

Light Treatment and Biological Rhythms

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EDITORIAL —

ADAPTATIONIST PERSPECTIVE

I forget to which person history was unkind enough to attribute the statement that there was no need for a patent office because there was nothing left to discover. I say unkind because the conviction—that all great discoveries are behind us—is as familiar as it is untrue.

This does not apply to our own field, of course. Chronobehavioral phenomena have many secrets still to yield and interventions are evolving rapidly. All the same, the seminal discoveries—that human mood varies seasonally and that mood and other behavioral rhythms can be influenced by light—seem startling and intriguing enough to seem a hard act to follow.

It is more than consolation, though, to recall that the very discovery of such phenomena and their treatment—the “what”—has evoked unanswered questions about the proximate and ultimate causes—the “how” and “why”—of such human behaviors. And while justly cautious, the pursuit of such questions in our field seems to enjoy some advantages not yet afforded the study of other human behavior disorders, namely a strong body of relevant animal models and research and a timely explosion of interest in evolution and behavior (see book review in this issue).

As for the evolution and behavior, seasonality, as deservedly as sociality or sexuality, has tempted adaptationist speculations which may have been too successfully resisted to date. As understanding of seasonal and other rhythmic phenomena progresses, reconsideration of the role of such behav-

iors as evolved responses to specific and predictable environmental opportunities or threats remains of inherent interest, and may provide relevant insights for the study of mechanism. Thus, in complement to descriptive and mechanistic considerations, *LTBR* invites and will attempt to include reconsideration of adaptationist approaches to chronobehavioral disorders.

The tough act to follow, then, consists of the conscientious and successful efforts of the founders of the field to disseminate information, generate interest, and attract growing numbers of contributors to the field. But follow we must. I am grateful to Scott Campbell and to the board of SLTBR for the opportunity to serve on the Bulletin.

—David Schlager, M.D.
Associate Editor

In This Issue

Edwin M. Tam and Raymond W. Lam
Treatment of Seasonal Affective Disorder 32

Jürgen Aschoff
An Attempt Toward a Constant Routine
50 Years Ago 39

David Schlager
on *Why We Get Sick: The New Science of*
Darwinian Medicine 40

Scott Campbell
Flash(light) Poll Results 42

Bulletin Board 43

Also: *Letter from the President, Flash(light) Poll*

TO REACH SLTBR ...

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interest. Reviews in 1989 and 1990 concluded that bright light was an effective treatment for SAD (Lam et al. 1989; Wehr and Rosenthal, 1989; Blehar and Lewy, 1990). In 1989, Terman et al. analyzed the light treatment data from 14 research centers with a pooled clustering technique (Terman M et al. 1989c). These 332 SAD patients represented the subjects of all studies done prior to 1988. Bright light (>2500 lux), using light boxes with fluorescent tubes, produced significant improvement in most studies: mean 21-item Hamilton Depression Rating Scale (HDRS) scores dropped from approximately 18-23 to approximately 8-12 post-treatment. Dim light controls (100-300 lux) produced small but statistically significant reductions of 3 points to yield post-treatment HDRS scores of 20. Morning bright light exposure was the most effective (53% remission rate), followed by morning-plus-evening light; they were the only two conditions yielding post-treatment HDRS scores below 10. The baseline severity was a factor in determining time of day effects: while evening and dim light response rates did not change with severity, the superiority of morning light over evening light declined as baseline severity increased.

Since then, treatment research has focused on exploring optimal parameters of light therapy, different types of light devices, and pharmacotherapy of SAD. Some common methodological problems in treatment studies of SAD have been discussed (Blehar and Lewy, 1990) but merit summary here. SAD studies have involved relatively small samples of patients and very short treatment periods. Many controlled studies have used a crossover design. While this design increases the power of a study for a given sample size, there are confounding factors including sequencing effects of treatment conditions, differences in patient expectations after crossover, and differences in relapse of symptoms during washout periods. The nature of a suitable placebo is perhaps the most controversial issue since, unlike drug trials, subjects in light studies cannot be blind to the treatment received (Brown 1990, Eastman 1990, Stewart J 1990). SAD patients are likely to have a sizable placebo response rate similar to outpatient treatment studies of non-SAD depression. Many studies used dim light as a placebo condition, but questions remain about the expectations of subjects regarding light intensity and the possibility that dim light is itself an active treatment. Other studies have used novel placebos such as deactivated ion generators, but differential expectations may still complicate results. Results from the light visor studies (q.v.) also raise issues about placebo response and the intensity-response relationship. With these methodological issues in mind, this article will review the published treatment studies of SAD from 1989 to the end of 1994.

