



Society for Light Treatment and Biological Rhythms

Program and Abstracts

Volume 20

20th Annual Meeting, June 26 – 28th, 2008
Vancouver, British Columbia, Canada

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Program Organizers: Victoria Revell and Ybe Meesters

Local Arrangements: Raymond Lam and Erin Michalak

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SLTBR 20TH ANNUAL MEETING PROGRAM

Thursday, June 26, 2008

- 3:00 – 5:00 p.m.** **SLTBR Board Meeting**
- 6:00 – 9:00 p.m.** **Registration**
- 7:00 – 9:00 p.m.** **Poster session with discussion**
(Guest discussant: Dr. Norman Rosenthal)
A unique British Columbia wine and cheese tasting will be featured prior to the poster session.

Friday, June 27, 2008

- 7:45 - 8:45 a.m.** **Registration, breakfast**
- 8:45 - 9:00 a.m.** **President's welcome**
- 9:00 – 11:00 a.m.** **Symposium I: (Chronobiological aspects of ADHD)**
- 9:00-9:30** **CORRELATION BETWEEN THE DLMO PHASE ANGLE
DISPLACEMENT FROM MID-SLEEP AND COGNITION AND
ATTENTION RATINGS IN ADOLESCENTS WITH ADHD.**
G. Keepers, E. Collings, N. Mishra, L. Maron, A. Lewy
- 9:30-10:00** **DISRUPTED CIRCADIAN RHYTHM IN ADULTS WITH ADHD AND
CHRONIC SLEEP ONSET INSOMNIA**
M.M. Van Veen
- 10:00-10:30** **CIRCADIAN PREFERENCE AND NEUROPSYCHOLOGICAL
FUNCTION IN ADULTS WITH ADHD: A CANADIAN SAMPLE**
R.D. Levitan, Y. Rybak , B. Mackenzie, U. Jain, H.E. McNeely
- 10:30-11:00** **A STUDY OF LIGHT THERAPY FOR ADULT ADHD**
Y.E. Rybak, H.E. McNeely, B.E. Mackenzie, U.R. Jain, R.D. Levitan
- 11:00 – 11:30 a.m.** **Break**

- 11:30 – 11:45 a.m. PRESENCE OF CIRCADIAN PHASE RESETTING IN RESPONSE TO BRIGHT LIGHT BEHIND THE KNEES?**
A.J. Lewy, J.S. Emens, J. Songer, A.F. Rutherford, J.N. Rough,
N. Mishra
- 12:00 – 1:30 p.m. Industry Sponsored Symposium and Lunch (Preventative Strategies for Managing Seasonal Major Depressive Disorder)**
Note: This session is located at the Metropolitan Hotel.
- 12:10 – 12:15 INTRODUCTION**
N. Goel
- 12:15 – 12:35 NON-PHARMACOLOGICAL STRATEGIES FOR THE PREVENTION OF SEASONAL MAJOR DEPRESSIVE DISORDER**
R.W. Lam
- 12:35 – 13:05 NEW PHARMACOLOGICAL STRATEGIES FOR THE PREVENTION OF SEASONAL MAJOR DEPRESSIVE DISORDER**
N.E. Rosenthal
- 13:05 – 13:20 PANEL DISCUSSION**
- 1:30 – 3:30 p.m. Oral presentations I**
- 1:30 – 1:50 SHORT EXPOSURE TO BLUE-ENRICHED WHITE LIGHT DOES NOT IMPACT ALERTNESS LEVEL WHEN USED AT THE END OF THE NIGHT**
A.Sasseville, J.Houle, M.Hebert
- 1:50 – 2:10 BLUE-ENRICHED LIGHT IN THE WORKPLACE INCREASES SELF-REPORTED ALERTNESS, PERFORMANCE, AND SLEEP QUALITY**
L.J.M. Schlangen, A.U. Viola, L.M. James, D.J. Dijk
- 2:10 – 2:30 BRIGHT BLUE-ENRICHED VERSUS BRIGHT WHITE LIGHT TO PHASE ADVANCE THE CIRCADIAN CLOCK**
M.R. Smith, V.L. Revell, C.I. Eastman
- 2:30 – 2:50 POLYCHROMATIC LIGHTING COUNTERMEASURES FOR SPACE EXPLORATION**
G. Brainard, M. James, K. Cecil, M. Jablonski, B. Warfield, K. West, J. Ricker,
B. Byrne, E. Gerner, M. Rollag, J. Hanifin
- 2:50 – 3:10 THE ACUTE AND PHASE SHIFTING EFFECTS OF SHORT WAVELENGTH LIGHT EXPOSURE IN OLDER INDIVIDUALS**
T.L. Sletten, V.L. Revell, B. Middleton, K.A. Lederle, D.J. Skene
- 3:10 – 3:30 BRIGHT LIGHT: A NOVEL TREATMENT FOR POSTTRAUMATIC STRESS DISORDER**
S.D. Youngstedt, J.P. Ginsberg, D.A. Powell, C.E. Kline, M.R. Zielinski

- 3:30 – 4:00 p.m. Break**
- 4:00 p.m. SLTBR Annual Business Meeting**
- 7:00 p.m. Annual Banquet**
Kirin Restaurant, City Square Centre

Saturday, June 28, 2008

- 7:45 - 8:30 a.m. Registration, breakfast**
- 8:30 - 10:00 a.m. Symposium II (Antidepressants, light and circadian rhythms)**
- 8:30-9:00 CIRCADIAN EFFECTS OF ANTIDEPRESSANTS**
 D.B. Boivin
- 9:00-9:30 EVIDENCE-BASED USE OF ANTIDEPRESSANTS FOR SEASONAL**
 AFFECTIVE DISORDER
 R.W. Lam
- 9:30-10:00 COMBINATION OF ANTIDEPRESSANTS AND LIGHT THERAPY FOR**
 SEASONAL DEPRESSION
 A.J. Levitt
- 10:00 -10:30 a.m. Break**
- 10:30 - 12:00 p.m. Oral presentations II**
- 10:30 – 10:50 A WINTER STROOP IN SUB-CLINICAL SAD USING HIGH-DENSITY**
 ERPS AND S-LORETA
 F. Jaspers-Fayer, I. Taake, L. Buchy, M/ Liotti
- 10:50 – 11:10 COMORBIDITY OF DELAYED SLEEP PHASE AND AFFECTIVE**
 DISORDERS
 D.F. Kripke
- 11:10 – 11:30 A PILOT fMRI STUDY OF EMOTIONAL REACTIVITY IN SEASONAL**
 AFFECTIVE DEPRESSION
 M. Liotti, F. Jaspers-Fayer, R. Lam
- 11:30 – 11:50 PREDICTORS OF WINTER DEPRESSION: LATITUDE, LONGITUDE,**
 AGE AND SEX
 M. Terman, T.M. White, S. Fairhurst, G.H. Musa
- 12:00 – 1:30 p.m. Lunch**

- 1:30 – 3:30 p.m.** *Symposium III (Light Therapy: Looking to the Future)*
- 1:30-2:00** **EFFECT OF BRIGHT LIGHT ON FATIGUE IN BREAST CANCER**
S. Ancoli-Israel, V. Trofimenko, M. Rissling, L. Natarajan, F. He, L. Liu
- 2:00-2:30** **THE ALERTING EFFECTS OF LIGHT**
M. Gordijn
- 2:30-3:00** **QUANTIFYING CIRCADIAN ENTRAINMENT AND DISRUPTION**
M.G. Figueiro, A. Bierman, J.D. Bullough, M.S. Rea
- 3:00-3:30** **EFFECTS OF LIGHT ON BRAIN ACTIVITY RELATED TO WORKING
MEMORY AND EMOTION PROCESSING ASSESSED IN HUMANS
USING FMRI**
G. Vandewalle
- 3:30 p.m.** **Closing remarks**
- 4:00 – 6:00 p.m.** **Optional social event: *Architectural walking tour of the ‘city of glass and
light’***
- 4:00 – 6:00 p.m.** **Optional public educational event: *‘Update on SAD and hot topics from
the 2008 SLTBR meeting’ at UBC Robson Square Conference Centre***
- Talks with discussion, 4.30-5.30 p.m.**
- Dr. Namni Goel**, University of Pennsylvania, providing
‘Highlights of the 2008 SLTBR meeting’
- Dr. Raymond Lam**, University of British Columbia, providing an overview of
‘SAD and light therapy’
- Dr. Robert Levitan**, University of Toronto, President, SLTBR, talking on
‘Bodyclocks and ADHD’
- Dr. Erin Michalak**, University of British Columbia, talking on
‘Self-management strategies for depression’

SLTBR 20TH ANNUAL MEETING

POSTER PRESENTATIONS

REST ACTIVITY CYCLES ACCORDING TO TIME MANAGEMENT IN BENEDICTINE MONASTERIES

R. Ciancaglini, S. Baccanelli, S. Riva

A RANDOMIZED, PLACEBO-CONTROLLED TRIAL OF BRIGHT LIGHT AND DIM GREEN LIGHT FOR TREATMENT OF SEASONAL AFFECTIVE DISORDER

R.K. Flory, B.B. Bowers

PATTERN OF ROD ERG MODULATION BY RECENT LIGHT HISTORY: A POSSIBLE MARKER OF SEASONAL AFFECTIVE DISORDER

A.M. Gagné, M. Hébert

CORRELATION BETWEEN THE DLMO PHASE ANGLE DISPLACEMENT FROM MID-SLEEP AND COGNITION AND ATTENTION RATINGS IN ADOLESCENTS WITH ADHD.

G. Keepers, E. Collings, N. Mishra, L. Maron, A. Lewy

SPECTRAL CHARACTERISTICS OF LIGHT THERAPY LAMPS

S. Kyburz, V. Bromundt, P. Oelhafen, R. Steiner, C. Cajochen, A. Wirz-Justice

NEUROIMMUNE FUNCTION IN PATIENTS WITH SEASONAL AFFECTIVE DISORDER

R.W. Lam, C. Song, E.M. Tam, E.E. Michalak, L.N. Yatham

CIRCADIAN PREFERENCE AND NEUROPSYCHOLOGICAL FUNCTION IN ADULTS WITH ADHD: A CANADIAN SAMPLE

R.D. Levitan, Y. Rybak, B. Mackenzie, U. Jain, H.E. McNeely

CORTISOL AS PREDICTOR IN MAJOR DEPRESSION

K. Martiny, M. Lunde, M. Unden, H. Dam, P. Bech

SEASONAL PHOTOPERIODISM IN ZEBRAFISH – EVIDENCE OF DAYLENGTH EFFECTS ON PITUITARY HORMONE EXPRESSION

J. Olsen, D. Whitmore

LACK OF EFFICACY OF ARMODAFINIL IN SEASONAL AFFECTIVE DISORDER IN A SMALL CONTROLLED STUDY

S.S. Shreeram, H. DiFebo, B. D'Souza, N.E. Rosenthal

EVENING MELATONIN RELEASE AND CONTRAST SENSITIVITY IN PATIENTS WHO RECEIVED LIGHT THERAPY FOR BIPOLAR DISORDER

D. Sit, M. Terman, E. Waxman, B. Hanusa, K. Wisner

THE ACUTE AND PHASE SHIFTING EFFECTS OF SHORT WAVELENGTH LIGHT EXPOSURE

T.L. Sletten, V.L. Revell, B. Middleton, K.A. Lederle, D.J. Skene

OSCILLATING RIGHT-LEFT VESTIBULAR DYSFUNCTION IN BIPOLAR DISEASE

A.M. Soza Ried, B. Certanec, J. Reyes

TEMPORAL VARIATION IN DEPRESSIVE SYMPTOMS AND RUMINATION IN WINTER

J.C.H. Tan, D. Dupuis

EATING CHARACTERISTICS IN SEASONAL AND NONSEASONAL MOOD CHANGES

J.C.H. Tan, K. Prystanski

DISRUPTED CIRCADIAN RHYTHM IN ADULTS WITH ADHD AND CHRONIC SLEEP ONSET INSOMNIA

M.M. Van Veen

SEASONALITY IN AFFECTIVE DISORDERS

W.H. Winthorst, P.P. Mersch, Y. Meesters, B. Penninx, W.A. Nolen

BRIGHT LIGHT TREATMENT FOR HIGH-ANXIOUS YOUNG ADULTS

S.D. Youngstedt, J.P. Ginsberg, C.E. Kline, M.R. Zielinski

THE MULLER CELLS' FUNCTION AS AN INDICATOR OF OVERDOSE IN LIGHT THERAPY

M. Zueva, I. Tsapenko, S. Zaguskin

SOCIETY FOR LIGHT TREATMENT AND BIOLOGICAL RHYTHMS ABSTRACTS 2008

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EFFECT OF BRIGHT LIGHT ON FATIGUE IN BREAST CANCER**S. Ancoli-Israel^{1,2,3}, V. Trofimenko^{1,2}, M. Rissling³, L. Natarajan⁴, F. He⁴, L. Liu^{1,2}**¹Department of Psychiatry, University of California, San Diego; ²VASDHS; ³SDSU/UCSD JDP in Clinical Psychology; ⁴Department of Family and Preventive Medicine

Objectives: Women with breast cancer complain of poor sleep and fatigue before and during chemotherapy. We have shown that women undergoing chemotherapy have little bright light exposure, yet it is known that bright light can improve sleep and might have an alerting effect. We present preliminary data from an on-going study that addresses whether bright light improves sleep and fatigue in women with breast cancer undergoing chemotherapy.

