

Light Treatment and Biological Rhythms

Bulletin of the Society for Light Treatment and Biological Rhythms



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President's Message

Sonia Ancoli-Israel, PhD

As we begin a new year, I want to thank you for your support of the Society for Light Treatment and Biological Rhythms – support rendered by your dues, your readership and comments on our publications, your visits to the website, your contributions to the Annual Meeting by your attendance and abstract presentations, and sharing your ideas and perspectives. Together we are fulfilling our mission statement by building an organization that fosters research and our professional development.

This issue of the newsletter brings you highlights of the annual scientific meeting, and I want to give you some of the details on our annual business and board meetings. More than 100 members, corporate members and supporters met in June at the Nobel Forum in Stockholm, Sweden, for three days of outstanding science, a stimulating exchange of ideas, conversation and absolutely delightful hospitality.

A main topic of discussion in Stockholm was our mission statement and goals. After 13 years, SLTBR is alive and well. We have a solid and expanding core of members, (we gained 20 regular members since last year and two new corporate members). Now we need to determine whether or not our mission statement needs refining or redefining. We need to find out what you, our members, want from your organization. I've asked the SLTBR past presidents to work as a committee to look at our mission statement, review our goals and evaluate their appropriateness in defining who we are and what we want to accomplish.

What does it mean to foster research, professional development and clinical applications in the fields of light therapy and biological rhythms? Should we be offering or participating in more scientific and clinical programs? Should we play any role in quality assurance issues? Should we deal with more clinical issues? Should we broaden our scope? Should we get involved in gaining recognition with insurance carriers for the services of our clinician members?

Should we establish outreach programs at APSS, APA, etc.? Should we continue the annual meeting or go to a biannual format? How should we spend our resources? Please take a few moments to jot down your thoughts on these questions and send them to me at sltbrinfo@aol.com.

Your officers and Board members would be happy to hear from you – your ideas, thoughts, and suggestions for strengthening the Society and enhancing member benefits.

I hope you will encourage your colleagues who are not yet SLTBR members to visit our web site, see what we're about, and join us. Encourage them to attend the 14th Annual Meeting in San Diego, California, June 13-15, 2002, at the quaint and lovely Horton Grand Hotel. Our meetings provide a wonderful opportunity to see old friends and colleagues and meet new ones. I hope you will plan to attend and share your knowledge and expertise with us. Check the web site (www.sltbr.org) for registration information and abstract submission details.

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Light Treatment and Biological Rhythms*Bulletin of the Society for Light Treatment and Biological Rhythms*

Editor

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President's Message (continued)

We plan to use our web site and Yahoo Groups, the List Serve feature, to post the newsletter, and bring you regular updates on important news in the field of light treatment and biological rhythms. (Contact our office at sltbrinfo@aol.com if you'd like more information on Yahoo Groups.) Dr. Dan Oren has graciously volunteered to select and post a monthly article or abstract of interest to our members. Beginning in January 2002 we will update and post the membership directory to the website on a quarterly basis. All these publications, electronic and paper, are available to members only.

Thank you for your continuing interest and support; I look forward to seeing you at our meeting in San Diego in June 2002. And my best wishes for a healthy and prosperous new year.



President Sonia Ancoli-Israel, Anna Wirz-Justice and Namni Goel relax at the Vasa Museum

SAVE THE DATE**June 13-15, 2002****Horton Grand Hotel
San Diego, California**

**See the website for details
www.sltbr.org**

ANNUAL MEETING RATES HIGH MARKS IN ALL CATEGORIES

By Robert Levitan, MD, Editor

The 13th annual meeting of the Society for Light Treatment and Biological Rhythms was a major success in every way. The science was outstanding, providing many new directions for future research, while the overall setting, organization and social events were of the highest quality. The Karolinska Institute and Nobel Forum provided an inspiring but relaxed ambiance that set the tone for the entire meeting.

Particular thanks to Bengt Kjellman who took a primary role as both a program chair and local arrangements director; Barbara Parry who played a primary role in the scientific program arrangements, and Torbjörn Åkerstedt and Mats Gillberg who did an outstanding job with local arrangements. We also owe great thanks to Kathleen Matikonis, the executive director of SLTBR, for coordinating the administration of the meeting, in particular helping with links between the North American and European sites. Thanks go out as well to SLTBR president Sonia Ancoli-Israel for her hard work and ongoing leadership.

