



Society for Light Treatment
and Biological Rhythms

Program and Abstracts

Volume 19



19th Annual Meeting
June 28-30, 2007
Copenhagen, Denmark



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SLTBR 19th ANNUAL MEETING PROGRAM

Thursday, June 28

- 3:00 – 7:00 PM Registration (*Room ABC/Ground Floor*)
- 4:30 PM Board of Directors Meeting (*Room E/6th floor*)
- 7:00 – 9:30 PM Reception (*Room ABC/Ground Floor*)
Poster Session with Discussion

Friday, June 29

- 7:30 – 8:45 AM Registration, Continental Breakfast, Corporate Exhibits (*Room ABC*)
- 8:50 – 9 AM Welcome: Robert Levitan, MD, FRCP, SLTBR President (*Room ABC*)
- 9 – 9:10 AM Plenary Session I: Light Therapy for Non-seasonal Depression
Introductions: Klaus Martiny, MD, PhD, Consultant Psychiatrist,
Frederiksborg General Hospital, Denmark
- 9:10 – 9:35 AM The Impact of Light on Human Circadian Physiology
Anna Wirz-Justice, PhD, Professor, Centre for Chronobiology, Basel,
Switzerland
- 9:35 – 10 AM Light Treatment for Chronic Depression
Namni Goel, PhD, Assistant Professor of Psychology in Psychiatry,
University of Pennsylvania School of Medicine, USA
- 10 – 10:25 AM Augmentation of Antidepressants by Light Treatment
Klaus Martiny, MD, PhD, Consultant Psychiatrist, Frederiksborg General
Hospital, Denmark
- 10:25 – 10:40 AM Coffee Break
- 10:40 – 11:15 AM What Is the Evidence for an Antidepressant Effect of Light Treatment in
Non-Seasonal Depression?
Arja Tuunainen, MD, PhD, Assistant Professor, University of Helsinki,
Finland
- 11:15 – 11:30 Discussion
- 11:30 – Noon Junior Investigator Presentation: Morningness – Eveningness and
Diurnal Variation in Energetic Arousal, Tense Arousal, and Hedonic
Tone
Konrad Jankowski, University of Warsaw, Faculty of Psychology
- Noon – 1:30 Lunch (sandwiches and beverages will be served)

- 1:30 – 3:45 PM Oral Presentations I (*Room ABC*)
- ADHD and the Circadian Rhythm
J.J.S. Kooij
- Circadian Rhythm Profiles in Night Eating Syndrome
Namni Goel, PhD
- Light and Dark, Activity and Rest in Day-shift and Night-shift Nurses
Mark Rea, PhD
- Seasonality in Homicides, Suicides, and Date of Birth of Suicide Victims
in Greenland
K. Sparring Björkstén, MD, PhD
- The Effects of Short and Medium Wavelength Light on Subjective
Alertness in the Young and Elderly
T.L. Sletten
- Light Interference and the Response of Prothrombin Time (Pt) in the
Laboratory Rat *Rattus Norvegicus*
Abraham Haim, PhD
- Testing Polychromatic Light as a Circadian Stimulus for Space Travel
George Brainard, PhD
- 3:45 – 4:00 PM Coffee Break
- 4:00 PM SLTBR Annual Business Meeting (*Room ABC*)
- 7:00 PM Banquet (*Tivoli Garden at the Groften Restaurant*)
*All paid attendees please meet at 7 PM at the Tivoli main entrance: Vesterbrogade 3.
Additional tickets can be purchased at the entrance. Dinner begins at 7:30. The
Litebook grant award will be presented at this time.*

Saturday, June 29

- 7:30 – 8:30 AM Registration, Continental Breakfast, Corporate Exhibits (*Room ABC*)
- 8:30 – 10:30 AM Oral Presentations II (*Room ABC*)
- In Vivo* Response of Colon Cancer to Photoperiod Manipulations and
Melatonin
Abraham Haim, PhD
- Bright Light Effects on LH and FSH
Daniel Kripke, MD
- Degree of Pineal Calcification (DOC) Is Associated with
Polysomnographic Sleep Measures
Dieter Kunz, MD

Light-induced Melatonin Suppression in Humans with Polychromatic
and Monochromatic Light
V.L. Revell, PhD

Rod System Light Modulation Disparities between SAD Patients and
Normal Controls
Marc Hébert, PhD

Differential Effects of Short-Term Light Exposure on Melatonin
Excretion
Dieter Kunz, MD

- 10:30 – 10:45 AM Coffee Break
- 10:45 – 10:50 AM Plenary Session II: Light Treatment, Light at Night and Risk of Cancer
Introductions: George Brainard, PhD, Professor of Neurology, Thomas
Jefferson University; Josephine Arendt, PhD, Emeritus Professor of
Endocrinology, Centre for Chronobiology, University of Surrey, UK
- 10:50 – 11:20 AM Risk of Cancer in Night Shift Workers. The Melatonin Hypothesis
Eva S. Schernhammer, MD, PhD, Assistant Professor of Medicine, Brigham
and Women's Hospital and Harvard Medical School, Boston, USA
- 11:20 – 11:50 AM Experimental Evidence for Light at Night-Induced Circadian/Melatonin
Disruption as a Risk Factor for Human Cancer Growth
David E. Blask, MD, PhD, Senior Research Scientist and Head, Laboratory
of Chrono-Neuroendocrine Oncology, Bassett Research Institute, The Mary
Imogene Bassett Hospital, Cooperstown, NY and Department of Medicine,
Columbia University, NY, USA
- 11:50 – 12:20 PM Effect of Frequent Phase-Shifts on Cancer Growth
Elizabeth Filipski, PhD, INSERM U776, Université Paris XI, Hôpital Paul
Brousse, Villejuif, France
- 12:20 – 12:50 PM Exposure to Light at Night and Risk of Cancer
Johnni Hansen, PhD, Head of Research Unit, Institute of Cancer
Epidemiology, Danish Cancer Society, Copenhagen, Denmark
- 12:50 – 1 PM Discussion and Closing Remarks
(Sandwiches and beverages will be served)
- 2:00 – 7:00 PM *Social Event (additional): Bus ride to the north of Zealand, with guided
picture exhibition at Frederiksborg Castle and afternoon coffee and sweets
at the Fredensborg Old Inn. Expected return to the Admiral Hotel at 7:00
PM.*

SLTBR 19TH ANNUAL MEETING

POSTER PRESENTATIONS

- A. Bader. *Light Therapy for Antepartum Depression: Ongoing Randomized Controlled Trial*
- V. Bromundt. *Rest-Activity Cycles and Circadian Rhythms in Women with Borderline Personality Disorder*
- V. Bromundt. *Rest-Activity Cycles, Negative Symptoms and Cognition in Schizophrenia—Preliminary Results*
- R. Ciancaglini. *The Association between Depression and Somatization (Anxiety) Levels and Pain Thresholds in Adult Subjects with Orofacial Pain*
- R. Ciancaglini. *Relationship of Depression and Somatization (Anxiety) Levels with Exposure to Open-air Daylight in Adults with Orofacial Pain Disorders*
- K. Danilenko. *Bright Light Therapy for Weight Loss*
- M. G. Figueiro. *Blue Light as an Alerting Stimulus at Night*
- M. Gimenez. *Artificial Dawn Effects on Performance after Wake-up: Does Melatonin Play a Role?*
- F. Jacobsen. *Effects of Earlier Daylight Savings Time in Winter Depression and Non-Seasonal Affective Illness*
- I. Kloog. *Exposure to Light at Night and the Incidence of Breast and Prostate Cancers in Israel*
- R. Levitan. *A Birth-Season/Dopamine-D4 Receptor Gene Interaction Predicts Obesity in Women with Bulimia Nervosa: More Evidence for a “Seasonal Thrifty Phenotype”*
- R. Prichard. *Interactions between Sleep Quality, Light Exposure, Mood, and Academic Performance in University Students*
- M. Rea. *Light and Dark, Activity and Rest in Day-shift and Night-shift Nurses*
- M. Terman. *Controlled Release Melatonin in a Physiological Washout Profile*
- M. van de Werken. *Artificial Dawn Effects on Subjective Ratings of Sleepiness and Activation, and on the Awakening Cortisol Response*

LIGHT THERAPY FOR ANTEPARTUM DEPRESSION: ONGOING RANDOMIZED CONTROLLED TRIAL

A. Bader^{1,2}, A. Riecher-Rössler², U. Frisch², K. Wolf², R.-D. Stieglitz², J. Alder², J. Bitzer², I. Hösli², M. Terman³, K. Wisner⁴, A. Wirz-Justice¹

¹Centre for Chronobiology, Psychiatric University Clinics Basel, Switzerland; ²University Hospital Basel;

³Columbia University, New York, USA, ⁴University of Pittsburgh, USA.

Objectives: The aim of the study is to examine the efficacy of morning bright light therapy to treat pregnant women with non-seasonal major depression. Affective disorder during pregnancy is a common condition: one in ten pregnant women suffers from a major depressive disorder (MDD). Antepartum depression is a difficult situation that requires careful judgment for treating the depression without harm to the foetus. Recent studies report adverse effects on the foetus of antidepressants administered during pregnancy. Out of caution, many pregnant women refuse medication. However, untreated depression in itself can negatively influence birth outcome and neonatal behaviour. Thus, non-pharmaceutical treatment is urgently needed, and light therapy may provide a solution. Preliminary trials of light therapy have shown promising results (1, 2), which prompted a randomised controlled trial with larger sample size. **Methods:** Pregnant women who fulfilled DSM-IV criteria for MDD without seasonal pattern were randomly assigned either to 7000 lux fluorescent bright white light therapy or 70 lux dim red light as a placebo control, taken in the morning upon awakening for 1h/day in a 5-week trial. Clinical state was monitored weekly using a validated German version of the 25-item SIGH-ADS interview (3) with a rater blinded to conditions. Patients wore an activity and light monitor throughout the trial. They collected serial evening saliva samples under dim light conditions at home at baseline and after treatment, for melatonin radioimmunoassay (Bühlmann Laboratories). **Results:** Patient recruitment began in October 2004. By May 2007, out of 61 study applicants 26 had been enrolled, 20 completed the trial, with 6 dropouts. SIGH-ADS scores declined significantly from 26.2 ± 3.9 (mean \pm SD) at baseline to 13.1 ± 9 ($p < 0.01$) after 5 weeks (placebo dim and bright light combined).

