

Light Treatment and Biological Rhythms

Bulletin of the Society for Light Treatment and Biological Rhythms



Volume 13, Number 2

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President's Message

Sonia Ancoli-Israel, PhD

This is my last presidential letter, as my term will end at this year's annual meeting. Writing a letter like this makes one reflect on the past. I came into the position with trepidation. After all, as I said in my first letter, I was following in the footsteps of some great people in our field – Dan Oren, Ray Lam, Chris Gillin, Anna Wirz-Justice, Michael Terman, Norm Rosenthal, Al Lewy – those were big shoes to fill. How much work would it take to be successful? How much would I be able to accomplish?

As it turned out, being president of SLTBR was a wonderful experience. Yes, it was work, but it was work made easy by my wonderful team of advisors (our past presidents and our board) and by our Executive Director, Kathy Matikonis. Kathy made this job not just easy, but enjoyable. Kathy and I spoke every Wednesday for the last two years (give or take a few). We knew we were in a routine when Kathy would answer the SLTBR phone with, "Hi Sonia." (If any of you happened to call at 11:00 on a Wednesday, you too would have been greeted that way – much to our embarrassment). In this way we were able to stay on top of all the issues.

What do I feel I've accomplished in the last two years? One of my goals was to increase membership, and I believe we have. Since last year's meeting, we've welcomed 28 new members to the Society and three corporate members. We also have a membership chair again and a new Board member, Dr. Namni Goel, who has helped with our recruitment efforts.

I have asked our distinguished past presidents to review our mission and present to us a new mission statement that better reflects who we are and what are goals should be. (We'll have an opportunity to discuss their recommendations at our business meeting on Friday, June 14.)

We held an outstanding meeting in Stockholm that surpassed our expectations in terms of attendance and science, hospitality and entertainment, thanks to Bengt Kjellman and his organizing committee.

At the Stockholm meeting, we welcomed several new members to the Board of Directors: David Harper assumed the job of treasurer, and Josephine Arendt was appointed as a Board member along with Michael Terman who graciously agreed to serve another term on the Board.

My most recent accomplishment and perhaps the legacy I leave for SLTBR is our association with the journal, *Chronobiology International* (CI). Discussions with Michael Smolensky, editor of CI, led to an agreement to publish our meeting abstracts in the journal. Our science is excellent, and it is time we were able to share it with the world and not just amongst ourselves.

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Bulletin of the Society for Light Treatment and Biological Rhythms



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President's Message...continued

This agreement will make *Chronobiology International* available to SLTBR members at a discounted subscription rate. The board will also be discussing whether to make CI our official society journal.

And last but not least, we will be holding another fabulous meeting in San Diego this June. Michael Young, our program chair, has put together what promises to be an exciting and stimulating scientific meeting. Although this is not Stockholm and the sun does set before 2:00 AM, San Diego is not a bad place to meet. The meeting will take place at the Horton Grand Hotel, a quaint Victorian hotel in the center of the Gaslamp District – a lovely area filled with great restaurants and shops. Our banquet will be held at the famous San Diego Zoo where we'll enjoy insiders' information on an adventurous after-dinner stroll through the Zoo's Nocturnal Canyon.

I hope you will join us for the 14th annual meeting, June 13-15 in beautiful, sunny San Diego, as I pass the gavel to Anthony Levitt.

Thank you for the help and support I have received from all of you.

SAVE THE DATE

June 13-15, 2002

**Horton Grand Hotel
 San Diego, California**

**See the website for
 details**

www.sltbr.org

A Consumer's Guide to Psychiatric Genetics: Are there signals in all that noise?

Robert Levitan, MD, Editor

Interpreting the multitude of psychiatric genetics studies now appearing on a daily basis is not an easy task. One day a gene seems to be linked to disorder A, the next day we see three negative studies with the same hypothesis. How can we detect signal from noise in this constantly changing space?

Firstly, one has to step back and consider the task at hand. Contrary to initial hopes, it seems fairly clear at this point that there are no major genes, transmitted in classic Mendelian fashion, that cause a given psychiatric disorder. If there were we would have found them by now. Rather we are dealing with complex disorders defined by many weak genetic effects working in tandem.

