Society for Light Treatment and Biological Rhythms

Program and Abstracts: Volume 21

21st Annual Meeting, June 24th – 27th, 2009
Berlin, Germany

Namni Goel, SLTBR President
Program Committee: Anna Wirz-Justice, Klaus Martiny, Marijke Gordijn, Dieter Kunz
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SLTBR also gratefully acknowledges the artist Andreas Horlitz, well known for his many installations on chronobiology themes, who has kindly installed three SLTBR-related works in the DIN auditorium. The "light box" with engraved actigraphy motifs will illuminate the speakers, and two symbolic composite prints will frame the entrance door. (www.andreas-horlitz.de)

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SLTBR 21ST ANNUAL MEETING PROGRAM

Wednesday, June 24th, 2009

4:30-6:30 pm	**SLTBR Board Meeting**
7:00-10:00 pm	**Registration and opening reception at Käfer Restaurant – Reichstag** (Platz der Republik 1, 11011 Berlin)

Thursday, June 25th, 2009

7:45-8:45 am	Registration
9:00 - 12:10 pm	**CME Course (intended for psychiatrists, physicians, architects, light planners, etc.)** Introductory Course on Chronobiology, Clock Genes, Light Technology, and Clinical Applications *Chair: Dieter Kunz (Berlin, Germany)*
9:00-9:40 am	**Basics in chronobiology** *Marijke Gordijn, University of Groningen, The Netherlands*
9:40-10:20 am	**Molecular mechanisms in chronobiology** *Steven Brown, University of Zürich, Switzerland &* *Achim Kramer, Charité Berlin, Germany*
10:20-10:50 am	Break
10:50-11:30 am	**Technical issues of light** *Horst Rudolph, Trilux, Arnsberg, Germany*
11:30-12:10 pm	**Practical light therapy** *Michael Terman, Columbia University, USA*
12:10-1:15 pm	Lunch
1:15 - 1:30 pm	**President's Welcome** *Namni Goel, University of Pennsylvania, USA*

Lighting and Architecture Focus

1:30 - 3:35 pm	**Symposium I: What Can Chronobiology Offer Architects and Lighting Designers?** *Chairs: Anna Wirz-Justice (Switzerland) & Phillip Mead (USA)*

1:30-1:55 pm	**Visual neuroscience and architectural design** *John Eberhard, USA (architect), Founder of the Academy of Neuroscience for Architecture*
1:55-2:20 pm	**The built environment and the human response to (day-)light** *Mirjam Münch, Switzerland (chronobiologist and sleep researcher), Solar Energy and Building Physics Laboratory, EPFL*
2:20-2:45 pm	**How can a lighting designer use light in buildings for well-being?** *Jens Christoffersen, Denmark (lighting engineer), Danish Building Research Institute*
2:45-3:10 pm	**The future and sustainability of precision color-controlled architectural light sources** *Fred Maxik, USA, Lighting Science Group Corporation*
3:10-3:35 pm	Break
3:35 - 5:00 pm	**Forum: "Biological" Lighting and Architecture - What Do We Know, What Do We Need to Know?** *Chair: Colin Fournier, Architect, Professor of Urban Design, Bartlett School of Architecture, University College London*

Architecture and Lighting Experts participating in the Round Table discussion with SLTBR Chronobiologists

Kristin Feireiss & Hans-Jürgen Commerell	*Architecture Forum Aedes, Berlin, Germany*
Tanya Scholze	*Architect Bob Gysin Partners Zürich, Switzerland, Winner of Velux Daylight Building Award*
Bob Venning	*Lighting designer, ARUP Engineering, London, UK*
Jean-Louis Scartezzini	*Solar physics, daylighting lab LESO, EPFLausanne, Switzerland*
Joachim Stormly Hansen	*Adviser, Optical Indoor Environment, Grontmij/Carl Bro, Denmark*
Dieter Lang	*Physicist, scientific consultant, OSRAM, Germany*
Luc Schlangen	*Scientific consultant, Philips, Eindhoven, The Netherlands*
Toine Schoutens	*The Light & Health Research Foundation, University of Technology, Eindhoven, The Netherlands*
Peter Roos & Peter Dehoff	*Biological lighting researchers, Zumtobel, Austria*
Atto Harsta	*Foundation Living Daylights, The Netherlands*
Andreas Horlitz	*Artist, lighting installations, Berlin, Germany*
Philippe Rahm	*Architect, lighting installations, Paris, France*

7:00 – 9:00 pm **Poster Session with Discussion**
Discussion led by Raymond Lam, University of British Columbia, Canada

Friday, June 26th, 2009

7:45-8:45 am Registration

8:45 - 10:15 am **Symposium II: EUCLOCK: Entrainment in Humans and Animals**
Chairs: Vikki Revell (UK) & Marijke Gordijn (Netherlands)

8:45 - 9:00 am **Entrainment of the human circadian clock**
Till Roenneberg, MPI Munich, Germany

9:00 - 9:15 am **Circadian photoreception: from photic mechanism to clinical strategies**
Claude Gronfier, Inserm, France

9:15 - 9:30 am **Insights into the mechanisms of entrainment using phase response curves in mice (*Mus musculus*)**
Marian Comas, University of Groningen, The Netherlands

9:30 - 9:45 am **A molecular look at chronotype and aging**
Lucia Pagani, University of Zurich, Switzerland

9:45-10:05 am **ClockWatcher and LightWatcher, new techniques for ambulatory measurements in humans**
Jakub Späti, University of Basel, Switzerland &
Marijke Gordijn, University of Groningen, The Netherlands

10:05-10:15 am **General discussion: Where does EUCLOCK go from here?**

10:15-10:45 am Break

10:45-12:15 pm **Oral Presentations I. Photobiology**

10:45-11:05 am **Melatonin phase shifts to dawn simulation and bright light, with photic and non-photic controls**
M. Terman, J. Su-Terman

11:05-11:25 am **Timing light treatment for eastward and westward travel preparation**
M. Paul, J. Miller, R.J. Love, H. Lieberman, S. Blazeski, J. Arendt

11:25-11:45 am **Seasonal changes in peripheral and central serotonin transporter parameters**
M. Willeit, N. Praschak-Rieder, H.H. Sitte

11:45-12:05 pm	**Seasonal fluctuations in platelet inositol trisphosphate receptor (ip_3r) levels in women with Seasonal Affective Disorder and normal controls** *R.D. Levitan, D. Nacuta, P. Li, J. Warsh*
12:30-1:30 pm	**Lundbeck-Sponsored Lunch Symposium: Melatonin, Circadian Rhythms, Mood and Sleep**
12:30-12:40 pm	**Introduction to melatonin symposium** *Namni Goel, University of Pennsylvania, USA*
12:40-1:05 pm	**Melatonin and REM sleep in healthy subjects and patients** *Dieter Kunz, Charité Berlin, Germany*
1:05-1:30 pm	**Phase-delayed circadian misalignment correlates with symptom severity in non-seasonal depression and healthy subjects** *Alfred Lewy, Oregon Health and Science University, USA*
1:45-3:15 pm	**Oral Presentations II. Biological Rhythms and Sleep**
1:45-2:05 pm	**Gender-specific sub-clinical dysphoria correlates with phase-delayed circadian misalignment in healthy women** *J. Emens, A.J. Lewy, J.N. Rough, J.B. Songer, A.L. Laurie*
2:05-2:25 pm	**The impact of activiva light on sleep, circadian phase and health during the polar winter** *V. Mottram, B. Middleton, P. Williams, J. Arendt*
2:25-2:45 pm	**Effects of reducing (blue) light intensity on human's sleep characteristics and melatonin rhythms** *M.C. Giménez, P. Bollen, M.C.M. Gordijn, D.G.M. Beersma*
2:45-3:05 pm	**Role of the circadian gene, *PER3,* in sleep homeostatic and neurobehavioral responses to chronic partial sleep deprivation** *N. Goel, S. Banks, E. Mignot, D.F. Dinges*
3:15-3:45 pm	Break
3:45-4:00 pm	**J. Christian Gillin Junior Investigator Research Award Presentation** **The effect of timed blue-green light on sleep-wake patterns in women with Alzheimer's Disease** *L. Nowak, J.E. Davis*

4:00-5:00 pm	SLTBR Annual Business Meeting
7:00 pm	Annual Banquet (Hugos Restaurant, 14th floor of the Intercontinental Hotel; Budapester Strasse 2)

Saturday, June 27th, 2009

7:45-8:45 am	Registration
8:45 - 10:20 am	**Symposium III: Sleep Deprivation, Light Therapy, Phase Advance: Chronotherapeutic Adjuncts to Medications in Major Depression** *Chairs: Klaus Martiny (Denmark) & Michael Terman (USA)*
8:45-9:10 am	**Chronotherapeutics for depression: a decision strategy for clinicians** *Anna Wirz-Justice, Psychiatric Hospital of the University of Basel, Switzerland*
9:10-9:35 am	**Clinical efficacy and feasibility of chronotherapeutics in psychiatric care** *Cristina Colombo, Instituto Scientifico Universitario Ospedale San Raffaele Milano, Italy*
9:35-9:55 am	**Results from a study in unipolar patients using sleep deprivation in combination with bright light therapy and sleep timing control** *Klaus Martiny, Psychiatric Research Unit, Hillerød, Denmark*
9:55-10:20 am	**Results from a study in bipolar patients using sleep deprivation, sleep phase advance and bright light therapy** *Joseph Wu, University of California, Irvine, USA*
10:20-10:40 am	Break
10:40-12:20 pm	**Oral Presentations III. Light Therapy: Treatment Beyond Seasonal Affective Disorder**
10:40-11:00 am	**Light therapy for nonseasonal depression: status report** *R.W. Lam*
11:00-11:20 am	**The effects of light therapy in non-seasonal depression with atypical features. Preliminary results** *P.M.J. Haffmans, P. Leydens, M.Hysaj, M. Blom, K. de Boer*

11:20-11:40 am	**A double-blind placebo-controlled randomised trial of light therapy for antepartum depression** *A. Bader, A. Riecher-Rössler, U. Frisch, K. Wolf, R.-D. Stieglitz, J. Alder, J. Bitzer, I. Hösli, M. Terman, K. Wisner, A. Wirz-Justice*
11:40-12:00 pm	**Can light treatment improve well-being of patients with emotional instability of the borderline type? – preliminary results** *V. Bromundt, A. Wirz-Justice, C. Cajochen*
12:00-12:20 pm	**A multistage chronobiologic intervention for the treatment of depression: a pilot study** *L. Moscovici, M. Kotler*
12:20-12:30 pm	**President's Closing Remarks** *Namni Goel, University of Pennsylvania, USA*
12:30-2:30 pm	**Optional Event:** *Tour of the newly renovated ("chronobiological lighting") Department of Psychiatry, in the Vivantes Klinik Berlin (headed by Professor Jürgen Staedt)*

SLTBR 21st ANNUAL MEETING

POSTER PRESENTATIONS

CIRCADIAN RHYTHM IMPAIRMENT AS A RESULT OF CHEMOTHERAPY FOR BREAST CANCER
S. Ancoli-Israel, J. Savard, L. Liu, L. Natarajan, F. He

LIGHT THERAPY FOR SEASONAL AFFECTIVE DISORDER: WHAT'S LUX GOT TO DO WITH IT
J.L. Anderson, C.A. Glod, J. Dai, Y. Cao, S.W. Lockley

RECALL, NUMBER AND EMOTIONALITY OF DREAMS DURING A MULTIPLE NAP PARADIGM: ARE THERE DIFFERENCES IN DEPRESSION?
S.L. Chellappa, S. Frey, A. Birchler-Pedross, V. Knoblauch, C. Cajochen

REDUCING SYMPTOMS IN WOMEN WITH CHRONIC ANOREXIA NERVOSA. A MULTIPLE SINGLE CASE STUDY ON THE EFFECTS OF LIGHT THERAPY
P. Daansen, P.M.J. Haffmans

INCREASE IN SLOW WAVE SLEEP DURING MULTIPLE NAPS IN WOMEN WITH MAJOR DEPRESSION: SLEEP ON HIGHER SLEEP PRESSURE?
S. Frey, A. Birchler-Pedross, P. Brunner, T. Götz, V. Knoblauch, C. Cajochen

IMPACT OF RED VS BLUE EXPOSURE ON ERG: MODULATION DISPARITIES BETWEEN PATIENTS WITH SEASONAL AFFECTIVE DISORDER AND NORMAL CONTROLS
A.M. Gagné, P. Gagné, M. Hébert

THE IMPACT OF PHOTOPERIOD MANIPULATIONS AND MELATONIN ON BREAST AND PROSTATE CANCER - THE USE OF MICE FOR IN VIVO STUDIES
A. Haim, Y. Pilosof, A.Yukler, F. Fares

POLYCHROMATIC BLUE-ENRICHED FLUORESCENT LIGHT FOR MELATONIN SUPPRESSION AND CIRCADIAN PHASE RESETTING
J. Hanifin, S. Lockley, K. Cecil, K. West, M. Jablonski, B. Warfield, M. James, M. Thiessen, B. Byrne, E. Gerner, M. Rollag, G. Brainard

SEASONAL PERIMENOPAUSAL INTERACTION IN AFFECTIVE ILLNESS
F. Jacobsen, L. Comas-Díaz

ACTIGRAPHIC SLEEP AND ACTIVITY PATTERNS IN OLDER PEOPLE DURING 'BLUE-ENRICHED' AND CONTROL WHITE LIGHT ADMINISTRATION
K.A. Lederle, B. Middleton, T.L. Sletten, V.L. Revell, D.J. Skene

THE EFFECTS OF LOW INTENSITY BLUE-ENRICHED WHITE LIGHT TREATMENT COMPARED TO STANDARD LIGHT TREATMENT IN SAD
Y. Meesters, M.J. Ruiter

CONTINUOUS MONITORING OF AMBIENT LIGHT LEVELS IN UK CARE HOMES FOR OLDER PEOPLE
B. Middleton, E. Cope, I. Eyers, D.J. Skene

CIRCADIAN EFFECTIVENESS OF SOLAR AND ARTIFICIAL RADIATION IN DEPENDENCE ON AGE
H. Piazena, L. Franke, D. Kockott, R. Uebelhack

IS PHYSICAL EXERCISE THE TREATMENT OF CHOICE FOR WINTER DEPRESSION?
A.A. Putilov

IMPROVEMENT IN FATIGUE, SLEEPINESS AND HEALTH-RELATED QUALITY OF LIFE WITH BRIGHT LIGHT TREATMENT IN SEASONAL AFFECTIVE DISORDER (SAD) AND SUBCLINICAL SAD – A SUBGROUP ANALYSIS
C. Rastad, J. Ulfberg, P. Lindberg

ATTENTIONAL BIAS IN SEASONAL AFFECTIVE DISORDER
M.J. Ruiter, P.J. de Jong, Y. Meesters

IS IT FEASIBLE TO ALERT PEOPLE AT RISK FROM SEASONAL AFFECTIVE DISORDER BASED ON KNOWLEDGE OF THE WEATHER?
P. Sachon, P. Marno, T. Laing-Morton, C. Wilson, K. Simpson, J. Mcevoy

USE OF SUNLIGHT EXPOSURE AND MELATONIN AS A TREATMENT APPROACH TO ELDERLY PSYCHIATRIC INSTITUTIONALIZED PATIENTS WITH SLEEP DISTURBANCES
A. Santa-Clara, A. Diniz, L. Seixas, C. Teixeira

LIGHT EFFECTS ON CIRCADIAN ACTIVITY RHYTHMS OF DJUNGARIAN HAMSTERS WITH AN ATTENUATED ABILITY TO SYNCHRONIZE
K. Schöttner, D. Weinert

WINTER-SUMMER VARIATIONS IN OVARIAN FUNCTION IN WOMEN AT 55º N LATITUDE
O.J. Sergeeva, K.V. Danilenko

EXPLORING THE ROLE OF MELANOPSIN IN PUPILLARY RESPONSES TO LIGHT
P. Teikari, L. Mure, H.M. Cooper

SEASONALITY IN AFFECTIVE DISORDERS
W.H. Winthorst, W. Post, P.P. Mersch, Y. Meesters, B. Penninx, W.A. Nolen

MOTION SENSOR ASSESSMENT OF ADHERENCE TO BRIGHT LIGHT TREATMENT
S.Youngstedt, C. Gore

SOCIETY FOR LIGHT TREATMENT AND BIOLOGICAL RHYTHMS ABSTRACTS 2009

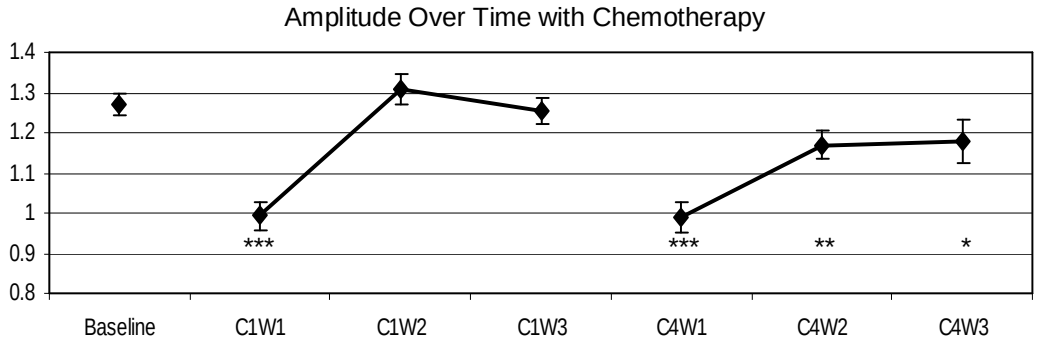
CIRCADIAN RHYTHM IMPAIRMENT AS A RESULT OF CHEMOTHERAPY FOR BREAST CANCER

S. Ancoli-Israel,[1] J. Savard,[2] L. Liu,[1] L. Natarajan,[3] F. He[3]
[1]Department of Psychiatry, University of California, San Diego; [2]School of Psychology, Université Laval and Laval University Cancer Research Center; [3]Department of Family and Preventive Medicine

Objectives: Prior cross-sectional studies have shown that cancer patients have sleep-wake activity cycles that show little distinction between daytime and nighttime, a pattern indicative of circadian disruption. This pattern is seen both before and during cancer treatment. Long term data are needed, however, to assess to what extent circadian rhythm impairments evolve over the course of chemotherapy. The goal of this study was to assess the longitudinal course of sleep-wake activity rhythms before and during chemotherapy for breast cancer.

Methods: Ninety-five women scheduled to receive neoadjuvant or adjuvant anthrocycline based chemotherapy for a stage I-III breast cancer participated. The participants wore a wrist actigraph for 72 consecutive hours at baseline (pre-chemotherapy), as well as during the weeks 1, 2 and 3 (W1, W2, W3) of cycle 1 and cycle 4 of chemotherapy. Sleep-wake circadian activity variables were computed based on actigraphic data.

Results: Compared to baseline, with the exception of acrophase (time of the peak of the rhythm), all circadian rhythm variables examined, including amplitude (peak of the rhythm; see Fig), mesor (mean), and the strength of the rhythm were significantly impaired on the first week of both chemotherapy cycles. Although the circadian variables approached baseline values during W2 and W3 of cycle 1, most remained significantly more impaired during W2 and W3 of cycle 4.



N=95; For comparisons between each time point vs. baseline: * p < .05; ** p < .01; *** p < .0001

Conclusions: These data suggest that the first administration of chemotherapy is associated with transient circadian disruption, while repeated administration of chemotherapy results in progressively worse and more enduring impairments in sleep-wake activity rhythms.

Keywords: Cancer, Circadian rhythms, Sleep-wake activity, Chemotherapy

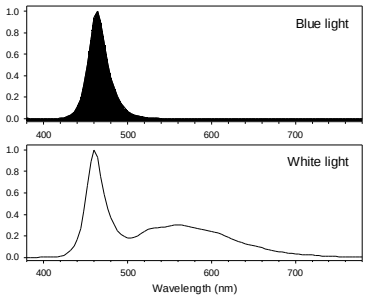
Funding Support: NCI CA112035, NCI CA85264, NIH M01 RR00827, NIH P60MD00220, Moores UCSD Cancer Center NCI P30 CA023100, the Research Service of the VASDHS and the Fonds de la Recherche en Santé du Québec.

LIGHT THERAPY FOR SEASONAL AFFECTIVE DISORDER: WHAT'S LUX GOT TO DO WITH IT

J.L. Anderson[1], C.A. Glod[2,3], J. Dai[2], Y. Cao[2], S.W. Lockley[1]
[1]Brigham & Women's Hospital and Harvard Medical School, Boston MA USA; [2]Bouvé College of Health Sciences, Northeastern University, Boston MA; [3]McLean Hospital Developmental Studies Program, and Harvard Medical School, Belmont MA

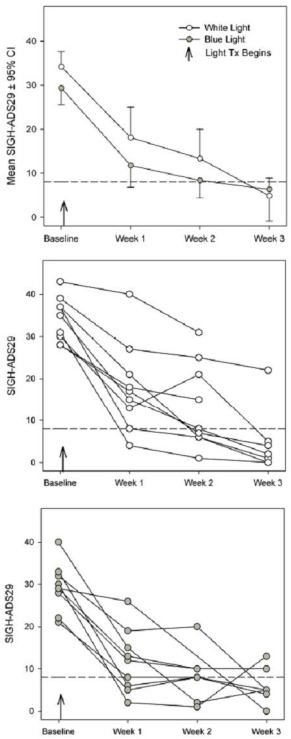
Objectives: Published dosing guidelines for light treatment of Seasonal Affective Disorder (SAD) refer to photopic *lux*, which is not appropriate for short-wavelength light. However, short-wavelengths have been shown most effective at stimulating multiple non-visual responses to light via a recently discovered photoreceptor system (Brainard et al. *J Biol Rhythms* 23:379-384 2008). If SAD therapy were mediated by the same system, standards utilizing *lux* pose the risk of overestimating necessary dose. We investigated antidepressant responses and tolerability to light using two LED sources, each emitting substantial short-wavelength light, but < 2500 *lux*.

