

Light Treatment and Biological Rhythms

Bulletin of the Society for Light Treatment and Biological Rhythms



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ANNUAL MEETING ISSUE

This issue reflects some of the goings on at last June's 8th Annual Meeting in Bethesda. The meeting was very well programmed by Dan Oren and included new research talks and posters, five symposium presentations and a CME course. The meeting's events are broadly summarized in Alexander Neumeister's overall meeting review while more substantive coverage is provided by Norman Rosenthal in his review of two particularly important presentations by Terman and Terman and Eastman et al., on recently concluded, multi-year placebo-controlled studies of light treatment for winter depression. Dan Oren's piece on humoral phototransduction represents a summary of both his symposium presentation and his previously published theoretical paper on the subject.

This issue also brings news of Scott Campbell's "active retirement" as editor of this publication. His contributions, equal parts wit and wisdom, will be missed. At the same time, we welcome Dr. Larry Morin, noted chronobiology researcher at SUNY Stony Brook as co-editor of the SLTBR bulletin and recognize with appreciation J.P. Smith's ongoing efforts as managing editor.

—David Schlager, Co-editor

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FROM THE PRESIDENT

It's a pleasure and an honour to be SLTBR president this year. I recall vividly the excitement of the organizing meeting for the fledgling society in 1988 in Montreal, and I have been pleased to see the SLTBR grow and prosper in the years since. Our recent successful 8th Annual Meeting in Bethesda shows that the SLTBR continues to have an active and pro-

ductive membership. Congratulations to Dan Oren for organizing and hosting such a wonderful meeting. (I am looking forward to working closely with Dan, as President-Elect, along with Chris Gillin, as Past President, on SLTBR issues. I'm sure all of you will be glad to hear that Chris Gillin has fully recovered from the illness which kept him from our Annual Meeting in June and is back to his usual hectic schedule. And I would like to welcome the new members of the SLTBR Board of Directors: Bengt Kjellman, Lawrence Morin, and David Schlager.)

As an aside, I predict that Norman Rosenthal's after-banquet speech will rapidly become an SLTBR legend. To those of you who weren't able to attend the Annual Meeting, we hope that you will join us next year (perhaps in Vancouver!), where Barbara Parry will preside as Program Chair.

Communication and Membership are the themes I have chosen for my presidency. Both are essential aspects of the

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Please visit the page (<http://www.websciences.org/sltbr/>) and give us your feedback. What other information should we include? How can we improve the site?

The other major initiative is the SLTBR e-mail Discussion Forum. The forum will be a place where SLTBR members can discuss new technologies, research findings and studies in the literature. We will also encourage members to use the forum for clinical questions about light therapy and other chronobiological treatments. We believe this will be a useful service to clinical members whose questions can attract answers and discussion from the experts in the field. SLTBR announcements can also be widely and easily disseminated. The forum will be restricted to SLTBR members only, to ensure a high "signal-to-noise" ratio for messages. To join, please send an e-mail message to me (rlam@unixg.ubc.ca) or to the list address (SLTBR-L@unixg.ubc.ca). I hope to be "talking" with many of you soon in cyberspace!

Finally, don't be shy about advertising the SLTBR. Approach your colleagues (and your students!), and sign up a new member this week. Mention the SLTBR in any talks or interviews that you give. We also have a colourful slide (available without charge, on request) that includes the SLTBR addresses, etc., to use in your presentations. Only with your help and enthusiasm can we keep SLTBR a strong and vibrant organization!

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HUMORAL PHOTOTRANSDUCTION

"The facts, however, have not yet been sufficiently grasped. If ever they are, then credit must be given rather to observation than to theories, and to theories only if what they affirm agrees with the observed facts."—Aristotle

Following Lewy's seminal discovery that light could suppress melatonin secretion in humans (Lewy et al., 1980) and Kripke's first trials of light as an antidepressant (Kripke, Risch and Janowski, 1983), the 1984 paper by Rosenthal and colleagues demonstrating that light could treat winter depression (Rosenthal et al., 1984) opened an intriguing new

SLTBR. We must communicate to other organizations and to the public as to who we are and what we stand for. We must also continually improve communication between our members. Our outstanding newsletter (now capably co-edited by Larry Morin and David Schlager) and the Annual Meetings have thus far been the primary means of communication for the SLTBR. Two recent initiatives will supplement these tools for SLTBR communication.