We need to keep in mind what it is that genes ultimately code for. If you think about it, human evolution is unlikely to have been based on the DSM-IV, and while I have not read Darwin's works, people who have tell me that the DSM was not mentioned at all (ICD-11 was mentioned briefly). This is problematic in that until recently, almost all genetic association studies were based on a given gene and a given disorder. A newer approach that makes a lot more sense mechanistically is to put aside the DSM, focusing instead on traits, behaviors or quantitative biochemical markers that have a more proximal relationship to the very genes we are studying. In SAD for example, rather than hypothesizing that a particular melatonin receptor gene variation is present in all patients with the disorder, one could develop a more precise hypothesis that only a subset of individuals, perhaps those with a markedly delayed DILMO, have SAD because of this genetic variant. In this case one determines whether different variants of the gene are associated with different patterns of the response. The notion of looking at subsets of individuals with a particular biological marker is well established in other areas of medical genetics and has considerable appeal at a scientific level. It is also more rewarding to develop and test a genetic hypothesis that is well thought out mechanistically and based on a clear, objective phenotype.

There are many methodological issues to consider when interpreting genetic studies. The most important is the issue of population stratification. Whenever you read about an apparent association between a given genetic variant and a disorder, always ask yourself what the comparison group was. Because of convenience and lower costs,

most studies have used a case-control method, whereby the controls are usually a mix of graduate students, hospital staff and people who happen to frequent the local restaurant. The point here is that for a control group to be valid, it needs to be very closely matched to the psychiatric group under consideration with respect to ethnicity, gender, age etc. If the match is not good, there is a strong likelihood that the control group will differ from the target group at a given gene based on factors unrelated to the hypothesis at hand.

For popular genes such as those related to serotonin, we now know the base rates of various polymorphisms that are expected in different ethnic and/or geographic populations based on prior research. So one way to check if a control group is valid is to compare its allele frequencies with prior studies of the same gene in the same general ethnic/geographic domain. If all other studies show allele A of the serotonin 1B receptor to be present in 50-55% of individuals, something is wrong if the new control group has the same allele at only 31%. Many a paper has been published whereby the associations reported are due to unusual allele frequencies in the control group, while the affected group has allele frequencies in line with controls from prior studies.

The best controls of all are family-based controls analyzed using the transmission disequilibrium test or TDT. TDT looks at all the heterozygous transmissions that have occurred in a given sample, and for each allele compares the "actual" number of transmissions to offspring with a particular phenotype, to the number of transmissions "expected" according to random meiotic segregation. A deviation from random transmission suggests that the particular allele is associated with the common phenotype of the probands. This method effectively takes into account errors due to conditions of non-random mating in the previous two generations, while controlling for population stratification. The TDT can also be used to study quantitative measures such as 24-hour-melatonin levels. However, the problem with the TDT is simply that it is very difficult and expensive to recruit parents and sibs, and homozygous parents provide little useful information for this test. So even after putting in the hard work to recruit families, many parents end up being discarded at the last step. The TDT is great when available, but has practical limitations that may limit its long-term popularity.

A new development that is likely to catch on rapidly is the use of genomic controls. Here one uses the general case-control method described above; however, cases and controls are matched based on a statistical analysis, which evaluates 40 markers across the genome.

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Levitan... continued

Comparison of allele frequencies across these 40 markers enables identification of the kinds of population substructure that can lead to false positive findings in case-control studies. If differences attributable to varying allele frequencies by ethnic group are found, a statistical correction is applied. Genomic controls have great appeal because they allow for use of general population controls, which are easy to recruit, while minimizing issues related to population stratification.

Another basic issue that one always has to keep in mind is that of multiple testing. The extreme example of this is the genome scan; however, even basic case-control studies have this problem if several genes are tested in the same group of subjects. If one were to analyze all the serotonin system genes in one study, chances are the cases and controls will differ at one or two sites by chance alone. How do you get around this? One might simply follow a rule that no matter how well done, all genetic association studies are truly preliminary in nature until replicated by several subsequent studies, preferably by independent groups. It is important here to consider the quality of the replication studies, and to make sure the phenotype under consideration is standardized across studies. It is also possible that a given polymorphism is associated with trait Z in one well-defined geographic population but not others; in this case replication within that population is key.

As it is with all areas of research, converging evidence is what to look for.

References:

- Spielman, R.S., & Ewens, W.J. (1996): The TDT and other family-based tests for linkage disequilibrium and association. *Am J Hum Genet*, 59, 983-989.
- Risch, N. & Merikangas, K. (1996): The Future of Genetic Studies of Complex Human Diseases. *Science*, 273, 1516-1517.
- Devlin, B., Roeder, K., Bacanu, S.A. (2001): Unbiased methods for population-based association studies. *Genet Epidemiol* Dec; 21(4):273-84.