Scientific Program

As per tradition the meeting kicked off with a series of poster presentations covering several important areas of work. As we have come to expect, Raymond Lam provided a comprehensive summary of the poster session "on the fly".

Several posters looked at light therapy treatment in non-seasonally depressed groups. In severe Alzheimer's disease, bright light therapy may help with both morning agitation (Ancoli-Israel et al) and depression (Martin et al), however dawn dusk simulation (DDS) did not work in patients who had disturbed circadian rest/activity cycles at base line (Gasio, Wirz-Justice et al). A theme that emerged in both the poster and oral presentations relates to possible activating or energizing effects of light (Gordijn et al, Hoppen et al), an important consideration for shift workers in particular. Regarding post-partum depression, Corral, Patton and Kostaras presented preliminary data showing light therapy responses, and described a small subgroup of women reporting high seasonality scores.

Thalén et al showed that depressed patients with a seasonal pattern improved more than those with a non-seasonal pattern independent of various hormonal markers and timing of treatment. Rüger et al found that ocular light affected body temperature and sleepiness while extra-ocular light did not. Lainey et al presented initial data on a novel portable head-mounted light

delivery system. Regarding pathophysiology, Lam et al showed that catecholamine depletion results in significant clinical relapse in SAD patients in the summer remitted state, pointing to a possible trait marker for SAD. Lowden et al compared the effects of high carbohydrate versus high lipid meals on alertness and performance finding that high carbohydrate meals had a small tendency to increase sleepiness. Michael Young et al presented interesting new data dealing with the measurement of seasonality, and reported a novel two-stage remission pattern including both an alteration in the rate of change of SAD symptomatology with the spring equinox and a separate, monthly rhythm related to the menstrual cycle.

Jo Arendt Named ALPCO-Buhlman Distinguished Lecturer

The high quality of the poster session set the tone for an outstanding oral presentation program. Dr. Josephine Arendt, the ALPCO-Buhlman distinguished lecturer, kicked off Monday's session with a talk entitled "Visions from Antarctica". Jo had conducted long distance research at the British base of Halley (75 degrees south) since 1985, before recently visiting the base for the first time (how about that for a site visit!). After hearing about the roughest seas on earth and other experiences on this remote area, one appreciates Jo's enormous dedication to this project.

Regarding scientific findings, she reported that adaptation to night shift occurs consistently within a period of about one week, however re-adaptation back to day shift is particularly difficult in the winter. Appropriately timed light treatment hastened this re-adaptation. In general, various sleep parameters are better during the night versus day shift. Based on self-reports, sleep was a problem during the winter with eleven of sixteen individuals reporting sleep difficulties. A major goal of Dr. Arendt's particular visit this year was to re-evaluate prototype personal UV monitors from Cambridge Neuro Technology Limited that Jo demonstrated to us throughout the meeting.



Dr Lennart Wetterberg with Dr Jo Arendt, the ALPCO-Buhlman Distinguished Lecturer

Young Investigator

Erin Michalak received the SLTBR Young Investigator Award, sponsored by Apollo Light Systems, for her work on Negative Life Events and Social Support in SAD. Perhaps because of the current DSM definition of SAD, there has been a tendency to underestimate the potential effects of social factors and social support on the onset and course of seasonal depression. In her talk, Erin reported a novel relationship linking negative life events, poor social support and increased seasonality. We look forward to follow-up work in this emerging area.

Rounding out the oral presentations for the morning, Paul Desan presented data once again showing that extra-ocular light was not helpful for the treatment of winter depression. Kathelijne Koorengelvel looked at the issue of whether the circadian pace maker is involved in the pathogenesis of SAD. Using a forced de-synchrony protocol in both SAD patients and controls, it was found that the impact of the pace maker and sleep-wake cycle on the regulation of mood was similar in both groups. Rigmor Stain-Malmgren found a reduction in platelet serotonin transporter density in symptom-free SAD patients, pointing to a possible trait marker for the disorder. On the other hand, increased density of 5-HT₂ receptors appears to be related more to the state of depression. Finishing off the morning, Michael and Juan Su Terman revisited the classic question of whether Seasonal Affective Disorder is characterized by delayed circadian phase in winter. Using the morning/evening questionnaire designed by Horne and Östberg, the Termans found that both morning types and evening types are well represented in the overall SAD population. Morning types did not experience much change in their morningness/eveningness ratings during springtime, while evening types had a significant increase in morningness during the springtime. Overall, the morning types showed the greatest stability of their circadian phase, suggesting that the advancing spring time sunrise has less effect on their subjective night than it does for evening types.