Methods: A 3-week randomized, double-blind, clinical trial compared daily treatment (45 minutes) with narrow-band blue-appearing LED light (λ_{max}=464 nm) (goLITE®) to blue-enriched white-appearing LED light in 18 depressed outpatients (12F, 49.1±9.5 yrs, SIGH-ADS ≥20). Both sources emitted ~3.4 x 10^{14} photons/cm^2/s within the short-wavelength range (424-532 nm), but the white source emitted twice as many photons overall and 7-fold more *lux* (blue 98 *lux*; white 711 *lux)*. [see Fig 1, Anderson et al. *Acta Psychiatr Scand* in press]



Results: SIGH-ADS29 decrease averaged 82% (SD=17%) from baseline (p<.0001) in both white- and blue-light groups. [see Fig 2 Anderson et al. *Acta Psychiatr Scand* in press] Both sources were well tolerated.

Conclusions: Current dosing guidelines are insufficient for informing clinical practice and risk overestimating the necessary dose. If SAD light treatment is mediated by the same short-wavelength-sensitive photoreceptor system as other non-visual light responses, the optimal wavelength response will be blue-shifted and therefore illuminance measurement in *lux*, which assumes photopic spectral sensitivity, will be inadequate as a standard for dose. Consequently, large clinical trials of short-wavelength light should not be restricted to treatment of >2500 *lux*. Further research is warranted to thoroughly assess effects of a broader range of devices and dosing strategies that incorporate wavelength as well as duration and irradiance of therapeutic light exposure and assess long-term safety. Narrow-bandwidth light devices require further evaluation. Understanding the spectral sensitivity of therapeutic effects of light is required before light dosing for clinical applications can be quantified definitively.



Keywords: Seasonal Affective Disorder, Phototherapy, Melanopsin

Funding Support: This study was supported by an investigator-initiated grant from Apollo Health, Inc., which provided light treatment devices but had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript. NCT00114322, 2005-P-000160: - Light-Emitting Diode (LED) Light for Seasonal Affective Disorder (SAD) Treatment http://www.clinicaltrials.gov/

A DOUBLE-BLIND PLACEBO-CONTROLLED RANDOMISED TRIAL OF LIGHT THERAPY FOR ANTEPARTUM DEPRESSION

A. Bader[1, 2], A. Riecher-Rössler[2], U. Frisch[2], K. Wolf[2], R.-D. Stieglitz[2], J. Alder[3], J. Bitzer[3], I. Hösli[3], M. Terman[4], K. Wisner[5], A. Wirz-Justice[1]
[1]Centre for Chronobiology, Psychiatric Hospital, [2]Psychiatric Outpatient Department, and [3]Women's Hospital, University of Basel, Switzerland; [4]Columbia University, New York, USA; [5]University 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 depression. Antepartum depression is a difficult situation that requires careful judgment for treating the depression without harm to the fetus. Light therapy may provide a non-pharmaceutical alternative. Preliminary trials of light therapy have shown promising results (1, 2), which prompted this placebo-controlled randomised trial. We predicted that morning bright light is more efficacious than dim light.

Methods: Pregnant women who fulfilled DSM-IV criteria for major depressive disorder (MDD) without seasonal pattern were randomly assigned either to 7000 lux fluorescent bright white light therapy (SphereOne) or 70 lux dim red light as a placebo control, administered in the morning upon awakening for 1h/day in a 5-week trial. Clinical state was monitored weekly by a blind rater using a validated German version of the 17-item Hamilton Depression Scale. To determine dim light melatonin onset (DLMO), evening saliva samples were collected, for melatonin radioimmunoassay (Bühlmann Laboratories), under dim light conditions at the patient's home at baseline and after treatment.

Results: Patient recruitment began in October 2004 and was completed in October 2008. Out of 99 study applicants, 46 were enrolled, 34 completed the trial (12 dropouts), and 7 were excluded because of adjunct therapy or low compliance. We present here a preliminary analysis of the two main endpoints, the observer depression rating and the timing of evening dim light melatonin onset (DLMO, defined as 3pg/ml threshold crossing time). HAMD-17 scores declined significantly from 17.8±5.1 (mean±SD) at baseline to 6.6±4.1 at week 5 for the bright light group (N=16), and from 17.7 ± 4.0 to 10.6±6.0 for placebo dim light (N=11). The two groups did not differ at baseline (T=0.05, df=25, p=0.96), whereas at week 5 patients in the bright light condition had significant lower depression levels than those in the dim light condition (T=-2.11, df=25, p=0.02, 1-sided). Changes of HAMD-17 scores over time analysed in the context of the General Linear Model with a repeated measures analysis of variance were not significant for the factor 'treatment group' (F=0.46, df=1, p=0.50) but highly significant for the factor 'time' (F=25.89, df=5, p<0.0001). The response rate (>50% reduction of initial HAMD-17 score) was signficantly higher in the bright light condition than in the dim light condition (12/16 vs. 4/11; χ^2=4.03, df=1, p=0.02). Even though there was a high remission rate (HAMD-17 score reduction >50% and final score ≤7) in the bright light group, it only showed a tendency to be different from the dim light group (10/16 vs. 4/11; χ^2=1.78, df=1, p=0.09). The DLMO (3pg/ml threshold) was slightly but not significantly earlier after bright light treatment, changing from 21.3±1.6h at baseline to 20.9±1.1h after 5 weeks; N=12 (paired t-test, T=0.96, df=11, p=0.18, 1-sided). There were no differences in DLMO before and after dim light (21.3±1.3h vs. 21.2±1.7h; N=10). There was no correlation between clinical improvement (change in HAMD-17 score) and phase shift of DLMO (r^2=-0.05, N=12, p=0.88).

Conclusions: Recruitment of patients to participate in this study was challenging, even though many patients were attracted by the possibility of a non-pharmacological treatment for their depression. We invested in widespread publicity throughout German-speaking Switzerland, but received only few referrals from other institutions. Many women who screened positively did not want to continue, and many found the study too time consuming. Thus, the final number of patients included was small for a treatment trial. This first analysis of our data shows that the bright light group attained lower depression ratings at the end of 5 weeks treatment than the placebo group (ΔHAMD-17=4.1), even though the classical statistical analysis over the entire time course was not significant. However, this degree of improvement compares well with other trials of light therapy in non-seasonal MDD and with large N drug treatment trials.

Keywords: Major Depression, Pregnancy, Light Therapy, Salivary Melatonin Phase

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

References: (1) Oren et al, Am J Psychiatry 2002;159:666-69. (2) Epperson et al, J Clin Psychiatry 2004;65:421-25.

CAN LIGHT TREATMENT IMPROVE WELL-BEING OF PATIENTS WITH EMOTIONAL INSTABILITY OF THE BORDERLINE TYPE? – PRELIMINARY RESULTS

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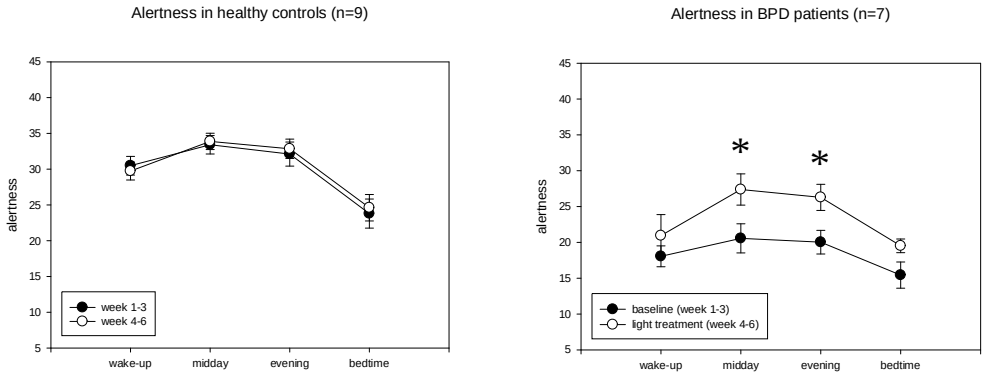
Objectives: Borderline personality disorder (BPD) is characterised by pervasive instability of mood, depression, anxiety, unstable self-image and relationships and self-injurious behaviour. Disturbances in sleep and rest-activity cycles are a common complaint in this patient group. In an ongoing study, we are investigating circadian rest-activity rhythms in women with BPD and whether light treatment can stabilise rhythms and improve well-being.

Methods: Patients (with and without medication) were diagnosed with BPD according to DSM-IV criteria and the Borderline Personality Inventory (BPI). In the baseline interview chronotype (MEQ), seasonality (SPAQ+) and sleep disorders (PSQI) were evaluated. Throughout the protocol regular interviews and a range of questionnaires were used to assess clinical state. Light therapy was administered at home (Daylight, Uplift Technologies, Canada), individually timed in the morning according to the MEQ for 30-40 minutes. Rest-activity cycles were measured in real life settings of women (28.7± 2.9 y) with BPD during 3 baseline weeks, 3 weeks with light treatment and 3 weeks follow-up using actimetry and sleep logs. Healthy female controls, matched by age and daily commitments (<15h per week) followed the same protocol over 6 weeks without light therapy. Once a week they collected saliva samples over 27h for later determination of melatonin and cortisol, and filled in questionnaires concerning their well-being: mood, relaxed state, alertness by the multidimensional well-being questionnaire MDBF, anxiety state by STAI, and anger state by STAXI, at wake-up, midday, evening, and bedtime. Depression and borderline symptoms were assessed weekly by the Hamilton Depression Scale with Atypical Depression Supplement (SIGH-ADS), Beck Depression Inventory (BDI) and Borderline Symptom List (BSL).

Results: Seven BPD subjects and 9 controls have completed the study so far. Six of the BPD subjects fulfilled the criteria for SAD and 2 controls for Sub-SAD as measured by the SPAQ+. BPD had higher daytime sleepiness and worse sleep quality in the PSQI. SIGH-ADS (self-rating) depression scores improved with light treatment (rANOVA, factor treatment: $p \leq 0.038$). BPD subjects differed significantly from controls concerning well-being, anxiety, and depression at baseline as well as during light treatment. However, during light therapy, alertness in BPD improved significantly at midday (rANOVA: factor group*treatment $p=0.004$) and evening (rANOVA: factor group*treatment $p=0.014$; see figures). Actimetry analyses revealed that BPD slept longer than controls during baseline (unpaired t-test: $p=0.006$), but there was no difference in circadian parameters.

Conclusions: BPD is a heterogeneous group of patients with comorbidity in different domains. In addition, sleep disturbances, daytime sleepiness, and depressive mood are characteristic. It was surprising to discover how many are also suffering from SAD. Light therapy improves these symptoms (so far studied during winter), as well as some borderline symptoms. Further investigation will follow up these preliminary results.



Keywords: Light Treatment, Alertness, Seasonal Affective Disorder, Borderline Personality Disorder

Funding Support: This study is supported by the VELUX Foundation, Switzerland, and by the 2008 SLTBR grant sponsored by LUMIE, U.K.

RECALL, NUMBER AND EMOTIONALITY OF DREAMS DURING A MULTIPLE NAP PARADIGM: ARE THERE DIFFERENCES IN DEPRESSION?

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Objectives: Recall and content of dreams are both strongly modulated by the ultradian NREM-REM sleep cycle and are deemed to be higher after REM sleep. Here we investigated how dream recall, number of dreams and emotional domain characteristics of dreaming can change in relation to depression, after both NREM and REM sleep during a multiple nap paradigm.

Methods: Analysis of dream recall and sleep EEG (NREM/REM sleep) was performed in nine young healthy women (20-31 years) and 8 young depressed women (20-31 years) during a 40-hour multiple nap protocol paradigm (150 minutes of wakefulness and 75 minutes of sleep, thus comprising 10 naps) under constant routine conditions. A nap trial that contained only REM sleep stage in the last 15 minutes of a scheduled nap was defined as REM nap, whereas a nap trial without REM sleep stage but NREM sleep stages was defined as NREM nap. Dream recall was assessed at the end of each nap trial (10 naps in total) with the Sleep Mentation Questionnaire, which addresses dream recall, number of dreams and the emotional domain of dreaming. For the latter, an emotional composite score comprised emotionality, vividness, pleasantness, hostility and colourfulness.

Results: Dream recall and number of dreams varied significantly across the multiple nap paradigm (main factor 'nap', $p<0.001$). While dream recall did not differ between the healthy and the depressed conditions, the number of dreams elicited a significant interaction between factors 'state' (healthy vs. depressed) and 'naps' ($p<0.05$), with depressed women reporting more dreams after naps scheduled in the evening. The emotional composite score differed significantly for main factor 'state' ($p>0.001$), with depressed women exhibiting a higher emotional score, mainly due to more hostile and unpleasant dreams. When considering NREM and REM naps, no differences were elicited between the groups for both percentage of NREM naps (H=47%; D=56%, Mann-Whitney U-test $p>0.1$) and for REM naps (H=40%, D=36%%, Mann-Whitney U-test $p>0.1$). Depressed subjects recalled similarly after both NREM and REM naps, while healthy individuals recalled significantly more after REM naps ($p<0.05$). Interestingly, the comparison of the emotional composite score between both groups yielded significant differences for factor 'state' ($p<0.001$), with depressed subjects exhibiting a higher emotional composite score after NREM naps in relation to healthy women but not after REM naps. Furthermore, the significant interaction 'state' vs. 'type' (NREM / REM naps), indicated that healthy but not depressed women presented a higher emotional score after REM naps in relation to NREM naps ($p<0.05$).

Conclusions: Although depressed subjects appear to recall dreams similarly as healthy controls, they did not show a NREM-REM sleep specific modulation of emotionality in their dreams, but exhibit a comparatively higher emotional score, particularly after NREM naps. Therefore, it can be inferred that the emotional domain of dreaming in depression is particularly enhanced after NREM sleep, which does not appear to occur in healthy controls.

Keywords: Dream Recall, NREM/REM Sleep, Depression, Circadian Rhythms

Funding Support: Research supported by the Swiss National Science Foundation (START #3130-054991.98, #3100-055385.98 and # 320000-108108/1 to C.C.)

HOW CAN A LIGHTING DESIGNER USE LIGHT IN BUILDINGS FOR WELL-BEING?

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Objectives: Designing a good lighting environment seems to become more complex in the future. Traditionally, lighting designers, architects, engineers and lighting manufactures have concentrated on creating a lighting environment for visual functions and visual amenity, completely integrated with the building architecture and meeting the challenges of being energy efficient. However, ongoing biological and behavioural research suggests that the lighting environment should also support human health and well-being; but it is still unknown what implications it will have for architecture and lighting design.

Conclusions: Adequate lighting, both natural and artificial, is important as part of a person's well-being. A description of a person's well-being may be context-specific depending on the building design and include a number of parameters such as daylight and sunlight penetration, window views and content of view, enclosed or open space, crowding, visual and acoustical privacy, personal control of ambient conditions etc. Successful daylighting requires trade-offs and optimisation between competing design aspects by skilful integration of the facade layout with the space configuration and the choice of lighting system used. Surveys consistently show that people prefer daylight over electric light, a desire for windows and view is well-established, and daylight as primary source is believed to be more healthful. Also, work spaces often consist of changing visual tasks, and thereby different lighting requirements. A lighting designer needs to balance the intensity of the light used, its location and direction adequately. The design must fulfil national building regulations or standards and provide a scenario where the general lighting satisfies visual functions and visual amenity and includes lighting that supports individual needs (e.g. task lamps). Thereby the lighting environment would meet most individual needs, reduce possible nuisance and support a person's well-being. However, the lighting designer is challenged by the ongoing biological and behavioural research, which opens new areas for lighting and daylighting application. Does this cause significant changes in today's building design and practice or can we continue as now, if we apply context-specific, evidence-based lighting and daylight design? Maybe, maybe not, since lighting and daylight design are often introduced too late in the building design process, thus creating lighting environments that are difficult to improve, since building design rarely changes during the lifetime of a building. Therefore, the research community needs to bring its knowledge to the designer, as one of the main targets, and it is essential that the information provided is clear, simple and context-specific, in order to minimise poor design resulting in short- and long-term effects of the people within the building. The information is rich, but the readers may not have the necessary background knowledge or time to search for similar information and thus adopt research results into a building design that is completely different from the context in which they where found. So, to quote a recent publication by Veitch [1], she addresses one of the key issues why design guidance may not be the main target of the research community: *Many academics may think that these activities* [Design Guidance] *are unimportant and not rewarding. These forms of publication may not be among those counted towards tenure and promotion decisions, which constitutes a barrier to interdisciplinary research and to its application. Experience suggests that there are other rewards, most notably the awareness that one's applied research is being applied in buildings, with beneficial results for the well-being of the people in them.*

Reference: [1] Veitch, J. A. (2008). Investigating and influencing how buildings affect health: Interdisciplinary endeavours. *Canadian Psychology*, 49, 281-288.

CLINICAL EFFICACY AND FEASIBILITY OF CHRONOTHERAPEUTICS IN PSYCHIATRIC CARE

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

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

Chronotherapeutics offers then a benign alternative to more radical treatments for severe depression on psychiatric wards, giving to the patients similar rates of response but with the advantage of rapidity of onset and lack of side effects.

Keywords: Chronotherapeutics, Bipolar Disorder, Sleep Deprivation, Light Therapy

INSIGHTS INTO THE MECHANISM OF ENTRAINMENT USING PHASE RESPONSE CURVES IN MICE (*MUS MUSCULUS*)

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Objectives: Entrainment may involve responses to dawn, to dusk, and to the light in between these transitions. Theory on the entrainment of circadian systems has suggested that the entrainment by long photoperiods can be explained by the action of light at the very beginning and the very end of the photoperiod, with little influence of the light in between (Pittendrigh & Daan 1976 J. Comp. Physiol. 106:291). We studied how different parts of the light signal contribute to the phase shifts of the circadian rhythm. This distinction is of importance if we want to understand how circadian rhythms entrain to light-dark cycles with different photoperiods.

Methods: Phase Response Curves (PRC) obtained for three different protocols were studied.
Experiment 1: Laboratory mice (C57BL6J//OlaHsd) were exposed to single light pulses of 7 different durations (1, 3, 4, 6, 9, 12, and 18 h) given once per 11 days in otherwise constant darkness.
Experiment 2: A double 1-h light pulse protocol was used with different intervals of darkness in between (1, 2, 4, 7, 10, and 16 h) and the resulting PRC were compared to the full light pulse PRCs of corresponding durations obtained in experiment 1.
Experiment 3: A step-PRC protocol, classically used to assess the role of light-dark and dark-light transitions, was used with 3 different light intensities (1, 10, and 100 lux). Three groups of mice were kept in complete darkness for 14 days and experienced in day 15 a step-up in light intensity; 14 days later the step-down to 0 lux occurred for all mice, which then stayed in DD for another 14 days.

Results:
Experiment 1: Amplitude and shape of the Phase Response Curve were affected by light-pulse duration. Nine-hour light pulses yielded the maximal amplitude PRC. A simple phase-only model estimated that the first hour of light made a major contribution while the response to the subsequent hours was reduced by a factor of 0.22.
Experiment 2: Up to 6 hours, phase responses induced by double light pulses are virtually the same as by a corresponding full light pulse. We estimated with a phase-only model the response reduction due to light exposure and response restoration due to dark exposure of the system. The results suggest that after 1 h of light followed by less than 4 h of darkness, there is a considerable reduction in response to the second light pulse. Full response restoration requires more than 10 h of darkness.
Experiment 3: Step-PRCs showed mostly delays after lights-on and no clear tendency to either delay or advance after lights-off, and therefore appear incompatible with phase delays generated by light around dusk and advances by light around dawn. Overall there is little or no circadian modulation.

Conclusions: Contrary to standard interpretation of step-PRCs, responses to the transitions *per se* are unlikely. Results are compatible with an initial major contribution of the beginning of the light pulse followed by a reduced effect of the subsequent light. No special role is found for the last hour of light. Double pulses replace single full light pulses of a corresponding duration of up to 6 h due to a response reduction during light, combined with response restoration during darkness. Using this mechanism, mice can maintain stable entrainment to the external LD cycle without being continuously exposed to it. All the data can readily be explained by tonic velocity (parametric) effects.

Keywords: Circadian Clock, Phase Resetting, Phase Response Curve, Entrainment, Light Pulse

Funding Support: Our work is supported by the EC's 5th framework project BRAINTIME (QLRT-2001-01829) and the 6th Framework Project EUCLOCK (No. 018741).

REDUCING SYMPTOMS IN WOMEN WITH CHRONIC ANOREXIA NERVOSA. A MULTIPLE SINGLE CASE STUDY ON THE EFFECTS OF LIGHT THERAPY

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Objectives: The aetiology and pathogenesis of anorexia nervosa is still unknown. Studies show that after treatment 50% recovers fully, 30% partly and 20% becomes chronic as far as regaining weight and normalisation of the eating pattern are taken into account. And even after successful treatment many patients still have another psychiatric disorder as anxiety disorder (25%), mood disorder (22%), substance abuse (14%) or personality disorder (31%) (Steinhausen, 2002). Yamamotova and colleagues (2008) reported that in eating disorders the circadian rhythms of food intake are abnormal. Light therapy synchronized the circadian rhythm of hunger and had an anti-depressant effect on patients with eating disorders. In a controlled study by Lam et al (1994) light therapy reduced symptoms of depression, binge eating and purging. We investigated the effect of bright light therapy (BLT) in patients suffering from anorexia nervosa.