TREATMENT OF SEASONAL AFFECTIVE DISORDER

INTRODUCTION

Therapeutic issues in seasonal affective disorder (SAD) have attracted much attention since the first report of light treatment for a patient with winter depression (Lewy et al. 1982) and the first systematic description of SAD by Rosenthal and colleagues (1984). Given that seasonal changes in the daily light-dark cycle were the likely trigger for winter depression, bright light therapy emerged as the treatment of

LIGHT THERAPY

A. Light Boxes

The light box using fluorescent lights is the most researched light device to date. Studies since 1989 have continued to establish efficacy and to define the therapeutic parameters of light including intensity, wavelength, duration of daily exposure, and timing. Effectiveness of bright light using light boxes has been found in open trials (McIntyre et al. 1989; Stinson and Thompson 1990; Nagayama et al. 1991a; Richter et al. 1992; Lingjaerde et al. 1993a; Sugishita et al. 1993; Bauer et al. 1994; Terman J et al. 1994), and more rigorously examined in controlled parallel and crossover studies (Grota et al. 1989; Winton et al. 1989; Terman J et al. 1990; Lam et al. 1991; Magnussan and Kristbjarnarson, 1991; Eastman et al. 1992). In general, the studies comparing bright light to dim light placebo have validated the antidepressant effect of bright light (Winton et al. 1989; Stinson and Thompson, 1990; Terman J et al. 1990; Lam et al. 1991; Magnussan and Kristbjarnarson, 1991; Lingjaerde et al. 1993a; Terman J et al. 1994). However, a study by Grota et al. did not show superiority of bright light over dim (Grota et al. 1989), and Eastman et al.'s study with a deactivated ion generator placebo similarly showed no superiority of bright light over placebo (Eastman et al. 1992). The former study was conducted with evening dosing, which may have obscured the superiority of the bright light treatment. The latter study had a relatively low response rate to bright light therapy (28%). Possible explanations included sub-optimal intensity or timing of the bright light, exclusion of light-sensitive patients due to unusually sunny weather during the baseline phase, entry criteria requiring atypical symptoms, and/or effects of a placebo control.

The optimal wavelength for treatment has been studied for both the visible and ultraviolet (UV) spectrum. White light has been shown to be superior to green (Stewart K et al. 1991), as well as red and blue (Brainard et al. 1990), while green seems superior to red (Oren et al. 1991a). However, the differences between conditions were small and of limited clinical significance. Broad spectrum and cool-white fluorescent lights were found to be equivalent (Bielski et al. 1992). An initial study suggested that atypical symptoms responded preferentially to light with UV wavelengths (Lam et al. 1991), but a larger follow-up study did not show any difference between bright light with or without UV-A transmission (Lam et al. 1992a).

The duration of light exposure in most studies using 2500 lux light boxes was generally 1-2 hours a day. Some studies suggest a therapeutic plateau for exposure time, since 2500

lux for 2 hours was as effective as 4 hours (Doghramji et al. 1990), and 3300 lux for 15 minutes of light produced the same results as one hour (Partonen 1994). In contrast, studies using 2500 lux light found that 2500 lux for 4 hours was superior to 1 hour of treatment (Terman M et al. 1989a), and 6 hours was superior to 2 hours (Winton et al. 1989). There is thus some rationale for increasing the time of exposure for non-responders. There may also be a reciprocal relationship between intensity and duration, as remission rates with 10,000 lux for 30 minutes were similar to those with 2500 lux for 2 hours (Terman J et al. 1990).

The optimal timing of light has been explored by comparing morning to evening light exposure. Most crossover studies show morning light to be superior (Avery et al. 1990; Sack et al. 1990; Terman J et al. 1990; Avery et al. 1991) while some parallel studies have shown no difference (Meesters et al. 1993a; Wirz-Justice et al. 1993; Lafer et al. 1994). In the crossover studies, a sequencing effect has been described whereby morning light therapy may have carry-over effects that diminish the effects of evening light (Terman M and Terman J, 1992).

The length of treatment has not been addressed in controlled studies. Relapse of symptoms generally occurred within days of light therapy discontinuation in previous studies (Lam et al. 1989; Terman M et al. 1989c). However, in two trials, Meesters found that giving five days of light at the first sign of winter depression often produced improvement lasting the whole season (Meesters et al. 1993a; Meesters et al. 1993b). A related study showed that giving light at the beginning of winter before the emergence of depressive symptoms conferred no protection (Meesters et al. 1994). However, Terman was unable to replicate these results in a study that showed most patients relapsed when light was only used early in the winter episode (Terman J et al. 1994).

B. Head-mounted Units

One drawback of the light box is the lack of mobility during treatment. Attention turned to head-mounted units which could provide the same therapeutic results while allowing the wearer free range of activity. A controlled crossover study showed that a light visor using incandescent light produced similar results to a light box (Stewart K et al. 1990). Since then, three other controlled parallel trials using a similar light visor have compared varying intensities of light to further assess efficacy. While the light visor produced significant improvement in depressive symptoms (with response rates ranging from 36% to 65%), the brighter light conditions were not superior to putative dim light controls (Teicher et al. 1992; Joffe et al. 1993; Rosenthal et al. 1993). An-

other study of a light cap using red light from a light emitting diode (LED) also failed to show differences between bright and dim light (Levitt et al. 1994). Investigators have proposed several possibilities to explain these findings. First, since many light box studies have demonstrated superiority of bright light over dim light, the antidepressant effects in the head mounted unit studies may be due solely to nonspecific placebo effects. A second possibility is that light is active, but that the delivery system has a major impact on the dose-response relationship. The light source of a head-mounted unit is much closer to the eye than that of a light box. This may be seen as being more efficient (i.e., that dim light is active) (Joffe et al. 1993) or less efficient (Rosenthal et al. 1993). A clear dose-response may be obscured because of ceiling effects (effects seen below the minimum intensity studied), floor effects (effects seen above the maximum intensity studied), a therapeutic window (effect at some intensity between those studied), lag effects (study duration too short to show effects) or underdosing effects (treatment period too short to show effects) (Levitt et al. 1994). A third possibility is that there are more prominent confounding factors with head-mounted units that prevent an accurate assessment of the dose-response relationship. For example, the subjects may not be wearing the units properly, the measurements of light exposure may not accurately reflect the light actually reaching the retina (Brainard et al. 1993), and/or the eye may adapt to this light source more readily. Finally, there are many measures of the physical properties of light and it is possible that illuminance (as measured by lux) may not be the critical parameter for biologic or therapeutic effects of light. Thus, there are still many issues that need to be clarified for head-mounted units.