CME COURSE**Bright Light Treatment: Indications, Methods & Devices**

Dr Dan Kripke, chair of this year's CME program, has planned an excellent course for meeting attendees.

The course will teach treatment with bright light for patients with seasonal and nonseasonal depression, premenstrual dysphoric disorder, bulimia, and circadian rhythm sleep disorders. Topics include methods and devices for bright light treatment, indications, timing, duration, and risks. Key clinical trials and evidence for efficacy will be critiqued. The emphasis will be on clinical methods of initiating treatment, with brief discussion of the physiology of light treatment. The faculty include some of the foremost American practitioners of bright light treatment.

Light Treatment of Seasonal Affective Disorders, PMDD and Bulimia

Raymond Lam, MD

Light Treatment of Nonseasonal Depression

Dan Kripke, MD

Treating Circadian Rhythm Sleep Disorders

Roger Cole, PhD

Panel Discussion:

Course participants will discuss light treatment with panel members and have an opportunity to question the panel about treatment approaches and clinical methods. Variations in strategies and opinions will be explained and debated.

Panel: Michael Terman, PhD; Barbara Parry, MD; Raymond Lam, MD; Dan Kripke, MD, and Roger Cole, PhD

**SLTBR 14TH ANNUAL MEETING
PRELIMINARY PROGRAM**

THURSDAY, JUNE 13

7:00 PM - 9:30 PM
7:30 PM - 9:30 PM

Registration
Poster Session: Discussion led by Norman Rosenthal, M.D., Professor of
Clinical Psychiatry, Georgetown University
Reception

FRIDAY, JUNE 14

7:30 AM - 8:00 AM
8:00 AM - 8:10 AM
8:10 AM - 9:00 AM

9:00 AM - 9:30 AM
9:30 AM - 9:45 AM
9:45 AM - 11:45 AM
12 Noon - 1:30 PM
1:30 PM - 3:00 PM
3:00 PM - 3:15 PM
3:15 PM - 4:00 PM
4:00 PM - 5:00 PM
7:00 PM

Registration; Continental Breakfast
Welcome – Michael Young, PhD
Keynote Address: **Photoperiodism in Humans**
Tom Wehr, MD, Chief, Clinical Psychobiology Branch, NIMH
Refreshment Break
Young Investigator Apollo Award Talk
Paper Session I
Lunch on your own
Symposium I
Refreshment Break
President's Address – Sonia Ancoli-Israel, PhD
Business Meeting
Banquet at the San Diego Zoo

SATURDAY, JUNE 15

8:00 AM - 9:00 AM

9:00 AM - 10:00 AM
10:00 AM - 10:30 AM
10:30 AM - 12:00 PM

ALPCO-Buhlman Distinguished Lecturer: Randy Nelson, Distinguished
Professor of Social and Behavioral Sciences, Ohio State University
Seasonality and the Immune System
Paper Session II
Refreshment Break
Symposium II

2:00 PM - 5:00 PM

CME COURSE

6:00 PM

OPEN HOUSE:

The Human Circadian Pacemaker Laboratory is
hosting an open house for all SLTBR meeting
attendees on campus in the School of Medicine at the
University of California, San Diego

SLTBR at the Horton Grand...

History, Science and Charm

In 1986, two turn-of-the-century hotels were painstakingly rebuilt, brick by time-honored brick, in the heart of San Diego's historic Gaslamp District. Join us at the 14th Annual Meeting and experience the elegance of the Victorian Era at the Horton Grand Hotel, a superbly crafted recreation of San Diego history and Victorian architecture. The Grand Horton was an elegant, ornate structure built by a German immigrant as a replica of the Innsbruck Hotel in Vienna, Austria. Opened in 1886, the hotel was one of many constructed during the "Boom of the Eighties" to accommodate the influx of people. Some 26,000 visitors flocked to the little town of 5,000 during 1886, after the arrival of San Diego's first trans-continental train in 1885.

The Brooklyn-Kahle Saddlery Hotel, less formal with a cowboy, Victorian flavor, sprang up at about the same time. It was originally a prominent saddle and harness shop that occupied the ground floor.

Both hotels were scheduled for demolition in the late 1970's and were purchased from the City of San Diego for \$1.00 each. The redwood infrastructures were swapped for the labor needed to dismantle the hotels brick by brick. More than 10,000 pieces were catalogued and stored in a warehouse until they were used to rebuild the hotels in their present location.