Methods: Five female patients (mean age: 34.2 years; range 24-53) were recruited for this study at the Eating Disorders & Obesity Department of the psychomedical centre PsyQ in The Hague. Written consent was obtained by all participants. To assess current and lifetime psychopathology immediately prior to the start of the study all patients were interviewed by an independent psychiatrist using the SCID-I. In all cases the diagnosis anorexia nervosa was confirmed. Comorbidity included generalised anxiety disorder (n=2), major depression (n=2) and dysthymic disorder (n=1). None of the patients had a normal menstrual cycle (one hysterectomy, two had no menses at all, one a very irregular period). On average the duration of illness was 15.3 years (range: 8 –22 years). The mean BMI for all 5 patients was 16.8 k g/m² (range: 12.7 – 20.8) and mean weight of all patients was 47.7 kg (SD=7.9). Four questionnaires were performed at baseline and after treatment with BLT. Overall psychopathology was measured by the SCL-90 (Dutch Version). Mood and affect were measured by the Dutch Beck Depression Inventory. Core eating disorder behaviour was measured by the Dutch version of the EDI-2. A sleep/wake diary was used to examine the quality of sleep, starting one week before treatment. In this design patients are considered to be their own controls. On 5 daily sessions of thirty minutes at 8.30 AM in the morning the patients were exposed to bright light (10.000 lux) from a light therapy device with constant background lighting. After treatment and at 3 months F.U. period, patients had an appointment with their psychiatrist to check diagnosis and menstrual cycle since it was expected that one of the first effects of light therapy would be a change of the menstrual cycle.

Results: No significant differences were found on the subscales depression, anxiety, sleeping problems and total score of the SCL-90 and BDI before, after treatment and f.u. with BLT. However differences were found on the EDI subscales ‘drive for thinness’ ‘bulimia’ ‘body dissatisfaction’ and ‘interoceptive awareness’ .Global distress of the individual is measured by the total score of all 90 items on the SCl-90. On group level there is a mean decrease of global distress from high to below average. Summarizing the global distress of all patients shows a clinical important improvement. The menstrual cycle, although returned after BLT in 3 patients.

Conclusions: Light therapy might be a new and promising intervention for chronic anorexic patients. Remarkable is that after treatment three patients had a return of their menstrual cycle without any clinical significant weight gain. As expected most patients had a decrease of their depressive symptoms and core eating disorder symptoms as bulimia, drive for thinness and total pathology decreased immediately after treatment. At follow-up after 3 month the benefits were partly lost. Therefore it is advisable to repeat treatment after one month and treatment period should be extended to 2-3 weeks.

Keywords: Anorexia Nervosa, Circadian Rhythm Desynchronisation, Menstrual Cycle, Light Therapy

VISUAL NEUROSCIENCE AND ARCHITECTURAL DESIGN: CHRONOBIOLOGY APPLICATIONS

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What would architects (and their lighting consultants) like to know about chronobiology?
Architects usually receive the design criteria for heating, cooling, ventilation, and light from their clients along with the functional space requirements. Both architects and clients would benefit from knowledge of neuroscience – including chronobiology. Examples are: 1) Biochemicals released as a reaction to stress can cause damage to the hippocampus – can this be modified by light and pleasant views? 2) Stimulation has been shown to increase neurogenesis – can light provide this stimulation? 3) Patients with Alzheimer's disease appear to become more agitated, confused and aggressive late in the day – can this be related to chronobiology? If so, can architects provide "blue light" late in the day to help?

What does a chronobiologist know that can be applied to school classroom lighting design?
Architects know that light in classrooms is a good thing, but they do not appear to have criteria that change the design of classrooms from kindergarten to the sixth grade. We know there are very large changes in children's brains from the age of 5 to 12. It also seems that the first level of circadian regulation undergoes change during this period. We do not yet know how these changes in rhythm affect children during this critical development stage. If we had the required knowledge, we might design classrooms that adapted to these changes. It seems to be true that *One size does not fit all.*

An example of neuroscience applied to the design of Neonatal Intensive Care Units.
There is a time in the course of fetal development when each in a series of events is designed to occur. The senses of taste, touch and smell develop early. The auditory cortex is formed in the third trimester of life. The visual cortex is not formed until the auditory cortex is completed. Problems may arise due to untimely occurrences resulting from premature birth. Thus, it becomes important to design the environment and the care practice of the Neonatal Intensive Care Unit (NICU) to support and facilitate development, and minimize interference. Light is a source of energy and capable of producing injury under a variety of circumstances. The risk of damage from light is related to the wavelength, the intensity, the duration, characteristics of the eye, the maturation of the eye and the eyelids, etc. Neuroscience research has shown that individually controlled lighting for each infant is critical in NICUs.

An example of chronobiology applied to the design of facilities for the aging.
Architects design facilities for aging populations, including residential units, assisted-living units, and long-term care units. Since chronobiology focuses on circadian and homeostatic regulation of sleep, alertness, cognitive performance, mood, memory consolidation and thermoregulation there should be many applications to facilities for the aging. Persons who are over 65 have sleeping problems ranging from chronic insomnia to difficulty staying alert during normal daylight hours. Elderly residents in assisted living facilities often are living with cognitive problems associated with memory – taking medication at the right time and in the correct amount. Patients living in long-term care facilities are often depressed – a mood related behavior. There is some evidence from chronobiology research that there are ways to use light to alleviate the distress of depression.

What is the Academy of Neuroscience for Architecture?
In 2003 I was part of a group of neuroscientists and architects that formed the Academy of Neuroscience for Architecture. As the first president I organized a series of workshops devoted to 1) healthcare 2) elementary schools 3) facilities for the aging 4) justice facilities and 5) laboratories. Many hypotheses were posed for neuroscience from these workshops – some of which should be of interest to chronobiologists.

Keywords: Architecture, Neonatal-Care Units, Classrooms, Facilities for the Aging

GENDER-SPECIFIC SUB-CLINICAL DYSPHORIA CORRELATES WITH PHASE-DELAYED CIRCADIAN MISALIGNMENT IN HEALTHY WOMEN

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Objectives: The hypothalamic circadian pacemaker (biological clock) controls endogenous oscillations in multiple parameters, including mood. We have previously demonstrated a circadian component to winter depression (seasonal affective disorder, SAD) and, more recently, to non-seasonal depression. In both cases, the degree of misalignment between the timing of the pacemaker and the timing of sleep correlated with symptom severity. We then sought to determine whether a correlation between circadian misalignment and mood existed in healthy, euthymic individuals as well.

Methods: Subjects (16 women, 9 men) were first-year medical students at Oregon Health & Science University (OHSU) recruited from among those participating in a student research project. One subject was excluded because she was taking an antidepressant medication and two other subjects were excluded because they were routinely exposed to light during the night (both of which might affect the timing of the biological clock). The remaining 22 subjects were in generally good physical and mental health as documented by a Health and Screening Questionnaire. Subjects kept a sleep/wake schedule of their choosing at home for seven weeks and maintained a written sleep/wake diary to document sleep/wake times. An assessment of circadian phase was conducted at the end of weeks 1, 3, 5 and 7 via six hours of hourly saliva sampling in dim light (< 10 lux) in the OHSU Clinical and Translational Research Center. Samples were assayed for salivary melatonin. Circadian phase was estimated using the dim light melatonin onset (DLMO) which is the time at which the salivary melatonin concentration rises above a threshold of 3 pg/ml. Just prior to beginning saliva collections subjects completed the Profile of Mood States, brief form (POMS-B) mood rating scale. Circadian misalignment was measured using the phase angle difference (PAD), defined as the time interval between the DLMO and the average midsleep of the prior week.

Results: Subjects were 26.0 ± 3.5 years old. The mean (± SD) total mood disturbance (TMD) score was 19.6 ± 13.6 (range: -4.25 to 52.25). Average bedtimes and waketimes were 23:33 ± 0:31 and 07:18 ± 0:29, respectively. In two subjects reliable salivary data was not obtained. The average DLMO for the remaining 20 subjects was 21:13 ± 01:17. Average PAD was 6:12 ± 01:00 h. There was a negative correlation between the TMD score and the PAD: shorter (more phase delayed) PADs were associated with worse mood ($r = -0.58$, $p = 0.008$). PAD and TMD score were highly correlated among the women ($r = -0.83$, $p = 0.0008$) but not among the men ($r = 0.34$, $p = 0.42$).

Conclusions: We have found a gender-specific correlation between circadian misalignment and mood in a small number of healthy individuals. Although subjects' mood fell within the normal range and both the timing of the DLMO and PAD were consistent with historical controls, we found that a delay of the endogenous circadian pacemaker relative to the timing of sleep was associated with worse mood among women but not in men. Whether this relationship is causal, as it appears to be in SAD, remains to be determined. However, the data suggest that circadian misalignment may play a role in every day variations in mood, at least among women. The presence of a circadian mood component in normal individuals further suggests that circadian misalignment may also play a role in symptom severity across multiple psychiatric and sleep disorders (including non-restorative sleep), although the clinical consequences of circadian misalignment may vary among different disorders. Future work on intra-individual correlations between mood and circadian misalignment is also indicated.

Keywords: Circadian Misalignment, Melatonin, Dim Light Melatonin Onset (DLMO), Phase Angle Difference (PAD), Non-Seasonal Unipolar Major Depressive Disorder (MDD)

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INCREASE IN SLOW WAVE SLEEP DURING MULTIPLE NAPS IN WOMEN WITH MAJOR DEPRESSION: SLEEP ON HIGHER SLEEP PRESSURE?

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Objectives: Homeostatic sleep-wake regulation has been hypothesized to be impaired in depression. However, it remains still unclear whether the buildup of homeostatic sleep pressure (Process S) during wakefulness or its decline rate during sleep or both may be altered in depression. In an ongoing study, we aim at quantifying process S in women suffering from major depression and healthy controls during a multiple nap paradigm (i.e. short sleep-wake cycles) under constant routine conditions.

Methods: Eight women with major depression (mean age 23y, SD ± 4.12y) and nine healthy young women (mean age 25.3, SD ± 4.03y) underwent a 40-h multiple nap paradigm comprising 10 short sleep-wake cycles of 150-min wakefulness and 75-min sleep in a chronobiology facility under constant light and temperature conditions. Polysomnographic recordings were carried out continuously. Additionally, subjective sleepiness was assessed by the Karolinska Sleepiness Scale. Slow wave sleep and subjective sleepiness were each subjected to a repeated two-way ANOVA with the factors “group” (depressed vs. healthy subjects) and “nap” (sleep episodes) or “time” (for sleepiness ratings) respectively. Post-hoc comparisons were based on the LSMEANS procedure in SAS with a Tukey-Kramer alpha level adjustment. Furthermore, EEG slow-wave activity (SWA, EEG power density between 1-4.5 Hz, averaged across all naps), as a marker of process S, was subjected to a two-sided T-test at Fz, Cz, Pz, and Oz derivations.

Results: Results disclosed a main effect of the factors “nap” ($p<0.001$), “group” ($p<0.01$), and an interaction effect of “nap x group” ($p<0.05$) for slow wave sleep. Post-hoc comparisons revealed that women with major depression had significantly more slow wave sleep in naps which occurred in the evening during the wake maintenance zone ($p<0.05$). For both the control and depressed groups SWA exhibited a frontal predominance with decreasing values from anterior to posterior sites. SWA in frontal brain regions (Fz) was significantly ($p<0.05$) higher in the group with major depression compared to the healthy controls. Results for subjective sleepiness showed a main effect of the factors “session” ($p<0.001$) and “group” ($p<0.01$) whereas no interaction effect “session x group” was observed. Post-hoc analysis on subjective sleepiness ratings yielded significantly higher scores for almost all time points during the 40-h nap protocol for women with major depression compared to healthy women.

Conclusions: Our data indicate that women with major depression sleep on an elevated sleep pressure level despite the fact that multiple naps encourage low sleep pressure conditions. This can be explained by either a faster build up of process S or a weaker circadian alerting signal, particularly during the wake maintenance zone in depressed women.

Keywords: Major Depression, Sleep Regulation, Process S, Slow-wave Sleep

Funding Support: Research supported by the Swiss National Science Foundation Grant # 320000-108108

IMPACT OF RED VS BLUE EXPOSURE ON ERG: MODULATION DISPARITIES BETWEEN PATIENTS WITH SEASONAL AFFECTIVE DISORDER AND NORMAL CONTROLS

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Objectives: Seasonal affective disorder (SAD) is characterized by a mood lowering occurring in fall and/or winter when the photoperiod decreases and remission during spring and/or summer when the duration of sunlight increases. Even though the aetiology of the disease is still nebulous, the strong link between light and symptoms suggests that a retinal mechanism could be involved. Supporting this hypothesis, we recently found that SAD people do not react the same way as normal controls to recent light history. The latter protocol included light exposures of 60 minutes (performed on different days) to 3 intensities: 5 lux (dim environment), 100 lux (normal indoor lighting) and 10,000 lux (phototherapy). In normal controls, the 5 lux condition yielded to the highest maximal rod response (Vmax) whereas the 100 and 10,000 lux yielded to similar Vmax rod ERG. In SAD patients, the 5 and 100 lux yielded to similar rod Vmax that were similar to the 100 and 10,000 lux condition observed in controls, whereas a decrease was observed in the 10,000 lux condition. No change across seasons was observed suggesting that this pattern of response may represent a trait marker. The decrease after the 10,000 lux exposure in SAD (not observed in normal controls) could be related to the blue light component of the white light spectra, as higher amount of blue light could impact melanospin, a photopigment involved in retinal light adaptation (Hankins & Lucas, 2002) and thought to be affected in SAD (Roecklin et al., 2008). Our goal was to challenge SAD ERG rod and cone response following two light exposure of different color: Blue (to which melanopsin is reactive) and Red (to which melanopsin does not react).

Methods: 10 healthy subjects and 10 SAD diagnosed patients have been exposed in a random order for 60 min to two different light colors (Red or Blue, presented in a Ganzfeld, in the same proportion of that observed in the 10,000 lux white light phototherapy device) separated by an interval of at least 1 day. Cone ERG luminance response function has been assessed 10 min after light exposure followed by a 30 min dark adaptation before acquiring the rod luminance response function using various intensities of stimulation. All the subjects have been tested in winter.

Results: A two-way Anova indicates that blue light decreases the maximal ERG response (Vmax) in both groups in photopic ($p<0.05$) and scotopic condition ($p<0.01$).

Conclusions: The main finding of this experiment is that blue light seems to reduce photoreceptor responses which suggest that melanopsin is involved in retinal adaptation following recent light history. However, the fact that SAD patients do not present a greater reduction suggests that their melanopsin system is performing as in controls.

Keywords: Seasonal Affective Disorder, Electroretinogram, Melanopsin, Light Exposure, Retina

EFFECTS OF REDUCING (BLUE) LIGHT INTENSITY ON HUMAN'S SLEEP CHARACTERISTICS AND MELATONIN RHYTHMS

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Objectives: Beyond vision, light has a great impact on our everyday lifestyle. First, light is the signal that sets the phase of our biological clock, which in turn synchronizes our physiological and psychological rhythms to the 24h rhythm of the environment. Second, light has acute alerting and activating effects, and it acutely suppresses melatonin at night. The recent discovery of photosensitive retinal ganglion cells has triggered new research into the importance not only of light intensity but also its spectral composition. In this study we investigate how an artificial reduction in (blue) light intensity (as occurs during aging by changes in lens transmission) affects human's sleep characteristics and melatonin rhythms under real-life conditions.

Methods: Via the use of soft orange contact lenses (OL) we were able to obtain a decrease in light intensity, particularly in the blue range. 15 subjects participated in this study. In randomized order they started with the control (15 days of wearing their own contact lenses) or with the experimental condition (15 days of wearing the OL). During the experiment actigraphy data were collected and sleep-diaries were filled in. For the last two nights of each 15-days session subjects came to our facility in order to collect saliva samples to assess both undisturbed melatonin profiles (< 10 lux) and the suppression of melatonin in response to 2h of white light from 24:00h to 2:00h (600 lux, Osram tubes). On a separate night outside the 15-days sessions subjects came to our facility to assess the acute effects of wearing the OL on melatonin suppression.

Results: After wearing the OL for 15 days no shift in the dim light melatonin onset was found in comparison with the control condition nor were there any changes in the amplitude of the nocturnal melatonin rhythm. Furthermore, no significant differences were observed between the control and the OL condition in the amount of melatonin suppression by 2h of light starting at midnight. In contrast, however, the suppression of melatonin production immediately after starting to wear the OL was significantly reduced. Sleep parameters were changed by the use of the OL; sleep was less efficient and more fragmented.

Conclusions: The results show that after 15 days of wearing the OL the system adapted to the change in light exposure by becoming more sensitive. Although small in size, the OL effects on sleep characteristics are somewhat similar to the sleep changes that occur with aging.

Keywords: Light Intensity, Light Spectral Composition, Melatonin Rhythms, Melatonin Suppression, Sleep, Humans

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ROLE OF THE CIRCADIAN GENE, *PER3*, IN SLEEP HOMEOSTATIC AND NEUROBEHAVIORAL RESPONSES TO CHRONIC PARTIAL SLEEP DEPRIVATION

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Objectives: The variable number tandem repeat (VNTR) polymorphism 5-repeat allele of the circadian gene *PERIOD3* (*PER3*$^{5/5}$) has been associated with greater cognitive decline at a specific circadian phase in response to a night of total sleep deprivation (TSD), relative to the 4-repeat allele (*PER3*$^{4/4}$). *PER3*$^{5/5}$ has also been related to higher sleep homeostasis, which is thought to underlie this cognitive vulnerability. To date, no study has used a candidate gene approach to investigate the response to chronic partial sleep deprivation (PSD), a condition distinct from TSD and one commonly experienced by millions of people on a daily and persistent basis. We evaluated whether the *PER3* VNTR polymorphism contributed to cumulative neurobehavioral deficits and sleep homeostatic responses during PSD.

Methods: 52 *PER3*$^{4/4}$, 63 *PER3*$^{4/5}$ and 14 *PER3*$^{5/5}$ healthy adults (aged 22-45 y) completed 2 baseline 10h time in bed nights, followed by 5 PSD nights at 4h time in bed in an experiment that involved assessments on a series of neurobehavioral measures (cognitive performance and executive function tests, subjective sleepiness, Maintenance of Wakefulness Test), and physiological sleep responses. Comparisons were made among genotypes. There were no significant differences in genotypic or allelic frequencies between Caucasians and African Americans.

Results: There were large phenotypic differences in PSD response in the *PER3*$^{5/5}$, *PER3*$^{4/5}$ and *PER3*$^{4/4}$ genotypes, and all 3 groups demonstrated equivalent cumulative decreases to PSD in cognitive performance (e.g., Psychomotor Vigilance Test, Digit Span), executive function (e.g., Hayling, COWAT) and alertness (e.g., Maintenance of Wakefulness Test, Karolinska Sleepiness Scale). *PER3*$^{5/5}$ participants had a greater sleep homeostatic response to sleep deprivation (as measured by non-REM slow-wave energy) than *PER3*$^{4/4}$ subjects. *PER3* homozygotes did not differ significantly at baseline in habitual sleep, physiological sleep structure, circadian phase, physiological sleepiness, cognitive performance, or subjective sleepiness.

Conclusions: The *PER3* VNTR polymorphism was not associated with individual differences in neurobehavioral responses to sleep restriction in a large cohort of healthy adults. It was, however, related to one marker of sleep homeostatic response during PSD. This suggests the *PER3*$^{5/5}$ genotype may contribute to differential neurobehavioral vulnerability to sleep loss that involves wakefulness at a specific circadian time in the early morning hours. The comparability of *PER3* genotypes at baseline and their equivalent inter-individual vulnerability to partial sleep deprivation indicate that *PER3* does not contribute to the neurobehavioral effects of chronic sleep loss.

Keywords: Sleep Deprivation, *PER3* Gene, Individual Differences, Homeostasis, Circadian

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LIGHTWATCHERS: A NEW AMBULATORY RECORDING SYSTEM IN HUMANS

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Objectives: Light acts as the main Zeitgeber to entrain circadian rhythms in humans. Recently it has been shown that the spectral composition of light, in addition to light intensity and timing of light exposure, play a major role in these non-image-forming effects of light. The discovery of the photosensitive retinal ganglion cells with a peak sensitivity to short wavelengths of light increased the interest in the spectral characteristics of light in the human environment. Knowledge of the exposure of the eye to dynamic changes of both light color and intensity over time is of major importance to come to a better understanding of the interaction of the circadian pacemaker with the environment under natural situations. Within the EUclock framework a prototype of a new ambulatory device to measure light has been developed; the LightWatcher (Sowoon Technologies, Lausanne, Switzerland). The LightWatcher is a portable recording system measuring irradiance with photodiodes covering the visual part of the light spectrum: red (620nm.), green (540nm.), and blue light (460nm), as well as the infrared (860nm) and the ultraviolet (UV, 350nm) part of it. The addition of the UV sensor makes it possible to distinguish between outdoor and indoor light exposure. Additional recordings include a 3-axial acceleration measurement to record rest-activity cycles and to control compliance, 2 temperature recordings, and sensors to measure pressure and humidity if desired. In a first exploratory study the device was tested in 15 people during 2 consecutive weeks in the summer of 2008. The LightWatchers were attached to glasses in order to have an optimal estimation of light exposure at eye level in the direction of gaze.

Results: The LightWatcher is capable of distinguishing between indoor and outdoor light exposure and differentiates between light sources with different color temperatures. Preliminary analysis in 7 subjects shows a clear difference in exposure to red, green, blue and UV light during working days and days off.

Conclusions: Further tests and calibrations under various artificial light sources are necessary to check the quantitative results of the LightWatcher. The first analyses show clear day-to-day differences in humans that are important for a better understanding of how our endogenous clock is able to predict time in a fluctuating environment.