Conclusions: The study will not be unblinded until the end of the 4-year trial. We can already divide responders and non-responders: patients who improved (13/20 with $\geq 50\%$ reduction of SIGH-ADS score) did so gradually over the 5 weeks. Also, the anonymised data showed circadian phase advances of melatonin onset in some subjects, consistent with an active treatment effect. Recruitment rate is sufficient for meeting the target sample size.

References: (1) Oren et al. *Am J Psychiatry* 2002;159:666-669. (2) Epperson et al. *J Clin Psychiatry* 2004;65:421-425. (3) Williams JBW, Terman M. Structured Interview for the Hamilton Depression Rating Scale with Atypical Depression Supplement (SIGH-ADS). New York, New York State Psychiatric Institute, 2003.

Keywords: Major depression, Pregnancy, Light therapy, Salivary melatonin, Non-pharmaceutical treatment of depression.

Funding Support: Swiss National Science Foundation Grant #320000-114110.

TESTING POLYCHROMATIC LIGHT AS A CIRCADIAN STIMULUS FOR SPACE TRAVEL

G. Brainard, B. Warfield, R. Fucci, E. Martin, M. Stone, M. James, B. Byrne, M. Rollag, J. Hanifin
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Introduction: Risk factors for the health and safety of astronauts include disturbed circadian rhythms and altered sleep-wake patterns. These physiological changes can result in decreased alertness, concentration, performance, and, in turn, can threaten the safety and objectives of space missions. In studies with astronauts, pre-launch light treatment has been used to help entrain circadian rhythms and sleep-wake patterns [1, 2]. Separate analytic action spectra in rodents, nonhuman primates and humans show that the peak wavelength sensitivity for the circadian system is in the blue portion of the visible spectrum, fundamentally different from that of the classical visual system [3]. Recent studies, based on selected monochromatic wavelength comparisons, have indicated that the acute alerting effects of light are shifted towards the shorter wavelength or blue part of the spectrum for healthy humans [4-6]. Working with both monochromatic and polychromatic stimuli, the goal of our research is to optimize light as a countermeasure for circadian and sleep disruption during space exploration [7].

Aims and Methods: The aim of this study was to compare the efficacy of standard white to blue-enriched polychromatic fluorescent light for their capacity to suppress melatonin in healthy females and males with normal color vision. The light exposure system consisted of a 119 x 120 cm flat panel with either white (4,200° K) or blue-enriched fluorescent lamps (17,000° K) 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. Two groups of 8 volunteers each (mean ages 23.9 ± 0.9 and 25.1 ± 0.9 , respectively) were exposed to nine irradiances of white (0.8 to $734 \mu\text{W}/\text{cm}^2$) or blue-enriched light (1 to $800 \mu\text{W}/\text{cm}^2$) and a dark control exposure with at least one week between each experiment. Blood samples collected were quantified for melatonin by radioimmunoassay.

Results: For both the white and blue-enriched light exposed groups, comparisons of pre- versus post-exposure raw melatonin values by paired, two-tailed t tests showed that middle-range to higher intensities induced a significant reduction of melatonin ($p < 0.05$ to 0.001). One-way ANOVA was used to compare both plasma melatonin % change scores and control-adjusted % change scores and both sets of data showed a significant intensity-related suppression of melatonin ($p < 0.001$). The mean and SEM melatonin control-adjusted % change scores were then plotted against a four parameter sigmoidal fluence-response curve and were shown to have a high coefficients of correlation ($R^2 > 0.90$).

Conclusions: Both the standard white and blue-enriched fluorescent lights suppressed plasma melatonin in healthy young subjects in a clear dose-response pattern with higher irradiances eliciting progressively stronger hormone suppressions. The data provide an important step towards characterizing the human circadian system's response to standard white and blue-enriched polychromatic fluorescent light. These findings open the door for optimizing light as a countermeasure for sleep and circadian disruption during space exploration as well as applications on earth.

References:

- 1) Stewart K.T. and Eastman C.I. (1996) In: *Biologic Effects of Light*. W. de Gruyter & Co. pp 340-347.
- 2) Dijk D.J. et al. (2001) *Amer J Physiol* 281: R1647-1664.
- 3) Brainard G.C. and Hanifin J.P. (2005) *J. Biol Rhythms* 20: 314-325.
- 4) Cajochen et al. (2005) *J Clin Endocrinol Metab* 90:1311-1316.
- 5) Lockley et al. (2006) *Sleep* 29:161-168.
- 6) Revell et al. (2006) *Neurosci Lett* 399:96-100.
- 7) Fucci et al. (2005) *Acta Astronautica* 56: 1017-1024.

This work supported by National Space Biomedical Research Institute through NASA NCC 9-58. Philips Lighting, BV, an NSBRI industrial partner, provided the lighting systems and lamps for this project.

Key words: Circadian Phototransduction, Light, Melatonin, Pineal Gland, Space Exploration

REST-ACTIVITY CYCLES AND CIRCADIAN RHYTHMS IN WOMEN WITH BORDERLINE PERSONALITY DISORDER

V. Bromundt¹, S. Kyburz¹, G. Dammann², C. Cajochen¹, A. Wirz-Justice¹

¹Centre for Chronobiology, Psychiatric University Clinics Basel, Switzerland; ²Psychiatric Clinics Münsterlingen, Switzerland

Objectives: Borderline personality disorder (BPD) is characterised by instability of mood, impulsive aggression, unstable self-image and relationships, depression, anxiety, and repeated self-injurious behaviour. Circadian and sleep disturbances are a common feature of psychiatric disorders, and also reported by BPD patients. We investigated rest-activity cycles and circadian melatonin rhythms in patients with BPD and their relationship to BPD severity.

Methods: Rest-activity cycles of 8 female outpatients, diagnosed with BPD by DSM-IV criteria, were continuously measured over a period of 21 days wrist actimetry, together with daily sleep logs and self-ratings (visual analogue scales) about their well-being, mood, sleepiness and urge to self-injury. Saliva samples were collected during 3 days (each separated by a 7-day interval) to determine the onset of melatonin secretion as a marker for circadian phase position (RIA, Bühlmann Laboratories). Clinical interviews and standardised questionnaires (Borderline Personality Inventory BPI, Pittsburgh Sleep Quality Index PSQI, Chronotype questionnaire MCTQ) were conducted to assess clinical status, medication, sociodemographic data and relevant parameters related to circadian rhythms.

Results: We found both disturbed and non-disturbed circadian rhythms in women diagnosed with BPD. By median-splitting the 8 patients according to their BPI scores, we were able to compare a mild to moderate BPD cohort (group M; median 11.5, range 8-27) with a severe BPD cohort (group S; median 35.5, range 27-46). PSQI and MCTQ revealed sleep problems (PSQI>5) in all individuals (group M: median 8, range 7-9; group S: median 10.5, range 6-13) and a high number of extreme chronotypes, either early morning types (MCTQ score<14) or late evening types (MCTQ score>21) (group M scores: 11, 13, 18, 25; group S scores: 26, 21, 7, 9) indicating distinctive circadian rhythm preferences in these patients. Objective actimetric data showed a lower diurnal amplitude in motor activity for group S compared with group M, as well as lower melatonin secretion in the evening. The melatonin onset in group S was either advanced (17:58, 17:24) or delayed (23:44, later than last sample at 1:00). In group M (21:42, 20:58, 20:00, 2:10), 3 patients showed normal melatonin onset times. Besides the diurnal and circadian measures, we found a negative significant correlation between subjective mood ratings and the urge to self-injurious behaviour ($r=-0.46$, $p<0.001$).

Conclusion: These preliminary data indicate that women with BPD show abnormal rest-activity cycles and circadian melatonin rhythms, which depend on BPD severity. We will investigate whether light therapy in BPD patients is able to correct these circadian abnormalities, and consequently, whether BPD symptoms such as depression and self-injury can be alleviated by light treatment.

This study is supported by the VELUX Foundation, Switzerland.

Key Words: Borderline personality disorder, Circadian rhythms, Actigraphy, Melatonin.

REST-ACTIVITY CYCLES, NEGATIVE SYMPTOMS AND COGNITION IN SCHIZOPHRENIA – PRELIMINARY RESULTS

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Objectives: Negative symptoms in schizophrenia are characterised by a lack of emotion and motivation, apathy, and poor social functioning. These symptoms may also occur in individuals with sleep disturbances, which are also a common complaint in schizophrenic patients. We are currently investigating the correlation between characteristics of the circadian rest-activity cycle, negative symptoms and cognitive functioning in schizophrenic patients.

Methods: Rest-activity cycles were recorded by wrist actimetry over a period of 21 days in schizophrenic outpatients, together with keeping sleep diaries. Saliva samples were collected during 3 days (interspersed by 7-day intervals) to determine the onset of melatonin secretion (DLMO) as an objective marker for circadian phase (RIA, Bühlmann Laboratories). Moreover, clinical interviews and standardised questionnaires (BPRS, PANSS, PSQI) were implemented to assess clinical status, medication and sociodemographic data. Cognitive functioning was assessed by neuropsychological tests (Trail Making Test A+B, Stroop interference task, verbal fluency test).

Results: The rest-activity cycles in five patients treated with the atypical antipsychotic risperidone showed abnormalities, in particular frequent awakenings during the main sleep episode. Circadian phase of DLMO, measured so far in 2 patients, showed a considerable delay. In a preliminary analysis of 6 patients we have found a weak relationship between negative symptoms and the degree of rest-activity cycle disturbance as measured by the Interdaily Stability index (IS). Additionally, we have observed a significant correlation between IS and executive cognitive functioning as measured by the Stroop interference task, whereas the correlation with the other neuropsychological tasks did not yield significance.