One is the new SLTBR page on the World Wide Web (WWW), developed by myself and Lonn Myronuk. The WWW is the most actively growing part of the Internet and we anticipate that our page will become an important window for SLTBR to the public and to prospective members.

avenue of neurobiology research. Light treatment had inherent research appeal on many levels, not least because of the physical and quantifiable nature of the intervention. But for those involved in such research, the manifest effects of light therapy in humans, whether as antidepressant or to reset the biological clock, has proven an intellectual challenge.

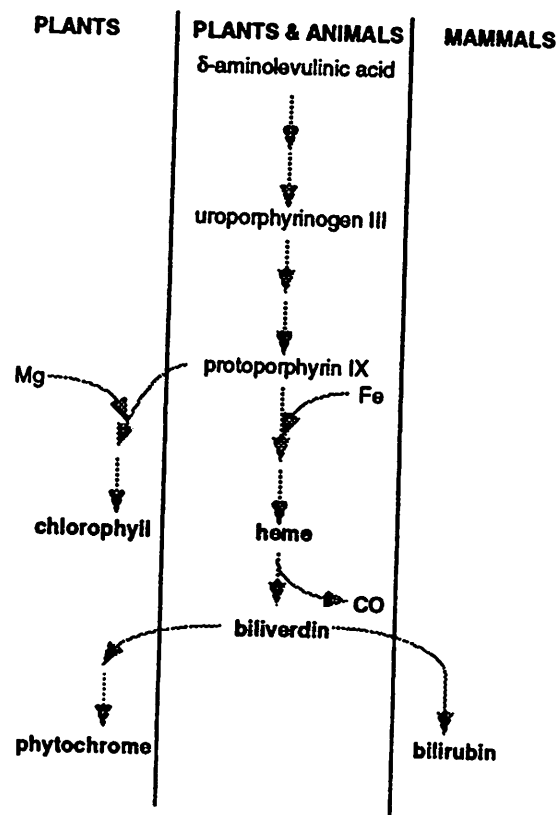
Despite decades of study of light absorption by organic molecules, the photon-absorbing molecules and photoreceptors which underlie the antidepressant and phase-shifting effects remain a mystery. This enigma is of critical importance because, as first articulated by Grotthus and Draper over a century ago in the First Law of Photochemistry, for light to have an effect on a molecule it must first be absorbed by the molecule. (There is subtle exception to this law that goes beyond the scope, but not the essence, of this discussion.) If our psyche is a mental representation of our molecules, and if light affects our psyche, then light must affect our molecules.

The enigma has been heightened over the past decade as scientists from various clinical and basic science disciplines have struggled to reconcile the conventional wisdom that the rod and cone photoreceptors of the retina mediate antidepressant and biological rhythm effects of light with a growing body of data that challenge that wisdom. The collected empirical work of investigators such as Brainard et al. (1994), Provencio and Foster, (1995), Czeisler et al. (1995), and myself (Oren et al., 1993), has, to date, failed to identify the photoreceptor molecules in question. Indeed, if anything, the collected evidence has suggested that some non-visual process might mediate the antidepressant and phase-shifting effects of light. In an attempt to resolve this paradox, I have introduced a theory of "humoral phototransduction," based on a molecular model of the evolution of behavior (Oren, 1996). The reader is also referred to the original manuscript for a more thorough outline of the model.

One premise of the model is that biological rhythms are ubiquitous. Everywhere in nature, one discovers rhythms, be they circadian, circannual or other. The absence of rhythmicity of a biological variable is far less common than the presence of such a rhythm. The rhythmicity of behavior as well, at least at the fundamental level of rest/activity cycles, is found in most forms of life. A second premise, advocated a century ago by the Austrian physicist and philosopher Ernst Mach, is that Nature is parsimonious—his concept of *denkonomie*. Thus from an evolutionary perspective, conservation of such responses is logical as light is the basic source of energy and the day-night cycle an environmental variable which affects all life.

In light of these premises, and with photoreceptors for animal circadian and antidepressant effects still unknown, I propose that we look to the plant kingdom for new models of behavior. The striking conservation of behavioral aspects of plant and animal biological clocks has been known for decades (Bünning, 1973). The role of chlorophyll as a transducer of solar energy for plant life is common knowledge, and the role of phytochromes in mediating plant biological rhythms have been elucidated more recently.

From this starting point, the highly conserved porphyrin biosynthetic pathways and the structural similarities between chlorophyll chromophores and heme moieties and between plant phytochrome chromophores and bile pigments raise the possibility that they share capacities for regulating biological responses to light.