Methods: 20 women (mean age=52.6 years, SD=8.7, range: 32-70 years) diagnosed with stage I-III breast cancer were randomized into two treatment groups: bright white light (BWL; n = 10) or dim red light (DRL; n = 10). Each woman was instructed to self-administer light therapy with Litebook for 30 minutes every morning during their first 4 cycles of anthracycline-based chemotherapy. Sleep/wake activity was recorded with actigraphy (Ambulatory Monitoring, Inc. and Mini-Mitter, Respironics) for 72-hours at baseline (pre-chemotherapy) and during cycles 1 and 4. Fatigue was assessed with the Multidimensional Fatigue Symptom Inventory – Short Form (MFSI-SF) pre-chemotherapy (baseline, BL) and during cycle 4 week 1 (C4W1). Mixed models were developed with group, cycle of chemotherapy, and the group-phase interaction included as covariates.

Results: In general, sleep and fatigue either improved or remained the same in the BWL group, but got worse in the DRL group (p<0.005).

	BWL (n=10)		DRL (n=10)	
	Baseline (mean [SD])	Cycle 4 (mean [SD])	Baseline (mean [SD])	Cycle 4 (mean [SD])
Total sleep time (min)	407 [95]	429 [81]	448	426
Wake time after sleep onset (min)	101 [72]	89 [40]	70 [33]	81 [44]
Fatigue (lower is better)	17.6 [8.5]	15 [7.1]	-1 [4.3]	19.1 [9]

Conclusions: Preliminary results suggest that bright white light may prevent a worsening of sleep and fatigue in women with breast cancer undergoing chemotherapy. We continue to collect data to examine the relationship between sleep, fatigue and light exposure.

Keywords: Light, Cancer, Chemotherapy, Sleep, Fatigue

Funding Support: Litebook Company Ltd., CBCRP 11IB-0034, NCI CA112035, Moores UCSD Cancer Center, and the Research Service of the VASDHS.

CIRCADIAN EFFECTS OF ANTIDEPRESSANTS

D.B. Boivin

Centre for Study and Treatment of Circadian Rhythms, Douglas Mental Health University Institute, Department of Psychiatry, McGill University

Objectives: Sleep-wake disturbances are frequent in major depressive disorder (MDD) and are characterized by insomnia, hypersomnia, excessive daytime sleepiness, and lack of energy. Nearly 80% of depressed patients report insomnia which is also a clear risk factor for developing depression. Patients recovering from depression are at greater risk of relapse if they present residual sleep disturbances. There is evidence to suggest that abnormal circadian rhythms and/or an abnormal temporal relationship between the sleep schedule and the endogenous circadian system might contribute to the severity of depression. Current antidepressant drugs were historically developed with a primary focus on their mood enhancing effects regardless of their action on sleep. The aim of the presentation is to review the simultaneous action of current antidepressant drugs on sleep and depression in the context of the clinical implication of sleep disturbances in MDD.

Methods: This presentation will briefly review evidences for a supporting a role of the circadian system in the physiopathology of MDD. We will also present results of an ultra-rapid sleep-wake cycle protocol conducted in a time isolation laboratory that was designed to investigate the circadian variation of sleep in bipolar affective disorder (BPD). Following this presentation, we will review the effects of several antidepressants on sleep of MDD patients.

Results: Sleep-wake cycle and circadian disturbances reported in MDD suggest a state of “over arousal” and are consistent with a circadian involvement in MDD patients. Our results from time isolation studies also support a disruption of sleep production and/or the circadian regulation of sleep in BPD. Various antidepressants exert different actions on the sleep-wake cycle, some improving sleep whereas others are disturbing sleep despite their antidepressant action.

Conclusions: These lines of evidence suggest that a misalignment between the endogenous circadian system and the sleep-wake cycle might contribute to the clinical status of patients suffering from MDD. In this context, antidepressants that simultaneously improve sleep and/or circadian disturbances appear advantageous for patients’ well-being.

Keywords: Depression, Circadian rhythms, Sleep, Antidepressant, Melatonin

Funding support: Canadian Institute of Health Research, Fond de la Recherche en Santé du Québec.

POLYCHROMATIC LIGHTING COUNTERMEASURES FOR SPACE EXPLORATION

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Objectives: Risk factors for the health and safety of astronauts and ground crews during space exploration missions include disturbed circadian rhythms and altered sleep-wake patterns [1]. Resulting in decreased alertness, concentration, and performance, such problems can threaten the safety and objectives of space missions. In studies with astronauts, pre-launch light treatment has been used to help entrain circadian rhythms and sleep-wake patterns [2-4]. Analytic action spectra employing monochromatic light exposures in rodents, nonhuman primates, and humans show that the peak wavelength sensitivity for the circadian system is in the blue portion of the visible spectrum, fundamentally different from that of the classical visual system [5]. Preliminary studies with two spectrally different white-appearing fluorescent light sources have shown that modifying the spectral content of a polychromatic light can modify its potency for neuroendocrine regulation in healthy human subjects [6,7]. The aim of the following study is to characterize a fluence response curve for melatonin suppression with a polychromatic fluorescent source that is so deeply blue-enriched that its emitted light no longer appears white.

Methods: Eight healthy females and males with normal color vision are participating in this study (mean age 23.9 ± 0.9). The light exposure system consists of a 119 x 120 cm flat panel with highly blue-enriched fluorescent lamps which subjects view face-on at a distance of 30 cm to achieve a full visual field exposure. The volunteers' pupils are freely reactive during the polychromatic light exposures between 2:00 and 3:30 AM. When the study is complete, each volunteer will have been exposed to nine irradiances of blue-enriched light (0.8 to 1500 $\mu\text{W}/\text{cm}^2$) and a dark control exposure with at least one week between each experiment. Blood samples are quantified for melatonin by radioimmunoassay.

Results: More than 60 of the planned 80 exposures have been completed. A preliminary one-way ANOVA was used to compare both plasma melatonin % change scores and control-adjusted % change scores. The data show a significant intensity-related suppression of melatonin ($p < 0.01$). A preliminary plot of the mean and SEM melatonin control-adjusted % change data against a four parameter sigmoidal fluence-response curve has a high coefficient of correlation ($R^2 > 0.95$).

Conclusions: Working with both monochromatic and polychromatic stimuli, the goal of our research is to optimize light as a countermeasure for circadian and sleep disruption during space exploration [8]. Preliminary assessment of data from the study shows that the highly blue-enriched fluorescent lights suppressed plasma melatonin in healthy young subjects in a clear dose-response pattern with higher irradiances eliciting progressively stronger hormone suppressions. Completion of this study will permit direct comparison to the potency of the white-appearing fluorescent light in our earlier studies [6, 7]. Together, these data provide an important step towards characterizing the human circadian system's response to differing spectral blends in polychromatic fluorescent light. These findings open the door for

optimizing light as a countermeasure for sleep and circadian disruption during space exploration as well as applications on earth.

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

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.

REST ACTIVITY CYCLES ACCORDING TO TIME MANAGEMENT IN BENEDICTINE MONASTERIES

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Objectives: In order to assess the timing and rest/activity proportion inside the life schemes (Regola) of benedictine monasteries, we carried out a survey by consultation of acknowledged literature and direct interviews (questionnaires).

Methods: We examined the duration of rest (sleep time, eating time and activities with a limited physical task like prayers, chants, meditation etc.) compared with high task activities (work) assessing the duration of the abovementioned in hours and minutes.

Results: The scheme of daily activity in wintertime was the following:

Rest/Activity	Total Hours (minutes)		
	Monastery 1	Monastery 2	Monastery 3
REST	5.30 (min. 330)	4.30 (min.270)	6.00 (min.360)
WORK	3.00 (min. 180)	4.30 (min.270)	1.45 (min.105)
REST	2.15 (min. 135)	2.30 (min.150)	2.45 (min.165)
WORK	2.15 (min.135)	2.00 (min.120)	2.45 (min. 165)
SLEEP	8.15 (min. 495)	8.00 (min.480)	8.00 (min.480)

Conclusions: The analysis of rest and activity (work) time clearly shows what follows:

- in the morning a mild/moderate activity and long rests are scheduled (prayers and chants)
- Such practices last approximately 5 hours (300 minutes) ranging from 4.30 (270 min.) to 6.00 (360 min.).
- the high task activities (work) performed in the morning last approximately 3 hours (180 min.) with wide differences between the monasteries ranging from 1.45 (105) to 4.30 (270 min.).
- After noon the working times (high task) follow the rest, and last about 2.30 hours (150 min) with little differences between the monasteries (min 2.15 - max 2.45).
- The duration of working activities results shorter of about 20% as an average when comparing the afternoon with the morning.
- An equal amount of duration in time devoted to rest and working activities is a common characteristic of the central daytimes.
- A long time for sleep (8 hours and over) is a common feature in the lifestyles in all the three monasteries investigated.

Keywords: Rest/Activity Cycles, Work, Sleep, Lifestyles

QUANTIFYING CIRCADIAN ENTRAINMENT AND DISRUPTION

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The suprachiasmatic nuclei (SCN) serve as the mammalian brain's internal master clock, orchestrating the circadian rhythms of a wide variety of biological functions, including sleep, core body temperature, hormone production, alertness, cell division, and DNA repair. Light and dark regulate SCN timing so that, in the natural world, every circadian rhythm would be coordinated with the 24-hour cycle of day and night. Several lines of research, from epidemiology to controlled studies with animal models, indicate that disruption of the natural, 24-hour light-dark cycle increases morbidity and mortality. Ecological studies of human exposures to light are virtually nonexistent, however, making it impossible to determine if, in fact, light-induced circadian disruption is related to human health.

A newly developed field measurement device, the Daysimeter, was used to record circadian light exposure and activity profiles in day-shift and in rotating-shift nurses. Using a technique from signal processing known as phasor analysis, it was possible to quantify circadian entrainment/disruption in these two groups of nurses in terms of the synchrony between light-dark exposure patterns and activity-rest patterns. As might be expected, the synchrony between light-dark and activity-rest patterns was high for day-shift nurses but low for the rotating-shift nurses. The same technique was applied to wheel running data for two groups of nocturnal rodents (*Rattus norvegicus*), one subjected to a conventional 12L:12D photoperiod and the other on a 48-hour reversing 12L:12D photoperiod. There was a remarkable correspondence between the magnitudes of circadian entrainment/disruption for the day-shift nurses and for the rats on the 12L:12D photoperiod and between the magnitudes of circadian entrainment/disruption for the rotating-shift nurses and the rats on the 48-hour reversing photoperiod.

Phasor analysis enables quantitative comparisons of circadian entrainment/disruption across species and should enable researchers to bridge actual human experiences of light and dark to parametric studies of light-induced circadian disruption in animal models used in health-related research. Phasor analysis should also enable systematic investigations of a wide range of biological functions as they are affected by circadian entrainment/disruption and may portend a very large leap forward in understanding of how light and darkness affects health in modern humans.

A RANDOMIZED, PLACEBO-CONTROLLED TRIAL OF BRIGHT LIGHT AND DIM GREEN LIGHT FOR TREATMENT OF SEASONAL AFFECTIVE DISORDER

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Objectives: Bright white light is an effective treatment for Seasonal Affective Disorder (SAD) but is not recommended for patients with ocular diseases or abnormalities. Although low-intensity green light is as effective as bright light in producing circadian phase advances in subjects with SAD (Lewy et al., abstract of SLTBR meeting, 4: 11, 1993), no study has directly compared the effectiveness of dim green with that of bright white light in treating this disorder. We evaluated the effects of dim green light, bright white light, and a placebo treatment (low-density negative ions) on the symptoms of SAD in women.

Methods: Each of 30 women with SAD was randomly assigned to receive 20 daily 30-minute sessions of either 10,000 lux bright white light, 400 lux dim 500 nm green light, or low-density negative ions ($\sim 4.0 \times 10^3$ ions/cm³). Each completed a treatment expectancy questionnaire prior to treatment, and each completed The Structured Interview Guide for the Hamilton Depression Rating Scale, SAD Version, Self-Rating (SIGH-SAD-SR) and the Beck Depression Inventory (BDI) prior to, at the midpoint of, and following the 20-day treatment period. Treatment sessions were scheduled during morning hours in January 2005 and 2006 when the daily photoperiod was relatively short.

Results: Pretreatment expectations did not significantly differ across treatment groups (Kruskal-Wallis test; $p = 0.086$). All measures (SIGH-SAD-SR, the 21-item Hamilton Depression Rating (HAM-D) and 8-item atypical SAD symptoms (ATYP) scales of the SIGH-SAD-SR, and the BDI) showed a significant decrease (p from ANOVA ≤ 0.001) across assessment times, and this decrease was greatest for the white light group. Bright light resulted in significantly lower post-treatment SIGH-SAD-SR and BDI scores (p from ANOVA ≤ 0.001) as well as HAM-D scores (p from ANOVA ≤ 0.05) than did the green light or placebo treatments. The percentage of participants meeting either of two clinical remission criteria was higher for the white light condition than for either of the other two treatments.

Conclusions: The antidepressant effect of bright white light was superior to that of dim green light or placebo as evidenced by its pattern of effect across treatment sessions as well as by its final effect on measures of SAD. The finding that dim green light showed some effectiveness in alleviating of SAD suggests that this treatment may be a viable option for SAD sufferers who have difficulty tolerating bright light.

Key Words: Seasonal Affective Disorder, Phototherapy, Negative Ionization

Funding Support: This research was supported by Hollins University Faculty Research Grants and by a Paula P. Brownlee Professorship Research Grant.

PATTERN OF ROD ERG MODULATION BY RECENT LIGHT HISTORY: A POSSIBLE MARKER OF SEASONAL AFFECTIVE DISORDER

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Objectives: In human, the rod ERG response appears to be modulated by the amount of prior light exposure (Gagne et al. Psychiatry Res, 2007). Following a protocol in which the electroretinogram (ERG) was recorded after a 60 min exposure to various light conditions (5, 100 and 10,000 lux), it was the 5 lux condition that yielded the highest rod ERG response. Since a decrease in rod sensitivity was shown to occur in winter in SAD patients (Hebert et al. Psychiatry Res, 2004) we challenged SAD patients to the same protocol in both winter and summer.