Conclusion: These initial findings in schizophrenic patients suggest that disturbed-rest activity cycles may be related to poor cognitive functioning, particularly for executive cognitive performance.

This study was supported by Bristol-Myers Squibb, Switzerland.

Key Words: Schizophrenia, Negative symptoms, Cognition, Actigraphy, Melatonin.

RELATIONSHIP OF DEPRESSION AND SOMATIZATION (ANXIETY) LEVELS WITH EXPOSURE TO OPEN-AIR DAYLIGHT IN ADULTS WITH OROFACIAL PAIN DISORDERS

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Objectives: Customary exposure to open-air daylight may positively influence affective disturbances and to some extent depression. We evaluated if the time of open-air daylight exposure may influence depression and somatization (anxiety) levels in orofacial pain subjects compared to healthy subjects.

Methods: Fifty-four adults with orofacial pain disorders (12 males, 42 females; mean age [SD] 44.1 [16.5] y) consecutively admitted at the same institution were age- and gender-matched with 54 healthy controls. Depression and anxiety were assessed by a standardized questionnaire (SLC-90) and scored according to the De Rogatis criteria. Severity of the orofacial pain disorder was classified according to the Helkimo index. Time of exposure to open-air daylight was recorded as the number of days/week of daily open-air exposure of one hour or longer.

Results: When compared to controls, orofacial pain subjects exhibited shorter open-air daylight exposure ($P=0.047$) and higher depression (mean difference [95% CI], 0.29 [0.08 to 0.51]) and anxiety (0.28, [0.06 to 0.50]) levels. In orofacial pain subjects a significant association was found between depression or anxiety and time of exposure to open-air daylight, even after adjusting for confounders (age, gender and severity of orofacial pain disorder), with an adjusted correlation coefficient of, respectively, $r=-0.356$ ($P=0.12$) and $r=-0.346$ ($P=0.013$). No significant association was found between depression or anxiety levels and time of exposure to open-air daylight in healthy controls.

Conclusion: Time (number days/week) of open-air daylight exposure may be a factor in the occurrence of and positively influence depression and anxiety levels in orofacial pain adult subjects. Additional longitudinal randomized trials need to clarify the effective mutual relationship of depression and anxiety with open-air daylight exposure in subjects with orofacial pain disorders.

Keywords: Anxiety, Somatization, Depression, Pain

The Association between Depression and Somatization (Anxiety) Levels and Pain Thresholds in Adult Subjects with Orofacial Pain

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Objectives:, Depression and somatization (anxiety) have been related to changes in sensitivity/perception of pain (pain thresholds). This study was conducted to examine whether any relationship may exist between depression and somatization (anxiety) levels with pain sensitivity in orofacial pain subjects.

Methods:, Fifty-four adults with orofacial pain (12 males, 42 females; mean age [SD] 44.1 [16.5] y) consecutively admitted at the same institution were age- and gender-matched with 54 healthy controls. Depression and anxiety were assessed by a standardized questionnaire (SLC-90) and scored according to the De Rogatis criteria. Pain thresholds (perceptive and objective) were detected by using tooth pulp electrical stimulation (constant current/square wave/ bipolar technique).

Results:, When compared to controls, orofacial pain subjects reported higher depression (median 0.92 vs. 0.55, $P<0.01$; Mann-Whitney test) and anxiety (0.83 vs. 0.42, $P<0.01$) levels, and higher perceptive pain threshold (17 vs. 14, $P<0.05$). Both in orofacial subjects and controls a significant negative association was found between objective pain threshold and both depression (Spearman correlation coefficient, $r,-0.619$ and -0.614 , $P<0.0001$) and anxiety ($r,-0.633$ and -0.648 , $P<0.0001$). Perceptive pain threshold was negatively associated with anxiety in orofacial subjects only ($r,-0.369$, $P<0.010$). Associations remained statistically significant ($P<0.05$) also after adjustment for age and gender.

Conclusion:, While a relationship exists between depression and anxiety levels with objective pain thresholds both in orofacial and healthy subjects, perceptive sensitivity to pain appears to be associated with anxiety in orofacial subjects only.

Keywords: Anxiety, Somatization, Depression, Pain

BRIGHT LIGHT THERAPY FOR WEIGHT LOSS

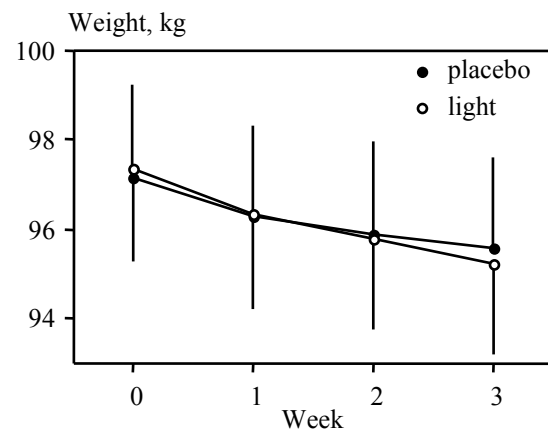
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Objectives: The aim of the study was to investigate whether bright light therapy can affect weight loss. A preliminary study found that exposure to bright light therapy resulted in weight loss (Bergan, 2002, unpublished data), however, the participants were not selected with respect to seasonality trait.

Methods: This was placebo-controlled, single-blind, crossover study performed between December 2006 – April 2007 in Novosibirsk (55° N). 43 volunteers (all but one, female) entered the study and 41 completed it, age mean $43.5 \pm \text{SD } 12.4$ y (20-67 y), body mass index 36.0 ± 6.1 (27.3-54.7). They were of good general health or on a stable dose of medication(s), if suffering chronic disease, and had normal sleep regimen. Individuals with SAD (Seasonal Affective Disorder) or sub-SAD according to the Seasonal Pattern Assessment Questionnaire (SPAQ; Rosenthal et al., 1987), short version, were excluded. Participants received a 3-week session of bright white light 4300 lux for 30' between 06:00-09:00 using Outside In light box at home and a 3-week placebo session by means of a deactivated ion generator. Participants were allocated to the two groups alternately. The off-protocol period between two sessions was 20-87 days (32.2 ± 11.0 days). The prescribed food intake during the two sessions was similar, usually less than 1800 kcal a day, i.e. mild hypocaloric diet.

Results: Patients' motivations and expectations towards weight loss were similar between light and placebo sessions. Calorific intake was equal: 1495 ± 288 vs. 1493 ± 284 kcal a day, respectively. Body weight decreased during both sessions but the difference was greater with bright light when taking into account the dynamics of subjects' weekly measurements (Figure; ANOVA, Intervention \times Time, $p=0.009$). However, when analyzing only the initial and final follow-up measurements recorded at the clinic, the enhanced effect of light was non-significant (ANOVA, Intervention \times Time, $p=0.14$). Post-hoc analysis revealed that this effect of light was more likely to be seen in participants who rated their seasonal changes in weight by SPAQ as moderate-to-marked ($N=15$, i.e. increase in fall-winter) than to those who responded as "no" or "slight" ($N=26$): -0.75 ± 0.94 vs. -0.04 ± 1.37 kg, $p=0.084$. Interestingly, appetite was decreased during both sessions, reaching significance for the light session (1-way ANOVA, $p=0.016$, weekly measurements using VAS-like scale). Mood improved during both sessions, but the effects were enhanced during light therapy (ANOVA, Intervention \times Time, $p=0.055$).



Conclusions: Bright light therapy aids weight loss in humans but only in those with seasonal-related weight changes i.e. increase in fall-winter.

Key Words: Overweight, Light Therapy, Weight Loss

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BLUE LIGHT AS AN ALERTING STIMULUS AT NIGHT

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Objectives: Exposure to light during the circadian night has been shown to increase alertness. Although the mechanisms associated with the nocturnal alerting effects are not fully understood, recent studies in neurophysiology and neuroanatomy have revealed the probable importance of the retinohypothalamic tract (RHT) and suprachiasmatic nuclei (SCN) in affecting wakefulness at night. Although previous studies have shown that blue light, which peaks close to the spectral sensitivity of the circadian system, can have alerting effects in humans at night, a functional relationship between different levels of blue light exposure and alertness has not been established. In this study, we utilized different levels of narrow-bandwidth blue light ($\lambda_{\text{max}}=470$ nm) to establish a functional relationship between blue light exposure and subjective and objective alertness at night. We then compared the relationships between blue light and alertness to predictions of nocturnal melatonin suppression.

Methods: Eight subjects were exposed to 50-minute durations of blue light at the cornea (5, 10, 20 and 40 $\mu\text{W}/\text{cm}^2$) during nighttime sessions. Subjects were exposed to all four blue light levels in one night in a counterbalanced manner. The ratio of electroencephalographic alpha power density with eyes closed to that with eyes open (alpha attenuation coefficient, AAC; an increase in AAC indicates a higher alertness level), and subjective ratings using the Norris mood scale were used to measure alertness.

Results: The AAC and subjective ratings of alertness increased monotonically with irradiance and were highly correlated ($r^2=0.95$, $p<0.05$). AAC values were also highly correlated with predictions of nocturnal melatonin suppression for each lighting condition, consistent with the inference that the RHT/SCN plays a role in human nocturnal alertness.

Conclusions: Our results show a monotonic relationship between blue light exposure levels and alertness measured objectively and subjectively. The close correlation between predictions of nocturnal melatonin suppression and alertness suggests a role of the RHT/SCN in nocturnal alertness.

Key Words: Blue light, Alerting stimulus

ARTIFICIAL DAWN EFFECTS ON PERFORMANCE AFTER WAKE UP: *DOES MELATONIN PLAY A ROLE?*

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Objectives: Although human sleep-wake rhythms show a clear 24-h alternation, not all humans sleep at the same time of day; with extreme early types and extreme late types as obvious examples. The late types tend to perform badly in the early morning hours. This could be due to the fact that their circadian phase in the early morning is not optimal for performance. Exposure to early morning light could theoretically improve performance after waking up by phase advancing the circadian pacemaker. The goal of the study was to test whether artificial dawn during sleep can improve people's performance after waking up and whether this is accompanied by a shift in the melatonin rhythm.