Schematic synthetic pathways of chlorophylls and heme-derived molecules in plants, animals and mammals.

Studies of the effects of light on heme moieties and bile pigments in animals have revealed that such molecules not only absorb light (as must be expected from their chemical struc-

ture) but that light also can act upon them to provoke other chemical effects. A large body of evidence supports the thesis that the eye is a primary site of phototransduction. Its prominent blood vessels provide ample opportunity for light absorption. The continual recirculation of erythrocytes through the retina may allow the integration and delivery of a circadian signal of day independent of the bleaching effects of light upon fixed retinal photopigments. It is the potential interaction between light and retinal *blood-borne* photoreceptors which might then explain observed antidepressant and rhythm-shifting effects of light in non-enucleated blind animals and people.

Recent discoveries that some neurotransmitters are gases give further credence to this viewpoint. Known for a century, but largely dismissed as an experimental curiosity, light's capacity to dissociate gases such as carbon monoxide (CO) and the free radical nitric oxide (NO) from heme moieties now acquires importance. More recent discovery that both CO and NO are capable of stimulating soluble guanylyl cyclase (GC) which in turn, stimulates the production of neuronal intracellular cGMP (Snyder, 1992) make consideration of the physiological importance of photodissociation of further interest. Bright light also stimulates nitric oxide synthase (NOS) to produce NO and heme oxygenase (HO) to produce CO.

When first presented, this model predicted that hemoglobin would have a physiologically important and unanticipated role as a transporter of NO and other neuroactive gases. Recent empirical data begins to support this prediction (Jia, Bonaventura, Bonaventura and Stamler, 1996). Therefore, light-induced release of neuroactive gases that normally bind to Hb, along with endothelial and intraerythrocytic synthesis of these gases can potentially convey photic information to the central nervous system and elsewhere.

Melatonin, Biliverdin, and Bilirubin

Other key moieties of time-keeping may be similarly conserved between the plant and animal kingdoms. Reiter and colleagues have identified melatonin in plant species (Dubbels et al., 1995 and Hattori et al., 1995), while N.J. Roberts, D.L. van Tassel, A.J. Lewy, and S.D. O'Neill (personal communication) have recently identified melatonin's presence in the Morning Glory ivy. Although the role of melatonin in plants remains to be explored, its presence in a plant like the Morning Glory, whose biological rhythm behavior is prominent, is most tantalizing.

Bilirubin and biliverdin have structures that are virtually identical to the plant phytochrome chromophore (see figure

above). As a molecular light switch, phytochrome assumes different conformations triggered by the absorption of the red versus far-red light at dawn and dusk and is capable of "resetting" the plant biological clock. Some forms of the flexibly structured bilirubin chromophore, acting as a chiroptical light switch, are also capable of reversible photoisomerization in vitro. One mechanism by which biliverdin might communicate a time signal of darkness in animals is its negative feedback inhibition of HO, the enzyme that forms biliverdin by opening heme rings to produce biliverdin in stoichiometric equivalence with CO.

While retinal vessel levels of CO and NO may decline at night, elevated nocturnal circulating levels of melatonin, biliverdin, and bilirubin—all antioxidants—have the capacity to quench unbound NO and other reactive molecules in the circulation and thus deliver a more generalized chemical signal of darkness. The nocturnal rise in the circadian rhythm of melatonin, bilirubin (Kanabrocki et al., 1988) and CO exhalation (reflecting biliverdin production) (Levitt, Elliott and Levitt, 1994) provide evidence of this pattern. Melatonin also suppresses NOS activity and is a cerebral vasoconstrictor. The presence or absence of ambient light may, therefore, regulate neuroactive gases in the retina and elsewhere and, in doing so, produce distinct humoral states throughout the body. This interplay between vasodilating gases such as NO and CO and vasoconstrictive molecules such as melatonin, biliverdin and bilirubin may therefore entrain and complement the endogenous circadian rhythms generated by the SCN.

Clinical Correlations

This model has physiological implications. For example, the known effects of NO in inhibiting indoleamine 2,3 oxygenase (which breaks down tryptophan) or stimulating serotonin transporters are consistent with the therapeutic enhancement of brain tryptophan uptake and serotonin levels thought important in several models of neuropsychiatric disease. Increased blood flow (Rieder et al., 1995) and serotonin levels (Lam et al., 1996) may explain some of the energizing and antidepressant effects of bright light. Bright light-stimulated elimination of bilirubin can remove the vasoconstrictive effects of biliverdin and potentially sedative effects of bilirubin during the daytime. (Such a model is consistent with those studies indicating greater efficacy of light when administered in the early morning—at a time of day when circulating bilirubin levels are at their highest.)