C. Dawn Simulators

Noting that light changes in nature tend to be gradual as opposed to the strict on-off quality of light therapy, Terman and colleagues explored a technique of simulating a dawn signal by gradually raising light levels in the morning, while the patient was asleep, to peak values below those of standard light therapy (<1000 lux). Initial open trials showed an antidepressant response to dawn signals given over 2 hours and peaking at 1000 lux (Terman et al. 1989b) or 2000 lux (Terman and Schlager, 1990a). A subsequent controlled trial by Avery's group found that a 2-hour dawn signal with a 1700 lux peak was not as effective as standard light therapy for 2 hours at 1700 lux (Avery et al. 1992b). Interestingly, a 2 hour dawn signal with a lower peak illuminance of 250 lux was superior to a 30-minute, 0.2-lux placebo dawn signal (Avery et al. 1993). Further complicating the issue is the fact that both rapid (10-minute) and gradual (2.5 hour) dawn simulation peaking at 275 lux were found to be of compa-

table efficacy (Avery et al. 1992a). This lack of superiority over a hypothesized placebo condition raises issues similar to those of the head-mounted unit.

D. Predictors of Response To Light Therapy

Predictors of response have been discussed in several of the studies cited above. The severity of atypical symptoms was correlated with good response to light treatment (Stinson and Thompson, 1990; Nagayama et al. 1991a), with hypersomnia being singled out in some studies (Lam et al. 1992b; Partonen, 1994). Diurnal mood variation (Meesters et al. 1993a) and the severity of typical depressive symptoms (Stinson and Thompson, 1990) have been negatively correlated with treatment response.

Three studies focused specifically on the issue of predicting response to light therapy. Oren et al. showed that hypersomnia, hyperphagia, and suicidality predicted response in female SAD patients (Oren et al. 1992), while Lam's study identified hypersomnia, increased eating and younger age at treatment as predictive factors (Lam 1994a). In contrast to these two studies, Kräuchi et al. (1993) used prospective measures of sleep and eating, and found that only a high intake of sweets late in the day predicted light therapy response.

E. Side Effects of Light Therapy

The side effects of light therapy were reported in a prospective study of 105 patients using the light visor: headache (19%), eyestrain (17%), feeling "wired" (14%), nausea (13%), and dizziness (11%) (Levitt et al. 1993). Most patients experienced a reduction in symptoms as treatment progressed. Furthermore, the emergence of these symptoms was not related to the intensity of light used. A retrospective study showed a similar, albeit somewhat higher, frequency of side effects (Oren et al. 1991b), while a smaller study showed a much lower incidence of side effects (Ozkan and Arik, 1994). A prospective study comparing morning and evening light found insomnia to be a problem for patients on the evening schedule (Labbate et al. 1994). Not surprisingly, dawn simulators have early morning awakening as a side effect, especially at higher intensities (Avery et al. 1992b; Avery et al. 1993). Light therapy, like other antidepressant treatments, may trigger a switch into hypomania in some patients (Kasper et al. 1990; Stewart K et al. 1991; Avery et al. 1992a; Avery et al. 1993; Levitt et al. 1993; Bauer et al. 1994; Labbate et al. 1994) and even mania (Schwitzer et al. 1990; Kantor et al. 1991; Kripke, 1991; Chan et al. 1994).

Ocular side effects of light therapy potentially involve the

retinal effects of visible light, and corneal and lenticular effects of ultraviolet light (Terman M et al. 1990b). Chronic UV-A or UV-B exposure may predispose to cataracts, and theoretically patients could achieve clinically significant UV exposure levels by staring directly at a 2500 lux fluorescent light source for 2 hours daily over a lifetime (Oren et al. 1990). The common practice of using UV filters and instructing patients not to stare constantly at the light minimizes this risk. One study of 10,000 lux for 30 minutes daily over 2 to 6 weeks did not find any pathological changes by ophthalmologic examination (Terman J et al. 1990). Another reported 5-year follow-up study found no clinical or electrophysiologic changes in the eyes of patients using 2500 lux light (Gorman et al. 1994). The need for routine ophthalmologic screening prior to light therapy is thus controversial. Some investigators feel it should be mandatory (Terman M et al. 1990b; Vanselow et al. 1991; Remé and Terman, 1992), while others have suggested that ophthalmologic assessment should be sought in high-risk patients only (Waxler et al. 1992; Rosenthal, 1993; Lam, 1994b).

