT) and the interpercentile range (IPRange, difference between the 90^{th} and 10^{th} percentile, 1/RT) were analyzed with a mixed model ANOVA with factors Group and Condition (HS: Days 2-4 vs. ES: Days 21-23) and subjects as a random intercept. For the SD interval, factors Group and Time awake were used.

Results: In the HS condition, TST was less for the short sleepers (mean±SE: 342±10 min) than for the long sleepers (535±8 min). During the ES condition, TST increased in the short sleepers (533±18 min, $p < 0.001$) but was unaffected in the long sleepers (530±16 min). In the HS condition, there were no differences in PVT performance between short and long sleepers. When given extended sleep opportunities, PVT performance improved in the short sleepers (ES vs. HS: lapses 1.0±0.5 vs. 2.4±0.5; median speed 4.09±0.23 vs. 3.95±0.17 s^{-1}; IPRange 1.46±0.12 vs. 1.86±0.12 s^{-1}, $p < 0.001$) but not in the long sleepers. ANOVA on PVT performance during SD revealed that the short sleepers showed fewer lapses (Group x Time awake, $p < 0.001$) and a more stable response pattern (IPRange: Group, $p < 0.04$) than the long sleepers, particularly in the latter part of the SD.

Conclusion: Individual differences between short and long sleepers in sleep duration may reflect a trait-like difference in tolerance to homeostatic sleep pressure rather than in the capacity to sleep. Short sleepers seem to possess a 'cognitive reserve' that becomes apparent when exposed to low and high levels of homeostatic sleep pressure.

Keywords: Circadian Rhythms, Homeostasis, Sleep Deprivation, Individual Differences, Vigilance.

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TIME-OF-DAY AND LIGHT MODIFY MARKERS OF HOMEOSTATIC SLEEP PRESSURE IN MICE

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Introduction: Sleep homeostasis refers to the increase of a pressure for sleep during wakefulness and its dissipation during sleep. The dynamics of this process is studied through EEG markers measured during non-rapid eye movement sleep (delta power: 1-4Hz) and wakefulness (theta power: 6-9Hz). Data suggest that these hallmarks are modulated by circadian time and light. We thus assessed the effects of time-of-day and acute light exposure on the dynamics of sleep pressure markers in mice.

Methods: Male C57BL/6J mice, implanted with EEG/EMG electrodes, were submitted to a 6h sleep deprivation (SD) by gentle handling starting at four different times of day: ZT0, ZT6, ZT12, or ZT18 (ZT0=Zeitgeber time 0: lights on). A week later, animals were submitted to the same SD but lights were turned off at the beginning of SD until the end of recording. Simulations were used to predict expected levels of delta power.

Results: We observed that the rebound in delta power was higher after the ZT6 and ZT12 SD than after the ZT0 SD. When the SD was repeated in the dark, the delta rebound was reduced for both the ZT6 and ZT12 SD. The increase in theta power during SD was lower for the ZT12 and ZT18 SD than for the ZT0 SD, but only the increase during ZT0 SD appears to be blunted in the dark condition. Importantly, simulations showed that the level of delta power during the first 10 min of recovery sleep could not be adequately predicted for the ZT6 SD but only when SD was performed in the light.

Conclusion: Our data suggest that sleep pressure dynamics depends both on time-of-day and environmental light. Further analyses are required to allow a precise estimation of the effect of these variables on sleep pressure markers.

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LIGHT EXPOSURE AND REST-ACTIVITY RHYTHMS IN OLDER PEOPLE: EFFECT OF LIGHT SUPPLEMENTATION IN COMMUNAL CARE HOME ROOMS

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Objectives: With advancing age ocular lens density changes reduce the transmission of short wavelength blue light. This and age-related alterations to the circadian timing system and the homeostatic regulation of the sleep-wake cycle may explain the increased prevalence of sleep problems in older people. Most light environments in homes for older people (care homes) are not adapted for the increased light requirements of older individuals. In addition with decreased mobility, residents may spend very little time outdoors in natural light. The aim of this study was to investigate the effect of a novel lighting condition (blue-enriched white light; 17000 K, 1000 lux) compared to a control white light (4000 K, 200 lux) and the care homes' original light condition (<100 lux measured at night) on actigraphic rest-activity rhythms and individual light exposure in care home residents. The hypothesis to be tested was that differences will be found between different light conditions for time spent in light above set light threshold levels (lux) and parametric circadian rhythm rest-activity parameters.

Methods: The 12-week study was a randomised, crossover design conducted in seven care homes from September to April in 2008/2009 and 2009/2010. After a baseline week of original care home lighting, each light intervention period (4000 K or 17000 K) lasted 4 weeks, with a 3-week washout period (WO) in between (original care home lighting). The experimental lights were installed in selected communal rooms regularly used by the participants. The environmental light conditions in the communal rooms were continuously recorded with lux meters (Hobos, Tempcon instrumentation Ltd, UK). Individual light exposure levels and activity data were recorded constantly using wrist worn Actiwatch activity and light monitors (Cambridge Neurotechnology Ltd) in recruited residents (MMSE score range 6 – 29, light data set n = 44, 4 males 40 females, 84 ± 8 years; activity data set n = 41, 5 males 36 females, 85 ± 8 years, mean ± SD). Using Actiwatch sleep analysis 5 software, time spent per day above a light threshold of 100, 500, 1000 and 2000 lux were determined for each subject in each light condition. Parametric cosinor analysis was used to quantify each participant's 24-hour rest-activity rhythm during each light condition (mesor, amplitude and acrophase). The effect of light condition on individual light exposure and rest-activity rhythms were compared using non-parametric and parametric ANOVA were appropriate.

Results: The time that participants spent in light levels >100, >500 and >1000 lux was significantly higher ($p<0.001$) during the 17000 K light condition (170 ± 19, 57 ± 10, 23 ± 5 mins/day mean ± SEM) compared to WO (87 ± 14, 16 ± 4, 6 ± 2) and the 4000 K light condition (107 ± 15 (not significant), 15 ± 4, 6 ± 2). There was no significant difference between light conditions for time spent in light levels >2000 lux (4000 K, 3 ± 1; WO, 2 ± 1; 17000 K, 5 ± 2 mins/day). Parametric cosinor analysis of all participants (mean ± SEM arbitrary units for mesor and amplitude and decimal time in hours for acrophase) revealed no significant differences between light conditions for mesor (4000 K, 4344 ± 420; WO, 4088 ± 381; 17000 K, 4280 ± 407), amplitude (4000 K, 2797 ± 316; WO, 2688 ± 313; 17000 K, 2819 ± 309) and acrophase (4000 K, 14.75 ± 0.44 h; WO, 14.81 ± 0.39 h; 17000 K, 14.68 ± 0.39 h).