Structural defects in hemoglobin or abnormal erythrocyte regulation of neuroactive gases may therefore impair neurotransmission and cause or contribute to some psychiatric

disorders. Several psychiatric studies report robust findings of abnormal erythrocyte electron-transfer enzyme function or abnormal erythrocyte structure. Also relevant to the model may be prior demonstration that abnormal hemoglobin structure has the capacity to induce production of abnormal isomers of bilirubin (Brown and Docherty, 1978).

While our membership has focused on the effects of ambient light, others in the photobiology community have observed in animals that different body tissues—especially the brain—are capable of emitting light and that this light may have a physiological function. This potential interaction, between endogenously emitted light and light-sensitive moieties found in many animal molecules, lends interest to the study of light's interactions with chromophores, i.e., photobiology.

In view of the failure of conventional models to explain the phototransductive process involved in the antidepressant and phase-shifting effects of light, I present this construct of humoral phototransduction as an alternate theoretical model. I hope that it might evoke interest from those of you who do have the resources to do the necessary empirical work that must be done to see, as Aristotle put it, if theories and facts agree.

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ANNUAL MEETING REPORTS—

Review and Summary of the 8th Annual Meeting, June 2-4, 1996

The 8th Annual Meeting of the Society for Light Treatment and Biological Rhythms took place at the Natcher Conference Center on the campus of the National Institutes of Health, Bethesda, Md. The scientific program was organized by Dan Oren.

The evening before the meeting began, a Continuing Medical Education (CME) course on the "Practice and Science of Light Therapy and Melatonin" was held at Bethesda Ramada Hotel. President-elect Raymond Lam began the course with a brief welcome followed by an excellent overview of opti-

Vin L. Bonaventura, C. Bonaventura, J. Stamler JS (1996) S-nitrosahae-

mal light therapy in the treatment of Seasonal Affective Disorder (SAD). Following, Scott Campbell and Ellen Leibenluft gave talks on the uses of light to treat shift-work and rapid cycling bipolar disorders, respectively. Josephine Arendt then reviewed the use of melatonin to promote sleep and prevent jet lag. Finally, Siegfried Kasper delivered an overview on the serotonin hypothesis of SAD and light therapy.

The formal scientific presentations began the following morning with the Poster Session. As in the previous year's meeting in Frankfurt, a wide variety of questions were addressed in the posters and participants were provoked to lively discussion both among themselves and with poster session discussant Norman Rosenthal. In trying to summarize the poster session, I must apologize to all those researchers whose work cannot be reviewed in this forum.

Among clinical studies, A. Kogan and coworkers showed that patients who benefit from a short-term trial of light therapy frequently prolong the daily treatment regimen and continue to show subjective benefit after three months of daily use. C. Clark's work indicates that switching from a light-box to a portable light visor does not disrupt the therapeutic effects of light therapy, although her study followed subjects for only one week after cross-over. The always lively discussion about prophylactic use of light therapy before onset of depressive symptoms remains unresolved since the studies of Kjellmann and that of Meesters revealed contradictory results. Several posters focused on treatment of Delayed Sleep Phase Syndrome (DSPS) patients, one study indicating that 3000 lux illumination administered late in the sleep period is superior to 500 lux which, in turn, is no different than placebo. Y. Dagan et al. found that, in a series of 67 hospitalized adolescents, those with Borderline Personality Disorder had a significantly higher probability of suffering from DSPS than subjects with any other psychiatric disorder. Underscoring the increasing importance of light therapy as a treatment in elderly patients, S. Youngstedt and D. Kripke as well as R. Pat-Horenczyk and colleagues demonstrated that increasing evening illumination to 1000 lux can produce considerable benefits in mood and/or sleep disturbance in these individuals. J. Eagles and colleagues presented epidemiological evidence of a small but significant seasonal fluctuation in well-being with no gender difference in elderly patients living in Scotland. M. Young presented data which support the hypothesis that short photoperiod is an etiological factor in SAD. D. Young presented evidence of increased incidence of manic symptoms among recent eastbound trans-meridian travelers and more depressive symptoms among westbound travelers, supporting the im-

portance of chronobiological factors in the pathobiology of affective disorders. G. Sachs and colleagues pointed out that personality characteristics may be state-related correlates of depression and therefore amenable to light treatment.