PHARMACOTHERAPY

The search for treatments of SAD has included the use of pharmacological agents. Limitations of these studies are similar to those of light studies: most involve small sample sizes, short treatment periods, and unreplicated results. Rosenthal et al. initially tried to mimic the effects of light by using a beta blocker, atenolol, to suppress melatonin secretion in the afternoon, with mixed results (Rosenthal et al. 1988). However, propranolol, a shorter-acting beta blocker, was shown in a placebo substitution trial to be effective in SAD when administered in the morning (Schlager, 1994). Melatonin was used in an open trial in an attempt to adjust the circadian rhythm directly, with no apparent effect (Wirz-Justice et al. 1990). Based on the hypothesis of abnormal dopaminergic regulation in SAD, a controlled trial of levodopa plus carbidopa was undertaken but was found not superior to placebo (Oren et al. 1994). D-fenfluramine, a serotonin-releasing agent without antidepressant properties, was found to be effective in two small studies (O'Rourke et al. 1987; O'Rourke et al. 1989). Tryptophan was compared to light in a small, complicated crossover study with some suggestion for benefit (McGrath et al. 1990). An open study of alprazolam also showed positive effects in SAD (Teicher and Glod, 1990).

It is somewhat surprising that there are so few antidepressant studies in SAD. Open trials have suggested that tranylcypromine (Dilsaver and Jaeckle, 1990) and bupropion

(Dilsaver et al. 1992) are beneficial. Only two placebo-controlled studies of antidepressants have been reported to date. Moclobemide, a reversible inhibitor of monoamine oxidase A, was investigated in a 3-week study in 34 patients (Lingjaerde et al. 1993b). No differences were found between drug and placebo, but major methodologic problems (e.g., poor diagnostic assessment, inadequate duration of treatment, suboptimal dose, small sample size) limit interpretation of these results. The other study compared fluoxetine (20 mg/day) to placebo in 68 SAD patients over 5 weeks, and found superiority of fluoxetine in the clinical response rate (59% vs. 34%) but not in the continuous HDRS scores (Lam et al. 1994c). The patients who were most markedly depressed at baseline showed the greatest benefit with fluoxetine.

Few studies have directly compared antidepressants to light treatment. The tryptophan study suggested that tryptophan response was similar to evening light (McGrath et al. 1990). A single case study of a well documented SAD patient found citalopram (a serotonin reuptake inhibitor) as effective as the patient's previous light therapy, albeit with a longer time course to improvement (Wirz-Justice et al. 1992). A more rigorous study comparing bright light plus placebo to fluoxetine plus dim light found similar response with both conditions (Ruhrmann et al. 1993), suggesting that antidepressants are as effective as bright light.

CONCLUSIONS

What conclusions can we make for treatment of SAD based on the clinical studies to date? The treatment most strongly supported by research studies is light therapy using a light box to administer bright white light (>2500 lux for 2 hours). Studies of higher intensity and shorter duration (10,000 lux for 30 minutes) suggest an equivalent response rate. Because this regimen is more convenient for patients, it has gained widespread clinical use. However, there is as yet limited data to suggest a linear intensity-duration relationship in light boxes. Because of potential side effects of chronic UV exposure, and since there has been no clear benefit from UV wavelengths in the therapeutic response, light therapy devices should have UV filters. Time of day of light exposure may not be important for the overall therapeutic response, but some patients may be selective responders to early morning light exposure. To prevent relapse, it would be prudent to continue the treatment throughout the winter season.

Studies of head mounted units have not yet demonstrated efficacy (i.e. superiority against a putative placebo control)

but the considerable response rates in the large sample studies using incandescent white light visors suggest that they are a reasonable alternative treatment when mobility is an issue. Dawn simulation is an interesting treatment that requires replication studies using larger samples before it can be recommended as a first-line treatment. Longer term studies of light therapy should be done to demonstrate that clinical effects are sustained over time. Further studies are also warranted to clarify the intensity-response relationship of light, the optimal treatment schedule for light exposure, and the long term safety of light treatment.

Side effects of light therapy appear to be mild and well tolerated. Because of the risk of hypomania or mania, patients should be carefully monitored by experienced clinicians during treatment. Studies have not shown that light therapy causes any eye damage, but these studies are limited and short term. While many clinicians would recommend pre-treatment ophthalmologic assessment only for individuals with risk factors (such as pre-existing retinal or eye pathology, systemic illnesses that involve the eye, use of photosensitizing medication, and older age), others have suggested routine pre-treatment eye screening.

Antidepressant medications such as SSRIs (fluoxetine, citalopram) also appear to be effective in SAD, especially for patients who are more severely depressed. Fluoxetine appears to be as effective as bright light exposure using light boxes. Interesting questions that require further study include the effectiveness of beta-blockers in SAD, and combination treatment with light therapy and antidepressants.

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Dear SLTBR Member:

A special goal for 1995 is the growth and expansion of SLTBR. The Society is the source of information, research and advocacy for light therapy. Anyone who reads our Bulletin, attends our meeting or reads our abstracts would agree unequivocally with this statement.

But this fact appears to be a well kept secret.

Help us share that secret by urging a professional colleague to join. You—as a member of SLTBR—are in the best position to know who among your professional colleagues should be counted as a member.

There are several ways to help the Society:

-Keep a few membership applications at your desk, when you meet a potential member pass one along.

-If you are presenting at a meeting attended by potential members, mention the Society (and the address). Better yet, plan ahead and have applications available.

-Let us make it even easier. On the form below, send the name(s) of potential members to staff and an application will be sent to them. Staff will keep track of new members who join and acknowledge the member sponsors in the Bulletin.

Be an active participant in SLTBR's growth. Sponsor a new member. We'll all benefit.