Methods: Eleven normal controls and twelve SAD patients were exposed for 60 min to three different light conditions (5, 100 and 10,000 lux) separated by an interval of at least 1 day. After each light condition, a 30 min period of complete dark adaptation was performed. In both seasons, rod ERG responses were recorded over a range of intensities to detect the saturating maximum response.

Results: Three-way ANOVA revealed an interaction Groupe X Condition ($F_{2, 20.9} = 33.69$; $P < 0.0001$). Compared to the 100 lux condition (which yielded to a similar rod saturating maximum in both groups), the 5 lux condition produced significantly higher rod response in normal controls whereas the 10,000 lux condition produced significantly lower rod response in SAD patients ($P < 0.0001$). This pattern did not differ across seasons.

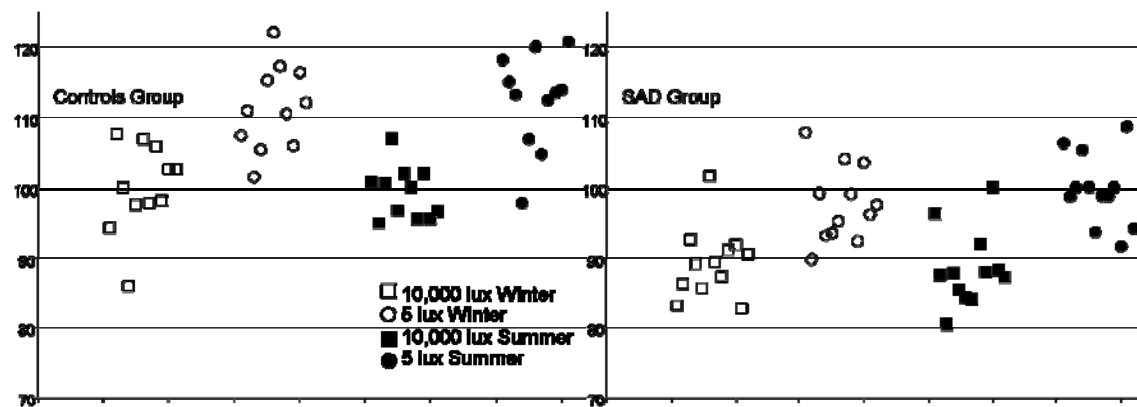


Fig.1: Individuals relative Vmax following 10,000 lux and 5 lux light exposure when compared to the controls (100 lux Vmax = 100%) in winter and summer.

Conclusions: In this study, 100 lux was used as a control condition because it represents normal indoor ambient light exposure. Of interest, both group responded similarly to this condition. However, when compared to this condition, 5 lux seemed to increase rod function in normal controls only, whereas 10,000 lux seemed to decrease it in SAD patients only. Although we cannot explain the underlying mechanism of these adaptation patterns, it is of interest to point out that the particular pattern observed in SAD may represent a marker of the pathology since it was observed even in the remitted state in summer.

Keywords: Seasonal Affective Disorder, ERG, Light, Retinal Sensitivity, Rod.

Funding support: This research was supported by a CIHR research grant to MH and by a doctoral research award to AMG.

THE ALERTING EFFECTS OF LIGHT

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Humans are diurnal, so the light phase relates to wakefulness. The relationship between light and wakefulness is more than a temporal coincidence: light has an acute alerting effect in humans, although, admittedly this has mainly been studied during the night. At that time, light exposure decreases sleepiness^{1,2}. A dose response curve for the alerting effects of light shows that compared to dim light (<10 lux), light levels between 100 and 200 lux already induce a 50% reduction of sleepiness¹, although it seems necessary to illuminate the whole retina to obtain these effects³. The spectral sensitivity of the photoreceptive system for the alerting effects of light is similar as for the phase shifting effects of light; short wavelength light (~460 nm) induces the largest reduction in sleepiness⁴⁻⁶.

Acute changes in physiological measures often accompany the alerting effects of light. At night body temperature and heart rate increase during light exposure and melatonin is suppressed⁷. In the morning, light induces an increase in cortisol^{8,9}. This increase in cortisol may facilitate waking up, which is shown by a reduction in sleep inertia and an increase in the awakening cortisol response after applying artificial dawn during the last half hour of sleep¹⁰. A few studies show that daytime light exposure also reduces sleepiness, despite the already low levels of melatonin, and without changes in cortisol, in body temperature, and in heart rate⁷. Nevertheless, fMRI scans at daytime show a light induced increase in thalamic activity in addition to the reduction in sleepiness¹¹.

Insight in the mechanisms underlying the acute alerting effects of light is important. It is a prerequisite for improving artificial indoor light conditions both during the day and (for shift workers) at night. Research should take into account the acute effects during light exposure, the short-term effects after light exposure, and the long life-time effects of altered light exposures on health.

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A WINTER STROOP IN SUB-CLINICAL SAD USING HIGH-DENSITY ERPS AND S-LORETA

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Objectives: Finding markers of low mood using brain imaging techniques could help to develop better diagnostic and treatment techniques for Seasonal Affective Disorder (SAD). Using a winter Stroop task, and studying people with symptoms of SAD, previous research (Spinks & Dalgleish, 2001) has found reaction time (RT) interference for winter words in both the summer and the winter. Our group has reported that although RT weakly differentiated the groups, ERP waveforms significantly differentiated between groups, and seasons (Jaspers-Fayer & Liotti, 2007). Specifically, in the winter an Emotional Anterior Positivity (EAP, 200-300ms) could be seen in the group with High Seasonal Pattern Assessment Questionnaire (SPAQ) scores, but not in the comparison group. This effect dissipated in the summer. The present study looks at the ERP results in brain space using s-LORETA, to determine neuro-anatomical underpinnings.

Methods: 64-channel EEG was recorded in 15 participants who scored high on the SPAQ (GSS>11, low mood in winter), and a comparison group (n=12) who scored within the normal range (GSS<11, no mood changes across the seasons).

Results: RTs to winter words (“ice”) compared to neutral words (“cup”), were marginally different between groups and seasons. The EAP was significantly different between groups and seasons. To look at the neural correlates of this task, standardized Low-Resolution Electromagnetic Tomography (s-LORETA) was performed on the grand-average waveforms. In the High SPAQ group the rostral Anterior Cingulate Cortex (rACC) had maxima during the 200-300ms time window ($t>3.0$).

Conclusions: The EAP distinguished winter words from neutral words in the sub-clinical SAD group, but not in the comparison group. This effect was significantly reduced when subjects were re-tested in the summer. The EAP may reflect automatic orienting towards a salient negative stimulus, and was localized in this study to the rACC.

References:

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Keywords: SAD, STROOP, ERPs, s-LORETA

Funding Support: MSFHR & CIHR (FJF); NARSAD & CFI (ML).

CORRELATION BETWEEN THE DLMO PHASE ANGLE DISPLACEMENT FROM MID-SLEEP AND COGNITION AND ATTENTION RATINGS IN ADOLESCENTS WITH ADHD.

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Objectives: Some evidence suggests significant sleep disturbance in ADHD (Ring et al., *J Learn Disabil* 31:572-8). Previous work of ours has shown unstable circadian rhythms in adolescents with ADHD. The mid-sleep phase angle displacement from DLMO (PAD) is related to SIGH-SADS depression score and treatment response in winter depression (Lewy et al: *PNAS* 103:7417-19). We hypothesize that ADHD patients will show sleep disruption, unstable circadian rhythms, phase delays, and seasonal variation in comparison to normal controls. We explore whether PAD may be related to the severity of ADHD symptoms.

Methods: Within 4 weeks of each solstice and equinox, adolescents with KSADS ADHD and controls are admitted for 4 overnight stays in < 30 lux light conditions. Seventeen Blood samples are drawn at ½ hourly and hourly intervals to determine melatonin levels by RIA. AW-64 Actiwatches measure activity levels. Initially, the KSADS, ADHD RSIV, Pediatric Sleep Questionnaire are collected. On each admission DLMO and DLMOff are determined and the ADHD RSIV is given. Actigraphy data are analyzed for sleep onset, time of awakening, number of times of awakening, total sleep time, and sleep efficiency. PAD was determined for each DLMO measurement in each subject. Canonical correlation analysis was used to examine relationships between PAD and ADHD symptoms.

Results: Seven subjects and two controls have entered with seasonal data available for 6 subjects. 4 subjects have data sets which are adequate for multiple measurements of PAD. Five of six ADHD had significant delays in DLMO which correlated with delayed sleep onset. Actigraphy data demonstrated that sleep onset is significantly delayed, total sleep is reduced and sleep efficiency is poor. Melatonin profiles show phase shifting and a high degree of variability in DLMO. ADHD symptomatology (averaged across subjects) was improved (ADHD-RS RCI $p < .05$) at the summer solstice. Measures of ADHD symptoms correlated with PAD. PAD was most strongly correlated with the ADHD index ($r^2 = .44$, $p < .001$).

Conclusions. These data are evidence for sleep disruption, phase delays, unstable circadian rhythms, and seasonal effects on circadian rhythm stability and symptomatology in ADHD. PAD may correlate with severity of ADHD symptoms but within subject variability complicates interpretation of the results.

Keywords: ADHD, Circadian Rhythm, DLMO, Phase angle displacement,

Funding support: Abracadabra Foundation

COMORBIDITY OF DELAYED SLEEP PHASE AND AFFECTIVE DISORDERS

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Objectives: Our group has been recruiting cases of delayed sleep phase disorder (DSPD) and DSPD-controls roughly matched for age, gender, ethnicity, and race. One goal is to identify genetic susceptibility factors which might contribute both to circadian and to affective disorders.

Methods: By solicitation of local sleep clinicians, word of mouth, radio and newspaper advertising, we recruited 205 nightowl participants and 221 controls (Kripke et al., *J Circ Rhythms*, 2008, in press). DNA was collected. Sleep and mood disorders were characterized by questionnaires including the BALM morningness-eveningness scales, the SPAQ global scale, the QIDS-SR depression scale, and the Mood Disorders Questionnaire (a screener for lifetime mania). DNA from larger samples of bipolar families and unipolar depression sib pairs were assembled from local and NIMH-sponsored repositories.

Results: A positive response to a screening question for lifetime history of major depression was obtained from 51% of DSPD, but only 23% of their controls ($P < 0.001$). Likewise, scores on the QIDS-SR averaged 6.0 for DSPS versus 3.4 for controls ($P < 0.001$). DSPS cases also reported more psychiatric consultation, more use of antidepressants, more hospitalization for depression, and more family history of depression. However, there was no significant difference between DSPD and their controls for reported manic symptoms, history of bipolar disorder, or family history of bipolar disorder. The SPAQ global score was not significantly associated. Bipolar disorder was associated with a number of single nucleotide polymorphisms in PER genes, CLOCK, and ARNTL, though these associations did not meet Bonferroni criteria. One polymorphism is being explored which appeared significantly associated with both bipolar disorder and DSPD, but no suggestively-significant polymorphisms were associated both with unipolar depression and with DSPD.

Conclusions: There is clear evidence for comorbidity of DSPD and unipolar depression (no mania), but we were surprised to find no evidence for comorbidity with bipolar disorder. In contrast, there is growing evidence for involvement of the circadian gene system in bipolar disorder, even though no common polymorphisms with high risk ratios have so far been discovered. Possibly we will eventually find many circadian polymorphisms each making only a very small contribution to expression of the bipolar phenotype. The evidence for genetic association of unipolar depression with the circadian system is minimal, and raises the question whether the comorbidity of DSPD and unipolar depression could be mediated by social and behavioral factors or a paucity of light.

Key Words: circadian, delayed, DSPD, bipolar, depression

Funding Support: HL071123.

SPECTRAL CHARACTERISTICS OF LIGHT THERAPY LAMPS

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Objectives: Light therapy lamps have been refined over the last 25 years with the objective of optimising their beneficial effects on the circadian system, while minimising possible adverse effects on the visual apparatus. In 1996¹, irradiance levels of single fluorescent tubes and plastic diffusing screens and filters commonly used in light therapy devices were measured, and recommendations for standards to prevent overexposure to damaging radiation by uncontrolled spectral characteristics of lamps were proposed. No such standards have been implemented in practice. The discovery of melanopsin-containing photoreceptors with spectral sensitivity in the blue range responsible for photic input to the circadian system has led to the development of many new therapeutic devices utilising enhanced blue wavelength components. However, artificial lighting may be involved in certain diseases of the retina and the lens, thus predicating caution.

Methods: We measured spectral intensity and illuminance of a selection of currently available light therapy lamps in Europe. Intensity measurements in the wavelength range between 350 nm and 1650 nm were performed using two diode array spectrometers MCS 501/UV/VIS/NIR and MCS 511/NIR (Zeiss, Jena, Germany) equipped with 1024 Si and 128 InGaAs diodes, respectively. The relative spectral sensitivity of the spectrometer setup had been calibrated at the World Radiation Center in Davos, Switzerland (EG&GINC: Lamp S/N: F240F). Illuminance was measured at determined distances from the light source with a Lux-meter (Mavolux 5032B).

Results: Our measurements could in no case confirm the specifications with respect to illuminance levels indicated by the respective producers. In addition, the spectral characteristics varied widely.