Keywords: Light Exposure, Spectral Composition, Humans, Ambulatory Measurements, Endogenous Clock

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CIRCADIAN PHOTORECEPTION: FROM PHOTIC MECHANISMS TO CLINICAL STRATEGIES

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Objectives: Entrainment of the circadian timing system to the 24h day is achieved through its daily resetting by light. It is well established that the resetting capacity of light depends on the intensity, timing, duration, pattern and spectral composition of the photic input. Studies in animals have shown that rods, cones and melanopsin-expressing ganglion cells are involved in circadian photoreception. However, the relative contribution of the classical and non-classical photoreceptors is unknown. In order to clarify the responsiveness of the human circadian system to light, we investigated 1) the acute effects of light exposure (spectral sensitivity), 2) the immediate after-effects of light exposure, and 3) the effects of combinations of monochromatic lights.

Methods: The sensitivity of light-induced melatonin suppression was assessed in healthy young males and females. In a within-subject design, each subject was exposed to monochromatic lights of equal photon density ($3.16x10^{12}$ photons/cm^2/sec) at 9 different wavelengths spread over the visual spectrum (420–620 nm) as well as combinations of monochromatic lights. Blood samples were collected every 15-60 min before, during, and after a 60-min nocturnal light exposure session in subjects with fully dilated pupils.

Results: Our results confirm a peak sensitivity of melatonin suppression to wavelengths between 460-480 nm, whereas wavelengths below 460 and above 500 nm are much less effective. From 440 to 420 nm, we find a marked decrease in the effect of light. Finally, the combination of monochromatic lights yields unexpected results, providing new insights into the mechanisms involved in circadian photoreception.

Conclusions: Our results confirm the exquisite sensitivity of the circadian timing system to mid-wavelength lights (460-480 nm). They also show that the effects of light on non-visual functions can be modulated by manipulation of prior light history. Our findings are relevant to for the optimization of current clinical photic strategies used for the treatment of chronobiological and affective disorders.

Keywords: Circadian, Photoreception, Non-visual Functions, Non-image Forming, Melanopsin

Funding Support: Cible Rhône-Alpes, FP6-EUCLOCK

THE EFFECTS OF LIGHT THERAPY IN NON-SEASONAL DEPRESSION WITH ATYPICAL FEATURES. PRELIMINARY RESULTS

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Objectives: In the DSM-IV three subtypes of depression are described: Depression with melancholic features, depression with atypical features (ATD) and psychotic features. ATD has a relatively chronic course, with a low response to antidepressants, more functional disabilities and high risk for relapse. Symptoms of ATD resemble the symptoms of seasonal affective disorder (SAD) including hypersomnia, hyperphagia, tiredness and fear for social rejection, however without the seasonal pattern. Since Bright Light Therapy (BLT) is the first choice of treatment for SAD, we investigated the effects of BLT on depression with atypical features.

Methods: 40 Patients, with a non-seasonal depression with atypical symptoms were asked to participate in the study. After written and oral information and written informed consent all patients were interviewed by an independent psychiatrist to confirm the diagnoses: depression, dysthymic disorder, depression NOS, bipolar II disorder with atypical symptoms. Excluded were patients with other axis I diagnosis, or patients with contraindications for BLT, psychotic symptoms, drug and alcohol dependency. All patients received psychoeducation on chronobiological issues in psychiatry and on the (side) effects of BLT. Patients were randomized to a waiting list (2 weeks) after which 2 weeks of BLT was applied (WL) or to BLT directly (2 weeks; LT). BLT was applied 2 consecutive weeks at 08.30 h AM, 10,000 lux for 30 min. Dim Light Melatonin Onset (DLMO) was measured the day before the first session of BLT and the last evening after BLT. The Inventory of depressive Symptoms (IDS) and the HRSD-SAD, both self-rating scales, were performed at baseline and at weekly intervals and 3 months follow-up period. Sociodemographic, somatic and psychiatric data were collected at baseline.

Results: 23 Patients completed the trial up till now. A significant decrease in the total scores of the IDS and HRSD-SAD were found after 2 weeks BLT. Patients in the WL condition showed a decrease in total scores during the 2 weeks after psychoeducation and before BLT was started. The most remarkable effects were on mood, sleep/waking pattern, eating pattern and concentration. At 3 months follow-up, these effects could still be found however, ‘desynchronization ‘or relapse occurred specifically in mood and carbohydrate craving, while the menstrual cycle was changed in most patients. The effects of BLT on the DLMO will be presented.

Conclusions: Light therapy might be a new and promising intervention for chronic depressed patients with atypical features. It should be emphasized that psychoeducation plays an important role and should always been linked/coupled with BLT. Further research on how to maintain this positive response on the long term, is needed.

Keywords: Atypical Depression, Hypersomnia, Hyperphagia, Circadian Rhythm Desynchronisation, Light Therapy

THE IMPACT OF PHOTOPERIOD MANIPULATIONS AND MELATONIN ON BREAST AND PROSTATE CANCER - THE USE OF MICE FOR IN VIVO STUDIES

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Objectives: Studies carried out on a country scale for breast cancer (BC) in Israel and world-wide for prostate cancer (PC) revealed a significant relation between light at night intensities for the two cancers while such relations were not revealed for lung cancer on both scales and neither for colon cancer on the global scale. Therefore it seemed of great interest to try and understand the biological background of the revealed results and for this purpose we used an animal model. To verify the revealed results on mice inoculated with BC or PC cells when kept under photoperiod manipulations and melatonin treatment.

Methods: For BC experiments we used BALB/c female mice which were inoculated with (4T1). Mice were short day (SD) acclimated and we used three groups: control, light interfered (LI) and LI-melatonin (MEL) treated. For PC experiments we used TRAMP-C2 inoculated into C57BL/6 male mice which were SD or long day (LD) acclimated. Each group as divided into two subgroups where SD-mice were LI treated while LD-mice were MEL treated. In both cases mice were compared with SD or LD untreated mice.

Results: In relation to PC, LD-acclimated mice had significantly bigger tumors relatively to SD-acclimated ones. However, MEL treatment to LD-mice significantly reduced the tumor growth while LI given to SD-mice tended to increase tumor size. In regards to BC, SD+LI had the biggest mean tumor size while LI+MEL treated mice had the smallest mean tumor size smaller than that of SD- acclimated mice, which were used for control.

Conclusions: According to our results MEL has an anti oncogenic effect on both BC and PC. However, we need still to understand the mechanisms through which MEL affects the cancer cells and this is being studied in our laboratory. LI to SD mice increased the BC-tumor significantly while in the case of PC it showed a tendency to increase the tumor size and this could be through abolishing MEL synthesis avoiding its anti oncogenic affects.

Keywords: Melatonin, Photoperiod Manipulations, Breast Cancer, Prostate Cancer

POLYCHROMATIC BLUE-ENRICHED FLUORESCENT LIGHT FOR MELATONIN SUPPRESSION AND CIRCADIAN PHASE RESETTING

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Objectives: Risk factors for astronaut and ground crew health and safety during space exploration missions include disturbed circadian rhythms and sleep-wake patterns (Longnecker and Molins, Bioastronautics Roadmap http://criticalpath.jsc.nasa.gov/, 2005). The goal of our research is to optimize light as a countermeasure for circadian and sleep disruption during space exploration. Monochromatic wavelength comparisons have indicated that circadian phase-shifting responses are shifted towards the shorter wavelength or blue part of the spectrum for healthy humans (Lockley, et al., JCEM, 88, 4502-4505, 2003; Warman, et al., Neurosci Lett, 342, 37-40, 2003). Testing of polychromatic blue-enriched fluorescent light at therapeutic light levels showed them to be no more effective for phase-advancing than standard fluorescent lighting used for bright light therapy (Smith et al., Sleep Med, in press, doi:10.1016/j.sleep.2008.05.005). The specific hypothesis being tested is that white polychromatic fluorescent light has increased efficacy for melatonin suppression and circadian phase resetting when it is enriched in the blue part of the spectrum.

Methods: The two lamps used in this study are 1) a standard white fluorescent with a correlated color temperature (CCT) of 4,000K or 2) a blue-enriched prototype lamp with a CCT of 17,000K predicted to have greater circadian potency than standard white lamps. The light exposure systems consist of 119 x 120 cm flat panels with an internal array of lamps that emit light through an opalized diffuser. Healthy, drug-free male (n=8) and female (n=6) subjects (mean age 22.5 ± 0.5 years) have completed studies with 4,000K or 17,000K exposures of equal photon densities. The seven day studies are being conducted in the Light Research Laboratory of Thomas Jefferson University in an environment free of time cues as outlined below:
Day 1: Baseline, 16h wake (90 lux), 8h sleep (0 lux).
Days 2-3: Circadian phase assessment using a 26h constant routine (CR1); constant wakefulness and posture (sitting in bed), food intake (hourly snack/fluid), dim light (<5 lux).
Day 4: Light exposure (LE), 6.5h in duration was given 9.25h before habitual wake time. Subjects seated upright in constant posture, panels viewed face-on at a distance of 30 cm to achieve a full visual field exposure.
Days 5-6: Circadian phase assessment using a 30h constant routine (CR2).
Day 7: Final 8h sleep before discharge.

Plasma melatonin is drawn through IV catheters placed on Days 2-6 with hourly plasma samples drawn during CR and every 20 minutes during LE. Blood samples are quantified for melatonin by RIA. Melatonin suppression is calculated from the difference in the area under the curve (AUC) between melatonin profiles during LE compared to the corresponding clock times during the previous melatonin cycle on CR1. Phase change is calculated as the difference in the time of onset of melatonin production between CR1 and CR2.

Results: This study is ongoing with 14 of the planned 20 exposures completed. Preliminary one-way ANOVA analysis of plasma melatonin suppression as calculated by AUC indicates that subjects exposed to 6.5 hrs of 17,000K blue enriched fluorescent light had significantly greater suppression of melatonin (79.6 ± 2.3%) compared with subjects exposed to 4,000K fluorescent light (43.3 ± 11.9%) ($p<0.005$). Phase resetting analysis is ongoing.

Conclusions: Currently, 10,000 lux white fluorescent light is used by NASA as a prelaunch circadian countermeasure while much dimmer lighting levels are used for illuminating the Space Shuttle and the International Space Station interiors. The preliminary melatonin suppression data support the hypothesis that blue-enriched 17,000K fluorescent light is a more potent circadian stimulus than the white 4,000K fluorescent light. The long-term goal of our research is to determine the best combinations of light wavelengths for use as a countermeasure during space flight, as well as for NASA ground crew and civilian shift workers.

Keywords: Circadian Phototransduction, Light, Melatonin, Space Exploration, Phase Shift

Funding Support: This work supported by the 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.

SEASONAL PERIMENOPAUSAL INTERACTION IN AFFECTIVE ILLNESS

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Objectives: Menstrual cycle dysfunction is not uncommon in women with affective illness and may be exacerbated by hormonal changes during the perimenopause (Rubinow et al, Psychopharm. Bull. 34: 289-290, 1998). Previously we described the phenomenon of winter amenorrhea in 10 affective disorder patients (Jacobsen and Comas-Díaz, Int. J. Neuropsychopharm. 7: 450, 2004). We now extend our original sample with a naturalistic longitudinal follow-up study of seasonal effects in women treated for affective illness while undergoing perimenopause.

Methods: Subjects were midlife women without a previous history of amenorrhea (missing three consecutive periods) or recent steroid use, who had been stabilized with outpatient psychopharmacology for recurrent affective illness (bipolar spectrum or unipolar) for at least 2 years and were otherwise healthy. Bimonthly evaluation included menstrual cycling, sleep, appetite, energy/activity, sexual function, cognition, and mood. Other data collected included menarche, parity, laterality, diurnality, sleep deprivation response, mood reactivity, headache and neurological history, ethnicity, family genetic history, and treatment history.

Results: In 19 women (12 bipolar, 7 unipolar) treated for mean 14.6 (±4.3 SD) years, amenorrhea occurred at age 49.7±4.2 years. Amenorrhea lasted 4.4±1.5 cycles during the fall/winter of at least one year. Patients reported menarche at 12.7±1.3 years, and varying lifetime premenstrual symptoms, with 15 of 19 women suffering menstrual migraine. Eight women reported histories of fall/winter depressions, but no patient showed increased depressive symptoms with winter amenorrhea. Menses resumed in all women during the spring. Surprisingly, two well-stabilized winter amenorrheic bipolars abruptly menstruated and became manic/mixed state following 7-8 days exposure to significantly increased intensity of sunlight and warmer environmental temperatures.

Conclusions: Winter amenorrhea followed by resumption of menstrual cycling during the spring in perimenopausal women treated for affective illness may suggest that a seasonally-associated melatonin increase superimposed onto midlife declining estrogen levels does not necessarily trigger depressive symptomatology. Sudden intense winter light exposure may dramatically alter the endocrine and affective symptomatology in vulnerable individuals. The phenomenon of winter amenorrhea in affective illness merits further study.

Keywords: Perimenopause, Seasonality, Affective Illness, Light

LIGHT THERAPY FOR NONSEASONAL DEPRESSION: STATUS REPORT

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Objectives*:* Light therapy has an established evidence base to support its efficacy in seasonal affective disorder (SAD). However, there are fewer rigorous studies of light treatment for nonseasonal major depressive disorder (MDD). This presentation will critically review the current evidence for efficacy of light therapy for MDD and present the study design for a new clinical trial.

Methods: An electronic literature search for English-language publications was conducted using the terms light AND depressive disorders. Randomized controlled trials, systematic reviews and meta-analyses were identified.

Results: There have been three published systematic reviews on light therapy for nonseasonal MDD. The first was conducted by the American Psychiatric Association and included studies published up to mid-2003 (Golden et al, 2005). A Cochrane systematic review was published in 2004 (including published and unpublished trials to end-2003) based on 20 studies meeting strict inclusion criteria (Tuunainen et al, 2004). The results of these two systematic reviews were discrepant, but both noted the methodological limitations of the included studies. Since the publication of the Cochrane review, there have been several trials addressing the issue of light therapy combined with antidepressants for MDD, including one well-designed trial conducted by Klaus Martiny and colleagues at a single centre in Denmark (Martiny, 2004). The third systematic review (Even et al, 2008) was published in 2008 and included these recent combination trials. However, the authors concluded that the quality and methodology of the studies were too heterogeneous to conduct a meta-analysis and therefore only provided a qualitative review. They found that there was not yet sufficient evidence to support efficacy of bright light as monotherapy, although there was better evidence for combination treatment with bright light and antidepressants. They also concluded that, given the limited data set, larger multi-centre trials are urgently needed. The LITE+MED trial was designed to address the methodological limitations of previous studies. This recently funded trial is a Canadian multi-centre study to investigate the efficacy of light therapy alone and in combination with antidepressants. The design of the trial will be presented.

Conclusions: Light therapy is a well-tolerated, non-pharmacological treatment that has good acceptability among patients. More evidence of its efficacy in nonseasonal MDD would be of great benefit for a condition in which current treatments are not optimally effective.

Keywords: Major Depressive Disorder, Light, Treatment, Randomized Controlled Trial

Funding Support: The LITE+MED study is funded by grant MCT-94832 from the Canadian Institutes of Health Research (CIHR).

References:

Even C, Schroder CM, Friedman S, et al: Efficacy of light therapy in nonseasonal depression: a systematic review. J Affect Disord 2008; 108:11-23.

Golden RN, Gaynes BN, Ekstrom RD, et al: The efficacy of light therapy in the treatment of mood disorders: a review and meta-analysis of the evidence. Am J Psychiatry 2005; 162:656-662

Martiny K: Adjunctive bright light in non-seasonal major depression. Acta Psychiatr Scand Suppl 2004; 7-28.

Tuunainen A, Kripke DF, Endo T: Light therapy for non-seasonal depression. Cochrane Database Syst Rev 2004; CD004050.

ACTIGRAPHIC SLEEP AND ACTIVITY PATTERNS IN OLDER PEOPLE DURING 'BLUE-ENRICHED' AND CONTROL WHITE LIGHT ADMINISTRATION

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Objectives: Aging is often accompanied by disturbed sleep and altered circadian rhythms. Reduced sensitivity to short wavelength (blue) light has been demonstrated in older people. Thus supplementation with 'blue-enriched' light may be beneficial for treating sleep problems. Actigraphy is a potent tool to measure 24 h motor activity patterns. This study investigated the effects of control light (colour temperature 4000 K) and 'blue-enriched' light (17000 K) treatment on activity and actigraphic sleep parameters in older people (> 60 years) with self-reported sleep complaints. In addition, it aimed to present activity patterns during the day and at night in this community-dwelling population.

Methods: Twelve healthy volunteers (65.3 ± 4.0 years; 7F, 5M) completed an 11-week light treatment trial (randomised, cross-over design) in their own homes. Following a baseline week, each light treatment (photon density ~ 3.62×10^{14} photon/cm^2/s, ~ 400 lux) was administered for 3 weeks; daily light exposure was for 2 h in the morning and 2 h in the evening. A 2-week washout period followed each light treatment. Subjects completed daily sleep diaries and continuously wore an Actiwatch-L (AWL) (Cambridge Neurotechnology Ltd., UK) on their non-dominant wrist. The AWL data provided actigraphic sleep variables using the AWL software package. Circadian rhythm analysis was performed by NPCRA (IV, IS, L5, M10, amplitude, RA) and cosinor analysis (mesor, amplitude, acrophase). The periods of day- and nighttime activity were defined using individual wake-up and bedtimes (both derived from the individual sleep diaries). Proc GLM was used to test for carry-over effects (t-test) and to compare light conditions (corrected for baseline). Weekly means were compared using RM one-way ANOVA (using time as a factor) with post-hoc Bonferroni comparison.

Results: No carry-over effect was observed for any actigraphic parameter. Control light produced significantly higher actigraphic sleep-efficiency than 'blue-enriched' light. This is partly in agreement with the increased subjective sleep efficiency observed during the third week of control light compared to baseline by 7.6 ± 9.2 % (mean ± SD). A significant advance of actigraphic wake-up time by approx. 25 ± 28 mins was observed during the second and third week of control light compared to baseline. This mirrors the significant advance seen for subjective wake-up time (36 ± 54 mins). Actigraphic time awake at night was significantly decreased by approx. 10 ± 6 mins in the third week of 'blue-enriched' light compared to the second washout week. Neither of the light treatments significantly affected any of the circadian rhythm parameters. Cosinor analysis of the activity data is presented in Table 1. No significant differences in day- and nighttime activity (activity counts/h) were observed before, during or after each light condition.

Table 1. Parametric variables (mean ± SD) obtained from cosinor analysis.

	Mesor (activity counts)	**Amplitude (activity counts)**	**Acrophase (decimal h)**
'Blue-enriched' light	12963 ± 4724	12000 ± 5338	13.8 ± 0.6
Control light	12729 ± 5258	11672 ± 5612	13.8 ± 0.7

Conclusions: This study provides a snapshot of the general activity patterns of older, healthy people living in the community. It shows that light treatment has significant, albeit subtle, beneficial effects on some actigraphic sleep parameters, e.g. advanced wake-up time and reduced nocturnal wake time. Control light significantly increased actigraphic sleep efficiency compared to 'blue-enriched' light. These results confirm previous findings for subjective sleep.

Keywords: Short Wavelength Blue Light, Actigraphy, Light Treatment, Age, Sleep

Funding Support: EU (MCRTN-CT-2004-512362), FP6 EUCLOCK (018471) and SomnIA Collaborative Research (RES-339-25-0009). Philips Lighting (The Netherlands) provided the light units.

SEASONAL FLUCTUATIONS IN PLATELET INOSITOL TRISPHOSPHATE RECEPTOR (IP_3R) LEVELS IN WOMEN WITH SEASONAL AFFECTIVE DISORDER AND NORMAL CONTROLS

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Objectives: To examine seasonal fluctuations of the platelet inositol trisphosphate receptor (IP_3R), part of the serotonin-2 receptor ($5\text{-}HT_2R$) signaling cascade, in women with SAD and matched normal controls.

Methods: 17 adult women with SAD and 15 matched controls provided fall/winter blood samples to assess levels of the IP_3R2 protein (the predominant IP3R subtype in platelets) as measured by Western blot in platelet lysates. Nine SAD subjects and 6 control subjects also provided a spring-summer sample for analysis.

Results: No difference in IP_3R2 levels was found between SAD patients and controls in either fall/winter or spring/summer. However, within-subjects comparisons across the two seasons demonstrated that IP_3R2 levels were significantly higher in spring/summer than in fall/winter in both SAD patients ($t = 3.83$, $df = 8$, $p = 0.005$) and healthy controls ($t = 3.04$, $df = 5$, $p = 0.029$).

Conclusions: There appears to be a robust seasonality to the expression of the platelet inositol triphosphate receptor IP3R2, which is part of the serotonin-2 signaling cascade. Consistent with several findings for serotonin activity per se, this seasonality appears to be occurring in the normal population as well as in subjects with SAD. Seasonality will be an important consideration in future studies of the IP3R signal transduction system in various normal and abnormal populations.

Keywords: Seasonal Affective Disorder, Second Messengers, Signal Transduction, Seasonality, Inositol Triphosphate Receptor

Funding Support: This work was supported by NARSAD.

Reference: Dwivedi Y, Janicak PG, Pandey GN. Elevated [3H]inositol 1,4,5-trisphosphate binding sites and expressed inositol 1,4,5-trisphosphate receptor protein level in platelets of depressed patients. Psychopharmacology (Berl). 1998 Jul;138(1):47-54.