Anna Wirz-Justice, Ph.D.
President

____ Please send me ____ applications to distribute. (Indicate number you need)

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AN ATTEMPT TOWARD A 'CONSTANT ROUTINE': 50 YEARS AGO

Recently, I was asked to contribute a historical note to a book on *Temporal Variations of the Cardiovascular System* (Aschoff, 1992). When discussing the effects of "masking factors," I referred to Mills, who first proposed the "constant routine" (Mills et al. 1978), and to some of his forerunners. Among these was Colombo (1899) who, in measuring daily variations in blood pressure, tried to avoid all "sources of error" such as body movements and meals.

Further attempts to demonstrate an unmasked "basic rhythm" had apparently not been published until about 70 years later. However, in checking the literature, I forgot a series of experiments which I, myself, carried out in 1944. At that time, I was interested in convective heat transfer by blood flow from the core of the body to the skin, and especially in the role played by the extremities. To that end, I measured the heat loss from the hands by making use of calorimeters suffused by water of constant temperature. The amount of heat lost to the water per unit of time was divided by the temperature gradient between core and skin of the hands, resulting in a unit called "conductance" ($\text{cal}/\text{cm}^2 \times \text{min} \times ^\circ\text{C}$) which is a reliable relative measure of peripheral blood flow (Wever and Aschoff, 1957). To put my hands into the calorimeters, I had to sit motionless in an upright position. (The old-fashioned recording devices, including light-beam galvanometers and self-made thermocouples, were operated by Mrs. Hilde Philippine Aschoff.)

In a first set of experiments, each lasting from morning to evening, I took my regular three meals per day, in between recording sessions. After each meal, there was a drastic increase in heat loss and conductance, indicating a strong effect of food intake on peripheral blood flow. This effect disappeared rapidly after breakfast and lunch, but lasted for quite sometime after dinner (see Figure 1). (The caloric content of meals was not measured, but lunch was certainly heavier than dinner). As a next step, then, I remained fasting (following dinner on the previous evening), and did not change my position for 16 consecutive hours, after the experiment had started at 1000h. The data from this experimental session, plotted in Figure 2, show the well established daily rhythm in rectal temperature, and for the first time, an almost inverse rhythm in heat loss and peripheral blood flow, respectively, under conditions which are not too far from what we have come to know as the "constant routine".

The experiment took place on the 26th of May, 1944; but publication was delayed (due to the war and its aftermath) for three years (Aschoff, 1947).

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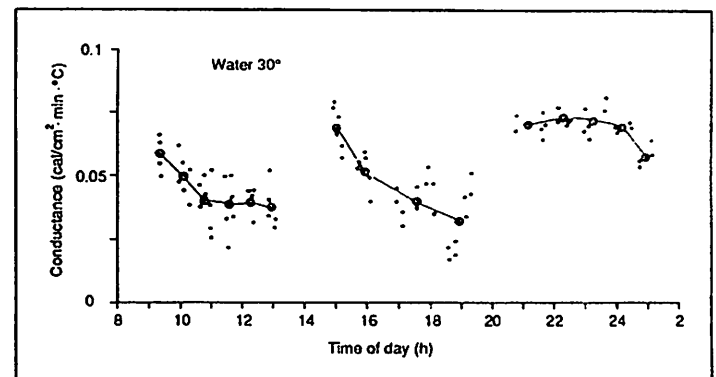


Figure 1. Heat loss from hands in response to running water of 30°C , converted into conductance from core to skin. Consecutive recordings from one subject (J.A.) who was sitting upright and took meals between recording sessions. Each small dot represents the measurement for one hand during about 15 min. The bold dots are the means of 3 to 4 measurements.

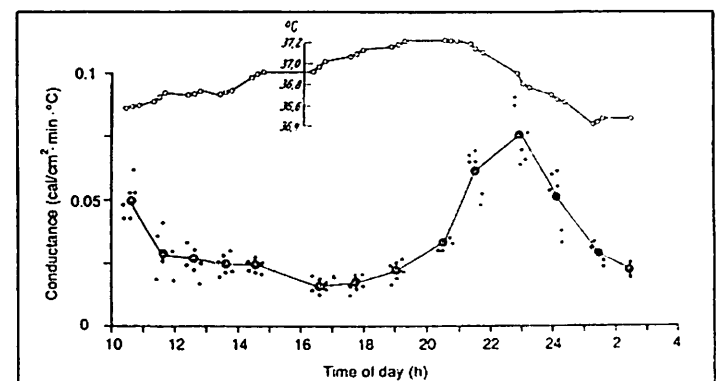


Figure 2. Circadian rhythm of rectal temperature and of conductance, as derived from heat loss from the hands in response to running water of 32°C . The fasting subject was sitting motionless in an upright position. Symbols on lower curve as in Figure 1.

BOOK REVIEW

Why We Get Sick: The New Science of Darwinian Medicine

By Randolph M. Nesse, M.D. and George C. Williams, Ph.D.
(Times Books/Random House, New York; 1994, 291 pp.,
U.S. \$24.00)

Now, as each of the parts of the body, like every other instrument, is for the sake of some purpose, viz. some action, it is evident that the body as a whole must exist for the sake of some complex action.

—Aristotle

Why are we born only to struggle, fret, suffer, and die? Because those in the past who did so, outreproduced the others.