Conclusions: The findings indicate that by increasing light levels in selected communal areas the amount of time that care home residents spent in bright light was increased 2-4 fold. The increased light exposure, however, was not sufficient to affect the circadian rhythm of rest-activity significantly. As this was not a homogenous group of individuals, further investigation is required to understand possible effects of other variables such as cognitive ability, visual acuity, mobility and individual light exposure times on rest-activity rhythms.

Keywords: Light, Ageing, Circadian Rhythms, Sleep Disorders

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EFFECTS OF PRIOR DAYTIME LIGHT EXPOSURE ON COGNITIVE PERFORMANCE, SUBJECTIVE SLEEPINESS AND HORMONAL SECRETION IN THE EVENING

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Objectives: In humans, environmental light is crucial to entrain the endogenous circadian pacemaker to the 24-h light-dark cycle. Thereby, light intensity, timing, exposure duration as well as spectral composition are important. We studied whether exposure to two different light conditions during the afternoon, similar to real life office situations, had an acute impact on hormonal secretion, subjective sleepiness and cognitive performance in the early evening hours.

Methods: Twenty-nine young subjects (12f, 17m) came twice and spent 8 hours (12:00-20:00) in our laboratory, where they were exposed for 6h to either artificial light (AL; 174.3±4.6 lx; mean ±SD in a vertical direction) or to mainly daylight (DL; 964 ± 462.6 lx mean ±SD in a vertical direction), in a cross-over study design. In the early evening between 18:00 and 20:00 we assessed their salivary melatonin and cortisol, subjective sleepiness and cognitive performance (n-back test) under dim light conditions (<5 lx).

Results: On average, we found no difference of prior light exposure on hormonal secretion and subjective sleepiness in the early evening hours. By comparing subjective sleepiness in the evening to mean assessments in the afternoon, subjects felt significantly more alert at the beginning of the evening after the DL condition, and they became significantly sleepier at the end of the evening after the AL condition ($p<0.05$). For cognitive performance we found a significant interaction between light conditions, mental load (2-back or 3-back task) and the order of light administration ($p<0.05$). On their first evening, subjects performed with similar accuracy after both light conditions (2-back task: $p=0.07$ and 3-back task: $p>0.1$), but on their second evening, that half of the subjects who had been exposed to DL performed significantly more accurately in both n-back versions and had fewer false alarms after the 2-back task when compared to to the AL group ($p<0.05$).

Conclusion: Taken together, even short-term lighting conditions during the afternoon can impact on cognitive task performance in the evening. This rapid effect was only distinguishable on the second day of training, i.e. when a difficult task had been sufficiently practiced.

Keywords: Office Lighting, Executive Functions, Cortisol, Subjective Alertness

Funding Support: Velux Foundation (Switzerland), Swiss Federal Office for Energy

COMPLEXITY AND REGULARITY OF CIRCADIAN MOTORIC ACTIVITY IN INDIVIDUALS WITH DEMENTIA AND AGGRESSION

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Objectives: When considering the multiple behavioural and psychological symptoms associated with the development of dementia, aggressive behaviour (AB) is decidedly one of the most disconcerting and difficult to manage challenges. While some literature points to unmet needs as the etiology for aggressive behaviour, there is evidence suggesting a temporal pattern for the symptom of aggression in dementia, which in turn may reflect a link to circadian dysfunction. The literature supports the fact that human motor control systems orchestrate regulate the rhythm and complexity of multiple physiologically interdependent temporally based circadian patterns. In dementia, it has been shown that the inability to maintain stable circadian rest-activity rhythmicity contributes to sleep pattern disruptions, and behavioural disturbances, such as aggression, and concomitant cognitive dysfunction
The importance of physiologic plasticity has been demonstrated in numerous studies, and has been exemplified by studies showing reduced complexity in terms of approximate entropy (ApEn) and fractal control in terms of fractal dimension (FD) with aging and under pathological conditions. The predictive value of reduced fractal complexity of cardiac measures of control with decreased survival rates has been demonstrated, and measures of ApEn have been used to quantify human mood over time. Despite the clear importance of fractal phenomena and the relationship of decreasing levels of approximate entropy with pathology, to date, no underlying mechanism has been established for control of these parameters in any neural or physiological system. While recent studies indicate that the endogenous circadian system is critically involved in the fractal control of motor activity at multiple time scales, little is known about fractal control and complexity or measures of approximate entropy in individuals with dementia with respect to circadian rest-activity patterns as they relate to behaviours, such as aggression, in individuals with dementia. The aim of the current study is to identify potential importance of nonlinear indices and complexity biomarkers in individuals with dementia and aggressive behaviours through assessing changes in regulatory function of the circadian rest-activity system at the level of the suprachiasmatic nucleus (SCN) utilizing measures of approximate entropy (ApEn) and fractal dimension (FD).

Methods: Motor activity data were collected via actigraphy in one minute epochs over 14 consecutive days from a sample (n=96) of demented participants living in the nursing home with (n=43) and without (n=53) aggression. Sampling rate for data collection was one per minute, providing 1440 data points available for each day and night. Data was initially analyzed as a single segment to examine fractal complexity and regularity using FD and ApEn of the time series, then values calculated separately for day and night. Subsequent data analysis was specific to the aims and working hypotheses of the study. Descriptive statistics were utilized to determine frequency distributions, percentage distributions, and means and standard deviations. Day-night differences were examined at several levels using one way ANOVA with 2 groups of subjects for the data and 2-way ANOVA with repeated measures ANOVA for day-night records of actigraphy. Appropriate post-hoc tests were utilized to further examine the differences between the two groups.

Results: Significant differences were observed between aggressive and control groups with respect to overall ApEn, and with respect to ApEn and FD at night, and between day and night within the aggressors. The aggressors exhibited significantly lower ApEn and FD levels than controls, especially at night.

Conclusions: Measures of ApEn and FD are methods sensitive to detecting and characterizing discrete changes in central motoric control and temporality of behaviours in dementia. Findings from this study have potential to identify nonlinear indices and complexity biomarkers in dementia, important for developing and testing the efficacy of interventions aimed at ameliorating circadian based symptoms of dementia.