Studies investigating the biological basis of SAD revealed some evidence for the importance of genetic factors in the manifestation of SAD, but the study of J. Freund et al. also indicated that environmental factors might influence the psychopathology of SAD. P. Arbisi and coworkers' study raised an intriguing question regarding the interaction between endogenous opioids and neurotransmitters. Investigating the serotonin hypothesis of SAD, A. Neumeister and colleagues presented a study showing no deterioration of depression after tryptophan depletion in untreated, symptomatic depressed SAD patients. The same group demonstrated in another poster that during tryptophan depletion, higher cortisol levels were observed than during control testing, thus providing further evidence for the importance of serotonin in the pathophysiology of SAD and the therapeutic effects of light. The evidence of serotonin's role in the pathobiology of SAD and the mechanism of light therapy was provided by R. Stain-Malmgren et al., who showed that light treatment increases platelet serotonin uptake. I. Neuhaus from the NIMH group presented data suggesting that SAD patients have elevated blood glucose levels during the winter. N. Praschak-Rieder and colleagues from Vienna, in her HMPAO-SPECT study, supported the hypothesis of a left hypofrontality in depression which normalized in patients who responded to light treatment. Correlations between mood and core body temperature circadian phase, as observed in a single-case study by D. Avery and D. Eder, supported prior observations among patients with forms of bipolar mood disorder.

The poster session was moderated by Norman E. Rosenthal who summarized, in his inimitable way, the findings of the hard work by all presenters and provoked an intensive and vivid discussion in the auditorium.

The three Oral Presentation Sessions focussed on different aspects of light therapy in SAD and provided new knowledge on pathophysiological mechanisms in SAD. Lam et al. as well as E. Turner and colleagues presented further evidence of serotonin's involvement in the mechanism of action of light therapy. The second session focussed on biological rhythms and photobiological mechanisms while the third session presented epidemiological data, a family study presented by E. Tam et al. and a treatment study by D. Schlager replicating an earlier finding of efficacy of early-morning beta-blockers in the treatment of SAD. B. Parry

provided evidence that in Premenstrual Dysphoric Disorder patients there is a delayed and blunted response to light in the symptomatic luteal phase.

It has become an important tradition of the SLTBR meetings to include symposia of more in-depth lectures on selected subjects. This year these lectures focussed on the state of the art of circadian rhythmicity, including melatonin and circadian photoreceptors. Specifically, the symposia included talks by David Klein on The Role of n-Acetyl Transferase, by Martin Lutz on The Effects of Light and Other Drugs on Melatonin in the Chick Pineal, by Ignacio Provencio on The Hunt for the Circadian Photoreceptor, by Dan Oren on Humoral Phototransduction and Evolution and, lastly, by David Schlager on SAD, Maternity, and Evolution.

In addition to all the scientific work which was done during the conference, this summary can not be properly concluded without expressing thanks to the organizers for the warm and cordial atmosphere they created during the whole meeting. At this point I want to remember the reader to the special lecture given by Norm Rosenthal after the banquet dinner in which he reminded us how unstable opinions and findings are in the scientific world. His fantastic and at times melodramatic demonstration described a "perfectly designed study" whose outcome, uncertain until the end, clearly supported dim light as the treatment of choice for winter depression—or was it finally bright light? (I can't remember exactly. Dr. Rosenthal: please provide us your lecture; and include the slides!)

Altogether, we, the members and friends of the SLTBR spent some time together, renewed friendships and established contacts. We look forward the 9th meeting of the Society in 1997.

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Of Placebos, Timing, Sequence and Ions: A Review of the Presentations of Eastman et al. and Terman and Terman at the 1996 SLTBR Annual Meeting

Of the many excellent and fascinating presentations at the latest meeting of the SLTBR in Bethesda this past June, two warrant a special mention: "Light Therapy for Winter Depression is More than a Placebo," by Charmane Eastman and colleagues (SLTBR Abstracts 1996; 8:5) and "A Multi-Year Trial of Bright Light and Negative Ions," by Michael

and Juana Su Terman (SLTBR Abstracts 1996; 8:1).