— Anonymous (paraphrased)

This new book is an elaboration, aimed at a wider audience, of a scientific paper published by the same two in *The Quarterly Review of Biology* (1991; 66:1-22). Dr. Williams is professor emeritus of ecology and evolution at SUNY Stony Brook, editor of *The Quarterly Review of Biology*, and a member of the National Academy of Sciences. He has written seminal works on natural selection and the evolution of senescence. Dr. Nesse is professor and associate chair for education and academic affairs in the Department of Psychiatry at the University of Michigan Medical School. He has been a central figure in the emerging field of evolution and human behavior.

Their thesis, using their own words liberally and not always sequentially, is introduced by some deceptively idle ponderings: "If evolution by natural selection can shape sophisticated mechanisms such as the eye . . . and brain, why hasn't it shaped ways to prevent nearsightedness . . . and Alzheimer's disease? . . . If our immune systems can recognize a million foreign proteins . . . why are we, after millions of years, still prone to streptococcal infections? . . . Why do we crave the very foods that are bad for us . . . and keep eating when we know we are too fat? . . . Why are so many of us constantly anxious, spending our lives, as Mark Twain said, "suffering from tragedies that never occur." . . . If we can live one hundred years, why not two hundred? . . . (If) an intricate system of arteries carries just the right amount of blood to every part of the body, (why do) many of us develop cholesterol deposits on their walls (with) the resulting blockage in blood flow causing heart attacks and strokes? It is as if a Mercedes-Benz designer specified a plastic soda straw for the fuel line! . . . Despite their exquisite design, our bodies have crude flaws. Despite our multiple defenses, we have a thousand vulnerabilities. Despite their capabilities for rapid and precise repairs, our bodies inevitably deteriorate

and ultimately fail . . . Before Darwin, physicians could only wonder at the incongruity of it all . . . and hope (that) our bodies (are) part of an unfathomable divine plan . . . or cosmic prank . . . (Since Darwin), an evolutionary approach transforms such mysteries into a series of answerable questions: "Why hasn't . . . natural selection . . . eliminated the genes that make us susceptible to disease? And why hasn't it selected genes that would perfect our ability to resist damage and enhance repairs so as to eliminate aging?"

The conventional answer, again in their words: ". . . —that natural selection just isn't powerful enough—is usually wrong! . . . Instead (the modern Darwinian answer lies in recognizing that) the body is a bundle of careful compromises" which are designed by natural selection to maximize fitness "not in the vernacular sense of strength, health, and longevity. Selection does not necessarily enhance the welfare of the species or the happiness of the individual . . . but rather the gene's ability to get itself replicated or, somewhat less accurately, the ability of organisms to gain genetic representation in future generations. In fact, many of the capacities for suffering seem to have been shaped by natural selection to serve special adaptive functions . . . If tendencies to anxiety, heart failure, nearsightedness, gout, and cancer are (or were) somehow associated with increased reproductive success, they will be selected for and we will suffer even as we "succeed" in the purely evolutionary sense."

This neo-Darwinian notion, that natural selection "selects" replicators primarily and vehicles of replications—i.e., "ourselves"—only secondarily and only in ways coincident with genetic interests, is at the heart of the evolutionary perspective of disease. It is a perspective which has already proved enormously fruitful in fields of animal behavior and ecology.

Why then "are there genes (or lack thereof) that make us vulnerable to disease? . . . Fewer (genes) than have been thought . . . arise from new mutations kept scarce by natural selection." Other explanations are presented in several categories:

- *Genes.* Some disease-causing genes cannot be eliminated because they cause no disadvantage until it is too late in life to affect fitness. Most "deleterious" genetic effects however, are actively maintained by natural selection because they have unappreciated benefits that outweigh their cost (i.e., vigor in youth that may result from genes that later cause aging). Some are maintained because of heterozygote advantage (i.e., sickle trait); some are selected because they increase their own frequency despite creating a disadvantage for the individual who bears them.

• *Novel environments/diseases of civilization.* Some disease results from exposure to environmental factors (e.g., nutritional abundances and shortages leading to obesity and vitamin deficiencies, respectively) not present in our evolutionary environment and thus not nearly enough to permit evolution of compensatory genetic factors.

• *Design compromises and historical legacies.* By being forced to work with only what is already there and to produce what works as well or better each step of the way, evolution often produces functional adaptations which might have been better designed by starting from scratch (e.g. crossed upper airway and digestive passages predisposing to choking, inside out retina responsible for blind spots and detachment).

• *Genetic Arms Races.* "Since we are not the only species with adaptations produced by natural selection . . . infection is not a happenstance encounter . . . but an arms race between host and parasite, with extraordinary elaboration of weapons, strategies, defenses, and counter-defenses . . . Infectious agents evolve so fast that our defenses are always a step behind."

The scope of medical phenomena subjected to the authors' analysis is wide-ranging, with chapters on infectious disease, injury, toxins, aging, allergy, cancer, sex and reproduction, and mental disorders. Some detail is provided in reviewing like-minded, prior research findings, including Paul Ewald's on the evolution of virulence in infectious disease, David Haig's on mother-fetus conflict-of-genetic-interest predisposing to common gestational disorders, and Williams' own enduring but largely unappreciated (at least in medicine) theory on the evolution of senescence. Complementing such few findings which have already produced relevant implications for medical practice and research, the authors provide a greater number of informed speculations about specific symptoms and diseases and propose testable questions of the type they believe exemplify a Darwinian approach to medicine.