	Illuminance (lux)			
Distance (cm)	25	50	75	100
Sanalux San 40	18100	6040	2940	1750
CET/Uplift Daylight	13200	4270	2020	1190
Philips Original Bright Light	9310	3920	2060	1270
Philips Bright Light Energy HF 3305	6900	2700	1370	860
Philips Wake-up Light	1040	331	164	101
Davita LD110	9010	3360	1670	1010

Conclusions: These results support the need for instigating standards. Moreover, labelling with respect to illuminance levels attained at a given distance may entail inopportune confidence in clinical efficacy. The advantages of blue light for phase shifting and alertness must be set in balance with putative long-term deleterious effects on the retina.

Reference:

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Keywords: Spectral Intensity, Illuminance, Light Therapy Devices, Retinal Hazards

EVIDENCE-BASED USE OF ANTIDEPRESSANTS FOR SEASONAL AFFECTIVE DISORDER

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Background: Shortly after the first description of seasonal affective disorder (SAD), studies emerged on using antidepressants to treat this condition. There are fewer studies of antidepressants than of light therapy in the treatment of SAD.

Methods: This presentation will briefly review the evidence for efficacy of various antidepressants in the treatment of SAD. The talk will focus on randomized controlled trials (RCTs) as the “gold standard” for demonstrating efficacy.

Results: There are few RCTs on antidepressant use in SAD. Fluoxetine and sertraline have been shown in placebo-controlled studies to have efficacy; more limited evidence supports the use of moclobemide. Several studies have compared fluoxetine to light therapy, showing similar rates of response for both treatment modalities, although light therapy had faster onset of action. A large RCT demonstrated that bupropion-XL was efficacious in preventing a seasonal major depressive episode.

Conclusions: Antidepressants are efficacious in treating SAD, with the greatest evidence for SSRIs in acute treatment and bupropion-XL for preventative treatment. Other studies support the use of moclobemide. Open label studies suggest that other medications, including agomelatine, duloxetine, escitalopram, and tranylcypromine, may also have benefit in SAD.

Keywords: Depression, Antidepressants, Selective serotonin reuptake inhibitors.

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NON-PHARMACOLOGICAL STRATEGIES FOR THE PREVENTION OF SEASONAL MAJOR DEPRESSIVE DISORDER

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Background: Light therapy is recognized as an efficacious treatment for acute winter depressive episodes in seasonal major depressive disorder (MDD), known colloquially as seasonal affective disorder. However, although by definition seasonal MDD is a recurrent condition, there has been little emphasis on maintenance or prevention of winter episodes by light treatment.

Methods: A systematic review of the literature was conducted using a PubMed search with search terms “seasonal affective disorder,” “prevent*,” and “maint*.” Relevant articles were screened and randomized controlled trials (RCTs) and prospective followup studies were selected for review.

Results: There are few controlled studies examining light treatment or other non-pharmacological treatments for maintenance treatment or prevention of seasonal MDD. Three studies examined a brief course of light therapy to prevent a winter episode, while two studies used continuous treatment. All were limited by small sample sizes. One preliminary pilot study suggested that cognitive-behaviour therapy may have enduring effects across subsequent seasons.

Conclusions: There is little evidence available for the efficacy of light treatment as maintenance or preventative treatment for seasonal MDD. Clinical recommendations for the use of light therapy as a preventative strategy must rely on expert opinion and be tailored for an individual patient.

Keywords: Depression, light therapy, seasonal affective disorder, prevention, maintenance treatment.

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NEUROIMMUNE FUNCTION IN PATIENTS WITH SEASONAL AFFECTIVE DISORDER.

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Objectives: Animal studies demonstrate marked seasonal changes in neuroimmune function in response to anticipatory winter stressors (Nelson et al, 2002). Neuroimmune dysfunction has also been implicated in the pathophysiology of depressive disorders (Leonard and Song, 1999). We investigated the hypothesis that patients with seasonal affective disorder (SAD) would show changes in proinflammatory cytokines in winter compared to healthy subjects (Lam et al, 2004); specifically that patients with SAD would show an increase in macrophage-produced proinflammatory cytokines and a “left shift” in cytokines produced by T-helper 1 and 2 lymphocytes (TH1 and TH2) indicative of a proinflammatory process.

Methods: We studied patients (N=20) with a DSM-IV diagnosis of major depressive disorder, seasonal pattern, currently depressed with a score on the HAM-29 of 20 or higher. Healthy comparison subjects (N=21), with no personal history or family history of psychiatric disorder and with Global Seasonality Scores of 6 or less on the Seasonal Pattern Assessment Questionnaire, were matched to patients according to age and sex. Patients and subjects were sampled during winter between November and January, inclusive. Blood samples were assayed for macrophage activity (by chemiluminescence), lymphocyte proliferation (by thymidin uptake) and cytokine release (by ELISA).

Results: The patients with SAD showed significantly higher macrophage activity and lower lymphocyte proliferation, with or without mitogen stimulation, compared to healthy subjects. There was also evidence for increased concentrations of macrophage-produced proinflammatory cytokines IL-1 β and TNF- α . Furthermore, the patients with SAD showed increased levels of the TH1-produced cytokine, IFN- γ . In contrast, there were no significant changes in TH2-produced cytokines.

Conclusions: Compared to healthy subjects, patients with SAD in winter show evidence for increased concentrations of proinflammatory cytokines and a shift in balance towards TH1-produced cytokines. These results support the hypothesis that neuroimmune dysfunction characterized by an increased inflammatory response is associated with the pathogenesis of SAD.

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Key Words: Seasonal affective disorder, immune function, cytokines.

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CIRCADIAN PREFERENCE AND NEUROPSYCHOLOGICAL FUNCTION IN ADULTS WITH ADHD: A CANADIAN SAMPLE

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Objectives: To review recently published results measuring circadian preference, and its clinical and neuropsychological correlates, from a Canadian cohort of adults with ADHD.

Methods: 29 adults with ADHD were assessed in the fall-winter season using self-report measures of ADHD, mood, seasonality and circadian preference. A standard battery of neuropsychological tests was also completed. Correlations between chronobiological variables and clinical/ neuro- psychological measures were performed.

Results: Based on the morningness–eveningness questionnaire (MEQ) which assesses circadian preference (N=27), 11 subjects (40.7%) were designated as evening types, and only 5 (18.5%) as morning types, a distribution highly discrepant with general population studies. Consistent with prior work in adult ADHD, high rates of seasonal depression were reported in this sample. Later circadian preference, independent of seasonality, was strongly correlated with both self-reported symptoms of ADHD and neuropsychological deficits including impulsive responding and poor target discrimination. None of these findings was attributable to state depression.

Conclusions: A mood-independent delay in circadian phase may contribute to both subjective and objective measures of core pathology in many adults with ADHD, at least during the fall/winter months. More work is needed to examine these same measures in the spring and summer months, and to compare these results to matched normal controls in the fall /winter period. These findings establish a potential target for chronobiological treatments such as light therapy in adult ADHD (see Rybak et al, this meeting).

Reference:

Rybak YE, et al. "Seasonality and Circadian Preference in Adult AD(H)D: Clinical and Neuropsychological Correlates." *Compr Psychiatr*, 48(6):562-71, 2007.

COMBINATION OF ANTIDEPRESSANTS AND LIGHT THERAPY FOR SEASONAL DEPRESSION

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Objectives: For the first several years of treatment research in Seasonal Depression, light therapy trials dominated. More recently trials have demonstrated that traditional antidepressant medications may also be effective and that response rates do not differ from light therapy. Nonetheless, there may be particular characteristics of patients with SAD that determine who might respond to light and who might respond to antidepressants. This has given rise to the suggestion that the combination of light and medications may be better than either treatment alone. Early literature on this combination has mostly been confined to open trials or case series, although double blind controlled trials have been conducted.

Methods: A search of existing literature was conducted using Medline and Psychinfo, using the keywords "seasonal + depression", and "light therapy" and "antidepressant". Reference lists from articles identified were scanned for further potential manuscripts.

Results: This presentation will review the existing literature and report on the potential risks and benefits the combination of light treatment and medication for SAD. In addition, the complex issues inherent in designing the "ideal" trial to determine whether the combination has some benefit over light treatment or medications alone will be discussed.

Conclusions: Although the literature is sparse, and although the benefits reported are small (but significant), there is at least theoretical support for the potential benefit of a combination of light therapy and antidepressant medication for SAD. Optimal trial design remains a substantial challenge.

Keywords: light therapy, antidepressants, seasonal depression, clinical trials

Funding Support: Servier Canada.

PRESENCE OF CIRCADIAN PHASE RESETTING IN RESPONSE TO BRIGHT LIGHT BEHIND THE KNEES?

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Objectives: To rule out the possibility that peripheral photoreception influences the circadian rhythms of a totally blind person. All totally blind people (without ocular light perception) studied under highly-resolved conditions [frequent melatonin onsets (MOs) for a complete circadian beat cycle] show relative coordination (RC) to as-yet-unknown weak zeitgebers (WZs). The pattern of RC is the same for all blind free-runners (BFRs), including those few whose intrinsic period (τ) is <24 hours: as the MO drifts between about 08:00-20:00, two-point taus (TPTs) are longer than the individual's average due to phase delays from the WZs; as the MO drifts between about 20:00-08:00, TPTs are shorter than average. However, the RC amplitude (longest TPT – shortest TPT) varies markedly between BFRs and is a bioassay for responsiveness to the WZs, as is circadian status (free running vs. naturally entrained).

Methods: A female BFR (with an average τ of 23.71) previously determined to have a robust RC amplitude has been going to bed with Biliblankets strapped behind each knee according to the method of Campbell and Murphy. A timer turns the light pads on between 01:00-04:00 to minimize interference with sleep. Every two weeks, hourly saliva samples are collected for 25 h and assayed for melatonin.

Results: Of the eight experimental data points obtained thus far (May 2008), most TPTs could be superimposed on the control TPTs. However, the TPT between MOs obtained from 07:00 (drifting earlier) to 23:00 was 23.32 (the shortest TPT in the control data set was 23.59, thus doubling the RC amplitude from .34 to .61h. Collection of experimental data continues.

Conclusions: To our surprise, we are apparently finding an effect in a subject chosen as an ideal test case for ruling out the influence of peripheral phototransduction to the endogenous circadian pacemaker. Thus far, the magnitude of the daily phase shift during the advance zone of the τ -response curve (16 minutes) is smaller than originally reported, which may be one reason why it was missed in studies (of sighted people, who may also be less sensitive, particularly males) that failed to confirm the Campbell and Murphy findings (Science:279;396-399,1998).

Keywords: Melatonin, blindness, peripheral circadian phototransduction, free-running, relative coordination

Funding support: 9R01 EY018312-09A1, R01 AG21826, R01 HD42125

A PILOT fMRI STUDY OF EMOTIONAL REACTIVITY IN SEASONAL AFFECTIVE DEPRESSION

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Objectives: Very few neuroimaging studies have been carried out in SAD. No studies have employed activation tasks involving emotional stimuli or various cognitive paradigms. Finally, no studies have employed the current state-of-the-art neuroimaging modality, i.e., fMRI. Here we report pilot data from a new study aimed at investigating the neural correlates of emotional reactivity in patients with SAD during winter relapse using a 3-Tesla Scanner.

Methods: Two tasks were employed: a block design version of the Affective Stroop Task, in which colour words were shown in 30 sec blocks of Depression, Positive and Neutral words, respectively (n=11), and a newly designed Season Scenes Task (n=5), in which patients were shown 30 sec videos of winter scenes (rain, snow, wind, umbrellas, dark skies) or summer scenes (warm sunny beaches, blue skies, etc) preceded by instructions to imagine how it would feel like being in the depicted scene, and followed by a screen asking patients to rate the subjective level of experienced sadness or elation.

Results: For the Emotional Stroop Task (eStroop), voxel-by-voxel contrasts of Depression vs Neutral and Depression vs Positive words revealed significant clusters of BOLD signal change in medial PFC BA9 and 10 (for Depression vs Neutral, $t = 4.58$, $p < 0.01$ uncorrected, cluster level significance $p = 0.011$). In the Season Scenes Task, results showed consistent changes in subjective ratings of affect following both the winter videos (mean sadness = 3.86 ± 0.63 , range 3.17-4.5) and the summer videos (mean elation = 4.06 ± 0.38 , range 3.67-4.67) showing that on average the task achieved the goal to produce affective changes in both directions. Importantly however, only the contrasts involving winter video scenes were accompanied by greater BOLD signal change in medial PFC BA 9/10/32, suggesting that this region is differentially activated by the impact of winter scenes in patients with SAD. These effects were significant at the cluster level in spite of the small sample size ($p < .001$, uncorrected, cluster size significance: $p < .00001$, $t = 17.1$).

Conclusions. Main results in the present study are consistent with a major role of MPFC in emotional conflict in the eStroop Task. Results in the newly designed Seasonal Scenes Task, tailored at winter-related environmental triggers of winter SAD, are particularly encouraging, in spite of the small sample size. These data provide a foundation for future studies investigating neuroimaging markers of Relapse and Remission in Seasonal Affective Disorder, including effects of phototherapy.

Keywords: Seasonal Affective Disorder, Functional Magnetic Resonance Imaging, Emotional Stroop Task, Medial Prefrontal Cortex, Season Scenes Task.

Funding Support: Canada Foundation for Innovation (CFI) and National Alliance for Research on Schizophrenia and Depression (NARSAD) to M.L.

CORTISOL AS PREDICTOR IN MAJOR DEPRESSION

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Objectives: Mild hypercortisolemia is a biological marker found in a subset of patients with major depression. The cause is supposed to be a malfunction in the corticosteroid receptor. Longstanding cortisol excess is toxic to nerve cells and the hippocampus especially seems vulnerable to hypercortisolemia. The well known memory and concentration difficulties found in stress and depressive illnesses are supposed to be partly caused by deterioration of the function of the hippocampus.