RESULTS FROM A STUDY IN UNIPOLAR PATIENTS USING SLEEP DEPRIVATION IN COMBINATION WITH BRIGHT LIGHT THERAPY AND SLEEP TIMING CONTROL

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Objectives: In contrast to the treatment of unipolar depression with medication, wake therapy (sleep deprivation) is known, through many years, to induce a rapid amelioration of depressive symptoms. Older studies did, however, show a marked tendency to relapse into depression when stopping wake therapy, but recently developed techniques seems to be able to sustain the acute response. These techniques are labeled chronotherapies as they incorporate the use of methods working on the circadian level such as wake therapy, light therapy and sleep time control. The absolute magnitude of the effect of chronotherapies in combination with antidepressant medications are often obscured by placebo responses as is the case in any therapy that cannot be blinded. The objective was thus to design a randomised controlled trial aiming at a balanced placebo response to assess efficacy. Furthermore we aimed at describing participants at baseline on a multi-axial (DSM-IV) approach to be able to predict response to the chronotherapeutic treatment.

Methods: Patients with a current diagnosis of unipolar or bipolar major depression according to the DSM-IV were included and randomized to a Chronotherapy group (Chrono-group) or an Exercise-group. The Chrono-group used a combination of three total sleep deprivations at the beginning of the study (intervention week), followed by sleep time control and daily bright light treatment. The Exercise group used a daily program individually tailored to a minimum of 30 minutes of moderate intensity. All patients were treated with a fixed dosage of duloxetine 60 mg daily. All patients were admitted to an open psychiatric ward in the intervention week to secure compliance and for safety reasons.

Results: From one week after the intervention, patients in the chronotherapy group showed a greater decrease in depression scores compared to patients in the exercise group and this difference between groups increased over the following weeks and reached statistical significance ($p=0.03$). Remission were obtained in 42 % of the patients in the Chrono-group compared to 14 % in the Exercise group at 4 weeks after the end of the intervention week ($p=0.007$). Self assessment scales showed the same pattern. Side effects of sleep deprivation, bright light therapy and exercise were rare and mild. The baseline expectancy ratings for the two groups were similar (Chrono-group 8.4, Exercise-group 8.6).

Conclusions: The chronotherapeutic intervention induced a rapid and sustained response superior to the response seen in the exercise group.

Keywords: Depression, Sleep Deprivation, Wake Therapy, Bright Light Therapy, Sleep, Exercise, Psychometrics

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ARTIFICIAL LIGHTING AND ITS EFFECTS

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Industrialized nations rely heavily on the use of light sources to brighten the nights and lengthen working hours. The Correlated Color Temperature (CCT) and Color Rendering Index (CRI) describe the visual quality of white light sources and help consumers choose the appropriate light for specific applications.

Today, there are several methods to produce light:

- Combustion
- Incandescence
- Electroluminescence
    - Solid-state lighting
- Gas discharge
    - Fluorescent
    - Low pressure sodium
- High Intensity Discharge (HID)
    - Metal halide
    - High pressure sodium
- Additive mixing of red, green and blue monochromatics

With growing knowledge of light's affect on certain human conditions, safety, agriculture, and biology, we can design future lighting systems and methods to deliver efficient lighting and effects while avoiding unintended consequences.

Thus, the study of light sources, their intended use, and their chromatic content is important for the enhancement of visual acuity, improvement of biological attributes, and enrichment of general well-being of bio-diverse populations.

THE EFFECTS OF LOW INTENSITY BLUE-ENRICHED WHITE LIGHT TREATMENT COMPARED TO STANDARD LIGHT TREATMENT IN SAD

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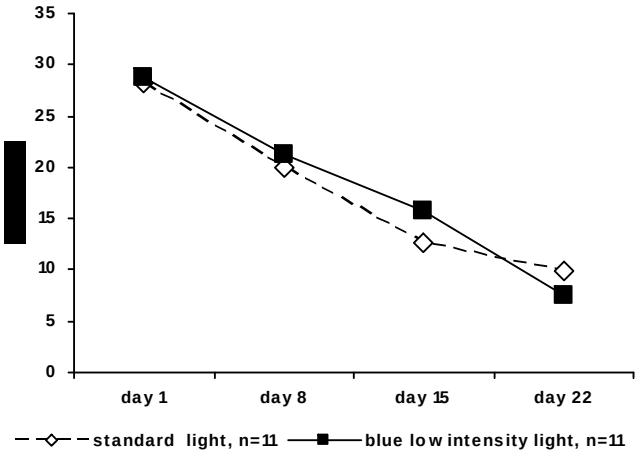
Objectives: Non-image forming (NIF) photoreceptors play a role in the phase-shifting effects of short-wavelength light. A previous study, Gordijn et. al, 2006, compared standard light treatment (SLT) of SAD with a treatment that used short-wavelength blue-enriched white light (BLT). Both treatments used the same illuminance (10 000 lux) and were highly, and equally, effective. A first explanation for this lack of a difference is that nor the NIF receptors nor the biological clock play a major role in the therapeutic effects of light. Alternatively, the effects may be (at least partly) mediated by the NIF receptors, which may already be saturated by the high illuminances used. The role of the NIF receptors and/or the biological clock in SAD and in the effects of light treatment, has been further explored in a new randomised controlled study (identical to the design used by Gordijn et. al in 2006). The study compares the effects of low intensity BLT against the effects of high intensity SLT.

Methods: In a 22 days design, 22 patients (40.4 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 (10 000 lux) for two weeks, on workdays between 7.30 and 8.30 a.m., in the winter of 2008/2009. 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 BLT (17000ºK) with a vertical illuminance of 750 lux using a prototype of the EnergyLight®, which emitted a higher proportion of short wavelengths. All participants completed questionnaires concerning mood, sleepiness and sleep quality on a daily basis starting at day 1 (3 days before treatment). SIGH-SAD ratings were obtained 4 times (on days 1, 8, 15, and 22).

Results: On day 22, SIGH-SAD ratings were significantly reduced compared to day 1 (SLT 64.8% and BLT 74.1%). Between the conditions, no statistically significant differences were found.
In the SLT condition were 72.7 % responders (SIGH-SAD reduction ≥ 50%), in the BLT condition 100%. In the SLT condition 54.5 % recovered (SIGH-SAD ≥50% and final score ≤ 8) and in the BLT condition 72, 7%. These differences were not statistically significant.



Conclusions: The sample size is small, so the conclusions can only be preliminary. The two treatment conditions were highly effective. The therapeutic effects of low intensity blue-enriched light were comparable to those of the standard light treatment. Even with an intensity of 750 lux blue-enriched light, it is still possible that saturation effects play a role. Further research is necessary to find the optimal intensity of blue-enriched light in treating SAD. The achievement of SAD therapeutic effects with blue enriched white light at illuminances as low as 750 lux helps to bring light treatments against SAD within reach of standard general workplace and educational lighting systems.

Keywords: SAD, Light Treatment, Blue-enriched Light, Short Wavelengths, Intensity

Acknowledgements: The light fixtures were courteously adapted and donated by Royal Philips Electronics B.V., The Netherlands.

Reference: Gordijn et al. (2006): SLTBR abstracts 18:6.

CONTINUOUS MONITORING OF AMBIENT LIGHT LEVELS IN UK CARE HOMES FOR OLDER PEOPLE

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Objectives: Age-related changes in the eye result in decreased visual acuity and reduced photic input to the circadian clock. Low lighting levels have previously been reported in institutions for older people. Increased lighting levels have been shown to lessen "sundowning" and increase circadian amplitude in people suffering from senile dementia. Improved lighting may decrease the number of falls in the older population as well as increasing daytime alertness and visual acuity. In previous studies ambient light levels have been measured as "snapshots" with measurements taken at discrete time points on sunny and cloudy days and failing to measure artificial lighting alone after sunset. Light sensors were thus placed in care homes to monitor light levels continuously across the 24 h day.

Methods: Light data were collected in 7 care homes in south-east England (51.3-51.5^{o}N; 0.2-0.76^{o}W) for 11.7 ± 2.4 days (mean ± SD) during March - October. Light levels were recorded at 5 min intervals at 12 locations within each care home using HOBO Dataloggers (Tempcon Instruments Ltd.,UK). Rooms monitored included communal lounges, dining rooms and reception areas plus individual residents' rooms, position and orientation were noted. The light sensors were suspended against the wall 1-1.5 m from the ground in a vertical direction (angle of gaze). Hourly average light levels were calculated for all records and mean number of hours above 500 lux (~ 1000 lux in horizontal direction) determined. Mean evening artificial light levels were also calculated. Data recorded in July and October were analysed in detail to determine the mean number of minutes above 500 and 1000 lux per 24 h plus maximum light intensity recorded.

Results: Within each individual care home there was great variability in the maximum light level (hourly means) recorded depending on the orientation of the room. Many room light intensities did not exceed 500 lux over the 24 h day even in the summer months. A clear effect of natural sunlight can be seen in rooms facing SE - SW. Lighting levels from artificial light alone are shown in Table 1. The average was 162 ± 24 lux. In care home (CH) 3 (July'07) depending on the room monitored time above 500 lux ranged from 673 ± 34 mins to 0 mins with a maximum of 8585 ± 1071 lux and a minimum of 216 ± 125 lux. In CH4 (October'07) time above 500 lux ranged from 162 ± 24 mins to 0 mins with a maximum of 1406 ± 132 lux and a minimum of 125 ± 10 lux.

Table 1. Summary of ambient light levels recorded in 7 care homes.

Care home	**Date**	**# of hobos recording levels < 500 lux**	**Mean evening light levels (lux ± SEM)**
1	March '07	2/4	157 ± 36
2	June '07	4/12	150 ± 27
3	July '07	3/12	252 ± 54
4	October '07	6/12	236 ± 33
5	March ' 08	4/12	123 ± 33
6	April '08	4/11	153 ± 26
7	June '08	6/10	65 ± 10

Conclusions: This study provides a detailed look at the lighting levels recorded in care homes in SE England. Some rooms reach adequate lighting levels with natural sunlight, areas without sunlight and artificial light alone did not exceed 200 lux. The lowest lighting levels were seen in the reception areas. As increased light intensity has been shown to have beneficial effects on wellbeing ambient lighting levels in those areas not receiving natural daylight needs further investigation.

Keywords: Care Homes, Light Monitoring

Funding Support: The SomnIA Collaborative Research project is funded by the Cross-Council New Dynamics of Ageing initiative (Grant number RES-339-25-0009).

A MULTISTAGE CHRONOBIOLOGIC INTERVENTION FOR THE TREATMENT OF DEPRESSION: A PILOT STUDY

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Objectives: Most antidepressant medications in current use have several disadvantages: a delayed therapeutic effect, side effects, stigmatization and concerns about safety for the developing fetus during pregnancy. Several chronobiologic techniques which are free of these disadvantages were proposed as an alternative. The current article reports the design and the initial outcome results of a new chronobiologic multistage intervention (CMI) that is comprised of the following techniques: (i) partial sleep deprivation during the second half of the night (wake therapy - WT), (ii) medium (green) wavelength light in combination with dawn simulation (DS), (iii) bright light therapy (BLT), and (iv) sleep phase advance (SPA).

Methods: The study was conducted as a set of 12 single-case designs with moderate-to-severe depressive volunteering patients. Depression, anxiety and tension measurements were taken on a daily basis beginning with a baseline measurement (T0), followed by a set of four consecutive morning measurements during the therapeutic intervention (T1-T4),and with a final measurement carried out at the end of 4 weeks of follow-up (T5).

Results: A clinically significant rapid improvement of the depressive symptoms was demonstrated and maintained for at least four weeks after the end of the intervention. No dropouts or compliance difficulties were observed. Patient satisfaction was high, and other than having to sleep for four nights at the Research and Development Unit, participants were not inconvenienced by the nature of the therapeutic design. Sleepiness in the late afternoon hours was reported by several of the participants, but did not reach a level that interfered with their ability to function. Levels of tension did not show a consistent improvement along the intervention procedure and were not maintained in follow-up. There was some unexpected improvement in the level of anxiety that persisted at follow-up. This latter finding requires further validation by additional studies.

Conclusions: These initial findings showed the procedure to be effective and well tolerated. It affords many advantages, such as the achievement of a rapid response, no extinction of the therapeutic effect after four weeks of follow-up, safety, high patient compliance and cost-effectiveness. These encouraging results warrant validation in further randomized controlled clinical trials.

Keywords: Depression, Chronobiologic Intervention, Wake Therapy, Bright Light Therapy

THE IMPACT OF ACTIVIVA LIGHT ON SLEEP, CIRCADIAN PHASE AND HEALTH DURING THE POLAR WINTER

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Objectives: The lack of natural sunlight during the Polar winter is associated with delayed circadian phase, delayed sleep timing, and sometimes free-run. The importance of short wavelength light to the circadian system prompted an initial study of sleep and circadian phase in 2003 with prototype blue enriched white lamps (Philips Lighting, 10000K) compared to standard white (1). The results suggested some advantages of blue enriched light, but that brighter light was needed to correct problems. The present study was designed to evaluate the effects of personal and communal blue-enriched, ActiViva Active lamps (Philips Lighting, 17000K) compared to standard white lamps, on sleep, circadian phase and general health during a 6 month period at the British Antarctic Base of Halley (75^0S).
Methods: From 3/3-12/10/2006 subjects (10M, 5F, 32.5±8 years) kept daily sleep diaries. 12 wore ActiwatchLs to monitor light exposure and activity. From 24/3-21/9/2006 light alternated between 4-5 week periods of standard white (W, 5000K) and blue enriched white light (B, ActiViva Active 17000K), with a 3 week no-treatment control (C) before and after the extra light. At the end of each period subjects collected sequential urine samples for 48h for analysis (RIA) of 6-sulphatoxymelatonin (aMT6s) as a marker of circadian phase, and completed the Rand 36 item general health questionnaire. Modelling was performed using rmANOVA (SAS version 9.1), data are mean±SD.
Results: In 2006 maximum light exposure was greater during sundown (11/5-11/8/2006) compared to 2003: 1864±643lux and 1039±28lux, respectively, without change in average exposure/24h (55±20lux and 64±21lux). Direct comparison of blue light with standard white indicated that sleep onset was slightly but significantly earlier (p=0.022), actual sleep time was longer (p=0.026) and sleep latency tended to be shorter with blue enriched white light (p=0.065). Using a full model including control periods, factors light, sundown, gender, age, maximum lux, average lux, observation day number, gave the following main effects (> = later/longer/higher): sleep onset, W>B>C (p=0.034), actual sleep time, C>B>W (p=0.002, Figure 1a), sleep quality (VAS) C>B>W (p=0.042), sleep efficiency, C>B and W (p=0.036) (overall sleep efficiency was C, 80.90±5.85, W, 79.36%±5.30, B, 79.04±4.86%). Compared to control there was no delay in wake-up during sundown. Delay in sleep onset during sundown compared to control was reduced compared to 2003: (1:06hmin (2003), 00:38hmin, (2006)). The ratio of maximum/average lux was associated with longer actual sleep (p=0.015). Gender provided the only significant effect in the Rand questionnaire, women had lower aspects of physical (PCS, p=0.029) and mental health (MCS, p=0.001). Circadian phase was earlier with blue enriched than with white light during sundown (normalised, p=0.022, Figure 1b).
Conclusions: Personal and communal use of blue enriched ActiViva Active light had beneficial effects on sleep timing, sleep length and sleep latency compared to standard white light during the polar winter. Higher maximum light exposure influenced positively sleep timing and duration.

Figure 1a

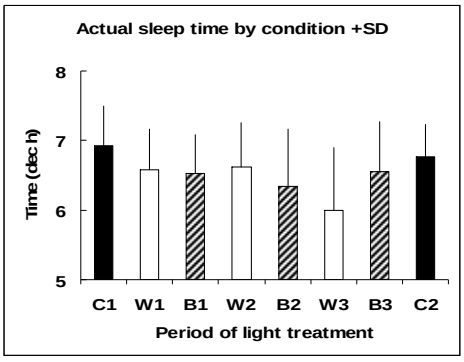
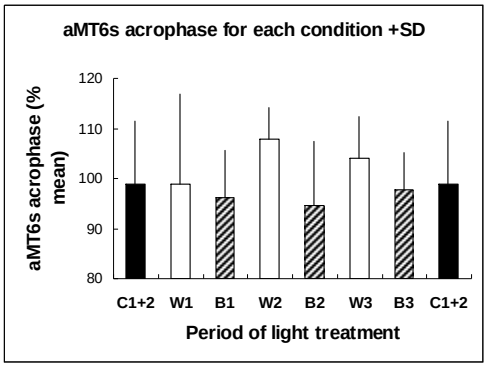


Figure 1b



Keywords: Sleep, Blue Light, Circadian, Polar Winter

Funding Support: British Antarctic Survey, Stockgrand Ltd, UK, Philips Lighting B.V., Eindhoven, The Netherlands (unrestricted research grant).
Reference: (1) Francis et al., J Sleep Res 2008.

THE BUILT ENVIRONMENT AND THE HUMAN RESPONSE TO (DAY-) LIGHT

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Light is not just for vision: it is the most important synchronizer between external time and the endogenous biological clock in humans. Beside rods and cones there is an additional so-called non-image-forming circadian photoreceptor in the retinal ganglion cells (with a photo pigment most sensitive to blue wavelengths), triggering many physiological and neurobehavioral responses. In modern societies, people spend a vast amount of their time indoors (at work or at home) subjected to varying lighting conditions with little or no possibilities to actively influence light quality. The often reported disturbances of sleep-wake rhythms, neurobehavioral performance, quality of life and health have been revealed to also be correlated with disturbances in circadian physiology. Therefore, a more intense future integration of chronobiological aspects in architecture and lighting design is warranted to help alleviate these problems in different populations and age groups.

What is relevant from a chronobiological point of view?

Three key properties of the circadian system are: 1) Circadian rhythms continue in the absence of light/dark cycles with an endogenous period close to but not exactly 24h. 2) The exact period length is a function of prior environmental conditions, and 3) Circadian phase can be reset by light. Based on these key properties, human physiology is further dependent on illuminance and irradiance levels, as well as the spectral composition of light; the time of day of exposure; the impact of age, photoreceptor sensitivity and prior light history (adaptation). Furthermore, only few results are available on exposure duration and the temporal pattern of exposure to light, however, recent findings showed differences between in- and outdoor workers during the winter season. Bright light also elicits many acute ('non-circadian') effects such as changes in subjective alertness, performance, heart rate, temperature or gene expression, all of which may interact with circadian rhythms (mechanisms so far unknown). Finally, the simultaneous interplay of wake-dependent homeostatic and circadian related functions strongly defines (among many other factors) the quality and quantity of our sleep-wake cycles.

How can this be implemented in architectural and lighting design?

As daylight is the most efficient and freely available light source, there are many possibilities to use it in architecture and in lighting design. Integrated day lighting systems make it possible to provide the majority of the room surface with sufficient daylight with minimal glare. Despite day-to-day variations (i.e. the differences between a mostly overcast and a completely clear day), daylight irradiance levels are most of the time higher than those found in most artificial lighting scenarios (Figure 1). Complementary light (when daylight levels are low or absent during the night) should be a well-considered trade-off between 'human factors' (e.g. chronobiological aspects, visual comfort, performance, health issues) and objective effectiveness (e.g. illuminating, safety, energy and costs). Currently, the discussion of how much blue-light we need (for the circadian system) is ongoing, and there are some limitations (blue light hazard).

Where do we need more trans-disciplinary research between chronobiologists and architects?

Experimental field studies are needed to investigate the high efficacy of daylight based on chronobiological aspects. Intelligent, user-related lighting systems, which allow the dynamic use of daylight together with complementary artificial light sources, have yet to be tested. Such lighting systems have to fulfill the requirements of the users' physiology (including circadian aspects) and subjective preferences (e.g. visual comfort, aesthetics) and of course, they have to be optimized in terms of the user's neurobehavioral performance. The different requirements of light in different populations (e.g. hospital patients, shift and office workers, older adults or school children) are not completely elucidated and far from optimal. Finally, the short and long lasting changes in human physiology and behavior in response to light need to be further explored in both laboratory and applied experiments. In order to (re-)evaluate the effectiveness of lighting in architectural settings, the definition of lighting quality should include chronobiological functions, leading to creation of new standards for architects and lighting designers to apply in future buildings.

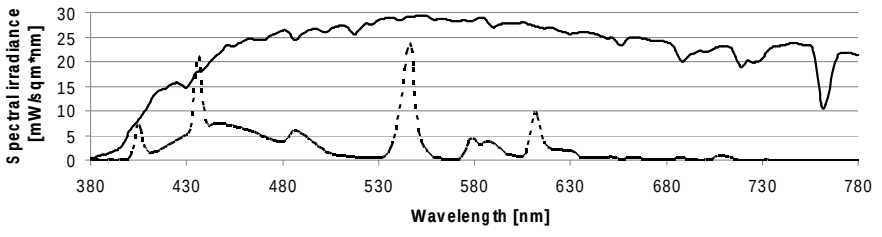

Figure 1: Vertical spectral irradiance levels of indoor daylight (solid line) and artificial light (dashed line) from a 17'000 K artificial light source (Philips, Activiva active). Both measurements were done in an office in our laboratory.

Keywords: Circadian, Chronobiology, Non-image-forming Photoreceptor, Architecture, Lighting Design
Financial Support: Velux Foundation,Switzerland (to MM); Swiss Federal Office of Energy, Switzerland (to FL)

THE EFFECT OF TIMED BLUE-GREEN LIGHT ON SLEEP-WAKE PATTERNS IN WOMEN WITH ALZHEIMER'S DISEASE

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Objectives: The occurrence of Alzheimer's disease (AD) is growing, with current projections estimating the prevalence of AD will nearly quadruple by the year 2050 (Brookmeyer & Gray, *Statistical Medicine, 19*, 148 1-93. 2000). These predictions are of special concern for women for two reasons: (1) they tend to live to ages at which AD is expressed at higher rates, and (2) AD pathology has been shown to be clinically expressed at higher rates in women (Barnes et al., *Archives of General Psychology, 62*, 685-691, 2005). Reversal of day-night patterns, disturbed sleep-wake rhythms, and excessive daytime sleepiness (EDS) are severe, common manifestations of AD that are extremely difficult to manage. The major objectives of this study were three fold: (1) to examine the effects of timed blue-green light (BGL) on the sleep and 24 hour rest-activity pattern in females with AD, (2) to explore the effects of timed BGL on global function (GF) in females with AD, and (3) to examine the duration of effect of timed BGL on sleep, 24 hour sleep-wake patterns and GF in females with AD. The central hypothesis of the study was that appropriately delivered timed BGL would synchronize disorganized circadian sleep-wake rhythms, thereby resulting in phase advancement of daily rest-activity pattern, improved sleep efficiency (SE), reduced sleep fragmentation (SF), reduced EDS, and resultant improvements in GF.