Methods: A modified artificial dawn waking up alarm (Philips DAP B.V., Drachten, The Netherlands) was used by 49 subjects for 42 days in their home environment. Every two weeks the maximum intensity of light reached by the waking up alarm (measured at the eye) was changed: 0 lux (control), 50 lux or 250 lux. The chronological order of conditions was randomized between subjects. At the end of every other two weeks subjects collected saliva samples in the evening under dim light for melatonin assessment. Questionnaires were completed to evaluate their performance after waking up.

Results: Out of the 49 subjects we could analyze 29 melatonin curves in all three experimental conditions. No significant differences were found in dim light melatonin onset time (DLMO) (time of crossing 15% of maximum level) with increasing artificial dawn intensity. DLMO for intensities 0, 50, and 250 lux were 21h13m (s.e.m. 11'), 21h21m (s.e.m.9'), 21h17m (s.e.m. 9') respectively ($F(2,56)=0.627$, $p=0.538$). Evaluation after 2 weeks showed a significant improvement of waking up quality, easy rising, energy and mood after the use of the wake up alarm. With increasing light intensity, the average estimated sleep inertia duration decreased significantly (one-tailed t-test, $p<0.05$), from 56.4' (s.e.m 8'), to 49.4' (s.e.m. 4.9'), and 40.5' (s.e.m. 4.0'), respectively. No differences were found in social interactions, concentration, and productivity aspects.

Conclusion: Several measurements, in particular sleep inertia, did improve by the use of the artificial dawn waking-up lamp. However the idea that a phase advance of the melatonin rhythm plays a role in establishing this effect is not supported.

Key words: Human, Artificial dawn, Sleep inertia, Melatonin rhythm, Performance

Funding support: This study was supported by Philips DAP B.V., CoC Vitality Care, Drachten, The Netherlands, and the 6th European Framework Programme EUCLOCK.

CIRCADIAN RHYTHM PROFILES IN NIGHT EATING SYNDROME

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Objectives: Night eating syndrome (NES) is characterized by evening hyperphagia and frequent awakenings accompanied by food intake. Patients with NES display a delayed circadian pattern of food intake but retain a normal sleep-wake cycle. These characteristics initiated the current study, in which the phase and amplitude of neuroendocrine and behavioral circadian rhythms in patients with NES was evaluated.

Methods: Fifteen women with NES (mean age \pm SD, 40.8 \pm 8.7 y) and 14 control subjects (38.6 \pm 9.5 y) were studied in the laboratory for 3 days. Blood was collected for 25 h (every 2 h from 0800 to 2000 h, and then hourly from 2100 to 0900 h) and assayed for glucose and 7 hormones [insulin, ghrelin, leptin, melatonin, cortisol, thyroid stimulating hormone (TSH) and prolactin]. Daily food intake also was measured. Statistical analyses utilized linear mixed-effects cosinor analysis.

Results: Control subjects displayed normal phases and amplitudes for all circadian rhythms. In contrast, patients with NES showed a phase delay in the timing of meals, and delayed circadian rhythms for total caloric, fat and carbohydrate intake. In addition, phase delays of 1.0 to 2.8 h were found in two food-regulatory rhythms — leptin and insulin — and in the circadian melatonin rhythm (with a trend for a delay in the circadian cortisol rhythm). In contrast, circulating levels of ghrelin, the primary hormone that stimulates food intake, were phase advanced by 5.2 h. The glucose rhythm showed an inverted circadian pattern. Patients with NES also showed dampened amplitudes in the circadian rhythms of food intake, cortisol, ghrelin and insulin, but showed heightened TSH amplitude.

Conclusions: In summary, patients with NES demonstrate significant changes in the timing and amplitude of various behavioral and physiological circadian markers involved in appetite and neuroendocrine regulation. Thus, NES may result from dissociations between central (suprachiasmatic nucleus) timing mechanisms and putative oscillators elsewhere in the central nervous system or periphery, such as the stomach or liver. As such, chronobiologic treatments for NES such as bright light therapy may be useful. Indeed, in case studies, bright light therapy has shown efficacy in reducing night eating and should be evaluated in controlled clinical trials.

Key Words: Circadian rhythms, Phase shifts, Amplitude, Night eating syndrome, Mixed-effects cosinor analysis

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LIGHT TREATMENT FOR CHRONIC DEPRESSION

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Objectives: In this lecture, part of the plenary session on “Light therapy for non-seasonal depression”, data from a randomized controlled trial investigating the efficacy of two non-pharmacologic treatments, bright light and high-density negative air ions for nonseasonal chronic depression will be presented. Both methods have shown clinical success for seasonal affective disorder (SAD).

Methods: Patients were 24 (75%) women and 8 (25%) men, ages 22-65 (mean age \pm SD, 43.7 ± 12.4 years), with Major Depressive Disorder, Single Episode (DSM-IV code, 296.2), Chronic (episode duration ≥ 2 years). Patients were entered throughout the year and randomly assigned to exposure to bright light (10,000 lux; $n=10$), or high-density (4.5×10^{14} ions/sec flow rate; $n=12$) or low-density (1.7×10^{11} ions/sec; $n=10$; placebo control) negative air ions. Home treatment sessions occurred for 1 hour daily upon awakening for 5 weeks. Blinded raters assessed symptom severity weekly with the Structured Interview Guide for the Hamilton Depression Rating Scale—Seasonal Affective Disorder (SIGH-SAD). Evening saliva samples were obtained immediately before and after treatment for ascertainment of circadian melatonin rhythm phase (dim light melatonin onset was the phase marker).

Results: SIGH-SAD score improvement was 53.7% for bright light and 51.1% for high-density ions compared with 17.0% for low-density ions. Remission rates were 50%, 50% and 0%, respectively. In this clinical trial, the presence or severity of atypical symptoms did not predict response to either treatment modality, nor were phase advances to bright light associated with positive response.

Conclusions: Both bright light and negative air ions are effective for treatment of chronic depression. Remission rates are similar to those for SAD, but without seasonal dependency or apparent mediation by circadian rhythm phase shifts. Combination treatment with antidepressant drugs or concurrent use of both bright light and negative air ions may further enhance clinical response.

Key Words: Bright light therapy, Negative air ionization, Chronic depression, Nonpharmacologic antidepressants, Placebo

LIGHT INTERFERENCE AND THE RESPONSE OF PROTHROMBIN TIME (PT) IN THE
LABORATORY RAT *RATTUS NORVEGICUS*

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Objectives: In humans as diurnal creatures, maximal blood coagulation activation is achieved during the morning hours. In rats as nocturnal species such values are expected during the dark period. We studied the effects of seasonality, as reflected by photoperiod manipulations and light interference of short day acclimated rats on prothrombin time (PT), as a marker of the coagulation profile.

Materials and Methods: Rats were acclimated to the following photoperiod conditions under a constant ambient temperature: long day 16L:8D; short day 8L:16D; and short day light interfered with lights on for 30min at midnight. Rats were anesthetized using a cocktail of (Rampun and Ketamine) blood samples of 1ml were taken by heart puncture into tubes containing sodium citrate. Plasma samples were stored at -70oC till clotting testing. Blood samples were collected at three different hours of the 24h cycle: 08:00' 16:00 and 24:00h and the samples were collected within one hour. During the dark period we used red dim light with the same intensity as in the acclimation room. For testing PT, a thromboplastin was added and the time for a fibrin clotting formation, by the extrinsic pathway was measured.

Results: Under a short-day acclimation a daily variation in coagulation time was noted with minimal PT values in the morning. However, light interference resulted in abolishing this daily variation and PT values were shortened at all time periods, which might reflect hypercoagulation stage.

Conclusions: The results of our study indicate that under short photoperiod, rather than under long photoperiod there are daily variations in blood coagulation time. Light interference leads to shorten the coagulation time, which might represent higher risk of thrombosis. The question to be asked is: if light interference will have a similar affect on humans? This will be studied in the close future.

Key Words: Coagulation , Light Interference, Seasonality, Prothrombin

In Vivo Response of Colon Cancer to Photoperiod Manipulations and Melatonin

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Objectives: *In vitro* experiments carried out on colon cancer cells of different lines revealed that addition of melatonin to cell cultures at various concentrations affected the viability of the cancer cells and DNA synthesis decreased. The aim of the study we are reporting on was to test the effects of photoperiod manipulations and melatonin treatment in an *in vivo* experiment with mice.

Materials and Methods: Mice (C 57BL-6 Harlan, Jerusalem) were acclimated for three weeks at least to short (8L:16D - SP) and long (16L:8D - LP) photoperiods under a constant ambient temperature of $26 \pm 1^\circ\text{C}$. Mice were treated with (MC38) 2.5×10^6 cells/mouse, injected *s.c.* Mice of each photoperiod acclimation were divided into two groups: 1) SP-acclimated control mice 2) SP-acclimated light interfered (LI) mice. Two weeks after injecting the cancer cells LI-mice were exposed every night for 30min to light seven hours after lights went off. LP-acclimated mice were also divided into two groups: 3) LP-control mice treated with saline 4) LP-experimental, treated with melatonin (5mg/Kg. W_b) injected *i.p.* six hours before lights went off, starting treatment two weeks after injecting the cancer cells for two weeks and then by adding to the drinking water (10/Kg. W_b). The size of the tumor was measured by a caliper and the volume estimated.

Results: A clear segregation was noted between the different photoperiod acclimations. The growth of the tumor under SP-acclimation was significantly slower than that of LP-acclimation. However LI accelerated the growth. Unexpectedly in LP-acclimated mice, treated with melatonin, the growth was also accelerated compared to the LP-acclimated control mice.

Conclusions: Our results show that *in vivo* growth of colon cancer in mice is affected by photoperiod. LI to SP-mice accelerates growth. Melatonin injected during photophase further accelerates the growth.