Keywords: Approximate entropy, Fractal, Dementia, Aggression, Circadian, Central motoric control

MELANOPSIN GENE VARIATIONS INTERACT WITH SEASON TO PREDICT SLEEP TIMING AND CHRONOTYPE

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Objectives: A sequence variation in the melanopsin gene (OPN4) has been reported to increase risk of seasonal affective disorder (SAD) in some individuals. The present study tests associations between OPN4 gene polymorphisms, self-reported sleep variables and seasonality, while controlling for confounding factors in a community sample.

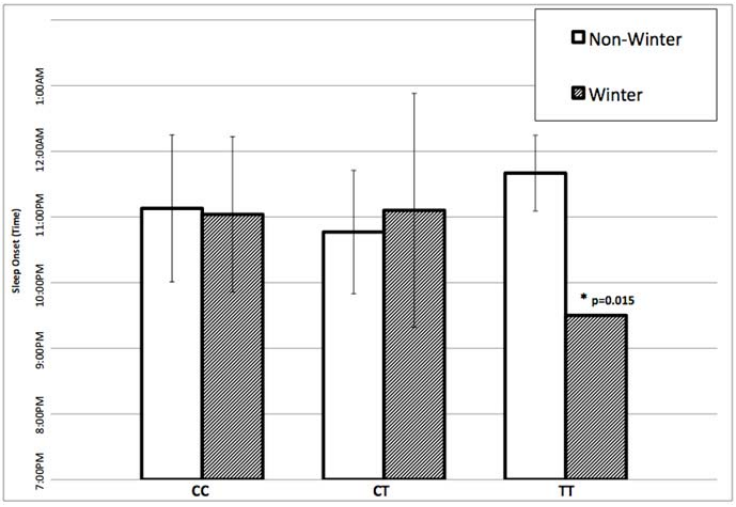
Methods: Community residents in the Adult Health and Behavior Project registry of non-Hispanic Caucasian ancestry (age 30-54 years) were genotyped for OPN4 gene polymorphisms using fluorescence polarization. Participants (N = 270), completed the Pittsburgh Sleep Quality Index (PSQI), and the Morningness Eveningness Quesionnaire (MEQ). Depression was measured with the Beck Depression Inventory 2nd Edition, and the Center for Epidemiological Studes - Depression scale, and included as covariates in all analyses, along with age and gender

Results: There was a significant interaction between P10L polymorphism genotype and time of self-reported sleep onset, $F(2, 262) = 5.249$, $p < .01$, $\eta^2 = .040$. Individuals with the TT genotype reported going to bed earlier when assessed in winter compared to non-winter months, whereas sleep times did not differ across seasons in the other two groups (*Figure 1*). MEQ total was associated with a significant T394I by season interaction, $F(1, 260) = 4.187$, $p < .05$, $\eta^2 = .017$. Specifically, individuals with two copies of the minor allele reported higher MES scores (morning types) when assessed in winter compared to non-winter.

Conclusions: These results suggest that OPN4 variations may interact with season to influence sleep timing and mood among individuals in the community. A better understanding of the role of melanopsin in mediating non-visual light responses may improve our understanding of a broad range of behavioral, circadian, sleep and mood responses to light.

Keywords: Psychopathology, Mood Disorders, Sleep, Melanopsin, OPN4

Figure 1. Interaction between P10L genotype and season of assessment predicting sleep onset times.



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THE UNIVERSITY OF VERMONT STUDY OF COGNITIVE-BEHAVIORAL THERAPY VS. LIGHT THERAPY FOR PREVENTING SAD RECURRENCE: DESIGN AND METHODS

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Objectives: The central public health challenge in managing seasonal affective disorder (SAD) is prevention of depressive episode recurrence over subsequent winter seasons. Bright light therapy is the established and best available acute SAD treatment. However, long-term compliance with clinical practice guidelines recommending daily light therapy from onset of first symptom through spontaneous springtime remission during every fall/winter season is questionable. Therefore, alternative treatments are clearly needed. An ideal alternative to light therapy would be time-limited (i.e., acute treatment completed in a discrete period vs. daily treatment every fall/winter indefinitely) and have effects that endure beyond the cessation of acute treatment to prevent the annual recurrence of these disabling symptoms. In prior studies, we found that a novel, SAD-tailored cognitive-behavioral therapy (CBT), alone or combined with light therapy, may be as efficacious as light therapy in reducing acute SAD symptoms (Rohan et al., J. Consult. Clin. Psychol. 75:489-500, 2007) and may have superior outcomes to initial treatment with solo light therapy during the subsequent winter (i.e., the winter season following the initial winter of acute treatment; Rohan et al., Behav. Ther. 40: 225-238, 2009).

Methods: The study design and methods for our R01-level clinical trial (underway since 2008) will be presented. The study is a larger, more definitive test of the efficacy of our CBT for SAD intervention against light therapy in a sufficiently powered, randomized head-to-head comparison on outcomes during the next winter. Community adults (N = 160) who meet criteria for Major Depression, Recurrent, with Seasonal Pattern on the SCID and criteria for a current SAD episode on the Structured Interview Guide for the Hamilton Rating Scale for Depression—SAD Version (SIGH-SAD) are randomly assigned to one of two 6-week treatments in the winter: CBT or light therapy. CBT is conducted in a small group format for 1.5-h sessions twice a week (12 sessions) and follows our manual. Light therapy is initiated using a 10,000-lux full-spectrum light box at home for 30-minutes each morning upon waking. Subsequently, the light therapy duration is individually adjusted weekly to maximize response. Light therapy participants can elect to borrow a light box for use the following winter. Follow-ups are conducted in the summer and annually in January or February of the next two winter seasons with the SIGH-SAD, the Beck Depression Inventory-Second Edition (BDI-II), and the Longitudinal Interval Follow-up Evaluation (LIFE) administered each time. The primary analysis will be an intent-to-treat (ITT) analysis of all randomized participants based on multiple imputation (MI) of missing scores. Outcomes will include recurrence (primary outcome) and remission status and continuous depression scores.
This study goes beyond our pilot studies in four important ways: (1) This study augments the generalizability of our prior studies by using a patient sample that is more representative of the SAD population (i.e., less restrictive inclusion/exclusion criteria to allow for comorbid Axis I disorders and stable antidepressant medications) and by demonstrating the feasibility of training community therapists to facilitate the CBT intervention. (2) We prospectively track depression recurrences and potential intervening variables that could affect outcome (e.g., retreatment, summer remission status) in the interim between treatment endpoint and the following winter. (3) This study includes a second annual winter follow-up to obtain preliminary data on the comparative effects of CBT vs. light therapy two winter seasons after initial study treatment. (4) This study will examine how potential modifiers influence the effects of CBT vs. LT, including demographic variables; baseline characteristics (e.g., depression severity, comorbidity, medications); and complete or incomplete summer remission status in the interim. In addition to treatment efficacy, we are also collecting data on potential mediators of treatment effects that may highlight modality-specific mechanisms behind CBT's vs. light therapy's acute antidepressant effects and on the cost-effectiveness and cost-benefit for the two treatments.