Methods: A two factor experimental design with repeated measures on one of the factors and convenience sampling was utilized. Twenty females with AD were randomized to the experimental or control condition. The study was conducted in five phases: screening and informed consent, collection of baseline data (7 days), application of the experimental/control light conditions (14 days), collection of post-test data (5 days), and collection of follow-up data at three two-week serial interval points (5 days at each interval). The experimental condition consisted of BGL at 12,000 lux and the control condition consisted of dim red light (DRL) at 5 lux. Both groups received light delivered via cap visor between 6-7am for 30 minutes for 14 consecutive days. Participants, their families, and facility caregivers were blinded to light condition. SE, SF and rest-activity pattern were measured via 24-hour wrist actigraphy. EDS was measured at mealtimes utilizing the Stanford Sleepiness Scale (SSS). GF was examined through qualitative interviews with family and facility caregivers post-light intervention and at each interval follow-up. Analysis of the raw 24 hour actigraphic data was performed by manufacturer algorithm. Descriptive statistics were used to determine frequency distributions, percentage distributions, means and standard deviations. Repeated-measures MANOVA and MANCOVA were used to determine the changes in response variables within subjects, between subjects, and within-subjects-by-between subjects interactions. To compare the difference in outcome variables from the baseline and subsequent treatments, the contrast and profile transformations in repeated-measures ANOVA were employed. For simultaneous testing of hypotheses, the Bonferroni method for controlling the overall error rate was used. Qualitative data on global function were analyzed utilizing the appropriate qualitative methodologies. Level of significance was set at $p \leq .05$.

Results: SE improved (p=.003) post-BGL, as did the number (p=.002) and length of SF (p=.04). EDS at breakfast (p=.002), lunch (p=.01), and dinner (p=.02) were all reduced post-BGL. The BGL group showed a reduction in sleep latency (p=.01) post-light. The BGL group spent less time awake at night (p=.001), less time in bed (p=.02), went to bed later (p=.01), and trended toward being up earlier in the morning (p=.06) post-light. Total minutes in bed were also reduced (p=.02) in the BGL group post-light. During the remainder of the study, changes in levels of SE, SF and EDS continued above baseline through the 6-week duration even though the changes in levels were not significant. Longitudinally however, EDS at breakfast remained (p=.02) improved from baseline at six weeks, and EDS at dinner remained (p=.01) improved from baseline at four weeks. Themes emerged from the caregiver interviews regarding the effect of light on GF, specifically in psychosocial areas (3 themes) and in cognition/language (4 themes).

Conclusions: Further research with continued rigorous methodology, larger sample sizes, and differing cohorts is needed. Included should be the examination of the effects of BGL and DRL on quantitative measures of the facets of global function identified in this preliminary work. Light visors have potential as a safe and manageable light delivery method, well-suited to managing sleep and circadian based symptoms in individuals with AD and dementia. Therapeutic light applications, once refined, have the potential to lengthen time of functional independence, improve quality of life, delay institutionalization, and compress AD associated morbidity to the end of life.

Keywords: Sleep, Light Therapy, Circadian Rhythm, Alzheimer's Disease, Daytime Sleepiness

A MOLECULAR LOOK AT CHRONOTYPE AND AGING

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Objectives: In animals and in humans, aging leads to several pathologies, including circadian rhythms disturbances. For example, a higher prevalence of early morning awakening and difficulties in maintaining sleep are observed in elderly individuals. Nevertheless, the causes of this phenomenon are unknown. Our study investigated if the age-related disturbances in circadian rhythms occur in every cell of the body. To address to this question we investigated whether circadian period in human primary fibroblasts, -- a known *in vitro* model for the study of the circadian rhythms (Brown S.A. et al., *PLoS Biology* **3**: e338, 2005) -- show age-related differences in their circadian period length that parallel differences in subject circadian phase *in vivo*.

Methods: For this purpose, we characterized the period length of circadian transcriptional oscillations in skin fibroblasts from 18 young and 18 elderly subjects (young: ≤ 30 years old; elderly: ≥ 60 years old; sex-matched). Fibroblasts were isolated from punch biopsies and infected with an engineered lentiviral circadian reporter (*mBmal-1::luc*) to analyse their circadian rhythms *in vitro* by bioluminescence imaging, either in the presence of 10% foetal bovine serum (FBS) or 10% human serum from young or elderly subjects. Similar measurements were conducted upon organotypic slices from mouse suprachiasmatic nucleus in the presence of the same sera. To investigate the phase of entrainment of fibroblasts, cells were incubated for 5 days in a temperature entrainment condition (8 hours at 37°C and 16 hours at 35°C) during bioluminescence measurement. In addition, chronotype of all subjects was analysed using the Munich Chronotype Questionnaire (MCTQ).

Results: From the analyses of the MCTQ, the young subjects recruited for the study had a later chronotype compared to the subjects belonging to the older group; however no influence of age on the circadian period length of fibroblasts was found. Under temperature entrainment conditions, identical phases were also observed between the two groups. Therefore, although age affected subject circadian behaviour, it did not affect the cell-autonomous properties of peripheral fibroblast cells. When the same measurements were conducted in the presence of different sera, though, the presence of sera from older donors significantly shortened circadian period length. Similar effects were observed regardless of the origin of the fibroblasts: from young subjects, older subjects, or even mice. Heat-inactivation of sera from older donors suppressed the observed reduction, but did not change period length with younger sera.

Conclusions: In our study, changes in chronotype and sleep-wake behaviour of older subjects reflected by the MCTQ questionnaire were not reflected in skin fibroblasts from the same individuals. Thus, the genetic properties of the circadian oscillator measured in peripheral fibroblast cells likely remain unchanged as humans age. However, fibroblast period was significantly shorter in the presence of serum from older individuals, suggesting the existence of hormonal factor(s) in aged individuals that shorten period. Since these factors affect peripheral cells but not the SCN itself, our observations might explain why elderly individuals show earlier phases of behaviour but no changes in free-running physiological period. They also suggest that age-related changes in circadian function might be pharmacologically reversible.

Keywords: Peripheral Oscillators, Circadian Rhythms, Aging

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TIMING LIGHT TREATMENT FOR EASTWARD AND WESTWARD TRAVEL PREPARATION

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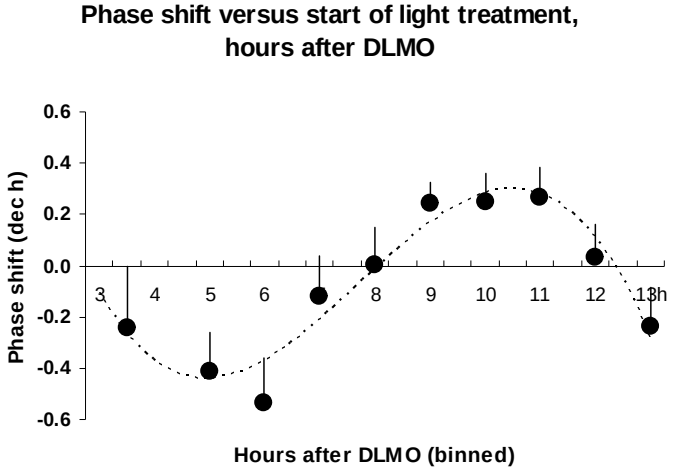
Objectives: The objective of the studies reported here was to determine, using a narrow bandwidth light tower (500 nm, www.sunnexbiotech.com) the optimum timing of a brief light treatment (illuminance 60 cm from the light source, 350 lux, irradiance, 98 $\mu W/cm^2$) to initiate appropriate circadian phase advance and delay prior to travel.

Methods: Three counterbalanced treatment order, repeated measures studies were conducted to compare melatonin suppression and phase shift across multiple light treatment timings. In experiment 1, 14 normal healthy volunteers (8 men and 6 women) aged 34.9 ± 8.2 yr; mean ± S.D., had light treatment at: A) 06:00 to 07:00 h, B) 05:30 to 07:30 h, and C) 09:00 to 10:00 h (active control). In experiment 2, 13 normal healthy subjects (7 men and 7 women) aged 35.6 ± 6.9 years, had light treatment at: A) 06:00 to 07:00 h, B) 07:00 to 08:00 h, C) 08:00 to 09:00 h and a no-light control (D) from 07:00 to 08:00 h. In experiment 3, 10 normal healthy subjects (6 men and 4 women) aged 37.0 ± 7.7 years had light treatment at: A) 02:00 to 03:00h, B) 02:30 to 03:30h, and C) 03:00 to 04:00h with a no-light control D) from 02:30 to 03:30h. Dim Light Melatonin Onset (DLMO) was established by 2 methods; 1) when salivary melatonin levels exceeded 1.0 pg/ml and 2) when salivary melatonin levels exceeded 3 times the 0.9 pg/ml sensitivity of the radioimmunoasssy.

Results: Using the 1.0 pg/ml DLMO, significant phase advances were found in experiment 1 for condition A ($p<.028$) and B ($p<0.004$). Experiment 2 showed significant phase advances in conditions A ($p<0.018$), and B ($p<0.003$) but not C ($p<0.23$), relative to condition D. In experiment 3, only condition B ($p<0.035$) provided a significant phase delay relative to condition D. Similar but generally smaller phase shifts were found with the 2.7 pg/ml DLMO. This threshold was used to analyse phase shifts against circadian time of the start of light treatment for all 3 experiments. The best fit curve ($R^2= 0.94$) provided a partial phase response curve with a maximum advance at approximately 9-11 h and a maximum delay at approximately 5-6 h following DLMO (see Figure).

Conclusions: These data suggest the largest phase advances will result when light treatment is started between 06:00 and 08:00 h clock time and the greatest phase delays from light treatment started at 02:00 to 03:00 h clock time in entrained subjects with a regular sleep wake cycle (23:00 to 07:00 h).



Relationship of phase shift (mean ± SEM) to the timing of the start of light treatment (hours after DLMO). Average N per point = 11. With DLMO at 21:00 h, 6 h after DLMO corresponds to 03:00 h clock time etc. Most significant fit was: $y = 2.3766 – 1.3509x + 0.2008x^2$, $r^2 = 0.94$, $p<0.001$, df=8.

Keywords: Jet Lag, Light, Phase Shift, Circadian

Funding Support: Canadian Forces.

CIRCADIAN EFFECTIVENESS OF SOLAR AND ARTIFICIAL RADIATION IN DEPENDENCE ON AGE

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Objectives: The aim of the investigation was to determine the threshold irradiance of sufficient melatonin suppression for persons of different age with free pupil adaptation by using polychromatic radiation with different emission spectra and with different angles of incidence on the cornea. These data were used to evaluate the circadian effectiveness of solar irradiance at the Earth's surface and of different lamp types for children, young adults and seniors.

Methods: Melatonin suppression was measured directly by analysing blood samples of healthy volunteers classified by their age and exposed by polychromatic radiation in dependence on its spectral distribution, on its irradiance and on its incidence angle on the cornea. Effective threshold irradiances to get saturation of melatonin suppression were calculated by using the circadian action spectrum.

Results: Depending on the age, effective threshold irradiance ranged between about 0.2 W m^{-2} and about 0.6 W m^{-2} in the case of half spherical geometry and of different emission spectra of white light lamps. In contrast, decreases of the incident angle resulted in decreases of melatonin suppression even if the luminance was increased to get equivalent corneal irradiance. However, the threshold irradiances experimentally determined for persons of different age are approximately in line with the thresholds calculated by extrapolation by using age-dependent spectra of eye transmittance and threshold irradiance data of melatonin suppression measured in young adults with dilated pupils and with monochromatic radiation.

Conclusions: This result is discussed as reference to the applicability of the *van Krefeld* law of photobiology to evaluate circadian effectiveness of polychromatic light sources by weighting with the circadian action spectrum, whereas the experimental data clearly show the violation of the *Bunsen-Roscoe* law as well as the need to establish "circadian weighted" measures to exclude confusion by using measures of visual effectiveness which result in misinterpretation of circadian effectiveness. In addition, aging effects of the eyes have to be considered to evaluate circadian effectiveness and effects of light. Outdoor sun light exposures during cloudless sky cause sufficient melatonin suppression between sunrise and sunset for persons of all ages, whereas the suitable daily periods are limited in case of cloud covered sky and depend on latitude, season, age, type of cloudiness and degree of cover. Circadian efficacy of lamps can be sufficiently controlled considering person's age by the choice of spectrum, irradiance, geometry of exposure and radiance.

Keywords: Melatonin Suppression, Circadian Effectiveness, Aging Effects, Geometric Effects

IS PHYSICAL EXERCISE THE TREATMENT OF CHOICE FOR WINTER DEPRESSION?

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Objectives: Bright light therapy (BLT) was proposed to be the treatment of choice for winter depression on the base of assumption that deprivation of light in wintertime is a key factor for development of this condition (Rosenthal et al., Arch Gen Psychiatry 41: 72-80, 1984). Indeed, the numerous investigations demonstrated that the symptoms of winter depression may remit after just one week of 2 to 4 hour daily exposure to bright light. The neurobiological basis of antidepressant action of BLT has been extensively studied. However, after 25 years of experimental research of this disorder, the following questions still remain to be open: 1) is winter depression a photoperiodically induced condition?; 2) is any specific component in the treatment of choice for winter depression?; 2) is any specific physiological system responsible for the alleviation of the symptoms of this depression?; and 3) is any causal link between the physiological and mood responses to BLT? To illustrate the issues of the research on the mechanisms underlying the antidepressant action of BLT, I resume here the results of several studies conducted by my group in winter seasons of 1988-2001 at the hospital of SB RAMS located near Novosibirsk (55 degree North).

Methods: A set of the investigational non-drug trials provided a possibility to compare the antidepressant effects of several one-week treatments in 265 female subjects with either winter depression or non-seasonal depression or without depression (n=115, 64 and 86, respectively). In the majority of the trials, the associations between clinical and physiological responses to the one-week treatments were determined.

Results: It was found that a total night sleep deprivation does not improve mood in non-depressed subjects, whereas the significant improvements of similar magnitudes were observed in seasonally and non-seasonally depressed patients. Any type of one-week treatment produced a notable reduction of depression scores in both depressed and non-depressed subjects. Winter depression responded better than non-seasonal depression to the treatments with physical exercise, bright light and combination of sleep deprivation with bright light (65-68% reduction of Hamilton Depression Rating Scale scores). It was also found that any used treatment, including placebo, prevents relapse after sleep deprivation in winter depressives. However, further significant reduction of depressive scores was obtained after bright lighting and after physical exercising rather than after blind administration of either melatonin or placebo. In overall, the results of the investigational non-drug trials suggest that winter depression could be well-treated with either physical exercise or bright light. Somewhat bigger reduction of Hamilton Depression Rating Scale score (81%) was seen only after one-week vocation in Firyuza resort (south of Turkmeniya, 38 degree North), but the difference was insignificant. The clinical data indicate that the midday treatments seemed to be as beneficial as are the treatments in other times of the day, although it is unlikely that the midday administration of bright light or physical exercise could markedly challenge patients' chronobiology. Physiological data showed that most physiological indexes in depressed patients tend to shift toward those observed in controls. However, no solid evidence was found for a strong dependence of any clinical response from a separate physiological response, such as advance of circadian phase, increase in energy expenditure, activation of sympatho-adrenal system, and intensification of non-rapid eye movement sleep. Most physiological systems responded to the treatment independently one from another. Highly significant correlation was noted between the number of favorable physiological responses and the number of favorable clinical responses to the treatment. However, the results of this correlational analysis do not prove the causal relationship between the physiological and clinical responses. Although the latter might be the cause of the former, the opposite causal relationship also can't be excluded.

Conclusions: It still remains to be clarified whether the primary and most important causes of seasonal depression are closely associated with the physiological shifts induced by seasonal variations in physical environment. The studied physiological responses to the visual non-drug treatments are not necessarily involved in etiology of winter depression and in beneficial clinical responses to these treatments. It seems that such a treatment mostly works as a powerful placebo. Therefore, winter depression and its beneficial response to bright light and physical exercise can't be fully explained without accounting for the non-seasonal factors of psychosocial nature, such as expectations, motivation, cognitions, personality traits, patient-physician communication, perceived social support, negative life events, etc.

Keywords: SAD, Non-drug Treatments, Bright Light Therapy, Sleep Deprivation, Melatonin

IMPROVEMENT IN FATIGUE, SLEEPINESS AND HEALTH-RELATED QUALITY OF LIFE WITH BRIGHT LIGHT TREATMENT IN SEASONAL AFFECTIVE DISORDER (SAD) AND SUBCLINICAL SAD – A SUBGROUP ANALYSIS

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Objectives: The first aim was to investigate treatment effects of bright light on fatigue, excessive daytime sleepiness and health-related quality of life in persons with winter fatigue and winter depression. The second aim was to explore and validate empirically derived subgroups in the sample and evaluate any differential treatment effects in the subgroups.

Methods: In a descriptive and comparative design, fifty adults (40 women and 10 men) from Dalarna (a district in central Sweden, lat 60.5 N) with clinically assessed Seasonal Affective Disorder (SAD) or Subclinical SAD (S-SAD) received treatment in light rooms for ten days in the morning (between 06.00 and 09.00 a.m. for 1.5 to 2 h daily on weekdays) during the period October to February. Measures used were the Epworth Sleepiness Scale (ESS), the Fatigue Questionnaire (FQ), the SF-36 (health-related quality of life) and VAS-scales of mood and sleepiness. Data were collected during the week before treatment, the week after treatment and at the one-month follow-up. Subgroups were explored with cluster analysis and measures used in the cluster analysis were baseline data for the two subscales (HAMD-21 and Atyp-8) in the 29-item SIGH-SAD/SR depression scale, the ESS and the FQ. The cluster solution was validated on measures not used in the cluster analysis, i.e. demographic data, results on the Seasonal Pattern Assessment Questionnaire (SPAQ), the SF-36 (health-related quality of life), VAS ratings and treatment effects over time.

Results: In the merged group repeated measures ANOVAs showed a significant reduction over time for the FQ (fatigue scale), $F(1.7, 79.4) = 24.7$, $p<0.001$ and the ESS (sleepiness scale), $F(2, 90) = 59.1$, $p<0.001$. There was a significant improvement over time for the SF-36 PCS (physical health summary scale), $F(2, 92) = 6.0$, $p<0.01$ and the SF-36 MCS (mental health summary scale), $F(2, 92) = 66.7$, $p<0.001$. There were similar improvements over time for the VAS mood and VAS sleepiness scales. The proportion with a total FQ (fatigue) score below the norms for a general population sample ($FQ\leq12$) was 6.4% at baseline compared with 72.3% at post-treatment and 83% at the one-month follow-up. The proportion with ESS (sleepiness) scores within the normal range ($ESS\leq8$) was 27.7% at baseline compared with 80% at post-treatment and 84.8% at the one-month follow-up. In the merged group, the SF-36 MCS (mental health) score was low at baseline (mean value 31.8, SD 10.4) compared with Swedish general population scores (mean value 50.0, SD 10.3). At the one-month follow-up, the SF-36 MCS scores were close to norms (mean value 49.8, SD 8.9). Thus, fatigue, excessive daytime sleepiness and health-related quality of life were improved at post-treatment. These results were maintained at the one-month follow-up. The subgroup/cluster analysis resulted in three distinct subgroups. These clusters were characterized primarily on the basis of differential degrees of depression and daytime sleepiness. Even though level of fatigue differed between the clusters, fatigue scores were high compared to the general population in all three of them. Hence the general denomination "Winter Fatigue" and the specific labels "Mildly depressed/Not sleepy", "Mildly depressed/Sleepy" and "Depressed/Sleepy" are introduced for the subgroups. All three subgroups improved following treatment with bright light and the effects were maintained during the one-month follow-up.

Conclusions: Fatigue, daytime sleepiness and health-related quality of life in persons with SAD and S-SAD improved in a similar way as depressed mood in persons with SAD and S-SAD. The results point to the usefulness of including a broader range of measures in future clinical trials of bright light therapy in SAD and S-SAD.

Keywords: Seasonal Affective Disorder, Bright Light Therapy, Fatigue, Health-related Quality of Life, Excessive Daytime Sleepiness

ENTRAINMENT IN HUMANS – FROM CHRONOTYPE TO MECHANISMS

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Objectives: To investigate entrainment in humans, we have defined the phase of entrainment (chronotype) as the mid-point of sleep on days without social constraints and without prior sleep deficits (the basis of the Munich ChronoType Questionnaire, MCTQ). We use chronotype to estimate *internal time* as an essential variable in many bio-medical issues, ranging from shift-work research to medical diagnosis and therapy but also for understanding the influence of zeitgebers on human entrainment and its underlying mechanisms. Human chronotype can also be used in the search for new genes that are involved in the entrainment of the mammalian clock.