Monday afternoon began with a symposium focused on the longstanding question of how light therapy works in SAD. Robert Levitan (yours truly) argued that light therapy may have a direct psychostimulant effect similar to that of amphetamine or methylphenidate. It was pointed out that children with attention deficit disorder (ADD) often become sluggish and fatigued as adults, a state highly reminiscent of SAD. In both SAD and ADD, there may be a core disturbance in energetic arousal mechanisms that contributes to difficulty initiating activities, prominent fatigue and sluggishness. Light therapy and psychostimulants may thus work by enhancing arousal mechanisms in SAD and ADD respectively.

Matthaeus Willeit, stepping in for Alexander Neumeister, talked about evidence for catecholaminergic mechanisms in SAD, summarizing a variety of studies including findings of decreased dopamine transporter density in SAD patients versus controls. This group has also demonstrated that catecholamine depletion induces relapse in SAD. Overall, the results of this elegant body of work strongly suggest that many different neurotransmitter systems are involved in the pathophysiology of SAD.

Michael Terman discussed the question of circadian phase at it relates to light therapy, suggesting that light treatment be implemented based on *circadian* time. Studies of eveningness/morningness in SAD patients have demonstrated early and late chronotypes, which can be identified using the Horne Östberg Score (which correlates highly with melatonin onset/offset); salivary melatonin may be impractical for daily clinical use. Michael always has a special bonus for his audiences, and in this case he described an automated version of the Horne-Östberg Scale, which is available over the Internet through the Centre for the Environmental Therapeutics; the web address is www.cet.org. Michael suggested that we all use the web-based version of the scale, which is scored automatically, with feedback provided, as this will further the development of this particular instrument.



Drs Juan Su and Michael Terman with Program Chair, Dr. Barbara Parry (center)

Dan Oren wrapped up the day's presentations with a discussion of the relationship between bilirubin and light responsiveness. It would appear that bilirubin gets *no respect*, suggesting that it may be the Rodney Dangerfield of the metabolic world (author's emphasis – I hope Rodney is not offended). Dan suggested that bilirubin may once again rise to prominence as a putative photo-transducer. He presented a fascinating hypothesis describing a putative bilirubin clock, and provided preliminary data supporting bilirubin's role as a marker of circadian time. Dan suggests that low nocturnal bilirubin levels and winter seasonal depression may be associated, and that light treatment may partially normalize bilirubin levels.

Tuesday morning's scientific session focused on studies of biological rhythms. Konstantin Danileko studied the sleep/wake cycle as zeitgeber. He demonstrated how a phase advance of the sleep/wake cycle, under stringently controlled, near dark conditions, phased advanced the core body temperature rhythm in parallel. Future analyses of melatonin rhythms will provide further data on whether the sleep/wake cycle is a potent non-photic zeitgeber. The next paper by Egemen Savaskan et al looked at the localization of melatonin receptors in hippocampal neurons and cerebrovascular tissue. It was pointed out that melatonin has antioxidant effects which might protect individuals from Alzheimers Disease. The finding of increased melatonin receptor reactivity in Alzheimers patients points to impaired melatonin levels at baseline. Melatonin may thus have a neuroprotective and cerebrovascular blood flow regulating effect of potential clinical benefit.

Shawn Youngstedt looked at the circadian phase response curves for both exercise and bright light. It was found that exercise can have a significant effect on human circadian rhythms, similar to the effects of bright light. It was suggested that this may be a particularly important consideration in older people who are less responsive to light as a zeitgeber. Rixt Riemersma presented a paper looking at the effect of indirect bright light therapy on sleep fragmentation in institutionalized demented patients. Both bright light and melatonin had a significant beneficial protective effect of sleep fragmentation. Melatonin worked particularly well on the subgroup of patients who were good sleepers at baseline.

Non-Seasonal Depression

Dr. Bengt Kjellman chaired the symposium on light treatment of non-seasonal depression. Francesco Benedetti gave a rousing talk on light treatment effects in Bipolar Disorder providing a comprehensive overview of studies in this area. Bipolar inpatients in rooms with eastern windows have shorter hospital stays than patients in western rooms suggesting that natural light can speed up response to antidepressant treatments in these patients. Light therapy might also improve the usefulness of total sleep deprivation in bipolar depression.