Conclusions: The study is progressing on target with 131 patients randomized to date. If successful, this work will develop a novel treatment with important public health implications for long-term management of winter depression.

Keywords: Seasonal Affective Disorder, Clinical Trial, Cognitive-Behavioral Therapy, Light Therapy

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A COMPARISON OF SUBJECTIVE AND POLYSOMNOGRAPHIC SLEEP ONSET LATENCIES ACROSS CIRCADIAN AND MENSTRUAL PHASES

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Objectives: A circadian variation of sleep propensity has been described using forced desynchrony and ultradian sleep-wake cycle (USW) procedures. Prior studies have documented discrepancies between subjective assessments of sleep onset latency (SOL) and objective SOL based on polysomnographic (PSG) criteria during nocturnal sleep episodes. To our knowledge, no study has investigated if these differences persist when sleep episodes are distributed throughout the 24-hour day. Our aim was to compare subjective and PSG-based objective measures of SOL across circadian phase, and to determine if these differences are modulated by the menstrual cycle.

Methods: Eight women with regular menstrual cycles participated in an USW procedure designed to assess the circadian variation of sleep during the mid-follicular (MF) and mid-luteal (ML) phases of the menstrual cycle. After a 3-week stabilization of the sleep-wake and light-dark cycles to an 8-hr sleep/darkness period, participants entered the laboratory for a nocturnal PSG sleep recording, followed by a 72-hour USW in time isolation (36 cycles of 60-minute wake episodes in constant conditions alternating with 60-minute naps) at MF and ML. PSG sleep was recorded during all naps throughout the USW, and scored in 30-sec epochs according to standard criteria. PSG-based SOL (P-SOL) was defined as the time from lights-out to the first appearance of at least 2 epochs of stage 1 sleep, or the first appearance of any deeper sleep stage. Subjective SOL (S-SOL) was assessed upon awakening from each nap by asking participants to report how long they thought it took them to fall asleep. The difference between PSG-based and subjective estimates (P-SOL minus S-SOL) was calculated for each nap episode.

Results: Two-way ANOVA (factors: menstrual phase x circadian phase) revealed a significant circadian variation of both P-SOL ($F_{11,77}$=19.86, $p<0.01$) and S-SOL ($F_{11,77}$=11.46, $p<0.01$), though menstrual phase differences were not observed for either measure. In both cases, SOLs were lowest during times spanning the habitual nocturnal sleep episode. The calculated difference between P-SOL and S-SOL showed a trend for a significant circadian variation ($F_{11,77}$=1.84, p=0.0611), but no menstrual phase differences. After pooling MF and ML data to compare overall P-SOL and S-SOL curves, a two-way ANOVA (factors: assessment type [i.e. P-SOL or S-SOL] x circadian phase) revealed a significant interaction between assessment type and circadian phase ($F_{11,77}$=3.25, p=0.0005). Simple main effects tests illustrated significantly increased P-SOL compared to S-SOL at circadian phase 120°, 150°, 180°, 240° and 270° (i.e. throughout most of the habitual daytime). The calculated difference between P-SOL and S-SOL after pooling MF and ML data showed a significant circadian variation ($F_{11,165}$=2.45, p=0.0073).

Conclusion:
This study demonstrated that, similar to nocturnal sleep periods, discrepancies exist between subjective and PSG-based objective estimates of SOL throughout the circadian cycle, and that these differences are not modulated as a function of the menstrual cycle. Interestingly, whereas prior work focusing on nocturnal sleep shows that participants tend to subjectively overestimate SOL, our findings illustrate that participants were more likely to underestimate SOL during naps when assessed throughout the circadian cycle. These underestimations were limited to the daytime, and did not appear during naps spanning the habitual nocturnal sleep period (i.e. when objective and subjective SOLs were ~10 minutes). These results may be useful in the assessment and treatment of sleep complaints associated with circadian rhythm sleep disorders, or in jet-lag and shift working populations.

Keywords: Circadian Rhythms, Sleep, Menstrual Cycle

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DAILY LIGHT EXPOSURE AND FEELINGS OF ALERTNESS AND VITALITY: INTERMEDIATE RESULTS OF A LONGITUDINAL STUDY

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Objectives: No two persons have the same daily light exposure. Among many factors, research has shown that light exposure is dependent on whether a person is indoors or outdoors, on time of day, season, and age. Daily light exposure is important for our biological rhythm. In addition, Hubalek and colleagues (Hubalek et al., Lighting Res. Technol, 42, 43-50, 2010) showed that daily light exposure had a significant and positive effect on subjective sleep quality, but not on self-reported pleasure and arousal at the end of day. Although these researchers did not find an effect on end of day feelings of pleasure and arousal, other studies suggest that light exposure can have an influence on feelings of alertness, vitality and psychological distress during daytime (Partonen & Lönnqvist, J Affect Disor, 57, 55–61, 2000; Phipps-Nelson et al., Sleep, 26, 695-700, 2003; Rüger et al., Am J Physiol Regul Integr Comp Physiol, 290, 1413-1420, 2005). In addition, research has shown that light treatment can be beneficial for people suffering from mood disorders, such as seasonal affective disorder (SAD), suggesting that light exposure can have an influence on mood. Two experience sampling studies by Ryan and colleagues (Ryan et al., J. Environ. Psychol*., 30,* 159–168, 2010) showed that being outdoors is related to subjective vitality. Results showed that participants who were outside for more than 20 minutes per day experienced greater vitality for that day, even when controlled for physical activity and social interaction. Presence in nature (partially) mediated the effect of being outdoors on self-reported vitality. Ryan et al. (2010) suggested that, in addition to nature, the presence of sunlight may have also induced experiences of vitality. In the current longitudinal field study, we recorded the amount of light falling on the eye during regular workdays, to gain insight into interpersonal differences and dynamics in light exposure throughout the day. Moreover, we investigated the relationships between light exposure during the day, sleep quality, and subjective alertness, vitality and tension, both on an hourly and daily basis, controlling for activities, contexts and person characteristics.