The Horton Grand is located in downtown San Diego's now exuberant Gaslamp Quarter historic restoration district (just 3 miles from San Diego International Airport). Third Avenue and I Street (now Island Avenue) was the heart of San Diego's notorious version of the Barbary Coast – the Stingaree District. Also called an "entertainment district," the Stingaree was the "wide open" section of the young, raw city of San Diego with an amalgamation of saloons, gambling halls, opium dens and brothels...with a few legitimate businesses mixed in. It was around Third and Island that the majority of the city's estimated 71 saloons and 120 bawdy houses sprang up during the "Boom of the Eighties." Despite occasional "clean-campaigns," the Stingaree remained the center of disreputable activity in San Diego for nearly three decades. The "Great Raid" on November 11, 1912, succeeded in cleaning up the area.

In the late 1980's the Horton Grand achieved a certain notoriety of a different sort. The hotel was supposedly haunted by at least one, possibly several, ghosts.

Make your hotel reservations before May 15 to insure that you get our special group rate:

US\$140 for a traditional room (one queen or one king bed, one or two people) and US\$150 for two queen beds, two people. Contact the hotel directly (Tel: 1-800-542-1886 or 619-544-1886; fax 619-239-3823) to book your accommodation. Be sure to mention that you are attending the SLTBR meeting.

Sunny San Diego... the quintessential Southern California beach city

Boasting Southern California's most beautiful and majestic coastline, near perfect climate and Mediterranean façade. San Diego offers a varied selection of shopping, dining, services, and attractions.

If you've never been to San Diego or your last visit was more than a few years ago, this relaxed and scenic city will hold some surprises for you. It's grown up. San Diego is no longer just a laid-back navy town – avant-garde architecture, sophisticated dining options, and a booming tourist industry all point to its coming-of-age.

Approximately 1.2 million people live in San Diego, making it the sixth-largest city in the United States (after New York, Los Angeles, Chicago, Houston, Philadelphia, and Phoenix). Although the city's population keeps increasing, you'll find that San Diego hasn't lost its small-town ambiance, and it retains a strong connection with its Hispanic heritage and culture.

The Gaslamp Quarter, where our meeting will be held, is the historic heart of San Diego. In recent years it has developed into the liveliest dining, entertainment and shopping district west of New Orleans.

Don't miss this year's banquet at the world famous San Diego Zoo. Relax with friends and colleagues and enjoy a private nocturnal tour to see what goes on after dark in the wild animal kingdom.

Located near downtown in Balboa Park, the zoo is home to 4,000 rare and endangered species, 6,500 varieties of birds, mammals and reptiles, and 6,500 varieties of exotic plants. Among its most striking features are the Polar Bear Plunge, Giant Pandas, Hippo Beach, Gorilla Tropics, Tiger River, Sun Bear Forest, the Children's Zoo and giant walk-through aviaries.

Check the links on the SLTBR website <http://www.sltbr.org/> for more information about San Diego and the San Diego Zoo.

14th Annual Meeting & CME Course Registration Form
Society for Light Treatment and Biological Rhythms
June 13-15, 2002
San Diego, California

Please submit one registration form for each participant. Type or print clearly. Mailed or faxed registrations will be accepted through June 1, 2002. After that date, a \$25 late fee will be added.

Name: _____
(Please print clearly) First Last Suffix
Title: _____

Affiliation: _____

Address: _____

City: _____ State: _____ Postal/Zip Code: _____

Country: _____

Telephone: _____ Fax: _____

Email: _____

(Registration confirmation will be sent via email.)

Annual Meeting Fees

☐ Corporate Member \$600.00

☐ SLTBR Member \$135.00

☐ Non-member \$220.00

☐ Student \$ 70.00

☐ Banquet (per person) \$ 85.00

☐ CME Course Fee \$100.00
(fee for Saturday PM course)

☐ Late registration fee) \$25.00
(after June 1)

Total \$ _____

☐ Enclosed is my check payable (USD) to SLTBR

check number _____

☐ Charge registration fees to my credit card

NOTE: A 5% SERVICE CHARGE WILL BE ADDED TO CREDIT CARD PAYMENTS.

☐ MasterCard ☐ Visa

Card Number: _____

Expiration Date: _____

Name of Cardholder: _____

Signature _____

FAX OR MAIL THIS FORM WITH FEES TO:
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