Methods: The cortisol awakening response (CAR) was measured in saliva by repeated saliva specimens (awakening, 20 min and 60 minutes after awakening) in patient participating in a double blind study using a fixed dosage of sertraline and randomised to either dim or bright light treatment. Cortisol measurements were made before medication and light treatment started. The hypothesis, stated in the protocol, was that saliva cortisol would have a predictive validity of the short term depression outcome.

Results: A statistically significant increase in cortisol levels was found during the first hour after awakening. The area under the curve (AUC) from the CAR results was calculated and was found to have a statistically significant predictive validity for depression scores and remission at endpoint. Thus, a statistically significant higher proportion of patients with low CAR values were in remission compared to patients with high CAR values. This effect was predominantly seen in the bright light treated group.

Conclusions: Patients with a high CAR were less likely to attain remission at endpoint. High CAR seemed to block the effect of light treatment.

Keywords: Major Depression, Light Therapy, Cortisol, Outcome, Remission.

SEASONAL PHOTOPERIODISM IN ZEBRAFISH – EVIDENCE OF DAYLENGTH EFFECTS ON PITUITARY HORMONE EXPRESSION

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Objectives: Seasonal photoperiodism is the biological response to changes in light exposure and duration over the annual year. Many species use this varying photoperiod as a cue for adaptation and anticipation of seasonal changes. A common output of seasonal photoperiodism is cyclic changes in reproductive endocrinology and mating behaviour. Seasonal breeding has been noted in both mammals (sheep, hamsters) and non-mammals (birds, lizards and some teleost fish such as Medaka). Here we investigate the effects of seasonal photoperiod in the popular genetic model organism, Zebrafish (*Danio rerio*).

Methods: Two series of experiments were performed:

- 1) Measurement of embryo production in both LD (Long Day; 16L/8D) and SD (Short Day; 8L/16D) photoperiods, and resulting changes in clutch size and health after seasonal changes in light exposure. Zebrafish were kept in 14L/10D to monitor breeding fitness before being moved into light cabinets (LD or SD). 4 alternating fish tanks were tested sequentially; mean clutch size, embryo survival rates, and developmental stage were assessed.
- 2) Differences in hypothalamic and pituitary hormone expression between LD and SD were assessed. Changes in a number of reproductive and non-reproductive endocrine targets were found in both adult (6-10 month) and embryonic (7 day) samples. Both PCR and qPCR strategies were used at this stage of research. RNA was isolated from brain and pituitary (in adults) and whole embryo RNA samples were taken at 4 circadian time points over the 24hr day (ZT 3/9/15/21). A minimum of 16 adults samples were pooled, and 50 embryos for each data point.

Results: Zebrafish breeding and embryo production is higher in long day (16L/8D) than short day (8L/16D) photoperiods. Changes in embryo survival at laying (live/dead) and the first 2 days of development are not significantly different. Switching 14L/10D entrained zebrafish into an SD light regime caused a drop in their breeding rate, which was restored upon LD exposure. Growth hormone (GH) expression is higher in LD entrained fish (2.08 fold higher), than SD entrained fish, as compared to a common calibrator (LD>SD; t-test, $p < 0.001$). GH expression also differs significantly between embryos kept in LD or SD from birth (LD>SD; t-test, $p < 0.001$).

Conclusions: These results suggest that zebrafish are responsive to alteration in seasonal light exposure through changes to both their fertility (number of live embryos produced per clutch) and fecundity (potential reproductive capacity, as measured by endocrine hormone expression). Increased expression of the somatotropic hormone GH in LD entrained fish (in both embryonic and adults) indicates significant downstream endocrine upregulation in response to light, and may later be linked with changes in tissue growth, metabolism and fertility. The demonstration of a photoperiodic response in a genetically approachable model system, such as zebrafish, will hopefully lead to an increase in our knowledge of this important phenomenon.

Key Words: Seasonal Photoperiodism, Zebrafish, Fertility, Growth Hormone

Funding Support: BBSRC (Biotechnology And Biological Sciences Research Council)

NEW PHARMACOLOGICAL STRATEGIES FOR THE PREVENTION OF SEASONAL MAJOR DEPRESSIVE DISORDER

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Introduction: Seasonal Affective Disorder (SAD) is a condition characterized by the predictable development of depressive symptoms in autumn and winter, and their remission in spring and summer. Symptoms include decrease in energy, fatigue, over-eating, over-sleeping, as well as sadness and anxiety.¹

Although light therapy has been the mainstay of treatment for SAD, there is evidence that antidepressants are also effective. Given its predictable course, SAD lends itself to anticipatory treatment with medications before the onset of symptoms in an attempt to prevent them.

Methods: In three similarly designed studies, 1042 patients with SAD were randomly assigned to treatment with Wellbutrin-XL (150 mg. to 300 mg.) or matched placebo in autumn or winter, before they developed their usual SAD symptoms. Studies were done at multiple sites across the United States and Canada. Subjects were monitored at regular intervals and relapse was defined according to the SIGH-SAD scale. Statistical analysis for the first two studies used the Kaplan-Meier survival calculation as a primary analytic tool, and relapse frequencies as a secondary tool. In the third study, the order of these analytic methods was reversed.

Results: Despite a reported average of 13 previous seasonal depressive episodes, almost 60% of patients had never previously been treated for depression. Major depression recurrence rates during the three studies for bupropion XL and placebo groups were 19% versus 30% ($p = 0.026$), 13% versus 21% ($p = 0.049$), and 16% versus 31%; yielding a relative risk reduction across the three studies of 44% for patients taking bupropion XL. Survival analyses for depression onset also favoured bupropion XL over placebo ($p = .081, .057, \text{ and } <.001$).²

Conclusions: Anticipatory treatment of SAD patients before they develop their symptoms in autumn and winter appears to be a useful treatment strategy for those individuals with a clear history of severe depressions in fall and winter.

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A STUDY OF LIGHT THERAPY FOR ADULT ADHD

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Objective: To assess whether morning bright light therapy might have utility as an adjunct treatment for adult attention-deficit/hyperactivity disorder (ADHD) in the fall/winter seasons.

Method: Non-randomized, open clinical trial. 29 adults meeting DSM-IV criteria for ADHD recruited through advertisements were administered a standard 3-week light therapy (LT) during the fall or winter months.

Primary outcome measures included percentage reduction on the Brown Adult Add Scale and the Conners' Adult ADHD Scale. Secondary measures were decrease in depression scores according to the Structured Interview Guide for the Hamilton Depression Rating Scale (SIGH-SAD) Seasonal Affective Disorder version; improvement on various neuropsychological tests; and shift toward an earlier circadian preference as measured by Horne-Ostberg Morningness-Eveningness questionnaire. Regression analyses determined which variables at baseline best predicted improvement on a given outcome measure and which variables changed in parallel with one another.

Results: Mean age of participants was 40.4 years. About half had ADHD inattentive subtype, slightly less than half had combined subtype, and 2 participants had hyperactive-impulsive subtype. The sample was highly educated. Of subjects, 41.4% had comorbid current MDD, 13.8% had full-syndrome seasonal affective disorder, and 27.6% had history of substance abuse disorder. LT was associated with a significant decrease in both subjective and objective measures of core ADHD pathology, improved mood symptoms, and a significant phase advance in circadian preference. Multiple regression showed that shift toward an earlier circadian preference with LT was the strongest predictor of improvement on both subjective and objective, neuropsychological, ADHD measures.

Conclusions: LT may be a useful adjunct in many adults with ADHD. Improvement is not attributable to improvement in depression scores. Phase advance in circadian preference was most strongly associated with in core ADHD pathology. Replication in the spring and summer months is needed to better characterize LT effects independently of seasonal and winter circadian changes.

Keywords: ADD, ADHD, Adult, Light therapy

SHORT EXPOSURE TO BLUE-ENRICHED WHITE LIGHT DOES NOT IMPACT ALERTNESS LEVEL WHEN USED AT THE END OF THE NIGHT

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Objectives: We have previously shown that wearing blue blockers in the morning after a night shift may increase sleep by an average of 30 min per day in night shift workers (Sasseville et al., SLTBR 2006). But, it was suggested that this strategy could be detrimental to vigilance since blue light (even of short duration) can be beneficial as demonstrated when used at the beginning of the night. In this study, we challenged the impact of blue light when used at 6 AM when vigilance is expected to be at the lowest.

Methods: Ten participants (5 M, 5 F) were maintained awake on two consecutive nights during which vigilance/performance tests; VAS and Conners' continuous performance test 2 (CPT II), were performed at 23h30, 1h30, 3h30 and 5h30. First night served as baseline where subjects were tested in dim light. On the next night, they were exposed to two 30 minutes pulses of bright light at 3h00 and 5h00, just before the vigilance/performance tests. The first pulse was a 1500 uW/cm²/s (LiteBook), while wearing blue-blockers reducing the light behind glasses to 500 uW/cm²/s and the second a 500 uW/cm²/s of blue-enriched white light (provided by the same lamp).

Results: Repeated measures ANOVA revealed no interaction for either measure. But a night [$F(1,7) = 6.12, P = 0.04$] and a time [$F(3,21) = 11.35, P = 0.003$] effects were observed for the VAS with subjective vigilance decreasing with time on both nights, but being better on the second night at all times.

Conclusions: Short exposure to blue light at 6 AM does not appear to impact vigilance. Subjective vigilance was better on the second night probably because participants were more tired on the first night due to the longer sleep deprivation period. Therefore, sleep appears to be the most important factor that can impact vigilance. This suggests that the focus should be on favouring means to improve day sleep quality (such as blocking blue light on the way home) rather than the maintenance of a short blue natural light exposure during the drive home that could be detrimental to sleep.

Key words: Vigilance, Sleep, Blue wavelength, Shift work

BLUE ENRICHED WHITE LIGHT IN THE WORKPLACE IMPROVES SELF-REPORTED ALERTNESS, PERFORMANCE, AND SLEEP QUALITY

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Objectives: Specifications and standards for lighting installations in occupational settings are based on the spectral sensitivity of the classical visual system and do not take into account the recently discovered melanopsin-based, blue light sensitive photoreceptive system. Laboratory experiments have shown that monochromatic blue light is effective in eliciting non-visual effects of light such as improvements in alertness and performance. We investigated the effects of blue-enriched white light exposure during daytime working hours in an office setting.

Methods: The experiment was conducted on 104 white-collar workers, divided into two groups. After baseline assessments under existing lighting conditions, the participants were exposed to blue-enriched white light (17000K) and white light (4000K). The typical illuminance on the work surfaces was around 400 lux. The duration of exposure to each condition was four weeks and the order of the conditions was balanced. Questionnaire and rating scale based assessments of alertness (KSS), mood (PANAS), sleep quality (PSQI), performance, mental effort, headaches and eye strain were made throughout the 8 week intervention period.

Results: 94 subjects (age \pm SD: 36.4 \pm 10.2) were included in the study. Blue-enriched white light improved subjective measures of alertness ($p < 0.0001$), positive mood ($p = 0.0001$), performance ($p < 0.0001$), evening fatigue ($p = 0.0001$), irritability ($p = 0.004$), concentration ($p < 0.0001$) and eye discomfort ($p = 0.002$). Daytime Sleepiness was reduced ($p = 0.0001$) and subjective nocturnal sleep quality ($p = 0.016$) was improved under blue-enriched white light.

Conclusions: Blue-enriched white light in the workplace during daytime working hours can improve subjective alertness, performance and mood and improve nighttime sleep quality, while at the same time reducing visual discomfort. Blue-enriched white light sources may be useful additions to existing artificial lighting systems.

Keywords: Office Lighting, Performance, Sleep Quality, Mood, Workplace

Funding Support: Philips Lighting B.V., The Netherlands.

LACK OF EFFICACY OF ARMODAFINIL IN SEASONAL AFFECTIVE DISORDER IN A SMALL CONTROLLED STUDY

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Objectives: Besides bright light treatment, some medications have been shown to be effective in preventing the onset of depressive symptoms in persons with Seasonal Affective Disorder (SAD) (Modell et al, 2005). Modafinil and armodafinil are approved agents for promoting wakefulness in patients with excessive sleepiness associated with obstructive sleep apnea, shift work disorder, and narcolepsy. Modafinil has been shown in an open-label pilot study to improve depressive symptoms in SAD (Lundt, 2004). The current pilot study seeks to evaluate the effect of armodafinil treatment in improving depressive symptoms in SAD.

Methods: The study was conducted in five cities in the northern United States. Subjects, recruited between October and mid-February using advertisements and practice databases, were required to meet the following inclusion criteria: 1) DSM-IV criteria for recurrent MDD with seasonal pattern (Seasonal Affective Disorder); 2) Score 20 or more on the Structured Interview Guide for the Hamilton Depression Rating Scale with Atypical Depression Supplement (SIGH-ADS); 3) Score 5 or more on the 8-item atypical subscale of the SIGH-ADS and, 4) a score of 4 or more on the Clinical Global Impression-Severity (CGI-S) scale. Exclusion criteria included: 1) Clinically significant medical or psychiatric conditions; 2) Predominance of “typical” depressive symptoms such as insomnia, decreased appetite or agitation; 3) Use of light therapy within 2 weeks of baseline; and 4) Plans to travel to a sunny region during the study. Eligible subjects were randomized to receive either placebo or armodafinil at dosages ranging from 100 to 200 mg/day for a period of 6-weeks, in a double-blind design. SIGH-ADS, CGI-S and the Clinical Global Impression-Improvement (CGI-I) scales at weeks 1, 2, 4, and 6 were used to evaluate the effects of armodafinil treatment on the subject’s SAD symptoms. Paired t-test equivalent to analysis of variance was performed on a modified intent to treat population.