Method: The method employed in this study was experience sampling, combined with continuous measurement of light exposure during three consecutive days from 8 am to 8 pm. Light exposure was measured continuously with a Daysimeter, worn at eye level. It records both photopic light intensity and intensity in the biologically effective range. Subjective self-reports were administered every hour between 8 am and 8 pm as feelings of alertness and mood seem to show diurnal variations. These measures included subjective feelings of vitality, alertness and tension, and the type of activity and location of the participant. In addition, participants reported their subjective sleep quality every morning and filled in questions concerning duration of being outdoors, duration of physical activity, time spent on social interaction and coffee consumption in a diary every evening before going to sleep.

Results: This study started in October 2010 and will run a full year, until October 2011. At the conference we would present the data collected until the end of May. Up to two persons participate each week, rendering data on a wide range of light exposures, activities, and settings. The results of these participants are analyzed using Hierarchical Linear Models with time of day and light exposure as fixed factors. Data collection and analyses are still ongoing, but the first results (N=29, 15 male and 14 female, at the time of submission of this abstract) indicate that feelings of vitality and alertness are related to time of day. In addition, the preliminary results show a significant positive relation between hourly light exposure, in terms of both photopic intensity and of the intensity in the biological relevant spectrum, and alertness and mood.

Conclusion: The first results suggest that there is a relation between light exposure and feelings of alertness and mood throughout the day. In addition, time of day seems to play an important role. Additional analyses will be performed to control these relations for personal characteristics, activities and contexts. In addition, the relation between light exposure and sleep quality will be assessed. The results of these additional analyses will be presented at the conference.

Keywords: Light exposure, Mood, Alertness, Biological rhythm, Human.

THE ROLE OF THE DEUBIQUITINASE USP2 IN CIRCADIAN RHYTHMS AND BEHAVIOUR

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Objectives: Ubiquitination has been proposed to have a role in the central nervous system (CNS) and neurodegenerative disease, though the expression of genes involved in this process has not been well characterized in the brain. It is known that ubiquitin ligases are involved in the regulation of circadian rhythms, endogenous cycles of 24h generated by a master clock located in the suprachiasmatic nucleus of the hypothalamus and clocks located in other tissues. However, it remains unknown whether deubiquitinases, which perform the reverse reaction, are involved in CNS function or the circadian clock. USP2 is a deubiquitinase that was found to cycle in most tissues, a rare property shared mainly by clock genes. Our aim is to study the role of USP2 in the circadian clock and in other brain functions. Specifically:
1) To determine the role of USP2 in locomotor activity rhythms
2) To determine the role of USP2 in other behaviours
3) To assess *Usp2* expression in the brain

Methods and results:
1) Through assessment of locomotor activity in running wheels, we found that *Usp2* knockout mice have a longer free-running period than WT littermates. Additionally, we identified an alteration of light response by the clock of *Usp2* knockout mice, as manifested by changes in the response to light pulses administered at different phases of the circadian cycle, and a modified ability to adapt to 6h shifts in the light-dark cycle.
2) We have assessed the behaviour of *Usp2* knockout mice on a battery of neurophenotyping tests. *Usp2* knockout mice show no difference in locomotor activity, motor coordination, spatial memory and depression-like behaviour, but present a decreased anxiety-like phenotype compared to WT mice in the elevated plus maze and the Thatcher-Britton test.
3) Using *in situ* hybridization, we have identified *Usp2* expression in the brain, supporting the idea that USP2 participates in various brain functions.

Conclusions: Our studies indicate that the deubiquitinase USP2 plays an important role in the suprachiasmatic nucleus clock, in addition to being involved in the control of complex behaviours in mice. Thus, these findings could have important implications for neurodegenerative diseases and psychiatric disorders.

Keywords: Ubiquitination, Suprachiasmatic nucleus, Clock genes, Mice, Neurophenotyping

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EFFECTS OF SPECTRAL MODULATION ON ACUTE ENDOCRINE, MOLECULAR AND BEHAVIOURAL RESPONSES TO NOCTURNAL LIGHT

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The human eye serves distinctly dual roles in image forming (IF) and non-image forming (NIF) responses when exposed to light. While IF responses mediate vision, the NIF responses affect various molecular, neuroendocrine and neurobehavioral variables. NIF responses can have acute and circadian phase-shifting effects on physiological variables. Irregular light-dark cycles are common in shift work and is associated with sleep disruption and impaired performance. Both the acute and phase-shifting effects induced by photic stimuli demonstrate short-wavelength sensitivity peaking around 450-480 nm (blue-light). We examined the molecular, neuroendocrine and neurobehavioral effects of completely filtering (0% transmission) all short-wavelengths <480 nm, all short wavelengths <460 nm, or partially filtering (~30% transmission) <480 nm from polychromatic white-light exposure between 2000 h and 0800 h in healthy individuals in a controlled laboratory conditions. Filtering short-wavelengths <480 nm prevented nocturnal light-induced suppression of melatonin secretion, increased cortisol secretion and disrupted peripheral clock gene expression. Furthermore, subjective alertness, mood and errors on an objective vigilance task were significantly less impaired at 0800 h by filtering wavelengths <480 nm as compared to unfiltered nocturnal light exposure. These changes were not associated with significantly increased sleepiness or fatigue as compared to unfiltered light exposure. The changes in molecular, endocrine and neurobehavioral processes were not significantly improved by completely filtering <460 nm or partially filtering <480 nm as compared to unfiltered nocturnal light exposure. In a separate field-based trial we also examined the effects of spectral modulation on sleep, mood and task performance in 10 healthy nurses (6 females and 4 males; mean age 28.7 years) working rotating shifts using a within-subject design. Behavioral and physiologic variables were assessed at baseline (2-weeks of rotating night shifts without spectral modulation) and during experimental intervention (2-weeks of rotating night shifts with spectral modulation during night shifts only). Changes in sleep were assessed by both polysomnography and subjective reports. Spectral modulation was associated with an earlier melatonin peak-time compared to baseline. Experimental intervention was associated with a significant increase in sleep duration, reduced sleep onset latency, reduced intrasleep awakenings, and increased sleep efficiency during night time sleep. There were no significant changes in daytime sleep compared to baseline. Task performance was less impaired at the end of the night shift with intervention compared to baseline as assessed objectively. There was a significant improvement in subjective mood and reduced daytime sleepiness with intervention compared to baseline. In conclusion, spectral modulation may facilitate adjustment to shift-work when used in a rotation-specific manner.