Enhancing darkness in manic patients was also considered. An emergent association between a variation in the 5HTT promoter gene and total sleep deprivation further strengthens the argument for strategic use of TSD in bipolar patients. Benedikt Bloching also looked at bright light as a stabilizer of antidepressant effects in late partial sleep deprivation. It was found that early morning bright light therapy, starting the day after late partial sleep deprivation, may prevent the relapse occurring after successful sleep deprivation. Dan Kripke presented data from a large meta-analysis

demonstrating that response to antidepressant medication is around 32% for placebo and 51% for medication establishing a 19% net effect of the active medication treatment. On the other hand thirteen controlled studies of light treatment in non-seasonal depression show net treatment effects of 12 – 35%. This suggests that bright light produces larger treatment benefits for non-seasonal depressed patients than does pharmacotherapy. In further support of this point, Namni Goel showed preliminary evidence that both early morning bright light therapy and early morning negative ion treatment are effective in treating chronic depression over five weeks. Clinical remissions were seen in over half of patients, similar to results in SAD. We will certainly look forward to follow-up data next year.

George (Bud) Brainard replaced Tom Wehr as the keynote speaker as Tom was recovering from an illness. We all wish Tom a speedy recovery. Dr. Brainard's talk was entitled "The Healing Light: Interface of Physics and Biology". Bud provided a comprehensive summary of the factors involved in light transduction. A number of factors will make a given light stimulus effective or ineffective including both the spatial and temporal distribution of the stimuli, various effects at the lens and pupil, and whether scotopic or photopic vision is in use. For the melatonin suppression response, wavelength is crucial with a fourfold difference in melatonin suppression between equivalent quanta of light at 505 vs. 555 nm. Clearly, lux is not the full story when it comes to light responsiveness, and many issues remain to be sorted out in this fundamentally important area. Thanks once again, Bud, for an inspiring and informative talk.

The afternoon was capped off with a symposium on light and work chaired by Torbjörn Åkerstedt. Arne Lowden looked at the effectiveness of bright light treatment on reducing sleepiness in an industrial work setting. Most work in this area has been based on laboratory work. The current study showed that light therapy works in an actual work setting, as it seems to in the lab, with reduced sleepiness and melatonin suppression. Sleep length following work was also easier to maintain. Bjørn Bjorvatn looked at the effects of bright light therapy in night workers on an oil platform in the North Sea. It was found that bright light treatment for only thirty minutes per day facilitated adaptation to night work at sea as well as helping readaptation following return home. The strongest effects occurred at home. Jo Arendt described a series of studies looking at adaptation to various patterns of shift work on the North Sea. Better adaptation to changing shifts occurred in March vs. November, suggesting that exposure to natural light affects the rate of adaptation. Jo also provided evidence for lipid intolerance and insulin resistance on the first night of a simulated night shift, suggesting that shift workers may be exposed to

metabolic stresses that may be deleterious to health during periods of adaptation. This work is of fundamental importance in helping us understand the stresses of adaptation to shift-work, and provides a scientific basis from which to design optimal adaptation parameters. Rikard Küller, Thorbjörn Laike et al have worked on the use of indoor lighting as a protective factor for SAD and sub-SAD in different settings. In northern countries, sitting close to a window in the work environment is particularly helpful in spring and fall, when outdoor light is still relatively abundant, but has minimal effect in the thick of winter. Clearly, there is a need to optimize artificial lighting strategies, above and beyond single light therapy units, to minimize fatigue and optimize performance in northern indoor work settings.



Dr. Al Lewy

Al Lewy examined the use of melatonin as a circadian phase resetter for nurses working seven nights every second week. Placebo had little effect, but on melatonin most workers shifted their endogenous rhythms in accordance with the work schedule. In addition, on off-work days, melatonin at night shifted their rhythms back to the usual time. This suggests that in addition to treating jet lag, strategic administration of melatonin can be used to optimize entrainment to changing circadian demands in shift workers.