Results: A total of 43 subjects were enrolled in all five sites, 32 (74.4%) of whom were women, and 11 (25.6%) men. Overall, 32 (74.4%) were White and 10 (23.3%) African American. Mean age was 42 years (range 22-62). There was no significant difference between the armodafinil group and the placebo group on SIGH-ADS total scores, atypical subscale, typical subscale, the CGI-I or the CGI-S.

Conclusions: Possible reasons for this finding and implications for future studies are discussed. Future studies to examine the usefulness of armodafinil in SAD should include larger numbers and should complete enrollment by late fall.

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Keywords: Seasonal Affective Disorder, Armodafinil, Pharmacotherapy

Funding Support: Cephalon, Inc., Frazer, PA

EVENING MELATONIN RELEASE AND CONTRAST SENSITIVITY IN PATIENTS WHO RECEIVED LIGHT THERAPY FOR BIPOLAR DISORDER

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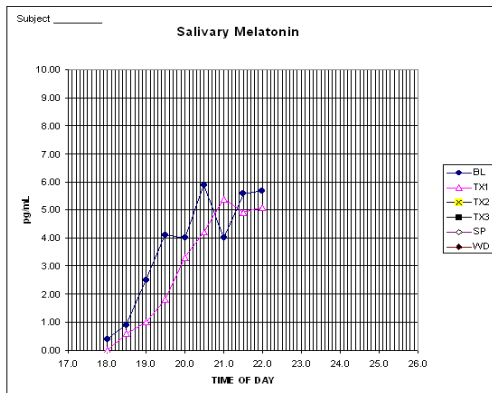
Objectives: A) The time of Dim Light Melatonin Onset (DLMO) serves as one reliable marker of the circadian timing system. We measured DLMO in patients who received light therapy (Sit et al, 2007) to ascertain the feasibility of the salivary collection method and assess circadian rhythm phase. B) Contrast sensitivity (CS) is a visual test that predicts function in the domains of driving, reading and facial recognition. CS requires intact visual information processing that may be impaired in bipolar patients (Friberg et al, 2000). We assessed baseline CS in our patient sample.

Methods: A) On the eve before starting light therapy (Sit et al, 2007), subjects collected 9 serial melatonin samples. The researchers instructed subjects to engage in minimal home activity (eg. watch TV), remain prone in a dimly lit room, and use dark goggles (ambient light <50 lux). The DLMO was defined as the time at which ascending salivary melatonin levels exceeded 3 pg/ml. B) The Pelli-Robson Test, which has been validated in healthy individuals, was used to measure CS.

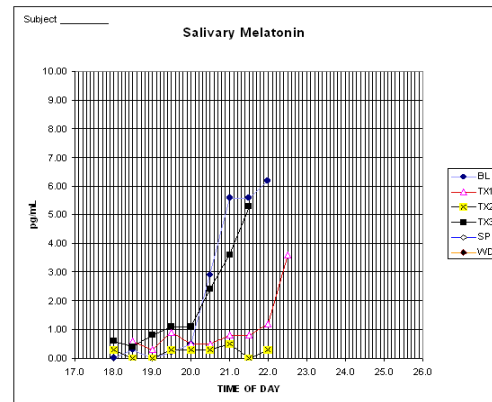
Results: A) Seven subjects collected complete samples; they separated into 2 groups [Figures]. Four subjects had an early time of DLMO (7:05-8:50PM) and three subjects had a late DLMO (9:55-11:25PM). The early DLMO group had longer intervals of time between DLMO and waking (11.5 ± 0.5 hrs); the late DLMO group had shorter intervals of time between DLMO and waking (8.7 ± 1.1 hrs). One patient each from the early and late DLMO groups developed a manic response to morning bright light therapy. B) Each value on the Pelli-Robson Test was converted into a z-score. All subjects had z-scores > 2 standard deviations from the mean.

Conclusions: The salivary collection method was feasible. In this limited sample, we detected a wide range of melatonin onsets that were not uniformly phase-delayed relative to norms. Subjects had significant reductions in sensitivity to contrast compared to age-equivalent norms. An expanded protocol is needed to further explore the associations between circadian phase parameters and treatment response, and the links between CS, the neuro-ophthalmic circuitry and bipolar illness.

Figures: Subject with Early Time of DLMO



Subject with Late Time of DLMO



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Keywords: Light Therapy, Melatonin, Contrast Sensitivity, Circadian Phase.

Funding Support: Stanley Foundation (PI - K. Wisner); Junior Faculty Scholars Program for D. Sit (PI – Pilkonis; 5 R25 MH060473-08).

THE ACUTE AND PHASE SHIFTING EFFECTS OF SHORT WAVELENGTH LIGHT EXPOSURE IN OLDER INDIVIDUALS

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Objectives: Age-related changes in the eye result in a reduction in the transmission of short wavelength light and may impair non-image forming light responses in older individuals. Indeed, reduced sensitivity to short wavelength light with age has been shown for light-induced melatonin suppression. The current study aimed to determine if a similar age-related reduction in response to short wavelength light occurs for circadian phase shifting and subjective alertness.

Methods: Eleven young (23.0 ± 2.9 years) and 15 older (65.8 ± 5.0 years) healthy males participated in two laboratory sessions that included a 2 h intermittent monochromatic light pulse ($\sim 6 \times 10^{13}$ photons/cm²/sec), individually timed to begin 8.5 h after their DLMO determined in a prior visit. Subjects were exposed to short wavelength light (456 nm) in one session and medium wavelength light (548 nm) in another; five older subjects participated in only a short wavelength light condition. The magnitude of phase advance was assessed as the difference in plasma melatonin onset and offset phase markers pre- and post-light exposure. Subjective alertness was rated on a 9-point scale during and for 5 h after light exposure.

Results: The two age groups exhibited similar wavelength sensitivity for the phase shifting response: short wavelength > medium wavelength light, but with smaller phase advances in the older group (non-significant). By contrast, the alertness response to short wavelength light was significantly reduced in the older group ($F_{1,24} = 23.6$, $p < 0.0001$), whereas the alertness response to medium wavelength light was not significantly different between the age groups.

Conclusions: The findings show that whilst there is reduced responsiveness to the acute effects of short wavelength light in older people (melatonin suppression, alertness) the response to phase shifting is not significantly impaired with age.

Keywords: Light, Alertness, Phase Shifting, Short Wavelength Light, Age

Funding Support: EU Marie Curie RTN grant (MCRTN-CT-2004-512362) and the 6th Framework Project EUCLOCK (018471).

BRIGHT BLUE-ENRICHED VERSUS BRIGHT WHITE LIGHT TO PHASE ADVANCE THE CIRCADIAN CLOCK

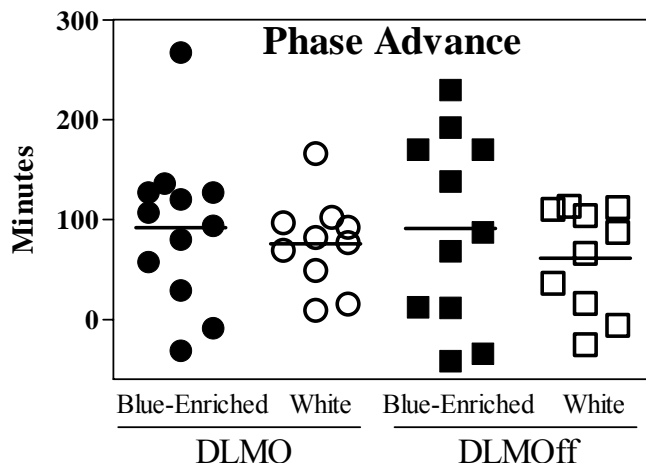
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Objectives: Previous studies have shown that the human circadian system is maximally sensitive to short wavelength (blue) light. Whether this sensitivity can be utilized to increase the size of phase shifts using light boxes and protocols designed for practical settings is not known. We tested whether bright polychromatic lamps enriched in the short wavelength portion of the visible light spectrum could produce larger phase advances than standard bright white lamps.

Methods: Twenty-two healthy young adults received either a bright white or bright blue-enriched 2-hour phase advancing light pulse upon awakening on each of four treatment days. On the first treatment day the light pulse began 8 hours after the dim light melatonin onset (DLMO), on average about 2 hours before baseline wake time. On each subsequent day light treatment began 1 hour earlier than the previous day, and the sleep schedule was also advanced. Salivary melatonin was collected during phase assessments before and after the light treatment days to determine the phase advance of the DLMO and dim light melatonin offset (DLMOff). The white light box (4,100K) delivered slightly more total photons than the blue-enriched light box (17,000K) (4.9 vs 4.2×10^{15} photons/cm²/sec) while the blue-enriched light box delivered more than double the number of photons between 400-490 nm (1.9×10^{15} vs 0.8×10^{15}). For the blue-enriched lamps, the illuminance was ~ 4000 lux and the irradiance was ~ 1640 μ W/cm², while for the white lamps the illuminance was ~ 6000 lux and the irradiance was ~ 1741 μ W/cm².

Results: Phase advances of the DLMO and DLMOff for the blue-enriched group (92 ± 78 and 91 ± 95 minutes, respectively) were not significantly different from that of the white group (76 ± 45 and 61 ± 53 minutes).



Conclusions: Bright blue-enriched polychromatic light is no more effective than standard bright light therapy for phase advancing circadian rhythms at commonly used therapeutic light levels.

Keywords: Blue Light, Human, Circadian, Phase Shift, Melatonin

Funding Support R01 NR007677. Philips Lighting donated the blue-enriched light boxes. Enviro-Med donated the white light boxes.

OSCILLATING RIGHT-LEFT VESTIBULAR DYSFUNCTION IN BIPOLAR DISEASE

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Objectives: The etiology of oscillation between depression and mania in bipolar disease is unknown, but it is likely that the chronobiologic system plays a role in it. Suprachiasmatic nuclei are responsible for regulating biological rhythms, which are altered in bipolar disease. Given the functional relationships that exist between suprachiasmatic nuclei and vestibular nuclei, vestibulo-ocular reflex can serve as an indirect measure of right and left suprachiasmatic nuclei activity.

Methods: We studied the vestibular function in two bipolar disease patients during different mood states. The vestibular activity was objectified through the recording of the vestibulo-ocular reflex (VOR). All measurements were taken between 8 and 11 a.m. using the same equipment (including a Tonnie's Optokinetic rotating chair).

Results: Bipolar patient 1's first recording showed a right/left ratio of 0.69 that was coincident to our previous studies showing a ratio <1 indicating right vestibular hypo activity in depression (Soza et Aviles, Neuroscience 144,128-134, 2007). The second recording, created on the seventh day after his lithium treatment was spontaneously discontinued (at which point the patient met DSM-IV criteria for mania), showed that the VOR record switched to a left vestibular hypoactivity with a right/left ratio of 1.27. The third recording was made when the patient resumed his lithium treatment, returning to his previous right vestibular hypo activity (0.54 asymmetry ratio) and to his previous mood state. In the other bipolar patient, the first recording showed an asymmetry ratio of 0.56, which coincides with a depressive state. The second recording, which was made during a maniac state, changed to a left vestibular hypoactivity with a ratio of 1.3.

Conclusions: In our research we found vestibular lateralized hypoactivity on the right side in depression and on the left side in mania. As the Suprachiasmatic Nuclei influences directly the vestibular neuronal centers, we hypothesize that those abnormal exams have their origin in Suprachiasmatic Nuclei alterations. We suggest that oscillation of suprachiasmatic nuclei asymmetry is probably involved in bipolar disease pathophysiology

Keywords: Bipolar Disease, Nystagmus, Raphe Nuclei, SCN, Brain Asymmetries, VOR.

TEMPORAL VARIATION IN DEPRESSIVE SYMPTOMS AND RUMINATION IN WINTER

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Objectives: We examined the temporal variation in depressive symptoms and three ruminative styles across 6 weeks in individuals who present with seasonal mood changes (SMC), with nonseasonal mood changes (NSMC), and without mood changes (Control). SMC is postulated to be linked to shortened photoperiod during the winter (Rosenthal et al., Arch. Gen. Psychiatry, 41: 72-80, 1984); rumination is associated with depression (Nolen-Hoeksema, J. Abnorm. Psychol. 109: 504-511, 2000). The findings might illuminate the link between rumination and depressive symptoms in seasonal and nonseasonal individuals.

Methods: Sixty-one university undergraduates (14 men, 47 women; age $M=22.69$ years) were categorized into 3 groups: SMC ($n=16$), NSMC ($n=19$), and Control ($n=26$). Classification measures used were the Structured Interview Guide for the Hamilton Depression Scale – Seasonal Affective Disorder version (Williams et al., New York State Psychiatric Institute, 2002) for depression severity, and the Global Seasonality Score (GSS; Rosenthal, Winter blues, 1984) for degree of seasonality and seasonal impairment. Average scores for each group were: SMC (total Hamilton = 44.62, GSS = 18.00, at least moderate impairment), NSMC (total Hamilton = 32.37, GSS = 7.74, none/mild impairment), Control (total Hamilton = 6.77, GSS = 5.35, no impairment). Participants rated themselves at the same time and same day of every week for 6 successive weeks in February and March on the Hamilton and a combined rumination scale (Roelofs et al., J. Behav. Ther. Exp. Psychiatry 37: 299-313, 2006). The Hamilton scale yielded 3 types of scores: total Hamilton, typical depressive symptoms, and atypical depressive symptoms. The combined rumination scale produced 4 types of scores: total rumination, rumination on sadness, rumination on causes, and rumination on symptoms.