BLUE ENRICHED ROOM LIGHT IN THE MORNING ENHANCES DAYTIME ALERTNESS AND NIGHT TIME SLEEP

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Introduction Basic research on the effects of blue wavelength light on wakefulness suggests that there are two distinct pathways of activating effects of bright light. One is an immediate pathway, causing cortical activation during task performance (Vandewalle et al, 2006). Another pathway is thought to act indirectly via the suprachiasmatic nucleus, controlling evening melatonin release and affecting the circadian pacemaker (Gordijn & Beersma; 1999; Hébert et al., 2002). However, it remains unknown whether these two mechanisms can be influenced in a real life environment by bright room light in the morning. The current study aims to compare biologically optimized room lighting to light bulb room lighting in the morning regarding subjective alertness, reaction times and night time sleep.

Methods In a randomized cross-over design ten healthy participants were exposed to an optimized lighting condition (637 lux;3400 Kelvin) and 7 days later to a light bulb lighting condition (20 lux; 2400 Kelvin) or vice versa. Light exposure took place on three consecutive days from 8 to 11 am. During light exposure subjective alertness and reaction times on the psychomotor vigilance task were measured every hour. In the evening light conditions were controlled and sleep was polysomnographically recorded.

Results During hours of optimized room lighting reaction times on the psychomotor vigilance task were significantly shorter compared to the light bulb condition (two-tailed paired t-test; $p < 0,05$). Similarly, subjective alertness in the optimized light condition was increased compared to the light bulb condition at all three of the hourly measurements (two tailed paired t-test; $p < 0.05$ at 9am; $p < 0.1$ at 10am and $p < 0,05$ at 11am). Interestingly, subjective alertness in the optimized light condition increased with every consecutive day, whereas this effect was absent in the light bulb condition (repeated measures ANOVA; interaction *light condition* * *day* * *time*: $p < 0.05$). Polysomnographic recordings revealed that after the optimized light condition participants experienced a mean of 29.4 minutes more total sleep time (two-tailed paired t-test; $p< 0.05$). Increased sleep was due to significantly more slow wave sleep ($p< 0.05$) and a trend towards more REM sleep ($p< 0.1$).

Conclusion The current data show that optimized lighting in the morning is of great importance not only for immediate alertness, but also for sleep quality at night. Furthermore, results suggest that the immediate benefits of optimized room light increase with every consecutive day of light exposure.
These results emphasize the importance of optimized lighting in schools and at the workplace regarding not only daytime performance but also night time sleep quality.

Keywords: Room lighting, Sleep, Alertness

Funding Support: Osram

PHASE RESPONSE CURVE TO A SINGLE 6.5-H LIGHT PULSE OF SHORT-WAVELENGTH LIGHT

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Objectives: The resetting response of the human circadian pacemaker to light depends on the timing of exposure and the direction and magnitude of the shift and is described by a Phase Response Curve (PRC). Previous PRCs in humans have utilized bright polychromatic white light. Given that the circadian photoreception system is most sensitive to short-wavelength visible light, the aim of the current study was to construct a PRC to blue (480 nm) light and compare it to a PRC to white light that had been constructed previously using a similar protocol.

Methods: Eighteen young (18-30 years), healthy male and female subjects were studied for 9-10 days in a time-free environment. Following three baseline days (16:8 h wake:sleep), subjects underwent an initial ~30-52-hour Constant Routine (CR) in <3 lux and, after an 8-hour sleep, were exposed to monochromatic 480 nm light (11.8 $\mu W/cm^2$) in a modified Ganzfeld dome for 6.5 hours centered in the 16-hour wake episode. The subjects' pupils were dilated 15 minutes prior to light exposure. The light timing for each subject was randomized to one of 18 circadian phases separated by 20^o intervals according to habitual wake-time. After an 8-hour sleep, subjects began a second CR (~32-55 h) followed by a recovery sleep and discharge. Blood samples were taken at regular intervals (20-60 min) to determine dim light melatonin onset (DLMOn). DLMOn for CR1 and CR2 was defined as the time when the rising part of the melatonin profile crossed through the 25% value of the fitted peak amplitude. Phase shifts were determined as the difference in clock time between the DLMOn measured on CR1 and the DLMOn measured on CR2, occurring three cycles later. For PRC construction, phase was determined as the time at which the onset of the light exposure was administered relative to the DLMOn estimate from CR1. The PRC was fitted with a two-harmonic function and adjusted R^2 was computed as a goodness of fit measure.

Results: Two subjects were excluded from final analysis due to missing data. The PRC derived from the melatonin data of 16 subjects shows a fitted peak-to-trough amplitude of 3.85 hrs, with a fitted peak of 1.29 h and a fitted trough of -2.55 h (adj. R^2 of fit = 0.88).

Conclusions: Exposure to 6.5 hours of 480 nm light resets the circadian pacemaker according to a conventional Type 1 PRC with average delays and advances of -1.62 hours and 0.67 hours for melatonin. The 480 nm PRC induced ~74% of the response of a previously constructed 10,000 lux white light PRC.

Keywords: Short-wavelength light, Phase Response Curve, Melatonin

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WHAT SHORT DURATION LIGHT PULSES CAN TELL US ABOUT HUMAN CIRCADIAN PHOTORECEPTION: RESULTS FROM MODELING AND EXPERIMENTS

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Objectives: Ocular light stimuli are potent stimuli for resetting the timing of the human circadian pacemaker. Single continuous exposures of several thousand lux of polychromatic light administered in the biological night induce delays of several hours in the human melatonin rhythm; similar circadian phase resetting to long-duration light exposures has been demonstrated in the non-primate mammalian circadian system. In animals, the circadian system is reliably reset by continuous duration exposures as short as 3 seconds over a range of light intensities, with the magnitude of the response greater than would be predicted using data from longer light exposures. The goal of our current experimental work was to determine whether the human circadian pacemaker has a significant response to short continuous duration light exposures as seen in animal studies.

Methods: Twelve subjects (6F; mean age ± SD = 23.3 ± 3.0 years; range 18-30 years) were studied using a 9-day inpatient protocol that has been used to probe the effects of longer continuous duration light exposures. Subjects maintained a regular sleep-wake schedule at home for at least 2 weeks prior to inpatient admission. The 9-day protocol consisted of (in sequence): 3 baseline days (8-hr sleep,16-hr wake) scheduled at the subject's habitual times, an 8-hr sleep episode, a 50-hr constant routine (CR) procedure in which subjects remained awake in a constant posture and received hourly meals, an 8-hr post-CR sleep episode, a 16-hr wake period with bright light exposure (LE), a post-LE 8-hr sleep episode, a 30-hr CR and a final 8-hr sleep episode before subjects were discharged to home. During LE subjects sat in a constant posture for 4.5 hours and a bright (~9500 lux) 2-minute LE was administered at a time centered approximately 6 hours prior to habitual wake, with a target onset between 0.5 and 4 hours after the melatonin marker $DLMO_{25\%}$ in order to induce a phase delay. Light levels during wake were 90 lux on baseline, and <1 lux from midway through baseline day 3 through the end of the study except during the 2-minute LE. Light levels during sleep were <0.3 lux. Circadian phase was assessed by computing the $DLMO_{25\%}$ from plasma melatonin collected every 30 minutes. Phase shifts are reported as the difference between the final phase estimate immediately prior to LE and the first phase estimate during CR2.