The study of Eastman et al. was, on the face of it, a very well-conducted, conventional controlled trial of light therapy for SAD, a parallel design with three treatment conditions: morning light treatment with 6000 lux for 1.5 hours per day, evening light treatment with the same fixtures and duration, and inactivated negative ion generators used in the morning for 1.5 hours. Treatment duration was over 5 weeks and the number of subjects treated, 96 over 6 years, was commendably large. The researchers found morning light treatment to be superior to both evening light treatment and to placebo.

In that previous studies have reached similar conclusions, one might conclude that there is little news here. For example, before Eastman's presentation, there was consensus among most researchers in the field that light therapy was acting as more than a placebo in the treatment of SAD. On the other hand, prior studies which compared efficacy of morning to evening light therapy have been less consistent in their findings. Researchers from the Pacific Northwest (Lewy and colleagues in Oregon, and Avery and colleagues in Seattle) found light treatment to be superior when administered in the morning as compared with the evening, whereas Wirz-Justice and colleagues found no difference between the two different timing regimens. The Columbia Group have previously suggested that such discrepant findings might be explained by differences in experimental design, with crossover designs (used by the Pacific Northwest group) yielding inferior results for evening light only when it followed morning light treatment within subjects in the crossover sequence. According to this line of reasoning, Wirz-Justice and colleagues had obviated this ordering effect by using a parallel design. The study of Eastman and colleagues thus broke new ground in finding a superior effect of morning light even when it is compared to evening light in a parallel design.

Interestingly, Eastman's group was able to demonstrate significant difference between morning light and placebo, and between the morning light and evening light, but only when strict categorical criteria for clinical response (commonly known as the Terman criteria) were used and not with conventional parametric analyses of rating score changes. Such discrepant findings between the two forms of analysis within a single light study have not previously been reported and suggest that patients who respond to treatment to a lesser degree are more likely to be placebo responders than those who respond in a more dramatic fashion. The distinction between truly active and placebo interventions might thus

Year Trial of Bright Light and Negative Ions," by Michael

be sharpened by comparing outcomes which exceed threshold values in terms of percentage improvement over baseline, final mood rating score, or both.

Two curious results of the study of Eastman and colleagues were: (1) the lack of efficacy of evening light treatment; and (2) the fact that they found a difference between treatment conditions only after three weeks of treatment. These findings are at odds with most of the rest of the literature, which finds that evening light treatment is somewhat effective for SAD and that a therapeutic effect is generally seen within one or two weeks of initiating treatment. It is difficult to reconcile the discrepancies between these present findings and the prior literature, especially on the basis of only the abstract and oral presentation. Possible reasons for the present unexpected findings include an overall lower efficacy of the active treatment and/or a higher efficacy of the placebo in this study.

When the history of light therapy is written, Eastman's name will be noted as its greatest skeptic and the researcher who most vigorously and impartially pursued the placebo effect. The title of her abstract therefore, "Light Therapy for Winter Depression is More than a Placebo," which might evoke a response of "so what? we all knew that," from true believers will be heard as a ringing endorsement of the treatment, coming, as it does from her research group. Ever since its modern inception, there has been no shortage of clinicians and researchers who have been skeptical of the efficacy of light therapy. Eastman, however, differed from these other skeptics in actually testing the question rigorously. There were times when she interpreted her data in a manner diametrically opposite from the conclusion she reached here. If she has not always been sufficiently respectful of the measures others took to create plausible placebo conditions or the degree to which they succeeded in that regard, she should be given credit for the ingenious placebo she did in fact create—the deactivated negative ion generator—and at the same time for spawning a whole new enterprise in evaluating the therapeutic potential of negative ions in SAD (see below for further details). In her presentation, Eastman graciously acknowledged that "it turns out that those of you who have said that light therapy is an effective treatment for SAD were right." It is equally true, however, that those of us who have made these claims all along owe a great deal to Dr. Eastman for her uncompromising quest for "the facts" which will certainly silence all but the most determined and eccentric of skeptics about the value of light therapy in SAD.

I now turn to the results of the multiyear treatment study by Drs. Michael and Juan Su Terman, which is surely one of

the most important studies in the annals of the treatment of SAD. In this massive study, the Termans treated a total of 144 patients (of 157 entered) with a series of interventions in a crossover study that resulted in sufficiently large cell sizes so that first pass comparisons could be made across treatment conditions, allowing for conclusions equivalent to those that can be drawn from a parallel design study. At the same time, the cell-sizes were sufficient to address the important question of ordering effects resulting from crossing patients from one light treatment to another in different sequences. In an ambitious additional wing of the study, these researchers also evaluated two dosing regimens of negative ion exposures, a low- and a high-dosage, although in the two groups receiving ions, the same dosing regimen was maintained across the first and second treatment regimens.