Key Words: Photoperiod, Light interference, Melatonin, Colon cancer

ROD SYSTEM LIGHT MODULATION DISPARITIES BETWEEN SAD PATIENTS AND NORMAL CONTROLS

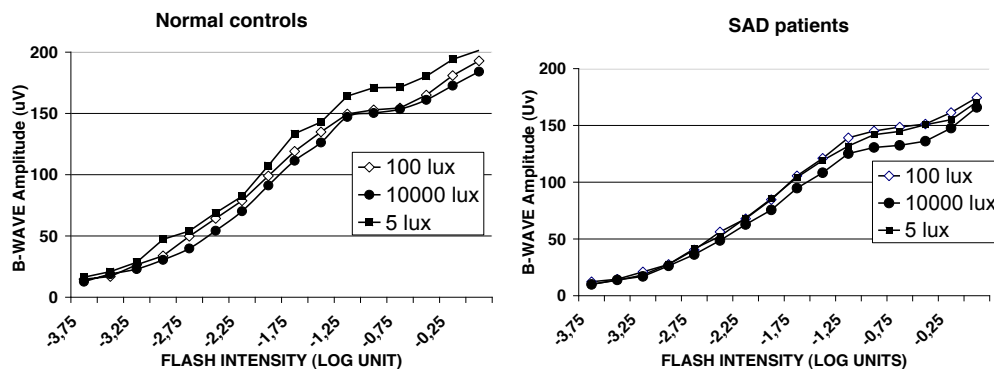
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Objectives: In normal controls the rod system appears to adapt to the amount of light received just prior to ERG testing (Gagne et al. Psychiatry Res, 2007). Since rod function anomalies have been reported in SAD patients (Hebert et al. Psychiatry Res, 2004) our goal was to assess for the first time in SAD patients, rod ERG response following various light exposures.

Method: Nine healthy subjects (2 males, 7 females, mean age 27 y.o) and 12 SAD diagnosed patients (2 males, 10 females, mean age 26 y.o) were exposed (in a random order) for 60 min to three different light intensities (10000 lux, 100 lux and 5 lux) separated by an interval of at least 3 days. Rod retinal function was assessed after each light condition using various flash intensities of stimulation in order to provide a luminance response curve.

Results: In normal controls, ANOVA followed by post-hoc revealed that it was the 5 lux condition which yielded to the highest maximal rod response ($p < 0,05$) whereas the 10000 lux condition yielded to a significant decrease in rod sensitivity (log K). In SAD patients, ANOVA followed by post-hoc demonstrated that it was the 10000 lux condition which yielded to a significantly lower rod maximal response ($p < 0,05$) whereas no change in sensitivity occurred between conditions.



Conclusion: In the retina, dopamine triggered by light, is detrimental to rods in order to favour cones function. In normal controls we suspect that 5 lux is not sufficient to trigger dopamine production which is why rod function is enhanced. However, with increasing light intensities, rod function decreases and loses its sensitivity, may be as a measure of protection against bright light exposure. In contrast, in SAD patients, rod response does not increase following exposure to 5 lux and decreases when exposed to bright light. Although we suspect that higher dopaminergic activity (in response to lower serotonin level) in SAD might explain the loss of gain in rod function after a 5 lux exposure, at the present time, we cannot understand why 10000 lux would yield to a decreased rod ERG amplitude. Further studies are needed to elucidate all neurotransmitters that are involved in the modulation of rod activity. However, such discovery could lead to a better understanding of the pathogenesis of SAD.

Keywords: ERG, Light, Retinal sensitivity, Rod.

Funding support: This research was supported by a CIHR research grant to MH.

EFFECTS OF EARLIER DAYLIGHT SAVINGS TIME IN WINTER DEPRESSION AND NON-SEASONAL AFFECTIVE ILLNESS

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Objectives: Evidence suggests that recurrent winter depressions may result from phase-delayed circadian rhythms. This year's 3 week earlier onset Daylight Savings Time (DST) in the U.S. raised concerns of adversely impacting winter depressives by returning their early morning sunlight exposure to darkness. A prospective study of stabilized depressives was undertaken to determine whether changes in sleep, mood or other symptoms would follow the clock delay.

Methods: DSM IV unipolars and bipolars pharmacologically stabilized for at least three months were rated ≤ 6 weeks before and ≤ 3 weeks after DST. Subjects were divided into comparison groups based upon a history of winter depression: 1) winter depressives using light therapy (WD +LT), 2) winter depressives not using LT (WD - LT), 3) depressives denying a history of seasonal depression (nSD). LT was 10,000 lux for ≥ 15 minutes upon waking each morning. All patients were blind to study hypothesis and received treatment as usual. Patients who reported changes in mood, sleep, appetite/food intake, and/or cognitive function following DST were rated on a 5 point change scale (0=none, 1=mild, 2=moderate, 3=severe, 4=incapacitating).

Results: Unexpectedly, 58 winter depressives using light therapy (45F, 13M: mean \pm SD age= 51.5 \pm 10.3 years) reported *more* mood/sleep changes (2/4) than 53 winter depressives not using light (2 mood/1 sleep) (38F, 15M: 53.7 \pm 9.3 years) and 54 patients denying seasonal depression (1 mood/1 sleep) (34F, 20M: 55.3 \pm 10.3 years. One-way ANOVAs for mood and sleep failed to reveal group differences ($F=0$, $df=3$, $p=NS$, for both). No patients reported appetite/food or cognitive function changes following DST.

Conclusions: A one hour phase delay 3 weeks early in the season appears to have negligible effects on most medication-remitted depressives, regardless of seasonal history or light therapy use. Further study is needed to determine the phase-shift magnitude and seasonal timing which may trigger symptoms in affective illness, particularly in light-responsive seasonal depressives.

Key Words: Winter Depression, Circadian Rhythm Phase-delay, Affective Illness, Daylight Savings Time

MORNINGNESS – EVENINGNESS AND DIURNAL VARIATION IN ENERGETIC AROUSAL, TENSE AROUSAL, AND HEDONIC TONE

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The aim of the presented study was to examine levels of energetic arousal (EA), tense arousal (TA), and hedonic tone (HT) in individuals with different circadian preferences during the course of a day. Selected from a large sample (N=500) using the MEQ, subjects were pure morning types (N=16) and pure evening types (N=15). They completed the UMACL every one and a half hour from 8:00 to 20:00h in laboratory conditions. The obtained data showed higher levels of TA and lower levels of HT in M-types over the whole day as compared to E-types and the most disadvantageous levels of these mood dimensions in morning hours. As for EA, M-types showed higher levels than E-types from 8:00 to 17:00h and no differences occurred between the groups at later hours. Both groups were found to exhibit similar diurnal patterns in TA and HT and dissimilarity between M-types and E-types appeared in the daily course of EA. The results show that three dimensional mood is more advantageous in M-types than in E-types during the hours of typical human activity.

Key words: Chronotype, Diurnal rhythm, Mood

EXPOSURE TO LIGHT AT NIGHT AND THE INCIDENCE OF BREAST AND PROSTATE CANCERS IN ISRAEL

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Objectives: Recent studies of restricted populations indicated that excessive exposure to light at night (LAN) may become a risk factor for breast and prostate cancers. However, no studies have yet attempted to examine the effects of LAN exposure in a general population. The present study attempts to investigate the links between local LAN levels and the incidence of two types of hormone dependent (prostate and breast) cancers, using cancer rates and LAN intensity data available for 165 individual urban localities in Israel. In particular, the present analysis attempts to answer the following question: Is there a link between local LAN levels and the incidence of breast and prostate cancers in urban localities after controlling for known potential confounders?

Methods: Nighttime satellite images were used to estimate LAN levels in 165 communities in Israel. Multivariate regression analysis was performed, to investigate the association between LAN and incidence rates of breast and prostate cancers across localities.

Results: In the multivariate analysis, LAN was found to be positively associated with risk of both cancers ($B=0.321$, $t=3.78$, $P<0.001$ for breast cancer, and $B=0.135$, $t=2.32$, $P<0.05$ for prostate cancer). *Per capita* income and *population size* of localities were also positively associated with cancer rates ($t>2.0$, $P<0.05$).

Conclusions: As the present analysis indicated, the incidence of breast and prostate cancers tended to increase, other things equal, by about 15-20% for each doubling in the ground LAN intensity. To the best of our knowledge, the present analysis is the first study in which the relationship between outdoor ambient LAN, and breast and prostate cancer rates were investigated on a general population level, using Geographic Information Systems (GIS) tools.

Keywords: Breast cancer, Prostate cancer, Light pollution, Pineal, Melatonin

ADHD AND THE CIRCADIAN RHYTHM

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Objectives: Children with ADHD may have chronic sleeping problems, associated with circadian rhythm disturbances. Little is known about sleep in adults with ADHD.

Methods: We studied the prevalence and type of sleeping problems using an interview questionnaire in 120 adults with ADHD.

Results: 78% of the 120 adults with ADHD had difficulty to go to bed in time (between 1 and 3 am). Almost 70% reported sleep onset problems, more than 50% had difficulty sleeping through. Almost 70% had difficulty getting up in the morning and 62% felt sleepy during the day. In more than 60% of patients these sleeping problems had been there all their lives. These results are very similar to earlier data presented by Dodson (Dodson, 1999). Several explanations for these sleeping problems may be considered (Kooij et al., 2001; Oosterloo et al., 2006; Boonstra et al., 2007). However, this frequent sleeping pattern of being a 'nightowl', with restless sleep and difficulty getting up in the morning may be associated with the delayed sleep phase syndrome, as was recently shown in children with ADHD and sleep onset problems (van der Heijden et al., 2006; van der Heijden et al., 2005). We currently study the circadian rhythm in adults by measuring the Dim Light Melatonin Onset (DLMO) in saliva in ADHD patients with sleep onset problems (ADHD+SO), compared to ADHD patients without sleep onset problems (ADHD-SO).

Conclusions: About 70% of adults with ADHD have sleep onset problems compatible with a delayed sleep phase pattern. First data of DLMO in adult ADHD patients with and without sleep onset problems will be discussed, as well as the possible relationship between chronically low levels of melatonin and risk of cancer in this group of patients.