Methods: We use an interactive systems approach involving databases, field studies, constant routines, biochemical, physiological and genetic analyses and modelling. The tools for collecting information for the databases are implemented online to ensure large numbers of subjects – an important prerequisite for discovery. Most of the internet-based tools can be accessed through www.theWeP.org or www.EUCLOCK.org (some online studies are only accessible by invitation to selected subjects). As of 2009, we had over 80,000 entries in our general chronotype database (increasing by approximately 950 per months). We are currently also building a database for shift-workers. In a cooperative effort involving the research networks EUCLOCK and CLOCKWORK, several computer-based tests and portable devices have been developed for measuring daily variations in the real world, from the biochemical and physiological levels to behaviour and cognition.
A series of field studies has been completed in 2007/08 in cooperation with SIEMENS, OSRAM, ARCELOR, and VW and further field studies will be completed in 2009. Genetic association studies for clock- and sleep related variables have been (or are still in process) across Europe, Asia and South America using both whole genome and candidate gene approaches. Several computer programmes for modelling entrainment conceptually and contextually (in defined laboratory conditions or in the real world, e.g., shift-work) have been developed and are involved in the iterative process described above.

Results: The reliable assessment of chronotype by a few simple questions (MCTQ) has been validated in many different studies against several different variables (ranging from sleep-logs and actimetry to cortisol and melatonin). Human entrainment is tightly coupled to the light:dark cycle, specifically to dawn. In urban societies, however, weak, irregular light cycles predominate, resulting in weak or dys-entrainment. Dys-entrainment can be quantified as the discrepancy between *internal* and *external* time (*social jetlag*). Although shift-work (20% of the working population; ≈ 9% of the total population) elicits probably the most severe form of *social jetlag* it is not the most common form: over 40% of the non-shift-working population suffers from a *social jetlag* of 2 hours or more. *Social jetlag* is closely associated with chronic sleep debt, which in turn is probably the most important variable underlying the detrimental health effects of dys-entrainment. Finally, our modelling efforts show that entrainment can be explained by much simpler formalisms than historically thought.

Conclusions: Nothing in entrainment makes sense except in the light of *internal time*.

Keywords: Entrainment, Chronotype, MCTQ, Social Jetlag, Shift-work, External Time, Internal Time

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ATTENTIONAL BIAS IN SEASONAL AFFECTIVE DISORDER

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Objectives: There has been a growing interest for the interplay between negative mood and (dysfunctional) attentional processes in non-seasonal depression. Part of this research focuses on comparing attentional characteristics in depressed patients and in healthy controls. These studies (e.g. Koster et. al., 2005) suggest that depressed patients direct their attention differently compared to healthy controls. They fail to direct their attention towards positive information and have difficulty in directing attention away from negative information. Both of these attentional biases are mood-congruent and confirm the relatively negative schemata depressed patients have. Recently, research has shown that patients with seasonal affective disorder (SAD) have similar cognitive impairments as patients with non-seasonal depression. This study was designed to investigate whether SAD-patients in depressed state have an attentional bias similar to patients with non-seasonal depression, and if this attentional bias is still found when in remission after light therapy.

Methods: Twenty patients (M= 40.6 y, sd = 12.9) with major depression with seasonal pattern (SAD) were included in this study. All had a score of ≥ 18 on the SIGH-SAD at day 1 and a score of ≤ 12 at day 22. Both at day 1 and at day 22 they completed an emotional modification of the exogenous cuing task (ECT; Posner, 1980)). In this reaction time task a target stimulus is presented on the left- or right-side on a screen. The target stimulus is preceded by a cue (a positive, negative or neutral word) at the same location as the target (valid trial) or at the opposite location of the target (invalid trial). In thee ECT used in this experiment, presentation times of the words (cues) was varied (500 ms, 1250 ms). Participants were asked to press the letter 'P' if the target was presented to the right and to press the letter 'Q' if the target was presented on the left. The task was to react as quickly as possible. In between the two measurements, the patients received light therapy, for two weeks at work days, 30 minutes per day.

Results: The 2(session) x 3(word valence) x 2(validity) x 2(presentation time) ANOVA revealed a marginally significant effect for the relevant four-way interaction ($F = 3.49$, $p = 0.51$, $\eta^2 = 0.27$). Further investigation of this interaction effect revealed that: 1. at short presentation times there was a facilitated engagement to depressive words when compared with attentional engagement to positive words, both in depressed state ($t = 2.47$, $p < .05$) and in remission ($t = 2.11$, $p < 0.05$); 2. in depressed state at short presentation times there was an impaired disengagement from depressive words, compared to disengagement from positive words ($t = 2.87$, $p < 0.05$).

Conclusions: Results seem to indicate that SAD patients direct their attention more easily to the location of depressive words compared to positive words, but only at short presentation times. This tendency is seen in both depressed state and in remission after light therapy. Furthermore, SAD patients have more difficulty in shifting their attention away from depressive words compared to positive words. This is only the case when in depressed state and this effect disappears in remission after light therapy. So, although SAD patients keep the tendency to direct their attention to depressive information, even when in remission, they have less difficulty shifting their attention away from that information when they are no longer depressed. This tendency might possibly be one of the factors that play a role in making SAD-patients vulnerable for relapse which is seen in the recurrence of depressive episodes (nearly) every year. More research is necessary to further explore this possibility.

Keywords: SAD, Attentional Bias, ECT

References:
Koster et al. (2005). Mood-congruent attentional bias in dysphoria: maintained attention to and impaired disengagement from negative information. *Emotion, 5*, 446-455.
Posner (1980). Orienting of attention. *Q. J. Exp. Psycho., 32*, 3-25.

IS IT FEASIBLE TO ALERT PEOPLE AT RISK FROM SEASONAL AFFECTIVE DISORDER BASED ON KNOWLEDGE OF THE WEATHER?

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Objectives: Met Office Health Forecasting uses the relationship between weather and health to forecast increased risk for patients. An example of this is the Healthy Outlook™ service whereby a forecast of "elevated risk" triggers contact with COPD patients to initiate anticipatory care and encourage self-management. The review of mental health service users in Cornwall, UK(.Dart C, Moses T, Cornwall & Isles of Scilly Primary Care Trust. September 2008) suggested that people with a range of mental health problems are affected by "gloominess". A collaboration between the UK Met Office, Cornwall Mental Health Commissioning Group and Outlook Southwest, a psychological services provider, was established to run a short study investigating if a weather based alert service as part of a care package could be delivered to people with Seasonal Affective Disorder and if there would be interest in this approach.

Methods: Participants were recruited from those currently in contact with Outlook Southwest and also via general media advertisements. Each person was given a self-help booklet based on cognitive behaviour therapy, an explanation of the service and a lightbox with advice how to use it. An algorithm using solar radiation measurements was developed to provide an assessment of 'gloominess' across 7 areas of Cornwall. Mean values were taken from hourly forecasts to assess the gloom on a particular day. Thresholds were identified which, when exceeded, would trigger an alert. Participants received a 2 day forecast of potential gloomy weather as well as a general forecast of how long it was likely to last. They were able to choose receiving the alert by email, text or automated voice message. The trial runs from February until the end of April 2009.

Results: A total of 67 people participated in the study. 54% (36) received alerts by text, 24% (16) by email and 22% (15) by voice message. To date, alerts were triggered in both February and March and reflected the geographical variation in gloom across Cornwall. Preliminary results suggest that participants responded well to the alerts and found the self-help material useful. It appeared to legitimise help-seeking behaviour and was acceptable to those traditionally more hard to reach with mental health services. The service generated interest both amongst potential users in other areas of the UK but also in local and national media

Conclusions: These results suggest that a targeted, direct to person forecast alert service coupled with self- help material was feasible and of interest to people affected by gloomy weather. A more extensive study is planned in Cornwall for Sep 09- Mar 2010.

Keywords: Health Forecasting, Light Therapy, Self-management, Seasonal, Depression

USE OF SUNLIGHT EXPOSURE AND MELATONIN AS A TREATMENT APPROACH TO ELDERLY PSYCHIATRIC INSTITUTIONALIZED PATIENTS WITH SLEEP DISTURBANCES

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Objectives: Circadian Rhythm disturbances, including sleep disturbances, occur in normal aging and are worse in patients with dementia. The relations between sleep, circadian rhythms and psychiatric disorders have been widely studied, and recommendations have been made on Chronotherapeutics both for Affective Disorders and for patients with Dementia. Our objective is to progressively remove neuroleptics and benzodiazepines (BZD) used as sedative at night or to treat disruptive behaviour during the day, in a population of 44 institutionalized women, most of them with moderate cognitive deficit (different Dementia types). All of them were diagnosed as having Mental Retardation or Chronic Psychosis.

Methods: Baseline evaluation included mental state evaluation (Mini Mental State Examination, MMSE), and autonomy evaluation (Barthel-ADL). Since October all patients are doing Light Therapy, "all day" (10:00 to 12:00 am and 2:00 to 5:00 pm) or "half day" (only morning or only afternoon) with natural sun light: they stay at a large sunny window while doing occupational activities and they go outside for a walk whenever possible. Those with insomnia without benefit from light alone, started slow-release melatonin (sr-MLT) 2 mg at bedtime and continued light treatment. Neuroleptics and BZD are being progressively removed. Up to now we have observational results form the psychiatrist, the nurses and the occupational staff concerning affective state, behaviour and sleep. Re-evaluation of MMSE and Barthel-ADL will be done by May 2009.

Results: At the present, data collected from 11 patients aged 51 to 85 years, diagnosed with Schizophrenia or Mental Retardation, with cognitive deficit, institutionalized for 30 to 50 years in this institution, show that: 1) sleep pattern was ameliorated in all cases, using either light therapy alone or with melatonin, with longer night periods of sleep (between 5 and 7 hours starting at the beginning of the night); 2) patients with psychomotor agitation, had remission of their sundowning and/or agitation during the day, after treatment with light, with or without sr-MLT and changes in their previous medication (removal of BZD and/or neuroleptics).

Conclusions: To the present, these preliminary data suggest that correctly timed use of sun light with and without melatonin administration, is a very good therapeutic approach to the elderly psychiatric institutionalized patients, allowing important reductions in the use of psychiatric medication, clear improvement in affective and behavioural outcomes and sleep/wake pattern.

LIGHT EFFECTS ON CIRCADIAN ACTIVITY RHYTHMS OF DJUNGARIAN HAMSTERS WITH AN ATTENUATED ABILITY TO SYNCHRONIZE

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Objectives: In Djungarian hamsters (*Phodopus sungorus*) bred in our institute, a specific amount of animals show activity patterns that seems incompatible with proper adjustment to a periodic environment (Weinert & Schottner, Chronobiol. Int. 24: 1065-1079, 2007). The activity onset in those animals is continuously delayed whereas the activity offset is stably coupled to "lights-on", leading to a compression of the activity time. We conducted experiments to evaluate the possible causes of the deteriorated ability of DAO hamsters (DAO-delayed activity onset) to synchronize.

Methods: To investigate free-running rhythms, hamsters were kept in constant darkness (DD) or constant light (LL) of different intensities (1, 10, 100 lx) for at least 3 weeks. Photic phase responses were studied in DD. Following a 3-weeks adaptation, animals were transferred to another room and exposed to light of 100 lx for 15 min, according to the individual circadian time (CT14 and CT22). The activity onset was taken as CT12. The motor activity of singly housed hamsters was investigated by means of passive infrared motion detectors. The impulses from the PIR detectors were stored and analyzed by means of the Chronobiological Kit® (Stanford University, Stanford, California, USA). The free-running period and rhythm robustness (PN-value) was estimated by means of the Lomb-Scargle Periodogram. To characterize the rhythms more formally, the mean total amount of activity per day was calculated. Also, the percentage of animals that became arrhythmic under constant lighting conditions was estimated. Activity onsets and offsets, period lengths, and phase shifts following light pulses were estimated on-screen using the software involved in the Chronobiological Kit®.

Results: Analysis of τ by means of 2-way-ANOVA revealed a significant effect of lighting conditions ($F = 54.427$; $p \leq 0.0005$). The phenotype had no significant effect but there was a significant interaction ($F = 6.627$; $p \leq 0.0005$). The free-running period (τ) of DAO-hamsters was significantly longer compared to WT-hamsters in DD. With increasing light intensity, it lengthened in both phenotypes, though not consistently. In LL of 1 lx, τ was significantly lengthened in WT-hamsters and even longer compared to DAO-animals. In the latter, τ increased significantly only in LL of 10 lx and was then no more different from WT-hamsters. The robustness of the circadian activity rhythm was highest in DD and decreased in LL. Statistical analysis revealed a significant effect of lighting conditions ($F=18.416$; $p \leq 0.0005$; 2-way-ANOVA), but no differences between phenotypes. The percentage of arrhythmic animals was low in DD but remarkably high in LL. Comparing the two phenotypes, the percentage of arrhythmic animals was always higher in WT-hamsters. This difference was significant in LL of 1 lx and 100lx. In hamsters of both phenotypes, the total amount of activity per day was highest in DD and decreased in LL. 2-way ANOVA revealed an effect of lighting conditions ($F = 4.671$; $p \leq 0.005$) and phenotype ($F = 6.397$; $p \leq 0.05$). DAO-hamsters were less active than WT-hamsters under each lighting condition. However, the difference was significant only under DD. Light pulses induced phase delays when applied at CT14 and phase advances at CT22 with advances being stronger than delays. At CT14, the phase response was not different between the two phenotypes. At CT22 animals of the two phenotypes did respond differently ($F=29.287$, $p\leq0.0005$). The phase advance of DAO-animals was significantly smaller in activity onset and offset compared to Wild-type hamster. Also, light pulses effected τ. If applied at CT14, τ did lengthen. At CT22 light pulses did cause a shortening. The differences between phenotypes were not significant (ANOVA).

Conclusions: The differences between the activity patterns of both phenotypes cannot be explained exclusively by differences in their free-running period and parametric light effects. Nonparametric light effects must be taken into account as potential causes for the delayed activity onset in DAO-hamsters. This was confirmed by the results of the phase response following photic stimulation. The phase advance at CT22 was less in DAO hamsters despite their longer τ.

Keywords: Circadian Rhythm, Locomotor Activity, Synchronization, Djungarian Hamster

WINTER-SUMMER VARIATIONS IN OVARIAN FUNCTION IN WOMEN AT 55º N LATITUDE

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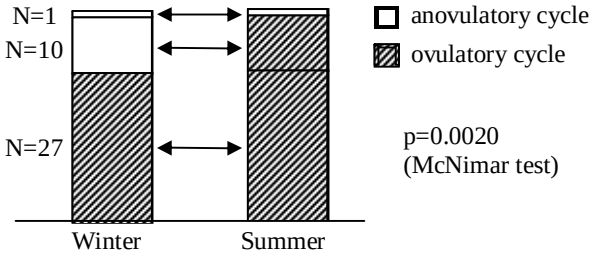
Objectives: The aim was to analyze the influence of seasonal change (Novosibirsk, 55º N) on menstrual cycle length, ovarian follicle size, ovulation and reproductive hormones secretion. Previous studies performed in northern Finland have shown seasonal changes in some of these indices in women [e.g., 1].

Methods: 1-year menstrual calendars were collected from 48 women (age 18-46 y) with fairly normal cycles of 21-35 days. A comparison was made between the length of the menstrual cycles ending in December–February vs. June–August. Thirty-eight women (age 19-39 y) completed ultrasound investigation twice a year (winter-summer). In a sub-group of 17 women, venous blood was taken on the same (within subject) day of the winter and summer menstrual cycles (the 3^{rd}-9^{th} day, median = 7^{th} day) to measure concentration of follicle-stimulating hormone (FSH), luteinizing hormone (LH) and prolactin.

Results: Menstrual cycle length was shorter in summer compared to winter (mean ± standard deviation): 28.0 ± 2.4 vs. 28.9 ± 2.3 days (p=0.0023, Wilcoxon test). Dominant ovarian follicle diameter was greater in summer: 17.7 ± 4.3 vs. 15.4 ± 5.6 mm (p=0.019, Wilcoxon test). There were also a greater number of ovulatory cycles in summer than in winter (Fig. 1). FSH levels tended to increase in summer (7.7 ± 1.5 vs. 6.8 ± 1.1 U/l, p=0.055, Wilcoxon test) although levels of other hormones (LH and prolactin) did not change.

Fig. 1. Ovulation frequency in winter and summer (N=38)



Conclusions: Pituitary-ovarian axis activity is greater in summer than in winter in women living at temperate latitudes (greater follicle size, frequency of ovulation, FSH secretion and shorter menstrual cycles). This could be due to the influence of natural light, as artificial light causes similar effects [e.g., 2].

Keywords: Seasonal Variations, Menstrual Cycle, Ovulation, Reproductive Hormones

Funding Support: The study was sponsored by Lumie®. OJS is paid by grant EUCLOCK (the EU 6^{th} Framework Project No. 018741).

References:

1. Kivelä A et al. Acta Physiol Scand 1988, 132: 321-327.
2. Danilenko KV, Samoilova EA. PLoS Clin Trials 2007, Feb 9;2: e7.

ESTIMATION OF HUMAN CIRCADIAN PHASE IN REAL LIFE CONDITIONS VIA A MULTI-CHANNEL AMBULATORY MONITORING SYSTEM

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Objectives: We aim at developing an easily applicable device and technique for estimating human circadian phase without the need of chronobiology laboratory studies under constant routine (CR) conditions and without the measurements of standard circadian markers such as core body temperature (CBT) and salivary melatonin. Multiple and nonlinear masking effects of everyday behaviour and environmental input on the measured variables in real life, such as physical activity and posture, light input, meals, and emotional activation make solving this problem a challenging endeavour**.**

Methods: In this ongoing study, subjects wear multiple ambulatory monitoring devices and go about their daily routine for approximately one week. After the ambulatory phase, the subjects enter the laboratory where they undergo a 32-hour CR procedure for measuring unmasked circadian phase and amplitude. The constant routine data represent a 'gold standard' for developing demasking algorithms for data recorded in the ambulatory part of the study.
The following monitoring devices are being used in both the ambulatory and laboratory parts:
1) For measuring CBT, physical activity, posture, cardiovascular and respiratory variables we apply multi-channel devices of two types: one specialized device prototype developed within the EUCLOCK project with wireless connectivity of sensors and a modified handheld computer for data recording, and another general-purpose monitoring device with wired sensors and custom-made amplifiers. The functionality of devices of both types is identical and each subject wears a device of one or the other type on a belt around the waist. After completing the study, issues such as subject comfort, ease of use, reliability, and data quality with the devices of both types will be analyzed and taken into account for designing a specialized second generation circadian ambulatory monitoring device.
2) A dedicated multi-channel device also developed within the EUCLOCK project is used to measure light spectral composition and intensity as well as ambient temperature. This device is mounted on a spectacle frame. Subjects that normally do not wear spectacles receive a frame with zero-dioptric glasses.
3) Skin temperatures are recorded with an array of eleven autonomous tiny sensors equipped with a microprocessor and non-volatile memory.
Additionally, behavioural factors or events are noted in an electronic diary on a Palm computer during the ambulatory part of the study.
To overcome the complex nonlinear masking effects of multiple confounding variables on circadian rhythm markers, advanced nonlinear demasking based on data mining and pattern recognition techniques will be applied for data analysis. After collecting data from 20 subjects we will apply these multivariate nonlinear techniques to determine circadian phase from ambulatory measurements and to discriminate between individuals with different circadian timing.

Results and Conclusions: As a result of this research, we expect to develop a second generation circadian ambulatory monitoring device with a minimal subset of sensors as well as advanced multivariate statistical techniques for reliable non-invasive ambulatory estimation of circadian phase in real life conditions. Such devices and techniques are expected to find their application in those fields where for optimal results it is desired to determine the circadian phase in humans without CR or invasive and expensive measurements of the conventional circadian markers, e.g. for therapy planning, scheduling shift work or physical training, etc.

Keywords: Circadian Marker, Circadian Phase, Ambulatory Monitoring, Constant Routine, Demasking

Funding Support: This research is supported by the 6th Framework Project EUCLOCK (No. 018741).

EXPLORING THE ROLE OF MELANOPSIN IN PUPILLARY RESPONSES TO LIGHT

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Objectives: In addition to rods and cones, the human retina contains a subset of light-sensitive ganglion cells containing melanopsin (mRGCs). The mRGCs have been shown to be involved in a range of non-image forming (NIF) responses to light including photic entrainment of the circadian clock, regulation of the sleep wake cycle, pupillary light reflex, and acute light-induced alertness. Melanopsin shares amino acid structure and signal transduction mechanisms of invertebrate photopigments (IRPs). IRPs are bistable photopigments in which light drives both sensory responses and chromophore regeneration required to restore responsiveness of the photopigment. To explore the bistable properties of melanopsin in humans we used the pupillary light reflex as a tool to define the photopigment response properties.

Methods: Monochromatic light stimulations were used to record consensual pupillary constriction responses with the pupil of one eye dilated with tropicamide. The pupil response (pupil aperture size) was recorded from the unilluminated eye using an infrared video pupil tracking system (ViewPoint, Arrington).

Results: The pupil response to light consists of several temporally distinct components. At light onset, a phasic pupil constriction is elicited by signals from rods and cones. Under continued illumination, the pupil redilates to a steady state level of constriction that is due to the sustained responses of melanopsin. This steady state response can be maintained unchanged for at least 10 min. At light offset the pupil displays a continued constriction to light that gradually (1-5 min) returns to the baseline (dark accommodated) level. This persistent response is under the control of melanopsin. We find that prior light exposure can modulate the amplitude of the steady state response in a manner consistent with predictions for bistable photopigments. Adapting long wavelength light increases while short wavelength light decreases the ability of the pupil to respond to light.

Conclusions: The expression of bistable properties of melanopsin could allow further optimization of spectral light distribution in industrial, domestic and in clinical phototherapy applications. It can also be hypothesized that bright light therapy would be more efficient when preceded by a long wavelength light to potentiate the response, as previously proposed by Mure et al. (2007). This possible optimization in light therapy would also reduce the amount of energy allowing shorter light exposures or reduced light intensities. In practice, this type of manipulation could be easily implemented with modern RGB-LED luminaires or by mixing two or more polychromatic light sources.