Wednesday morning began with talks on photobiology. George Brainard presented data on more than 600 nighttime melatonin suppression tests using nine monochromatic wavelengths in the 420-600 nm range. An action spectrum based on composite data fitted a vitamin A₁ retinaldehyde template, but with a peak sensitivity different from the four classical opsin photopigments. This supports the existence of a novel opsin photopigment in the human eye, which mediates circadian photoreception, a potential target for future work on the mechanism of light therapy. Julian Smith discussed bright light suppression of melatonin targeting

different visual fields in the elderly. Bright light applied above eye level was as good as direct light in suppressing melatonin, suggesting that the more comfortable indirect light may in fact suffice for this effect. More direct clinical comparisons are needed going forward. Returning to the theme of the direct energizing effects of light, Katherine Hoppen examined whether different wavelengths of light have differing alerting/performance enhancing properties. Consistent with prior work, different wavelengths of light had different abilities to suppress melatonin. It was also found that blue light was better at enhancing performance than both green and red light.

The final symposium, chaired by Robert Levitan, was on genetic vulnerability and phenotype definition in SAD. A theme stressed by all four speakers was the need to consider a variety of phenotypes and endo-phenotypes when studying the genetics of SAD and seasonality, moving beyond the basic DSM-IV definition of this disorder. Carolina Johansson summarized the various epidemiological studies that point to a strong genetic vulnerability to SAD and seasonality, and provided a thorough overview of the cutting edge methodologies available for psychiatric genetics studies. Most importantly, these strategies enable us to address the complex nature of disorders such as SAD.

Matthaeus Willeit presented data showing an association between polymorphic variations in the serotonin transporter promoter gene (5-HTTLPR) and neurovegetative symptoms in SAD. This gene also predicted the occurrence of PMDD in women with SAD. Timo Partonen and Robert Levitan both emphasized the need for hypothesis-based endo-phenotypic strategies in SAD, providing examples from their ongoing work related to the genetic control of the circadian period, serotonin metabolism, light sensitivity, carbohydrate craving, weight regulation and second messenger systems.

Overall, this symposium demonstrated that SAD genetics work is progressing extremely well with careful attention to cutting edge methodologies and hypothesis-based definition of phenotype. Preliminary findings from various centers point to several new areas of great interest. We look forward to future collaborations and further progress in this rapidly evolving field.

The meeting ended with a CME program chaired by Bengt Kjellman on the basics of light treatment, with contributions from Bud Brainard, Timo Partonen and Al Lewy.

Loaded with new information and several new ideas for future work, we headed home to reconvene in San Diego next year. Thanks again to Bengt Kjellman, Torbjörn Åkerstedt and Mats Gillberg for hosting a truly first class meeting.

SWEDISH HOSPITALITY PAR EXCELLENCE

Following a productive business meeting, Peggy Landstrom, president of the Stockholm City Council, welcomed us in style at the magnificent Town Hall where the Nobel Prize Awards are ultimately presented. Town Hall has a truly unique architecture, and the hospitality was second to none. We were treated to an exclusive tour of the Reception Hall and the dining room where the Nobel Banquet is held. To cap off the evening we enjoyed a relaxing boat cruise showing us both the old and new of Stockholm; a sunset that appeared to be suspended in time added much to the ambience.

Tuesday night was celebrated with the annual banquet at the VasaMuseum, where we were serenaded by the talented Karl Magnus Fredriksson of the Stockholm Opera. Further highlighting this event was an inspiring talk by Professor Lennart Wetterberg on the history of light treatment. A number of Nobel Prize winners over the years performed significant research on light, including Roentgen, Arrhenius, von Laue, Compton, Planck, Einstein and Bohr. As Dr. Wetterberg noted, the history of light treatment in the modern scientific era has just begun. Many potential areas of future work exist, and this bodes well for our Society over the next several decades. Although the evening ended towards midnight, we were still able to enjoy a late sunset in the land of the midnight sun.



Two of our hosts, Drs. Bengt Kjellman and Torbjorn Akerstedt, wonder how they managed to please so many people so many times

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LTBR GOES PAPERLESS

This is the last "snail mail" issue of LTBR – unless you tell us you want your copy via post. This issue and all subsequent issues will be posted on the web site and sent via our Yahoo Groups List Serve. Contact the SLTBR office with questions. (415-876-0716 phone; 415-751-2758 fax; sltbrinfo@aol.com).

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**Society for Light Treatment
and Biological Rhythms**
PO Box 591687
San Francisco, CA 94159-1687



Michael Terman, PhD
Department of Psychiatry
Columbia University
1051 Riverside Drive, Unit 50
New York, NY 10032
USA