Results: Separate Group (between-subject) x Week (within-subject) ANOVAs were conducted on *each* of the 7 dependent variables (DVs) consisting of 3 Hamilton scores and the 4 rumination scores. Bonferroni-split approach was used to control for overall Type I error, and Hyundt-Feldt corrections for violations of sphericity assumptions. Post-hoc Tukey and polynomial contrast tests were employed to investigate group differences and weekly trends, respectively. Results showed a Group effect ($p<.001$) with both SMC and NSMC > Control on all DVs. A Week effect on was observed for all DVs ($p<.001$ for all except atypical Hamilton at $p < .05$.) such that as the photoperiod increased, group scores on the DVs decreased. An interaction effect ($p<.05$) on atypical depression scores revealed a diametrically opposite profile across weeks for SMC and NSMC (Figure 1).

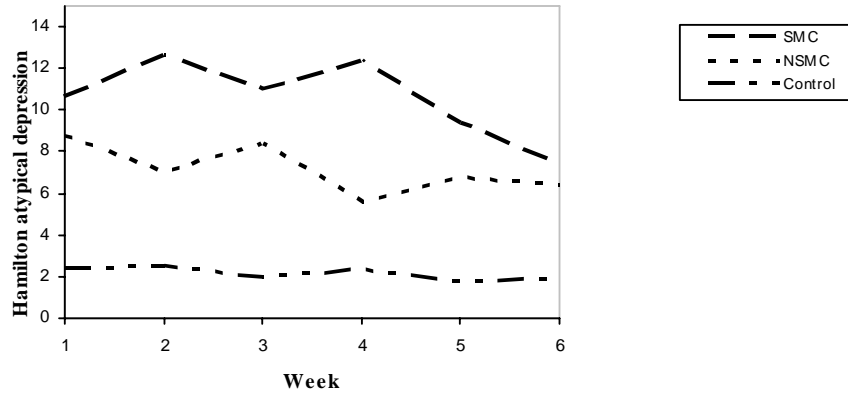


Figure 1. Averaged Hamilton atypical depression scores for each group by week.

Conclusions: As photoperiod duration increased, depression severity and rumination decreased in all 3 groups. Individuals with seasonal and nonseasonal mood changes showed diametrically opposite temporal trends in their atypical symptoms; when the atypical depressive symptoms in the seasonal group increased (decreased), the nonseasonal counterpart showed a decrease (increase).

Keywords: Seasonal Mood Changes, Depression Symptoms, Rumination, Temporal Variation.

Funding Support: Infrastructure grant from the Canada Foundation for Innovation.

EATING CHARACTERISTICS IN SEASONAL AND NONSEASONAL MOOD CHANGES

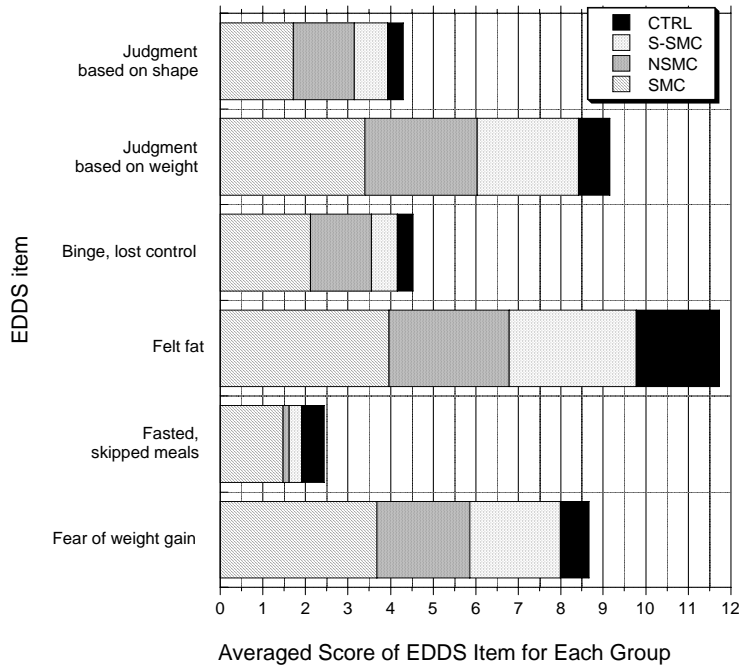
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Objectives: The winter vegetative symptoms in seasonal affective disorder (SAD) are similar to those found in bulimia nervosa (BN). BN is co-morbid with both major depression (O'Brien et al., *Clin. Psych.Rev.* 23:57-74, 2003) and SAD (Ghadirian et al., *Gen. Hosp. Psychiatry.* 21:354-359, 1999). This study compares disordered eating and compensatory behaviours (e.g., purging,) in individuals with seasonal mood changes (SMC), sub-syndromal seasonal mood changes (S-SMC) and nonseasonal mood changes (NSMC).

Methods: Ninety university undergraduates (27 men, 63 women; age $M = 22.38$ years) were classified into 4 groups: SMC ($n = 25$), NSMC ($n = 22$), S-SMC ($n = 24$), and Control ($n = 19$). Group classification was established with the use of the Structured Interview Guide for the Hamilton Depression Scale – Seasonal Affective Disorder version (SIGH-SAD, Williams et al., New York State Psychiatric Institute, 2002) to measure depression severity, and the Global Seasonality Score (GSS, Rosenthal, Winter blues, 1984) to assess the degree of seasonality and seasonal impairment. Mean scores for the groups were: SMC (total Hamilton = 41.72, GSS = 16.28, at least moderate impairment), NSMC (total Hamilton = 31.95, GSS = 8.00, no/mild impairment), S-SMC (total Hamilton = 15.20, GSS = 12.92, no/mild impairment), and Control (total Hamilton = 4.84, GSS = 4.54, no impairment). Participants also completed the Eating Disorder Diagnostic Scale (EDDS, Stice et al, *Psychol. Assess.* 12: 123-131, 2000) to measure BN symptoms.

Results: Results from ANOVAs and post-hoc Tukey tests on EDDS items showed that among all groups, SMC had the most fear of weight gain ($p < .001$), and used fasting or skipping meals most frequently to prevent weight gain ($p < .01$; see Figure below). Compared to Control, SMC reported feeling more fat ($p < .01$), and binged and felt out of control more frequently within the last 3 months ($p = .02$). NSMC had a greater fear of weight gain than Control ($p < .001$). Finally, compared to Control, the other 3 groups had a greater tendency to evaluate themselves as a person on the basis of weight ($p < .001$) or shape ($p < .001$). All other group comparisons were nonsignificant.



Conclusions: Individuals with seasonal mood changes are differentiated from their subsyndromal seasonal and nonseasonal counterparts on the basis of their greater fear of weight gain and use of fasting or skipping meals to prevent weight gain.

Keywords: Seasonal Mood Changes, Eating, Binge, Weight

Funding Support: Infrastructure grant from the Canada Foundation for Innovation.

PREDICTORS OF WINTER DEPRESSION: LATITUDE AND LONGITUDE IN RELATION TO PHOTOPERIOD AND SUNRISE

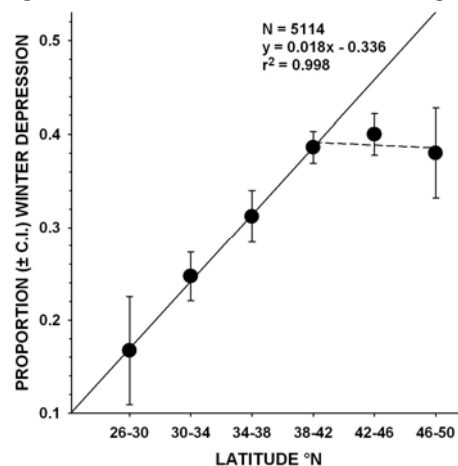
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Objectives: At previous SLTBR meetings we reported preliminary results of Web-based surveys of depressive symptoms, seasonality and chronotype. Now, with an expanded data set, several geographic and demographic factors have emerged that expand upon published population summaries.

Methods: We developed online versions of two instruments familiar in SAD research, presented on *cet.org*: the *Personalized Inventory for Depression and SAD* (PIDS), which includes a PRIME-MD/DSM-IV provisional diagnosis of major depressive disorder in the past year, SPAQ global seasonality scale with “worst” and “best” months, and a checklist of atypical neurovegetative symptoms emergent in winter; and the Horne-Östberg *Morningness-Eveningness Questionnaire* (MEQ). A demographic questionnaire recorded latitude and longitude of residence (via ZIP code), age and sex, among other variables, while maintaining anonymity. Respondents comprised a convenience sample recruited on the Web with IRB approval. Without random sampling we cannot ascertain population prevalence, but the data can be stratified to detect geographic, sex and age variations. Over three years of the study, 5114 subjects in the continental U.S., ages 18-60 (40.9 ± 12.1), provided complete data sets.

Results: The proportion of respondents with winter depression increased linearly with latitude by a factor of 2.3 across the lower half of the U.S., with no further increase above 38 °N. By contrast, longitude within time zones showed a significant effect above 38 °N, with 26% more winter depression among those living toward the western edge of time zones than toward the east. Women were 40% more likely than men to experience winter depression. There was 23% more winter depression between ages 30-50 than at ages 20-30 or 50-60, seen in both sexes. The MEQ score did not vary across latitude or longitude within time zones. Logistic regression confirmed significant effects only of latitude and sex below 38 °N. Above 38 °N, effects included longitude within time zone, sex and age.



Conclusions: The latitude cline for winter depression stops at about 38 °N, which could explain why prevalence studies farther north have failed to find such an effect. Increased winter depression toward the west of time zones supports the circadian hypothesis that later sunrise relative to sleep is depressogenic.

Key Words: Winter depression, Epidemiology, Latitude, Longitude

Funding support: Center for Environmental Therapeutics, New York State Office of Mental Health

EFFECTS OF LIGHT ON BRAIN ACTIVITY RELATED TO WORKING MEMORY AND EMOTION PROCESSING ASSESSED IN HUMANS USING FMRI

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Light exerts profound nonvisual effects on physiology and behavior in humans. Some of these effects are mediated in part by a recently discovered photoreception system which is most sensitive to blue (~470nm) light and recruits melanopsin. In the past 5 years, we conducted several neuroimaging studies investigating nonvisual effects of light on human brain activity. Our first experiments demonstrated that relatively short (~20min) white or monochromatic light exposures influenced brain activity related to cognitive tasks and alertness regulation. These effects were wavelength dependent: blue light exposures maintained activity levels, while in darkness or under green light exposure, activity decreased significantly.

We then investigated the brain mechanisms involved in the establishment nonvisual responses to light exposures by reducing the durations of the light exposures to less than a minute. We first used an auditory working memory task to show that the thalamus and the brainstem were involved in nonvisual brain responses to light within the first tens of seconds of the exposure. Brain response sensitivity to light was higher for 470-473nm, suggesting a prominent role of melanopsin ganglion cells as compared to the other photoreceptors (S-cones and M-cones).

Activity of the amygdala was also affected by the short light exposures. We therefore wondered whether light could affect emotion-related brain responses. Indeed light therapy is an effective treatment for seasonal affective disorder, but acute effects of light exposure on the brain emotional system have not been demonstrated. We used an auditory gender decision task (word-like utterances with angry or neutral prosody) to show that, as compared to green light, blue light increased brain activity related to negative stimuli in the amygdala and in the "voice area" of the superior temporal sulcus, both involved in emotion processing.

Our data show that light exposures lasting from a few tens seconds to a few tens of minutes induce dramatic changes in cognition- and emotion-related brain activity through a non-classical photoreception system that is most sensitive to blue light.

Funding Support: FNRS, FMRE, PAI/IAP, ULg, Wellcome Trust.

DISRUPTED CIRCADIAN RHYTHM IN ADULTS WITH ADHD AND CHRONIC SLEEP ONSET INSOMNIA

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PsyQ, psycho-medical programs, Program Adult ADHD, The Hague, The Netherlands.

Objectives: Previous studies have found evidence for the involvement of disturbances of the circadian timing system in children with ADHD and sleep onset insomnia. The current study was performed to replicate these findings in adults with ADHD.

Methods: Sleep logs and wrist actigraphy data were assessed during seven consecutive days and nights in 40 adults with ADHD, of which 31 did, and 9 did not report sleep onset insomnia. Salivary melatonin levels were assessed during one night and under dim light conditions. Actigraphic variables, sleep estimates, circadian activity variables and dim light melatonin onset were calculated and compared between groups.

Results: In this sample 80% of adults with ADHD complained of sleep onset problems. Indeed, sleep onset, sleep end and dim light melatonin onset (DLMO) were markedly delayed in this group, indicating a phase delay in the circadian timing system. The rest/activity pattern was less stable between days with a smaller difference between daytime and nighttime activity levels.

Conclusions: These findings demonstrate the involvement of a delayed circadian rhythm in adults with ADHD and sleep onset insomnia. Future studies are needed to further investigate the specific alterations of the biological clock in ADHD, especially considering the possible major impact on general health and quality of life.

SEASONALITY IN AFFECTIVE DISORDERS

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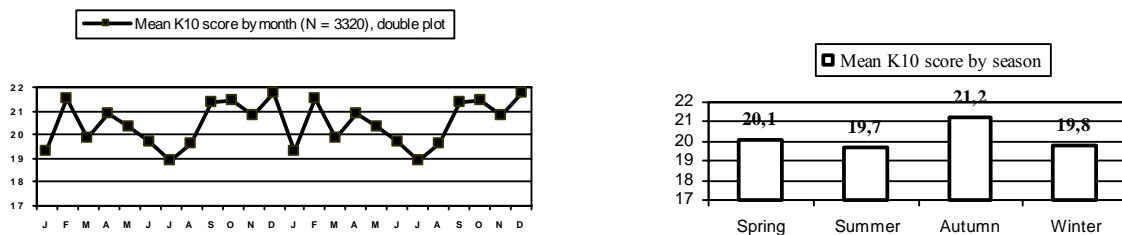
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Research question: Is there a seasonal variance in the prevalence and severity of depressive and anxiety symptoms among patients visiting their general practitioner?