Results: The mean +/- SD phase shift across 12 subjects was 35 +/- 19 minutes phase delay (median 33 minute phase delay); 11 of the 12 subjects had a phase delay (range 21-67 minutes phase delay) while one subject had a phase advance of 4 minutes.

Conclusion: Compared to previous studies conducted in the same facility with the same procedures, in which 6.5 hours of light administered at approximately the same circadian phase resulted in a ~180 minute delay of melatonin phase, these results demonstrate that ~22% of the resetting effect can be generated from only 0.5% of the stimulus duration. These results, therefore, suggest a non-linear response to light duration that was not predicted by current mathematical models of the effect of light on the human circadian pacemaker.

Keywords: Light, Phase shift, Circadian photoreception

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THE KINETICS OF THE BISTABLE MELANOPSIN SYSTEM – IMPLICATIONS FOR ARCHITECTURAL LIGHTING

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Objectives: In bistable photopigment systems, light elicits photosensory responses and drives photoregeneration of the chromophore to restore photic responsiveness. Melanopsin in the human retina has been shown to express bistable properties both *in vitro* and *in vivo* (Mure et al, PLoS ONE 4(6): e5991, 2009). These studies have shown that prior light exposure can modulate the amplitude of subsequent photic responses of melanopsin. In the present study, we attempt to model the kinetics of the melanopsin photopigment system in response to modulations of light spectrum and intensity.

Methods: We modelled the responses of the melanopsin photopigment system based on data for the equilibrium and difference spectra of melanopsin obtained by Mure et al. (2009) in our laboratory applying mathematical modelling. Light spectra of broadband natural and artificial light sources were used to generate prior light stimulations to drive the melanopsin system to a defined state of equilibrium. Theoretically, this corresponds to the proportions of melanopsin isoforms in the *11-cis* and *all-trans retinal* bound states. Mono- or polychromatic spectral templates were subsequently applied to examine the modulation of photic responsiveness.

Results: The results suggest that prior exposure to light sources dominated by long wavelength light increase the ability of the melanopsin system to respond to subsequent light exposures, while light sources dominated by shorter wavelength light decrease the response.

Conclusions: Exploiting the bistable properties of melanopsin could allow for optimization of elicited non-visual responses in industrial, domestic and clinical phototherapy in regard to energy efficiency. This could be integrated to the design workflow of architectural lighting design (Pechacek et al., Leukos 5(1):1-26, 2008) in order to have quantitative descriptors for non-visual aspects of light.

Keywords: Melanopsin, Bistable photopigment, Non-visual effects, Photoreception, Architectural lighting

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BLUE ENRICHED LIGHT AND DAYLIGHT- A HEAVY COMPETITION

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Objectives: Circadian regulation of human physiology and behavior (e.g., body temperature or sleep-timing) depends on the "zeitgeber" light that synchronizes them to the 24-hour day. In modern, western societies, the zeitgeber light is however weakened, since, especially in urban areas, employees spent their time indoors and the nights are brighter due to light infrastructure. To ameliorate this "light deprivation", one strategy is to increase the similarity between the spectral composition of daylight and indoor lighting. Yet, very little is known about the effects of blue-enriched light in real life settings, such as offices. To investigate the effects of blue-enriched light (8000K) at the work place as opposed to standard light conditions (4000K), we assessed sleep-wake and activity-rest behavior, as well as subjective wellbeing ratings.

Methods: An experimental group (N=27) that experienced the light change was compared with a non-intervention group (N=27) that remained in the 4000 K environment throughout a 5-week study period (14 January to 17 February). Sleep logs and actimetry continuously assessed sleep−wake behavior and activity patterns. Daily wellbeing ratings (on a scale from 0 to 10) were recorded via sleep log entries.

Results: Over the study period, the timing of sleep and activity on free days steadily advanced parallel to the seasonal progression of sunrise in the non-intervention group. In contrast, the temporal pattern of sleep and activity in the experimental group remained associated with the constant onset of work. Wellbeing ratings did not change systematically over the course of the study period and did not differ between groups over and above baseline differences.

Conclusion: The results suggest that artificial blue-enriched office light competes with natural light as a zeitgeber. While subjects working under the warmer light (4000 K) appear to entrain (or synchronize) to natural dawn, the subjects who were exposed to blue-enriched (8000 K) light appear to entrain to office hours, as seen in their sleep-wake and rest-activity behaviour on free days. The results confirm that light is the dominant zeitgeber for the human clock and that its efficacy depends on spectral composition. Yet, the positive effects of blue-enriched light on mood could not be detected in this study sample. The results indicate that blue-enriched artificial light is a potent zeitgeber that has to be used with diligence.

Keywords: Blue-enriched light, Office workers, Sleep-wake behaviour, Actimetry, Zeitgeber

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THE INFLUENCE OF FEVER AND INFLAMMATION ON PERIPHERAL CLOCK GENE EXPRESSION

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Objectives: The circadian clock is a 24-hour biological timer regulating most physiological systems through a series of interlinked transcriptional regulators termed core clock components. The master clock resides in the suprachiasmatic nucleus (SCN) and maintains synchrony among peripheral oscillators through a unique, yet unknown, set of humoral, behavioural and/or neurological cues. Recently, the proinflammatory factors interleukin-6 (IL-6) and prostaglandin E_2 (PGE_2) were proposed to influence peripheral clock dynamics, raising the possibility that fever and inflammation affect clock function.

Our aim is to elucidate the time-dependent effects of fever and inflammation on core clock components in peripheral tissues and understand the mechanism accounting for these effects.

Methods: Turpentine oil (TURP) injected into the hind leg of rats is a model of inflammation and fever. After the formation of a local abscess, one proinflammatory cytokine – IL-6 – is released systemically inducing PGE_2 expression in the brain resulting in fever. To assess the impact of TURP on clock dynamics, the core clock components *Per1, Per2,* and *Reverbα* in peripheral tissues were examined using quantitative PCR.