Key Words: Adult ADHD, Delayed Sleep Onset, DLMO, Circadian Rhythm, Cancer.

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BRIGHT LIGHT EFFECTS ON LH AND FSH

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Objectives: Previous small studies have provided inconsistent evidence that bedside lights at night can influence the menstrual cycle. Danilenko et al. (2007) showed that bright morning light could induce ovulation. Yoon et al. (2003) had shown that 1000 lux light at 5-6 AM awakenings increased luteinizing hormone in young men. Two further studies were done to explore reproductive endocrine effects of bright light.

Methods: In one study of bright light phase response curves, subjects were randomly assigned to receive 3000 lux white light at one of 8 times around the clock. Treatment was provided for 3 hours on 3 occasions 24-hours apart. Baseline and post-treatment urinary LH was assayed by ELISA. In the second study, 8500 lux white light was provided for 1 hour early each morning for 4 weeks at home. Urinary LH and FSH were assayed at baseline and at the end of the final week of treatment, with excretion averaged over 24 hours.

Results: In the first study, data were available for 98 subjects, including groups of females and males contrasting ages 18-31 and ages 59-75. As referenced to endogenous melatonin phase, treatments were randomly distributed in circadian phase. No significant treatment or time-of-treatment effects were demonstrated in LH. In the second study, data were available for 9 depressed subjects from 60-74 years of age, who showed no significant change in LH or FSH excretion.

Conclusions: Previous studies of bright light effects on reproductive endocrinology have yielded mixed results. These results add to the negative studies. In view of the study of Yoon et al., it would appear that 3000 lux for 3 hours on 3 occasions may have been an insufficient dose of bright light, either in quantity or number of days of exposure. In the second study, either poor adherence to the protocol or the age of the participants might explain the lack of significant response. Further studies are needed to isolate the parameters of bright light treatment which augment reproductive endocrine responses.

Key Words: Light, LH, FSH, Endocrine

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DIFFERENTIAL EFFECTS OF SHORT-TERM LIGHT EXPOSURE ON MELATONIN EXCRETION

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Objectives: The daily light-dark cycle synchronizes the circadian timing system (CTS) with the environmental 24-hour day. Using controlled lab-conditions long-term application of bright, high and low intensity light suppresses melatonin secretion. The aim of the study was to prove that low intensity blue light emitted by everyday lamps applied to healthy subjects in a naturalistic setting influences human physiology.

Methods: 9 healthy subjects (6 male, 3 female, aged 22-33 yrs.) kept their average bedtimes (+/-1h) during a 7-day entrainment phase (controlled by actigraphy). During the following 6-day experimental phase, subjects followed their habitual daytime schedules, only attending the laboratory in the evening hours from 7:00 pm until 12:00 pm under dim light conditions (<10lx). Light exposure was timed 1h before habitual bedtime. Melatonin excretion was measured by salivary samples every 30 min. except every 10 min. before, during and after light exposure (analyzed by Bühlmann Laboratories, Basel, Switzerland). Self-assessments of alertness, mood, and performance were performed every 30 min. using visual analogue scales. Night 1 was baseline condition (no light exposition). During nights 2-6, ordinary lamps with different functions (office, bathroom, industry) of different light intensity (130 thru 500 lux) and spectral distributions (four with , one without blue portions) were used for light exposure administered to the subjects in a cross-over design of groups of three subjects per condition.

Results: Graphical analyses of single subjects as well as statistical analyses of group data (Wilcoxon test) showed a significant reduction or interruption of the increase of melatonin excretion compared to the baseline curve immediately after exposure to all lamps with blue portions, but not for the lamp with no blue portion. The amount of melatonin suppression tendentially was related to the light intensity and the portion of blue light. Significant effects started as early as 10 min after the beginning of light exposure and reached a peak 10 min after exposure. Subjective alertness was significantly increased at the end of exposure to 3 of the 4 lamps with portions of blue light as compared to the baseline condition.

Conclusions: Data prove that 10 to 30 minutes of exposure to everyday lamps containing blue portions are sufficient to influence melatonin excretion as well as behaviour.

Key Words: Light, Melatonin, Circadian Rhythm Desynchronization

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DEGREE OF PINEAL CALCIFICATION (DOC) IS ASSOCIATED WITH POLYSOMNOGRAPHIC SLEEP MEASURES

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Objectives: Melatonin plays a key role in the proper functioning of the circadian timing system (CTS), and exogenous melatonin has been shown to be beneficial in cases of CTS and sleep disturbances. Nevertheless, the concept of “melatonin deficit” has yet to be defined. The aim of our study was thus to determine the relationship between the individual melatonin deficit marker DOC (degree of pineal calcification) and objective sleep parameters using polysomnography (PSG).

Methods: A total of 43 outpatients (22 women, 21 men, mean age 45.0 years; SD 14.4) with neuropsychiatric sleep-related disturbances were included. Following an adaptation night, a PSG recording night was performed. Urine samples were collected at predefined intervals over a 32-hour period that included both PSG nights in the sleep laboratory. 6-sulphatoxymelatonin (aMT6s) levels were determined using ELISA. DOC was estimated by means of cranial computed tomography.

Results: Controlling for age, aMT6s parameters did not correlate with any of the PSG parameters evaluated. In contrast, DOC was negatively associated with REM-sleep percentage ($r = -0.480$, $P < 0.001$), total sleep time ($r = -0.337$, $P = 0.013$), and sleep efficiency ($r = -0.341$, $P = 0.012$) and was positively associated with wake time after sleep onset ($r = 0.345$, $P = 0.011$).

Conclusions: DOC appears to be superior to measurements of the absolute amount of melatonin in the circulation as an indicator of melatonin deficit. High DOC values indicate changes predominantly in those PSG parameters that are governed by the circadian timing system. As such, DOC may serve as a marker of CTS instability.

Key Words: Melatonin, Sleep, Pineal calcification, Circadian rhythms

A BIRTH-SEASON/DOPAMINE-D4 RECEPTOR GENE INTERACTION PREDICTS OBESITY IN WOMEN WITH BULIMIA NERVOSA: MORE EVIDENCE FOR A “SEASONAL THRIFTY PHENOTYPE”

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Purpose: We have recently reported that among overeating women with seasonal affective disorder, probands born in the spring who carried the hypofunctional 7-repeat allele of the dopamine-4 receptor gene (DRD4) had a markedly increased risk of overweight and obesity (*Neuropsychopharmacology* 2006; 31, 2498-2503). To explain this finding, we proposed a *seasonal thrifty phenotype hypothesis* triggered by in-utero exposure to a fall/winter melatonin pattern. The goal of the current analysis was to test this same model in a second group of female overeaters i.e. young women with bulimia nervosa (BN). **Methods:** The current study sample consisted of 200 women with BN with or without a lifetime history of anorexia nervosa (AN). ANCOVA was used to test whether the previously described birth season/DRD4 interaction predicted maximal lifetime body mass index in BN, as it did in SAD, using age as a co-variate. DRD4 genotype was based on the presence or absence of the 7-repeat allele. **Results:** Strikingly, the birth-season x DRD4 interaction term was a significant predictor of maximal lifetime BMI in these women with BN ($F=2.77$, $df=7$, 191 , $p=.009$), thus replicating our overall findings in women with SAD. In contrast to our earlier study, in BN it was a fall birth, rather than a spring birth, that was associated with higher lifetime BMIs. Pairwise post-hoc testing revealed that 7R carriers born in the fall had a significantly higher maximal BMI than did probands in each of the other subgroups defined by the birth season, DRD4 interaction (at $p<.01$), with the exception of the spring birth/7R group (the high risk group from our SAD study). **Conclusions:** These data offer further evidence that unknown factors tied to birth season interact with the hypofunctional 7R allele of DRD4 to promote weight gain and obesity in young, female, overeating populations. More work is needed to elucidate the particular mechanisms involved, particularly as it relates to photoperiodic signaling in fall vs. spring.

Keywords: Bulimia, Birth Season, Weight Gain, Obesity, DRD4 gene, SAD

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AUGMENTATION OF ANTIDEPRESSANTS BY LIGHT TREATMENT

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Objectives: Antidepressants have a delayed onset of action and treatments are often associated with residual symptoms in patients with major depression. The developments of new augmentation strategies are thus needed. Two studies using light therapy as augmentation are presented.

Method: In the first study (1,2) patients with non-seasonal major depression were randomised to treatment with bright or dim light therapy in combination with 50 mg daily of sertraline and followed for 5 weeks with an additional follow-up period of 4 weeks after light treatment were stopped. In the second study (3), patient developing major depression, following a cerebral stroke, were randomised to treatment with two intensities of light in combination with 20 mg of citalopram and followed for 4 weeks.

Results: In the first study (1,2) patients treated with bright light had a statistically significantly faster reduction of depression scores at all visits in the first 5 weeks. However, this difference between groups disappeared in the follow-up period. The level of blinding was acceptable as evaluated on a post study self-assessment scale. Side-effects were mild. In the second study (3) a dose response effect were shown as patient treated with the highest light intensity had a statistically significant better outcome.

Conclusions: Together these two studies supports the use of bright light treatment as an augmentation strategy in non-seasonal major depression and raises questions on the optimal treatment duration and the possible use of light in a variety of other conditions in which patients develop major depression co-morbid to a physical illness.