Background: The epidemiological findings on the existence of seasonal variations in the prevalence of mental disorders and symptoms show opposing tendencies varying from a clear seasonal variation to no seasonal variation at all. In the general population the prevalence of Seasonal Affective Disorder varies from 0% -9, 7% (Mersch et al, Biol Psychiatry 45: 1013-1022, 1999). There are some findings of seasonal patterns in anxiety disorders (Graaf et al., Am.J.Epidemiol., 162, 654-661, 2005. Ohtani, T., et al., Psychiatry and Clinical Neurosciences 60.3: 379-83, 2006). Little is known of the long term course of depression in SAD in relation to non-seasonal depression and anxiety disorders (Murray, Seasonal Affective Disorder, practice and research. Partonen T., Magnussen A. red. Oxford press, 55-62, 2000).

Methods: The Kessler-10 screening questionnaire, extended with 5 additional anxiety questions, was sent to a random sample of GP patients aged 18-65 years who consulted the GP in the last 4 months (time period 2005-2007) irrespective of reason for consultation. The K-10 (scoring range 10-50) has shown to have good screening characteristics for affective disorders. A total of 23750 screening questionnaires were sent out by primary care physicians. 10774 questionnaires were returned (45%).

Results: Up to date for 1 out of 3 research sites (3320 subjects) the exact date of filling in the questionnaire could be recollected. The total mean score on the K10 for this sample was 20,3 (SD 8,53) with lowest scores for July (mean 18,9 SD 7,66) and highest scores for December (mean 21,7 SD 8,58). There is an overall difference in mean K10 score between the months ($F(11,3308) = 3,601$; $p < 0,001$). Clustering the data by season shows that the mean K10 score was highest in autumn in comparison with the other seasons. Method: Analysis of Variance; ($F(3, 3316) = 5,285$; $p = 0,001$).



Conclusions: Although small, the seasonal effect is in line with the finding of Mersch et al. in the general population. Our next research question will concern the seasonal variance in anxiety symptoms in this study. Furthermore we are interested in seasonal variation in the nature of depressive symptoms in patients with a current depressive and/or anxiety disorders. This research question will be addressed by the authors in the Netherlands Study of Depression and Anxiety (NESDA); a multi-site naturalistic cohort study.

Key Words: Seasonality, Affective Disorders, Seasonal Affective Disorder

BRIGHT LIGHT TREATMENT FOR HIGH-ANXIOUS YOUNG ADULTS

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Objectives: Anxiety is the most common mental illness in industrialized countries. A potentially attractive alternative or adjuvant anxiolytic treatment is bright light exposure. Our previous uncontrolled study found a significant anxiolytic effect of bright light in low-anxious adults. The aim of this study was to examine the influence of both acute and chronic exposure to bright light on anxiety in high anxious young adults.

Methods: Thirty subjects (mostly students) ages 18-35 years were assessed. Inclusion criteria included a high level of trait anxiety ($\geq 75^{\text{th}}$ percentile of the STAI), and absence of history of bipolar disorder or ophthalmic abnormalities. All but one of the subjects were diagnosed (via SCID) with an anxiety disorder. In an acute study, subjects were randomly assigned to 45 min exposure to (1) bright light treatment (via Litebook® devices) or (2) a placebo inactivated negative ion generator. At 10 min before and 30 min after the treatments, blood pressure and self-reported measures of state anxiety (Spielberger State-Trait Anxiety Inventory), depression (Beck Depression Inventory), and mood (Profile of Mood States) were assessed. Subjects were then assessed for 5 weeks, including a 1-week baseline, and 4 weeks of randomized daily exposure (45 min/day in the morning) to (1) bright light (via Litebook® devices) or (2) placebo negative ion treatment. Clinical ratings of anxiety (Hamilton Anxiety Scale) and depression (Hamilton Depression Scale) and Clinical Global Impression (CGI) were performed before and after the experiment. Sleep was assessed via actigraphy and a daily diary. Following each week, blood pressure and self-reported measures of state anxiety, depression, mood, sleep (Pittsburgh Sleep Quality Inventory), and side effects (SAFTEE) were assessed.

Results: Subjects reported equal expectancy for improvement between treatments. No significant differences were found following acute exposure to bright light vs. placebo. A significantly greater reduction in state anxiety (STAI) was found following chronic bright light vs. placebo treatment ($p < 0.05$). No significant treatment-by-time effect was found for the Hamilton Anxiety Scale. However, compared with placebo treatment, bright light elicited a marginally greater reduction in psychic symptoms of this scale ($p = 0.06$). There were no other significant differences between treatments in other clinical ratings, nor in other self-reported measures, blood pressure, or sleep.

Conclusions: The results are equivocal. The results might have been limited by considerable week-to-week variability in anxiety in the student sample, due to exams, spring break, etc. Further randomized controlled trials of bright light treatment of anxiety are needed.

Keywords: Anxiety, Phototherapy, Randomized Controlled Trial

Funding Support: Study supported by a Litebook Company 2006 Research Grant and a VA (VISN-7) Career Development Award

BRIGHT LIGHT: A NOVEL TREATMENT FOR POSTTRAUMATIC STRESS DISORDER

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Objectives: Posttraumatic stress disorder (PTSD) is the most common mental health diagnosis of veterans of current military conflicts in Iraq and Afghanistan. Bright light has had very positive effects on depression, anxiety, insomnia, and cognitive impairment, which are hallmark symptoms of PTSD. The aim of our 2 pilot studies was to assess whether bright light exposure could alleviate clinical and self-reported symptoms of combat PTSD.

Methods: Study 1 was an uncontrolled trial of veterans with PTSD (n=3) . Following baseline, subjects received bright light (5,000 lux, 45 min/day) for 2 weeks. At baseline and post treatment, subjects were assessed on Clinical Global Impressions Scale (CGI), and subjects completed the PTSD symptom checklist (PCL-M), Spielberger State-Trait Anxiety Inventory (STAI Form Y-2), Beck Depression Inventory (BDI-II), Pittsburgh Sleep Quality Inventory (PSQI), and SAFTEE side effects questionnaire. For Study 2, 9 combat PTSD subjects were randomized (following baseline) to two 2-week treatments (45 min/day): (1) bright light or (2) deactivated negative ion exposure. Blinded clinical interviews included the Clinician Administered PTSD Scale (CAPS-2) and the CGI. At baseline and post-treatment, PCL-M, STAI, BDI-II, PSQI, and SAFTEE were also assessed.

Results:

Study 1: Remarkable improvements in clinical assessment and/or self-reported symptoms were observed following bright light treatment (**Table 1**).

Table 1. Selected Data from Pilot Study #1

Subject	CGI		PCL-M		STAI		BDI	
	SEV	IMP	Base	Final	Base	Final	Base	Final
1.	4	1	70	35	61	35	20	5
2.	3	3	56	26	32	26	13	5
3.	4	---	59	---	53	42	32	18

CGI: Clinical Global Impression Scale. **SEV:** Baseline Severity (1=normal; 2-7= borderline, mildly, moderately, markedly, severely, and extremely ill, respectively). **IMP:** =improvement (1-3=very much, much, minimally improved, respectively; 4=no change; 5-7=worse).

Study 2: Compared with placebo, bright light elicited a greater improvement in CAPS-2 (**Figure 1**) and the CGI (**Figure 2**). Mean improvements in the other measures also favored bright light.

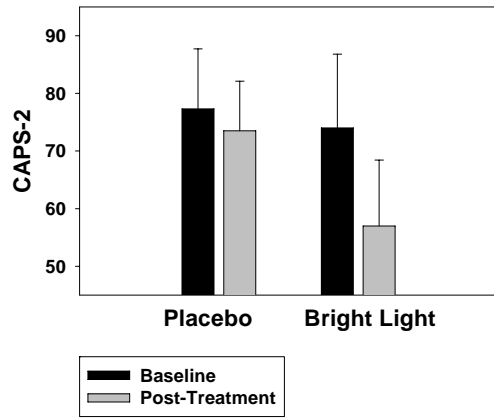


Figure 1.

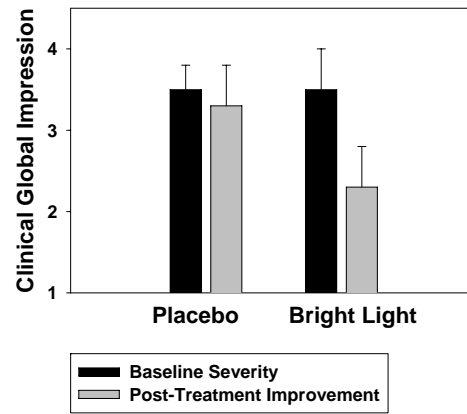


Figure 2.

Conclusions: The data suggest that bright light is an effective treatment for combat PTSD.

THE MULLER CELLS' FUNCTION AS AN INDICATOR OF OVERDOSE IN LIGHT THERAPY

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Objectives: It is known that the neuroglia in a brain and in a retina plays the important role of a regulator of various circadian functions of an organism, taking part in synchronization of neuronal activity rhythms. Due to complementary biochemical properties of Muller cells (MCs) and neurons, the uniform metabolic community 'neuron-neuroglia' functions in a retina as a self-regulated system with a feedback. Disturbances in metabolism and function of MCs seem to be one of the main links of a pathogenesis of retina diseases, and we assume that changes in glia-neuronal interactions can serve as signs of desynchronization. Our studies confirm that signs of neuroglia involvement in the retinal reaction can be found in retinal diseases of different nature, and may be found in various exogenous (damaging and therapeutic) influences upon the organism including phototherapy. MCs as well as bipolar cells are known to contribute to the ERG b-wave generation, but MCs cannot respond to flicker at more than 2Hz, and so the flicker ERG has a purely neuronal nature. Taking this into account, we examined the ERG dynamics to determine the MCs reaction to a phototherapy in age-related macular degeneration (AMD).

Methods: We used bio-controlled chronophysiotherapy (BCCT) techniques (Zueva M. et al. Vopr. Kurortol. Fizioter. Lech. Fiz. Kult. 5: 13-15, 1994) for low intensity light stimulation of visual fields in 12 patients with a dry form of AMD. In BCCT, frequencies of the light stimulation are corrected by a feedback principle at synchronization the influence with rhythms of pulse and breathing of the patient (Komarov F. et al. Klin. Med. (Mosk). 8: 17-20, 2000). The MCs/retinal neurons interactions we tested through comparative alterations of electroretinogram (ERG) to single-flash and flicker stimuli (EP-1000, Tomey). The glial index K_g was calculated as the single-flash ERG b-wave/12Hz-flicker ERG amplitudes ratio (Zueva M., Tsapenko I. Ross. Fiziol. Zh. Im. I.M. Sechenova. 90(8): 435-436, 2004).

Results: The photo-stimulation results in the increase of visual acuity (average from 0.09 to 0.25) in the most of patients, and this effect lasted near 3m. After the initial increase of glial index value, the significant reduction of the K_g was revealed, which dependent on the numbers of treatment séances. Visual acuity continued to increase during all 10 séances, while we showed the decrease in MCs' function after 4-5 séances of BCCT (fig.1). In the short course of phototherapy (5 séances), which took into account the critical point of glial index decrease, the K_g was gradually recovered to the values inside the norm range (fig.2) with the same positive effect to visual acuity as in the complete series of phototherapy. We consider the revealed MCs' reaction as a tension of compensator mechanisms, and the direct prescription to stop the therapy.

The schemes of tendencies in visual acuity and glial index Kg dynamics after the BCCT

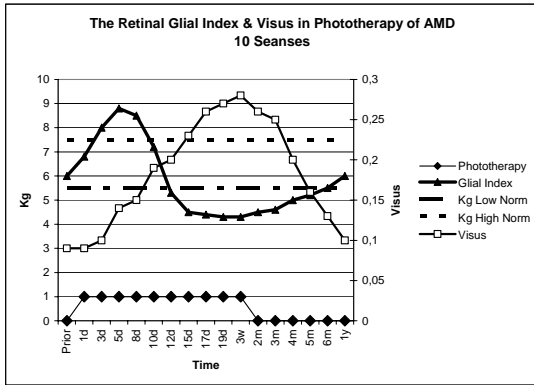


Fig.1

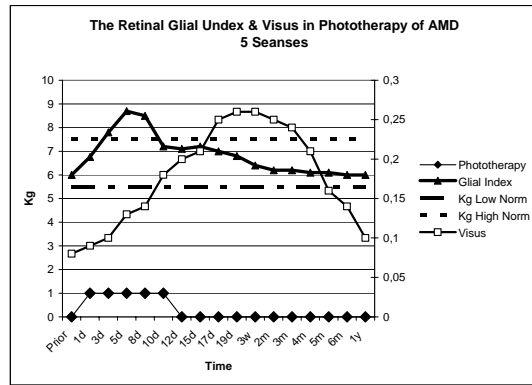


Fig.2

Conclusions: Our results suggest that even in a low-intensity rhythmic therapeutic influence, there is the danger to overdose, and the critical moment is predetermined by the reaction of Muller glial cells. The Kg, as a glia-neuronal interaction criterion, permits to optimize the existing phototherapy techniques and helps reducing the risk of complications from a possible overdose. The assumption, that neuroglia can be an acceptor of different nonspecific influences of environment, allows us to survey them as one of perspective targets when elaborating novel nonspecific therapy methods and agents, and, above all, a flicker light therapy.

Key Words: Light Therapy, Bio-Controlled Chronotherapy, Retinal Diseases, Muller Cells, Glia-Neuronal Interactions

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