The chapter on mental disorders includes reference to Daly and Wilson's increasingly compelling findings on child abuse and homicide, as well as considerations of anxiety, depression, and sleep. The section on depression, a syndrome too common to be attributed to mutation, includes reference to several extant hypotheses on its possible adaptive functions, and suggests that the recent eruption of thymoleptic use adds urgency to such considerations. The brief mention of SAD, while welcome, seems to reflect a conspicuous want of adaptationist analysis of this naturally amenable phenomenon.

From an evolutionary standpoint, all analyses are sophisticated but simply stated. Indeed, the review chapter on evolution by natural selection provides an elegant, if brief, review of important recent advances in what is arguably the most theoretically charming story in science. The book also succeeds in at least addressing, if not exhaustively refuting, many of the more common bugaboos—untestability, teleology, genes=destiny, political misuse of Darwinism, etc.—which plague the reception of evolutionary tracts among biomedical and other audiences. On the medical side, the disease entities are accurately detailed and the evolutionary implications for epidemiology and pathophysiology well-drawn.

Thus the case is made that evolutionary biology is a useful but greatly underutilized basic science for biomedical research and practice. And though the importance of their ideas must ultimately be judged by the body of insights they provoke, I believe their potential utility to behavioral chronobiology is well worth exploring.

If Darwin's theory provides its own answer to the question "What is the meaning or purpose of life" (to reproduce), then it seems inevitable that the same theory would have a say about the meaning of health.

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SIGH-SAD NOTE

Diurnal Variation Type A (item H18 on the *Structured Interview Guide for the Hamilton Depression Rating Scale—Seasonal Affective Disorder Version* [SIGH-SAD]) is scored zero if the patient is not currently depressed. In the self-rating instrument (SIGH-SAD-SR), however, it is possible for the respondent to report diurnal variation even when Depressed Mood (item H1) is absent. Closer agreement between interview and self-rating scores will be obtained if SIGH-SAD-SR item H18 is re-scored as zero when item H1 has been corrected accordingly. If you have related questions, please contact Michael Terman, Ph.D., or Janet B.W. Williams, D.S.W., New York State Psychiatric Institute, 722 West 168th Street, New York, NY 10032, Fax 212-960-2584.

FLASH(LIGHT) POLL RESULTS

The *Flash(light) Poll* solicits opinion from the membership, primarily in the form of a yes/no response, concerning a current, hopefully provocative, issue. The feature was introduced in the October issue of *LTBR*, with results of that poll reported in the January issue. Here, the results of the latest poll are presented.

The issue for debate was: *"I believe SLTBR or another professional association should establish an accreditation program for light therapists."*

This is an important issue that has the potential to affect a substantial proportion of our membership. As such, we anticipated a large and vocal response to the poll. We were wrong.

Only 36 of you found the issue worthy of a response. Of the respondents, 10 were researchers, 12 were clinicians, and 7 identified themselves as both researcher and clinician; we heard from 1 patient/consumer, 2 manufacturers/distributors and a lighting consultant and a retired physician; 1 respondent was both a clinician and a patient/consumer, and another was both a patient/consumer and manufacturer/distributor. Responses came from 14 states in the U.S., 2 Canadian provinces, 5 European countries (including Eastern Europe) and Australia. Seven respondents used e-mail, 8 people faxed me, 19 of you used "snail mail", and two responded in person.

Of the 36 respondents, two-thirds believed that SLTBR (or another association) should establish an accreditation program for light therapists. Two respondents suggested accreditation either by SLTBR or by another association (the American Psychiatric Association, the American Psychological Association, or the National Board of Certified Counselors).

Many of the "YES" responses were accompanied by specific qualifying statements, several concerning who should be included:

"... accreditation should be established IF counselors are included."

"This should encompass MD's, psychologists, social workers and other allied health practitioners ..."

"... as long as MD's are not the only ones entitled to become accredited."

"A light therapist should be able to explain the phase response curve and

apply light accordingly. An accreditation program would ensure the basics."

"... may give boost to insurance reimbursement issue."

"NO" respondents wondered about the timeliness and practicality of accreditation:

"Wait until the "science and practice" of phototherapy are unequivocally established ..."

"... use does not seem that complicated; it should be taught in residency programs."

"I don't think (accreditation) is the best use of time and energy when so much needs to be done."

"... the tiny size of SLTBR precludes its arrogating accreditation judgments."

Since clinicians would perhaps be most affected by such an accreditation program, it was of interest to examine the breakdown in responses as a function of profession. Whereas, 70% of the researchers believed that accreditation was desirable, and five of the seven researcher/clinicians believed this, only half of the 12 clinicians responded "YES". A Fischer's exact test revealed that this distribution did not differ significantly from chance.

In summary, one rather depressing conclusion that can be drawn from the response rate to the current Poll question, is that better than 90% of our membership has no interest in, and/or no opinion on, the issue of accreditation for light therapists. Alternatively, one might interpret the low response rate in terms of seasonal effects: perhaps a large percentage of our membership was too busy attending to SAD treatment and research projects, (or too depressed themselves), to respond to the Flash(light) Poll.

In any case, Spring is just around the corner, and editorial hope blooms eternal. To wit, you will find a form containing the next item for debate enclosed in your Bulletin. Let us hear from you!