Key words: Bright Light Therapy, Non-seasonal depression, SSRI, Stroke

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LIGHT AND DARK, ACTIVITY AND REST IN DAY-SHIFT AND NIGHT-SHIFT NURSES

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Objective: Environmental factors such as electric light at night (LAN) have been implicated as agents in endocrine disruption and, by extension, breast cancer. Night-shift has been used as surrogate for exposure to LAN with subsequent melatonin suppression. In order, however, to accurately study endocrine disruption, melatonin suppression, and cancer risk, it is necessary to accurately measure the primary exogenous stimulus for circadian entrainment and disruption, namely, the patterns of circadian light exposure for women actually working at night. **Methods:** As part of the Nurses Health Study, circadian light exposure and activity patterns from both day- and night-shift nurses were obtained for seven successive days and nights. These unique data were obtained with the Daysimeter, a new, light-weight, head-worn calibrated circadian light dosimeter with on-board, solid-state accelerometers that measure head motion. **Results:** Synchronies between the nurses' light-dark exposure patterns and their activity-rest patterns were examined. In general, all day-shift and all night-shift nurses have a dominant 24-hour pattern of light-dark exposure coordinated with activity-rest periods as revealed by periodogram analysis. It is unambiguously clear, however, that night-shift nurses have significantly less synchrony than day-shift nurses, although a few day-shift nurses also exhibit low synchrony due to irregularly occurring activities while awake. These analyses indicate that light-dark and activity-rest are tightly linked in a circadian pattern even in night-shift nurses. The main cause of the reduced synchrony in night-shift nurses appears to reflect their attempts to shift back and forth between diurnal and nocturnal activity patterns. **Conclusions:** The synchronies between light-dark, activity-rest and circadian hormone markers such as melatonin have yet to be compared; however, it appears that night-shift nurses, while certainly exhibiting less synchrony than day-shift nurses, still show a circadian pattern of activity-rest in concert with a 24-hour light-dark pattern

Key words: Nurses Health Study, Circadian disruption, Light at night, Shift work.

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INTERACTIONS BETWEEN SLEEP QUALITY, LIGHT EXPOSURE, MOOD, AND ACADEMIC PERFORMANCE IN UNIVERSITY STUDENTS

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Objectives: Among college students, poor sleep quality and irregular sleep patterns are commonplace, and are correlated with excessive daytime sleepiness, decreased mood, and poor academic performance (Buboltz Jr. et al., 2001; Brown et al., 2002). Furthermore, college students often create sub-optimal sleep/wakefulness environments (e.g., erratic schedules, excessive caffeine and alcohol consumption, and chronic stress). We sought to confirm and extend previous studies of college student sleep by evaluating additional environmental variables, such as nocturnal light exposure, as potential contributing factors to poor sleep quality.

Methods: All undergraduate students at the University of St. Thomas received an email invitation to take an online survey; 1157 completed the survey (21% response rate), which consisted of a series of sleep-related scales including the Horne Ostberg Morningness/Eveningness scale, the Epworth Sleepiness Scale, the Pittsburgh Sleep Quality Index (PSQI), a sleep environment survey, the Subjective Units of Distress Scale (SUDS), the Profile of Mood States, and questions concerning alcohol, caffeine and other drug use. In addition, a subset of these participants (n=15) wore a motion and light actigraph for one week and completed daily sleep diaries.

Results: Students reported poor sleep quality and high levels of stress; only 34% scored <6 on the PSQI, and over 50% scored >70 on the SUDS. Both of these scores were positively correlated with measures of depression, tension, fatigue, confusion and anger (for all cases, $r > .328$, $p < .001$). The lighting environment in the students' sleeping area was also related to sleep quality; students who regularly fell asleep with some form of ambient light (e.g., glow from a computer screen) reported higher scores on the Epworth Sleepiness Scale ($F_{4,963} = 9.25$, $p < .001$) and PSQI ($F_{4,950} = 3.55$, $p < .01$). Twenty-nine percent of students complained of too much light exposure during sleep. Actigraphy results also showed high nocturnal light exposure, and irregular sleep schedules; the mean variation in bed time and rise time during the week was 3.29 h and 3.98 h, respectively.

Conclusions: These results strongly suggest that sleep quality in college students may be impacted by light exposure during sleep, and that students and campus life professionals should be more educated in sleep hygiene practices, including the importance of the light environment.

Key Words: Sleep, Light, College students, Performance, Mood

LIGHT-INDUCED MELATONIN SUPPRESSION IN HUMANS WITH POLYCHROMATIC AND MONOCHROMATIC LIGHT

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Objectives: The relative contribution of rods, cones and melanopsin to non-image-forming (NIF) responses under different light irradiances, duration and spectral composition remains to be determined in humans. NIF responses to polychromatic light sources may be very different to that predicted from the published human action spectra data which have utilised narrow band monochromatic light and demonstrate short wavelength sensitivity. To test the hypothesis that only melanopsin is driving NIF responses in humans, we matched monochromatic blue light (λ_{\max} 479 nm) with polychromatic white light for total “melanopsin-stimulating” photons at 3 different intensities and assessed light-induced melatonin suppression.

Methods: A within-subject crossover design was used to assess the suppressive effect of nocturnal light on melatonin production in young male subjects ($n = 11$) aged 18 – 35 years (24.9 ± 3.8 ; mean \pm SD). A 30 min light pulse, individually timed to occur on the rising phase of the melatonin rhythm, was administered between 23:30 and 01:30 h. Regularly timed blood samples were taken for measurement of plasma melatonin. Repeated measures two-way ANOVA with irradiance and light condition as factors, was used for statistical analysis.

Results: Light-induced melatonin suppression showed a significant intensity dependent response ($p < 0.001$) with both light conditions. At all intensities, greater melatonin suppression was observed with the polychromatic light ($p < 0.01$).

Conclusions: Polychromatic light was more effective at suppressing nocturnal melatonin than monochromatic blue light matched for “melanopsin-stimulating” photons. NIF responses to polychromatic light thus cannot be predicted from the human spectral sensitivity studies with monochromatic light. The findings suggest a stimulatory effect of longer wavelength light either implicating M and L cones and/or melanopsin regeneration in the melatonin suppression response. The results of this study may be relevant to designing the spectral composition of polychromatic lights for use in the home, workplace and in treatment for circadian-rhythm disorders to ensure optimal stimulation of the NIF system.

Key Words: Human, Melatonin, Melanopsin, Monochromatic light, Polychromatic light

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THE EFFECTS OF SHORT AND MEDIUM WAVELENGTH LIGHT ON SUBJECTIVE ALERTNESS IN THE YOUNG AND ELDERLY

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Objectives: Non-image forming responses to ocular light in humans include acute increases in alertness. The alerting effects of light have been shown to be maximally sensitive to short wavelength light. However, age-related changes in the density of the ocular lens reduce the transmission of short wavelength light which may in turn impact light-induced changes in alertness in older individuals. The current study aimed to compare the ability of short and medium wavelength monochromatic light to increase alertness in young and older subjects in the morning.

Methods: Eleven young (22.9 ± 3.0 years, mean \pm SD) and 15 older (65.1 ± 4.3 years) men were pupil dilated and exposed to a 2-hour intermittent (25 min ON; 5 min OFF) light pulse individually timed to begin 8.5 hours after dim light melatonin onset. In a within-subject, randomised cross over design, volunteers were exposed to two different wavelengths of equal photon density monochromatic light ($\sim 6 \times 10^{13}$ photon/cm²/sec) on two separate occasions; short wavelength (λ_{\max} 456 nm) and medium wavelength (λ_{\max} 548 nm) light. Subjective alertness was verbally assessed on a 9-point scale every 15 minutes throughout the 2-hour light exposure. Alertness ratings were normalised against the baseline value immediately prior to lights on and ratings during each wavelength of light were analysed using two-way repeated measures ANOVA with age and time as factors.

Results: During exposure to short wavelength light, alertness ratings were significantly higher in the young compared with the older men ($F_{1,7} = 2.40$, $p = 0.049$). In addition, in the younger men, subjective alertness ratings were higher at the end of the light exposure compared to pre-light ($F_{1,24} = 23.58$, $p < 0.0001$). There was no effect of time or age group on alertness levels during exposure to medium wavelength light.

Conclusions: The results confirm the short-wavelength sensitivity of the alertness response to light in young subjects, and suggest impaired responsiveness to the short wavelength alerting effects of light in older people. This supports earlier findings of reduced responsiveness to short wavelength light in light-induced melatonin suppression in the elderly¹.

Key Words: Light, Alertness, Short Wavelength Light, Age

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SEASONALITY IN HOMICIDES, SUICIDES, AND DATE OF BIRTH OF SUICIDE VICTIMS IN GREENLAND

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Objectives: Greenland is the most extreme of human habitats regarding light-dark changes. We have previously reported an extremely high prevalence of suicides, almost exclusively violent, in West Greenland in 1968-1995 (n=833), and a seasonality with a midsummer peak and a winter trough*.

The aim of this work was to assess whether there was a seasonality in homicides, in suicides and in the season of birth of the suicide victims in all Greenland. Another objective was to assess whether there was a difference in seasonality North and South of the Arctic circle, the light-dark conditions being very different.

Methods: Official computerized registers on causes of death for entire Greenland from 1968-2002 were used. Data regarding homicides and definite suicides and date of birth for suicide victims were analyzed using Rayleigh statistics for circular distributions. Data were also analyzed separately for each side of the Arctic Circle.

Results: We found that there was a statistically significant seasonal variation 1) in all suicides with the annual peak occurring on June 11th, (n=1351, $r=Z=7,58$, $r=0,07$, $p<0,000$), 2) in suicides South of the Arctic circle with the annual peak occurring on May 27th, (n=769, $r=0,07$, $Z=3,76$, $p<0,05$), 3) in suicides North of the Arctic circle with the annual peak occurring on June 30th (n=577, $r=0,09$, $Z=4,45$, $p<0,01$) and 4) in suicides in the sparsely inhabited province of North Greenland with four months mid-night sun, the annual peak occurring on June 10th (n=33, $r=0,35$, $Z=4,11$, $p<0,01$)

Date of birth of suicide victims showed no seasonal variation. There was a non-significant seasonal variation in homicides (n=308, $r=0,08$, $Z=1,67$, $p<n.s.$) the annual peak occurring on May 2nd.

Conclusions: There was a seasonality in suicides with summer peaks, the seasonality being more pronounced in the North. The summer suicides may partly be caused by impulsive aggressiveness mediated by a serotonergic imbalance related to seasonal changes in light rather than by depression. The seasonal variation in homicide, however non-significant, may have similar explanations.