The study yielded answers to four critical questions in the treatment of SAD. They found that: (1) light therapy is an effective antidepressant for SAD; (2) morning light is superior to evening light therapy; (3) sequence of presentation of morning versus evening light therapy affects outcome; and (4) exposing SAD patients to high doses of negative ions has antidepressant effects. The first two conclusions nicely parallel those of the Eastman paper and really do definitively answer two questions about light therapy that have preoccupied the field. In Termans' protocol, the placebo condition was low-dose rather than Eastman's no-dose negative ion exposure, and low-dose ions were observed to be inferior to all other conditions tested including evening light. In this finding the Termans' paper differs from that of Eastman et al. and is more in line with the field as a whole. The Termans nicely replicate their earlier finding that evening light treatment is particularly inferior to morning light treatment if it is presented after morning treatment in the crossover sequence. The replication has the additional strength of being prospectively predicted as opposed to the original observation, which was derived from retrospective analysis of data. Finally, the finding that high-dose negative ion exposure is therapeutic is new, exciting and bound to foster further research into efficacy and mechanism.

The Termans were influenced by Eastman and colleagues into looking at their data according to both categorical and continuous response criteria. In this regard as well, however, they introduced an elegant new way of looking at data from all light studies, called signal detection analysis, which they had used in prior animal studies. This method of analysis enables one to compare treatments along a continuum of response criteria and to graphically represent the comparison in a way that readily shows which response criteria best illustrates any differences. This innovative analytic

strategy will surely exert an important influence on the field both in the interpretation of the results of future studies and in sending many of us back to reanalyze data already collected. There were, of course, many other wonderful papers and posters at the meeting, and this particular SLTBR member came away with the sense of the richness and diversity of our young and burgeoning field. But in my view,

these two papers all by themselves were worth the price of admission.

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GUIDELINES

1. Candidates shall not have passed their 35th birthday on January 31, 1997. If a senior investigator is listed as a co-author of the submission, the senior author should indicate in an accompanying letter the degree of independence represented by the candidate's contribution.
2. Although the research is not to be judged in comparison with the work of the more senior investigators in the field, special consideration will be given to the originality of the approach and independence of thought evident in the submission.
3. The candidate(s) must be still actively involved in the area of research described in the submission.
4. The submission should be in the form of a manuscript that describes empirical studies. The studies and data must not have been published elsewhere at the time of submission.
5. The winning authors will receive their awards and will be invited to present a scientific abstract based on their paper at the 9th Annual Meeting of the Society in the spring of 1997.
6. Submission will be welcomed from young investigators in any country.
7. Candidates need not be current members of the Society for Light Treatment and Biological Rhythms.

INSTRUCTIONS

1. Please submit manuscripts (six copies) of 10-20 pages

(double-spaced) in length, excluding references.

2. A brief biographical sketch (six copies) should be sent with the manuscript.
3. The deadline for receipt of submissions is January 31, 1997.
4. Submissions should be sent to Young Investigator Award, SLTBR, 10200 W. 44th Avenue, Suite 304, Wheat Ridge, CO 80033-2840.

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Authors contributing articles to *LTBR* are reminded that submissions should be written in the style consistent with the *Journal of Biological Rhythms*. This is especially true of references. Articles not submitted in the correct style may be returned to the authors for revision.

General guidelines for references include: Authors' given names are abbreviated as initials with no periods following surnames; volume numbers of periodicals are italicized with no space after the colon following the volume number, and journal titles are abbreviated as appropriate with no periods.

Examples of proper reference style are as follows:

Campbell SS, Dawson D, and Anderson M (1993) Alleviation of sleep maintenance insomnia with timed exposure to bright light. *J Am Geriatric Soc* 41:829-836

Okawa M, Hishikawa Y, Hozumi S, and Hori H (1991) Sleep-wake rhythm disorder and phototherapy in elderly patients with dementia. In *Biological Psychiatry*, G Racagni and T Fukuda, eds, pp 837-840, New York, Elsevier Science Publishers.

WELCOME NEW MEMBERS

Welcome to the following new members of the Society who have joined since publication of the May 1996 issue of *LTBR*.

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