BULLETIN BOARD

WELCOME TO NEW MEMBERS

We welcome new members who have joined SLTBR since publication of the January 1995 issue:

Regular Members

Alex Van Bommel, M.D., Ph.D.	Ron Peled, M.D.
Naoto Yamada, M.D., Ph.D.	Yung S. Chung, M.D.

The response to SLTBR's 1995 membership drive has been enthusiastic. A list of new members joining during the drive will appear in the next bulletin.

SLTBR ANNUAL MEETING TO BE HELD JUNE 9-11 IN FRANKFURT

SLTBR's 7th Annual meeting will be held June 9-11, 1995, at the Johann Wolfgang Goethe-Universität, Frankfurt am Main, Germany. This first meeting of the SLTBR outside the United States provides clinicians and scientists from throughout the world an opportunity to meet and exchange information. A particular focus will be to invite colleagues from Eastern Europe to participate. Conference organizers are Burkhard Pflug and Wilfried Köhler.

Included on the program are:

- Concepts of chronobiology, photobiology, and neurophysiology underlying light therapy;
- Chronotherapy of seasonal and non-seasonal affective disorders and sleep disturbances;
- Pharmacologic treatment of circadian rhythm-related neuropsychiatric illness and sleep disorders;
- Forum: patent law and ethics for scientists: can the use of light and melatonin be patented?
- Festive evening with after-dinner speech by Jürgen Aschoff.

The Postgraduate Teaching Course will be "The Practice of Light Therapy." The language of the meeting is English; the teaching courses will be carried out in English and German.

For further information contact *Dr. Wilfried Köhler, Zentrum der Psychiatrie Heinrich-Hoffmanstr. 10, D-60 528 Frankfurt a.M., Germany, Fax (01149)69-6301 5936 (from the U.S.) or (xx49) 69-6301 5936; or contact SLTBR, 10200 W. 44th Ave., Suite 304, Wheat Ridge, CO USA 80033-2840, Tel 303-424-3697, Fax 303-422-8894, E-mail 5686814@mcimail.com.*

APSS ANNUAL MEETING

The APSS Annual Meeting will be held May 30-June 4, 1995 in Nashville, TN. The meeting will present many aspects of chronobiology and light in relation to sleep. Further information from *APSS, 1610 14th St. N.W., Suite 300, Rochester, MN 55901, Fax 507-287-6008.*

RHYTHMS, BEHAVIOUR, AND MOOD

A Symposium on Rhythms, Behavior, and Mood is being organized as a Festschrift for Professor Rudi van den Hoofdakker, June 7-8, 1995 in the Department of Biological Psychiatry, University of Groningen, The Netherlands, with international participation. Information can be obtained from the Secretariat, Biological Psychiatry, P.O. Box 30.001, NL-9700 RB Groningen, The Netherlands, Fax (31)-50-696 727.

UNDERSTANDING THE BIOLOGICAL CLOCK

The American Physiological Society will sponsor a consensus meeting this summer entitled "Understanding the Biological Clock—From Genetics to Physiology." It will take place at Dartmouth Medical School, Hanover, NH from July 8-12, 1995 and is organized by Jay C. Dunlap and Jennifer J. Loros. Information may be obtained from *APS Membership Services, 9650 Rockville Pike, Bethesda, MD 20814-3991, Fax 301-571-8313.*

NEW DIRECTIONS IN AFFECTIVE DISORDERS

The 2nd International Conference on New Directions in Affective Disorders, to be held in Jerusalem Sept. 3-8, 1995, will have two Symposia of particular relevance to SLTBR members: "Seasonal Affective Disorders" (organized by N. E. Rosenthal and A. Pande) and "Chronobiological Aspects of Affective Disorders" (organized by M. Berger and P. Lavie). Information can be obtained from *The Secretariat: Peltours-Te'um, POB 18388, Jerusalem 91082, Israel, Fax (972)-2-637 572.*

CHRONOBIOLOGY AND CHRONOTHERAPEUTICS

The World Conference on Chronobiology and Chronotherapeutics (under the patronage of a number of Rhythm Societies) will be held Sept. 6-10, 1995 in Ferrara, Italy. The abstract deadline is May 2, 1995. Further information can be obtained from *Francesco Portaluppi, WCC c/o Institute of Internal Medicine, University of Ferrara, via Savonarola 9, I-44100 Ferrara, Italy, Fax (39)-532-295 816.*

FEDERATION OF SLEEP RESEARCH SOCIETIES

The Second Intentional Congress of the World Federation of Sleep Research Societies will be held in Nassau, the Bahamas, September 12-16, 1995. Entitled *The Mystery of Sleep*, this congress is designed to bring together sleep researchers, clinicians and technicians from throughout the world. For further information contact *Global Events, Congress Secretariat, 710 N. Trenton Drive, Beverly Hills, CA 90210 USA. Tel 310-247-8004; fax 310-247-8457.*

LIGHT SYMPOSIUM CONFERENCE

The Light Symposium Foundation has scheduled its 1995 International Conference for October 9-11, 1995 in Atlanta, Georgia. The deadline for completed abstract forms is February 1995. For more information contact *Michael Holik, M.D., Ph.D., Boston University School of Medicine, 80 E. Concord Street, M-1013, Boston, MA 02118 USA. Tel 617-638-4545; fax 617-638-8882.*