Reference: *Karin Sparring Björkstén, Daniel F Kripke and Peter Bjerregaard: Suicides in the midnight sun - Seasonality in Suicides in West Greenland . Psychiatry Research, 133, 2005, 205-213.

Keywords: Seasonality, Suicide, Homicide, Date of birth, Light

CONTROLLED RELEASE MELATONIN IN A PHYSIOLOGICAL WASHOUT PROFILE

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Objectives: A wide range of melatonin dosing in immediate and controlled release formulations has been used with mixed results. Timing has varied between shortly before sleep onset, about 2 h before sleep onset (to approximate endogenous melatonin onset) and about 6 hours before sleep onset (for phase advances of the circadian clock). There has been a trend toward lower dosing in the physiological range, although low doses may still produce a supraphysiological spike. We sought to devise a controlled release tablet that would maintain physiological levels throughout the night and wash out in morning.

Methods: Our formulation was devised using micronized melatonin in combination with safflower oil, carnauba wax, Micosolle, Methocel and ProSolv compressed into tablets that were tested for purity, specificity, consistency, microbial content, accelerated shelf life and dissolution rate *in vitro*. Under FDA IND #66,321, single-tablet *in vivo* tests of 0.2 mg, 2.0 mg, and placebo, spaced at 10-14 days, were conducted in blinded, randomized order in 10 healthy adults (age 50.3±3.9 y) without sleep disturbance. All were intermediate chronotypes and maintained a sleep schedule of 2300-0700 h throughout the baseline and testing period. On test days, subjects remained on a recliner or in bed under dim illumination ≤50 lux from 1400-1830 h, ≤5 lux until 2300 h, ≤0.03 lux until 0700 h, and ≤5 lux until 1200 h. The study tablet was administered at 2100 h. Blood samples for Bühlmann plasma melatonin radioimmunoassay were drawn from a forearm venous catheter from 1900-1200 h in 30 or 60 min intervals.

Results: *In vitro* dissolution followed an exponential approach to maximum with 82% dissolved at 6 h and 98% at 10 h. For *in vivo* testing under placebo, the average endogenous melatonin curve rose from 1.7 pg/ml at 1900 h to 19.3 pg/mL at 2100 h (the time of tablet administration). Peak levels reaching 54 pg/mL were maintained between 2200-0600 h, followed by an exponential washout completed by 1200 h ($t_{1/2}$ =71 min). Melatonin absorption and elimination followed a complex pattern of rapid rise to peak concentration from 2130-2300 h (0.2 mg, 328 pg/mL; 2.0 mg, 3467 pg/mL) followed by slow, parallel exponential declines. Under 0.2 mg, the curve superposed on the endogenous washout curve starting at 0700 h ($t_{1/2}$ =73 min). The 2.0 mg curve remained >10 pg/mL until 1200 h.

Conclusions: The 0.2 mg controlled release formulation provides a physiological dose of melatonin with concentrations ≥10 pg/mL lasting 8.7±2.1 h after ingestion. Taken 2 h before bedtime, washout coincides with that of endogenous melatonin. This formulation may be useful as a supplement taken around the time of melatonin onset for people with low endogenous melatonin production, and for those whose sleep would benefit by afternoon or early evening administration as a circadian phase-advancing agent.

Keywords: Melatonin, Pharmacokinetics, Circadian Rhythms, Sleep

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WHAT IS THE EVIDENCE FOR AN ANTIDEPRESSANT EFFECT OF LIGHT TREATMENT IN NON-SEASONAL DEPRESSION?

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Objectives: Efficacy of light therapy for non-seasonal depression has been studied without any consensus on its efficacy. The objective of this research has been to evaluate clinical effects of light therapy in comparison to the inactive placebo treatment for non-seasonal depression.

Methods: The work of our group, adhered to a structural format of the Cochrane Collaboration, has been published in The Cochrane Library in 2004. Based on a strictly defined protocol, extensive searches of databases and other relevant information were performed. All relevant randomized controlled trials were selected. Data were extracted and quality assessment was made independently by two reviewers. The authors of each study were contacted to obtain additional information. Twenty studies (49 reports) were included in the first-edition systematic review. As the Cochrane reviews are regularly updated, we have recently been searching for additional studies to be included in the review, the update to be published in The Cochrane Library in the near future.

Results: In the original version of the review, the meta-analysis results were based on 18 studies, since two studies had provided insufficient information. In general, the quality of reporting was poor, and many reviews did not report adverse effects systematically. Most of the studies had applied bright light as adjunctive treatment to drug therapies, sleep deprivation, or both. The treatment response in the bright light group was better than in the control treatment group, but did not reach statistical significance. The result was mainly based on studies of less than eight days of treatment. The response to bright light was significantly better than to control treatment in high-quality studies (standardized mean difference (SMD) -0.90, 95% confidence interval (CI) -1.50 to -0.31), in studies applying morning light treatment (SMD -0.38, CI -0.62 to -0.14), and in sleep deprivation responders (SMD -1.02, CI -1.60 to -0.45). Hypomania was more common in the bright light group compared to the control treatment group (risk ratio 4.91, CI 1.66 to 14.46, number needed to harm 8, CI 5 to 20). Recently we have found several new studies to be included in the update of the review, and few papers are awaiting more information from the authors to be evaluated. The updated results will be presented in detail at the meeting.

Conclusions: The original version of the systematic review concluded that for patients suffering from non-seasonal depression, light therapy offers modest though promising antidepressive efficacy, especially when administered during the first week of treatment, in the morning, and as an adjunctive treatment to sleep deprivation responders. Hypomania as a potential adverse effect needs to be considered. Several new studies have been identified since the publication of the original review. Up-to-date results, presented in the meeting, will show if conclusions of the original review have been confirmed.

Key Words: Depression, Light Therapy, Randomized Controlled Trials

Reference: Tuunainen A, Kripke DF, Endo T. Light therapy for non-seasonal depression. Cochrane Database of Systematic Reviews 2004, Issue 2. Art. No.: CD004050. DOI: 10.1002/14651858.CD004050.pub2.

ARTIFICIAL DAWN EFFECTS ON SUBJECTIVE RATINGS OF SLEEPINESS AND ACTIVATION, AND ON THE AWAKENING CORTISOL RESPONSE

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Objectives: Immediately after waking up from sleep, people suffer from sleepiness and performance decrement, called sleep inertia. At that time cortisol levels peak due to a diurnal cycle in secretory activity. This might have a function in activating the body. Here we investigate the effects of artificial dawn during sleep and the role of cortisol in waking up alertness.

Methods: The Philips Wake-up light[®] (Philips DAP B.V., Drachten, The Netherlands) was used to create artificial dawn (maximum 350 lux) starting 30 minutes before the alarm. Sixteen healthy subjects (average age = 22.8y ± 4.58) were selected, who need more than 1 hour to fully wake up, for at least 4 days a week. In the lab, subjects were exposed to 2 conditions, each lasting 2 nights. The first night served as baseline, the second night was either the control night in which the light was switched on simultaneously with the alarm (modified Wake-up light[®]), or the experimental night in which the light gradually increased before the audible alarm and remained on after the alarm. Subjective ratings of sleepiness and activation (KSS, Thayer) and saliva samples for cortisol analysis were taken at 1, 15*, 30, 45*, 60 and 90 minutes after the alarm (*no activation measurement).

Results: With the use of artificial dawn, subjects felt significantly less sleepy (main effect condition $F(1,15)=4.58$, $p<.05$) and more active ($F(1,15)=7.58$, $p<.02$) during the 90 min after waking up. The cortisol pattern changed significantly over time ($F(5,75)=32.0$, $p<0.001$) with a peak occurring 30 min after the alarm. During these 30 minutes the change in cortisol is negatively correlated (Spearman's Rho, 1-tailed) with a change in sleepiness ($r_s=-.683$ $p<.01$) and positively correlated with a change in activation ($r_s=.432$ $p<.05$). No differences in cortisol pattern between conditions were observed, neither in total production over 90 minutes ($F(1,15)=1.86$, NS) nor in temporal pattern ($F(5,75)=1.07$, NS). Similar conclusions were reached for the first 30 minutes

Conclusions: Artificial dawn during the last 30 minutes of sleep resulted in decreased sleepiness and increased activity ratings during the first 1.5 h after waking up. This effect could not be explained by an effect on cortisol production.

Key Words: Human, Artificial dawn, Sleep inertia, Awakening cortisol response, Performance

Funding Support: This study was supported by Philips DAP B.V., CoC Vitality Care, Drachten, The Netherlands, and the 6th European Framework Programme EUCLOCK.

THE IMPACT OF LIGHT ON HUMAN CIRCADIAN PHYSIOLOGY

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Light obviously has multiple effects in humans, from enabling vision to providing vitamin D through the skin. Importantly, light acts as the major zeitgeber to entrain the central circadian clock in the SCN and the sleep-wake cycle. In mammals, these non-visual responses to light involve novel photoreceptors located in intrinsically light-sensitive melanopsin-expressing ganglion cells, whose action spectrum show unique short-wavelength sensitivity very different from classical scotopic and photopic visual systems. Further evidence comes from studies demonstrating preferential response to blue vs. green monochromatic light in terms of melatonin suppression, phase shifting, alertness, core body temperature and heart rate. Although the melanopsin-containing ganglion cells are the major photoreceptors for the circadian system, mid-wavelength cones play a significant role, mainly observed for light exposures of short duration and toward the longer wavelength region of the spectrum. The SCN exhibits substantial heterogeneity in both its neurochemical and functional organization, with retinal input and oscillatory timekeeping functions segregated to different regions within the nucleus. Photoperiod is reflected in SCN firing rate as well as in clock gene expression patterns. Peripheral clocks are indirectly synchronised by the SCN; inertia in phase resetting does not originate in the SCN but is a systemic feature of the whole organism. Light also has direct "parametric" effects. Evolving knowledge of the complexity of light input mechanisms into the circadian system predicates caution in too-rapid attempts to translate these findings into simplistic therapeutic applications.

Keywords: melanopsin, phase shifting, monochromatic light, cones, SCN, clock gene expression