Results: We found that the time of TURP treatment affects the magnitude of cytokine response and clock gene expression. We show that animals treated with TURP at different times over 24hrs have the greatest IL-6 induction in the early night corresponding to the greatest deviation in clock gene expression. Further, the magnitude and time of sensitivity of clock gene expression to TURP treatment varied between peripheral tissues examined. Further, suppressing IL-6 expression with exogenous hrIL-1ra rescued some of the alterations in *Per1* and *Per2* caused by TURP, defining a possible of IL-6 in the deviations of clock gene expression to inflammation.

We intend to investigate the specific effect of PGE_2 on clock gene expression by suppressing PGE_2 expression with the COX-2 inhibitor celecoxib. Finally, we will investigate whether IL-6 and/or PGE_2 act directly on liver using primary hepatocyte cultures treated with exogenous IL-6 or PGE_2.

Conclusions: The time of day of TURP injection affects the responsiveness of both the proinflammatory cytokine induction and peripheral clocks. Further, the changes in clock gene expression correlate with the maximal responsiveness of cytokines and are tissue-specific. Using pharmacological techniques, we have established a possible role of IL-6 in the changes in clock gene expression but whether this effect is due to direct action on the peripheral organs or through a systemic response remains to be determined.

Keywords: biological rhythms, immunology, inflammation, peripheral clocks, cytokines

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SEX DIFFERENCE IN THE CIRCADIAN VARIATION OF DISTAL-CORE TEMPERATURE GRADIENT

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Objectives: Studies have shown that body temperature is influenced by various parameters including metabolic rate and subcutaneous blood flow, which is related to heat loss at the extremities. Interestingly, sex differences and circadian variations were found in both metabolic rate and the subcutaneous blood flow. The aim of the present study is to examine sex differences in the circadian variation of body temperature regulation.

Methods: After two consecutive weeks of a regular sleep-wake schedule, 10 healthy men (mean age ± SD: 25.77 ± 4.48 years) and 10 healthy women in their mid-follicular phase (26.01 ± 3.06 years) entered the laboratory to participate in a 72-hour ultradian sleep-wake cycle (USW) procedure. During the USW, participants alternated between 60-minute wake episodes in dim light (<10 lux) and 60-minute nap episodes in total darkness. Throughout the procedure, participants remained in time-isolation, maintained a semi-recumbent position, and were served iso-caloric snacks (1x/2 hours). Measures included core body temperature (CBT), distal skin temperature (DT), and a calculated distal-core temperature gradient (DCG). Data were binned according to circadian phase (30° bins).

Results: Neither significant interactions nor main effects of sex were found for CBT. As for DT, the main effect of sex approached, but did not reach, significance ($p=.056$), with males having lower values compared to females. DCG showed a main effect of sex, with women having significantly higher values than men ($p<.05$) throughout all circadian phases.

Conclusions: Parameters that could affect body temperature, such as activity level, food intake, and posture were controlled for by using the USW procedure. Women presented higher DCG throughout circadian phases even though statistical tests showed that both CBT and DT were comparable to men. Our results suggest a sex difference in thermoregulatory mechanisms.

Keywords: Circadian Rhythms, Sleep, Thermoregulation

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BRIGHT LIGHT TREATMENT FOR ANXIETY

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Objectives: The common co-morbidity and biochemical similarity of anxiety and depression provide rationales for expecting that bright light will have anxiolytic effects as well as antidepressant effects. We have been exploring this hypothesis in a series of studies. In an open trial [Youngstedt and Kripke , BMC Psychiatry 7:62, 2007], we found significant anxiolytic effects of acute bright light exposure. A subsequence randomized controlled trial [Youngstedt et al., 28:324-332, 2011] found less impressive benefits of acute or 4-weeks of bright light in high anxious young adults. Our ongoing research is examining the effects of bright light on posttraumatic stress disorder (PTSD), which is the most common mental health diagnosis of veterans of the present wars in Afghanistan [Operation Enduring Freedom (OEF)] and Iraq [Operation Iraqi Freedom (OIF)]. Current treatments for PTSD have had limited efficacy. Bright light could be an effective treatment for combat PTSD because of its positive effect on so many symptoms that characterize PTSD, including anxiety, depression, insomnia, cognitive dysfunction, and fatigue.

Methods: Following extensive screening and a 1-week baseline period, participants (n=37) 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 of cognitive function and they self-rated their PTSD severity (PCL-M). Sleep was assessed continuously via a 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=0.038) following bright light [from 57.9±4.9 to 37.4±5.0, Effect Size (ES)=0.95] compared with placebo (44.1±5.9 to 38.9±5.3, ES=0.23).
Post-hoc analysis showed that this effect could not be readily explained by baseline differences. Though not significant at this juncture, more favorable reductions in self ratings of PTSD (PCL-M) occurred following bright light (from 45.0±2.5 to 32.6±2.1, ES=1.25) compared with placebo (from 40.2±3.3 to 33.9±2.3, ES=0.53). Moreover, compared with placebo bright light elicited significantly greater reductions in state anxiety (p0.027, ES 0.47 vs. -0.02), PSQI-Global complaints (p=0.017, ES=0.93 vs. -0.22), and in PSQI-PTSD related complaints (p=0.018, ES=0.86 vs. 0.00)), and more favorable reductions in BDI (ES0.95 vs. 0.55).

Conclusions: The results suggest benefits of bright light treatment for PTSD in every type of variable assessed, including clinical and self-assessment of PTSD severity, self-ratings of depression and anxiety, sleep, and cognitive function.

Keywords: PTSD, Depression, Veterans

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CIRCADIAN VARIATION IN THE RESPONSE OF T CELL TO ANTIGEN

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Circadian variations in white blood cell counts and in infection-induced mortality have been shown in rodents and in humans. Cytokine secretion by innate immune cells in vitro has been shown to demonstrate a circadian variation, giving clues that there are functional aspects of the immune response under circadian control. The adaptive immune response begins in the lymph node, where antigen is presented to T cells, causing them to proliferate and gain the effector function that allows this specific immune response to control infection. However, little is known about the timing of T cell-mediated events.

We show that there is a circadian variation in T cell proliferation in response to stimulation of the T cell receptor (TCR) *in vitro*. We show that the core TCR signaling molecule ZAP-70 is expressed rhythmically, suggesting that it plays a role in this rhythmic response. Strikingly, T cells respond in a time-dependent manner in mice immunized with peptide at different times of day, which has important implications in the development of more efficient vaccination strategies.