Keywords: Melanopsin, Pupillary Light Reflex, Non-visual Functions, Non-image Forming, Photoreception

Funding Support: FP6-EUCLOCK, Cible Rhone-Alpes, PRES Lyon Mobilité européenne

Reference: Ludovic S. Mure, Camille Rieux, Samer Hattar and Howard M. Cooper. “Melanopsin-Dependent Nonvisual Responses: Evidence for Photopigment Bistability In Vivo.” *J Biol Rhythms* 22, no. 5 (2007): 411-424.

MELATONIN PHASE SHIFTS TO DAWN SIMULATION AND BRIGHT LIGHT, WITH PHOTIC AND NON-PHOTIC CONTROLS

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Objectives: Circadian phase advances are a major factor associated with the antidepressant response to postawakening bright light therapy for seasonal affective disorder (SAD).[1] Dawn simulation, which is also antidepressant,[2] presents gradually incrementing light of far lower intensity in the bedroom, before awakening. Early case studies of dawn simulation, with overnight serial plasma melatonin determinations, noted posttreatment phase advances. The present study compared phase shifts following treatment with bright light or dawn simulation in randomized, parallel groups, with both photic (brief dawn pulse) and nonphotic (negative air ionization) controls.

Methods: Research volunteers (N=103) with SAD were assigned to one of five groups: (a) postawakening bright light (30 minutes, 10,000 lux, 3000 K fluorescent [Uplift Technologies]); (b) dawn simulation (0.001–250 lux incandescent [Osram 66490] in the pattern of May 5 at 45 north latitude, beginning 93 min before wake-up time [MacLite algorithm]; (c) a dawn light pulse (13 min before wake-up time, 250 lux, with an illuminant dose of 3.25×10^3 lux·min, matched to the dawn); (d) negative air ionization at high flow rate (93 min before wake-up time, 4.5×10^{14} ions/sec [SphereOne]); or (e) ionization at low flow rate (93 min, 1.7×10^{11} ions/sec). The clock time of treatment was set according to the subjects' habitual sleep patterns. At baseline and at the end of 3 weeks of home treatment, subjects collected 9 samples of saliva under dim room light, using attenuating goggles. Samples were spaced at 30 min, timed to begin approximately 4 h before habitual bedtime. Saliva was assayed for melatonin (Bühlmann), with 3 pg/ml chosen as the onset phase.

Results: Bright light, dawn simulation and high-intensity negative air ions were clinically superior to the low-intensity ion control, but not significantly different from each other (2). ANOVA for melatonin phase shifts showed significant group differences ($F_{4,99}=3.83$, $P=0.006$). Bright light and dawn simulation showed similar phase advances (0.57±0.81 h and 0.58±0.62 h, respectively). Both were significantly larger than that of the controls, which did not differ among themselves: dawn pulse, 0.20±0.90 h), low-intensity ions (-0.19±0.70 h), and high-intensity ions (0.03±0.81 h).

Conclusions: Clinical response and phase advances to bright light and dawn simulation are similar, while dawn simulation presents a far lower photic dose. The relative efficiency of dawn simulation may be due to its earlier presentation on the post-crossover, phase-advancing interval of the phase response curve, the incremental waveform of the signal, or its presentation to the retina in the dark-adapted state. It is important to note that the incandescent dawn signal presented minimal short-wavelength visible radiation. The absence of a phase advance to high-density negative air ions suggests that its antidepressant action is independent of circadian timing.

Keywords: Light Therapy, Melatonin, Dawn Simulation, Seasonal Affective Disorder, Circadian Rhythms

Funding Support: US National Institutes of Health RO1-MH-42931.

References:
1. Terman JS et al. Arch Gen Psychiatry 58:69–75, 2001
2. Terman M et al. Am J Psychiatry 163:2126–2133, 2006

WHAT WE KNOW ABOUT THE EFFECTS OF LIGHTING ON PERFORMANCE, MOOD, AND HEALTH

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Objectives: Advances in photobiology have revealed neuroanatomical pathways separate from vision that mediate biological and behavioural effects of light in humans and other animals. This review will summarize what is known about the effects of lighting on human task performance, mood, and health, concluding with the implications of these effects for architectural lighting.

Performance: Provided that there is adequate light to see the task, there is limited evidence that increasing illuminance levels will improve task performance. Adaptation to higher illuminance might moderate the effects. Several studies of fluorescent lighting in offices and schools have sought to demonstrate task performance benefits attributable to changing the spectral composition of the light source on the expectation that light sources with higher correlated colour temperatures and better colour rendering would result in better performance than provided by light sources in the 3000-4000 K range. The results at 5000 K are inconclusive (largely because of methodological problems), although there is evidence that increasing the short-wavelength component to give CCT = 17000 K might improve self-reported performance.

Mood: Both experimental and correlational studies have found that increased light exposure is associated with improved mood and subjective well-being in healthy individuals. Exposure to illuminance > 1000 lx (measured at the wrist) has been associated with more agreeable, less quarrelsome, social interactions. The effect may be associated with immediate effects on tryptophan metabolism and serotonin function. Still other studies have found a wide range of individual differences in preferred illuminances; working under one's preferred illuminance results in more positive mood at the end of the working day. Working under lighting conditions that one identifies as being of high quality has been associated with more positive judgements of room appearance, more pleasant mood, and better end-of-day feelings of physical health.

Health: Therapeutic use of light is well-established for seasonal mood disorders and for circadian phase adjustment (e.g., to adapt to shift work and jet lag and for sleep disorders). Among generally healthy individuals, both experimental and correlational evidence shows associations between higher light exposure and general feelings of vitality or well-being. Two field experiments have found that light sources with CCT=17000 K resulted in reports of less daytime sleepiness, lower evening fatigue, and better night-time sleep quality.

Conclusions: There has long been speculation that lighting conditions could influence human performance, mood, and health. Studies have focused on variations in illuminance and spectral power distribution. Recent years have seen more use of sophisticated research designs and statistical analyses than formerly, and subtle effects have been revealed. There is too little information as yet to warrant changes to lighting recommendations and standards; however, increasing the appropriate use of daylight to reduce lighting energy use might result in additional benefits to health and well-being.

Keywords: Lighting, Task Performance, Mood, Health, Well-being, Architecture

*Unable to attend the meeting

SEASONAL CHANGES IN PERIPHERAL AND CENTRAL SEROTONIN TRANSPORTER PARAMETERS

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Objectives: Binding of the selective serotonin transporter ligand [^{11}C]DASB shows a clear seasonal variation in the brain of healthy human subjects, with higher binding occurring at times of lesser light, while binding diminishes with increased duration of sunshine during spring and early summer (Praschak-Rieder & Willeit et al., Arch Gen Psych 65(9):1072-1078, 2008). In human platelets, a well characterized peripheral model for brain serotonin transporters, efficiency of serotonin transport shows clear seasonal variation as well. Transport efficiency for serotonin is highest in fall and winter, and reduced in summer (Willeit & Sitte et al., Neuropsychopharmacology 33, 1503–1513, 2008). However, maximal binding capacity (Bmax) of the serotonin transporter ligand [^{3}H]β-CIT to platelet serotonin transporters failed to show significant seasonal variation. Similarly, k_d values, a measure for the affinity of a ligand to its receptor, failed to show seasonal variation. In order to better understand the inconsistency between brain and peripheral binding data, we carried out additional analyses on platelet serotonin transporter binding using 'binding potential values' analogue to brain PET outcome measures.

Methods: Platelets from were drawn from 73 patients with seasonal affective disorder and 70 healthy control subjects in Fall/Winter, again after four weeks of bright light therapy, and approximately 180 days after the first blood withdrawal, i.e. in early Summer (see Willeit & Sitte et al. 2008 for detailed description of study methods). A frequently used outcome measure of reference based PET data analysis is the binding potential (BP_{ND}). BP_{ND} values are calculated as ratio of Bmax over the dissociation constant k_d, a measure for the affinity of the ligand to its receptor. Since in high-affinity systems, the fraction of ligand-receptor complexes at low ligand concentrations increases rapidly and almost linearly with increasing ligand concentration, changes in BP_{ND} values are commonly assumed to reflect changes in Bmax rather than k_d in PET experiments performed at tracer doses. In analogy to the PET studies, a 'binding potential' ($Bmax/k_d$) was calculated using [^{3}H]β-CIT binding data to platelet transporters (further on termed BP_{PLT}). Data were evaluated for systematic changes between time points of blood withdrawals using repeated measures analysis of variance, 43 patients and 63control subjects had complete data sets for repeated measures analyses, paired t-tests were used for post-hoc testing.

Results: In contrast to Bmax ($F_{(2,104)}$=1.17, p=.31) and k_d values ($F_{(2,104)}$=0.31, p=.73), BP_{PLT} showed significant variation over time ($F_{(2,104)}$=8.50, p<.0004). While there was no difference between BP_{PLT} values before and after four weeks bright light therapy (p=.82), BP_{PLT} values before therapy (Fall/Winter) were significantly higher than BP_{PLT} values in summer (1.54±1.1 vs. 1.17±0.5; p=.0007).

Conclusions: Similar to what is found with [^{11}C]DASB and PET in the brain, BP_{PLT} values of [^{3}H]β-CIT binding to the platelet serotonin transporter shows significant seasonal variation. In good agreement with [^{11}C]DASB PET data, [^{3}H]β-CIT BP_{PLT} values were high in Fall/Winter and low in Summer. Combining relatively modest but opposite changes in the parameters Bmax and k_d helped detecting a seasonal signal of change in serotonin transporter properties in platelets. These changes are likely to be due to changes in oligomerization status, phosphorylation, or binding to associated proteins of the serotonin transporter 'regulome'. These results corroborate the finding of seasonal changes in serotonin transporter binding in the living human brain and they will advance our understanding of rhythmically expressed psychiatric disorders such as seasonal affective disorder.

Keywords: Serotonin Transporter, [^{11}C]DASB, PET, Platelet, Season

SEASONALITY IN AFFECTIVE DISORDERS

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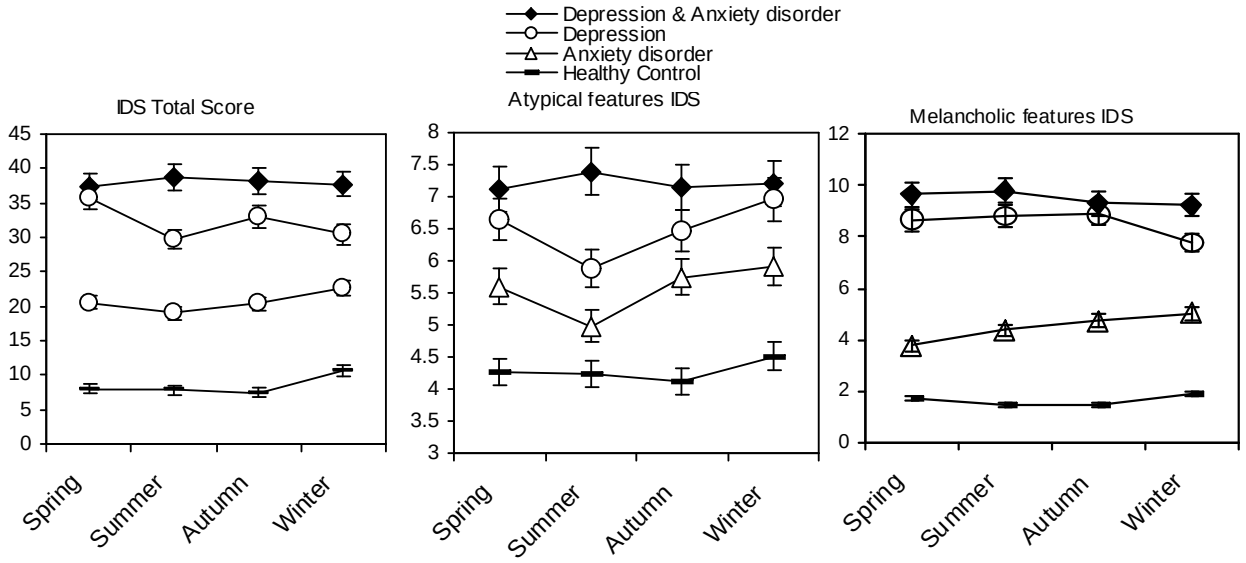
Objectives: Is there a seasonal pattern in the severity of (atypical /melancholic) depressive and/or anxiety symptoms in patients with a current (1 month prevalent) depressive and/or anxiety disorder as well as in healthy controls? There are some findings of seasonal patterns in anxiety disorders (Graaf et al., Am. J. Epidemiol., 162: 654-661, 2005. Ohtani et al., Psychiatry and Clinical Neurosciences 60: 379-83, 2006). Posternak evaluated 1500 patients in a psychiatric outpatient practice. Contrary to his hypothesis he did not find higher rates of onset of major depressive disorders in spring and fall. There were no higher rates of atypical depression in the winter (Posternak et al., Psychiatry Research 112:187–194, 2002).

Methods: Data are from 1,092 adults of the Netherlands Study of Depression and Anxiety (NESDA) cohort of 2,981 participants, 692 women (63.4%) and 400 men. The Composite Interview Diagnostic Instrument (CIDI) was used to diagnose depressive and anxiety disorders.
Participants were divided into four groups: 1] Healthy controls (465). 2] Major depression last month (131). 3] Any anxiety disorder last month (134). 4] Both major depression and any anxiety disorder last month (362). Outcome measures: Severity of depressive symptoms was measured with the 30-item Inventory of Depressive Symptoms self-report version (Rush et al., 1996). We constructed subscales for atypical features (5 items: scale 0-15) and melancholic features (8 items: scale 0-24). Severity of anxiety symptoms was measured using the Beck Anxiety Inventory (Beck et al., 1988), and the Fear Questionnaire (Marks and Mathews, 1979). Participants who completed the questionnaires more than 7 days before or after the diagnostic CIDI interview were excluded. The year was divided into the 4 meteorological seasons. Statistical analyses were conducted with SPSS: method multiple linear regression.

Results: Participants scored 2.9 points higher on the IDS (total score) in autumn (CI 0.5-5.3 p= 0.019), 6.3 higher in winter (CI 3.4-9.2 p= 0.000) and 2.7 higher in spring (CI 0.1- 5.4 p= 0.047) compared to summer. Depressive participants scored 3.7 points lower in winter (CI -6.3 - -1.1 p= 0.00) compared to summer. On average women scored higher than men: 4.7 (CI 2.3-7.0 p= 0.00) but contrary to our expectations women scored 0.6 points lower in winter p= 0.00). There was a marginal (significant) elevation of atypical symptoms in autumn 0.5 (CI 0.0-0.9) and winter 0.4 (CI 0.0 -0.6). Men scored higher in winter compared to summer on melancholic symptoms 1.1 (CI 0.16-1.93 p=0.021) but for women there was no difference between the seasons. There were no significant seasonal differences in anxiety scores (BAI and FQ).

Conclusions: Healthy controls and participants with anxiety disorders score lower on depressive symptoms in summer and higher in winter. Participants with depressive disorders score lower in winter on melancholic features and higher on atypical features. For participants with both depressive disorders and anxiety disorders there were no seasonal differences. Seasonal effects are limited and explain only a small portion of the total variance. These data suggest that seasonal changes in mood (seasonal affective disorder) require specific questionnaires like the SPAQ and the SHQ.



CHRONOTHERAPEUTICS FOR DEPRESSION: A DECISION STRATEGY FOR CLINICIANS

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Chronotherapeutics can be defined as controlled exposure to environmental stimuli that act on biological rhythms in order to achieve therapeutic effects. Chronotherapeutics for depression encompasses a set of treatments arising from research in chronobiology (light therapy) or from astutely following up clinical observations (sleep deprivation). Over the last thirty years the evidence base has grown sufficiently to promote these methods, and newly, their combinations (Table). In addition, exogenously administered melatonin can, like light, synchronise circadian rhythms and promote sleep, and has proved to be very useful for sleep-wake cycle disorders in persons with visual impairment, though without having have any major effects on mood.

TABLE Circadian and Wake Therapies for Major Depression

	Therapeutic Response	
	latency	**duration**
Total sleep deprivation = wake therapy (WT)	hours	~1 day
Partial sleep deprivation 2nd half of the night (PWT)	hours	~1 day
Repeated WT or PWT	hours	days/weeks
Repeated WT or PWT with antidepressants	hours	weeks/months
Phase advance of the sleep-wake cycle	~3 days	1-2 weeks
WT followed by sleep phase advance	hours	1-2 weeks
Single/repeated WT or PWT + light therapy	hours	weeks
Single/repeated WT or PWT + phase advance + light therapy	hours	weeks
Single/repeated WT or PWT + lithium, pindolol, or SSRIs	hours	months
Light therapy (winter seasonal depression)	days	weeks/months
Light therapy (nonseasonal depression)	weeks	weeks/months
Light therapy + SSRIs (nonseasonal depression)	1-2 weeks	weeks/months
Dark or rest therapy for mania or rapid cycling	days	while treated

No antidepressant has yet broken the time barrier with fast onset of action and minimisation of residual symptoms. In contrast, response to sleep deprivation works within hours. It has not entered the therapeutic armamentarium because patients usually relapse after recovery sleep, or even a nap. Now we have learned how to sustain this rapid effect with morning light therapy, sleep phase advance and a variety of medications. Practical experience shows that major depression can indeed remit quickly and remain remitted even in otherwise refractory cases. Light therapy has undergone widespread controlled, randomised clinical trials for seasonal affective disorder, and studies in non-seasonal depression show that light (as adjuvant or monotherapy) induces fast and substantial improvement.

The International Society for Affective Disorders convened a Committee on Chronotherapeutics (https://www.isad.org.uk/committees/chrono_therapy.asp), whose report on chronobiologic treatments for depression was published as an editorial in *Psychological Medicine*[1]. We have now written a treatment manual to provide theoretical and practical guidelines for wake therapy and light treatment in clinical practice[2] and implemented a discussion forum for practitioners (www.chronotherapeutics.org), thereby fulfilling an objective of our non-profit organisation (Center for Environmental Therapeutics, www.cet.org) to provide research-based, reliable information about these non-pharmacologic treatments.

Keywords: Light Therapy, Sleep Deprivation, Wake Therapy, Sleep Phase Advance, Non-seasonal Depression

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References:
[1]Wirz-Justice A et al. Chronotherapeutics (light and wake therapy) in affective disorders. Psychol Med 35, 939-944, 2005.
[2]Wirz-Justice A et al. Chronotherapeutics for Affective Disorders: A Clinician's Manual for Light and Wake Therapy. ISBN-13:978-3-8055-9120-1. S. Karger AG, Basel, 2009.

RAPID AND SUSTAINED ANTIDEPRESSANT RESPONSE WITH SLEEP DEPRIVATION AND CHRONOTHERAPY IN BIPOLAR DISORDER

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Objectives: The development of a rapid-acting and sustainable treatment for bipolar disorder (BPD) has been a goal for decades. The most widely-documented rapid-onset antidepressant therapy is sleep deprivation (SD) which acts within 24-48 hours in 40-60% of depressed patients. Conventional antidepressants usually require 2-8 weeks to meet response criteria. The delay prolongs suffering, may increase suicidal risk and underlines the urgency of alternative treatment strategies. This the first study to evaluate the combined efficacy of three established circadian-related treatments (SD, bright light, sleep phase advance) as adjunctive treatment to lithium and antidepressants.

Methods: Forty-nine BPD patients were randomly assigned to a chronotherapeutic augmentation (CAT) (SD+BL+SPA) or to a medication-only (MED) group. Clinical outcome was assessed using the Hamilton Rating Scale for Depression (HRSD).

Results: Significant decreases in depression in the CAT versus MED patients were seen within 48 hours of SD.

Conclusions: This is the first study to demonstrate the benefit of adding three non-invasive circadian-related interventions to SD in medicated patients to accelerate and sustain antidepressant responses and provides a strategy for the safe, fast-acting and sustainable treatment of BPD.

Keywords: Sleep Deprivation, Depression, Light Therapy

MOTION SENSOR ASSESSMENT OF ADHERENCE TO BRIGHT LIGHT TREATMENT

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Objectives: One limitation of assessing the efficacy of bright light treatment in participants' homes is the difficulty of objectively assessing treatment adherence. Wrist actigraphic light sensors have not been reliable for assessing adherence. Recently, a power sensor was developed (Desan et al., 2007), which can establish when an experimental light box is turned on, but not whether a participant is indeed receiving the prescribed light treatment. A video camera could be used to assess adherence, but would likely be judged to be an unnecessary invasion of privacy.

Methods: We have developed a device that assesses adherence to light treatment via a motion sensor. The device (size: 6.5"x6.5"x6.5"; 2.3 kg) is driven by a small, relatively quiet motor. A timer is programmed to allow the electronic device to operate daily within a prescribed window of time (e.g., 0600-0900 hr). When the participant is in the prescribed window of time, a 30 minute countdown timer is manually pressed to activate the electronic device. The device will operate as long as a participant is detected by a motion sensor. The device stops registering exposure after 1 minute if movement is not detected, but will rapidly restart once movement is again detected. Weekly visits allow staff to record total weekly exposure ($\leq$210 min) from a meter, and then reset the meter.

Results: Validation studies indicate that the device is quite accurate in assessing adherence to bright light treatment.

Conclusions: A disadvantage of the device is that it must be moved whenever a participant moves a bright light box. Moreover, the device is not invulnerable to deception by a participant, who could fake adherence, for example, by having a friend or pet sit by the device. Nonetheless, we believe that this device is a good alternative for assessing adherence to bright light treatment.

Keywords: Adherence, Phototherapy, Exposure Measurement

AUTHOR INDEX