Evidence of a Biological Effect of Light Therapy on the Retina of Patients with Seasonal Affective Disorder

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BACKGROUND: Retinal sensitivity anomalies have been reported in patients affected by seasonal affective disorder (SAD). We used the electroretinogram (ERG) to assess seasonal change in retinal function in patients with SAD and healthy participants, as well as in patients following 4 weeks of light therapy. METHODS: ERG assessments were obtained in 22 SAD patients (2 men, 20 women, mean age 31 +/- 9 years) in the fall/winter season before and after 2 and 4 weeks of light therapy and in summertime. Matched healthy participants (2 men, 14 women; mean age 29 +/- 8 years) were evaluated once in the fall/winter and once in summer. The 29-item Structured Interview Guide for the Hamilton Depression Rating Scale, Seasonal Affective Disorder version was administered. Standard ERG parameters were derived from the photopic and scotopic luminance response functions. Salivary melatonin concentration during ERG was assessed in both groups but during fall/winter assessments only. RESULTS: A significantly lower cone ERG maximal amplitude and lower rod sensitivity was found in SAD patients before light therapy compared with healthy participants. Following 4 weeks of light therapy, a normalization of cone and rod ERG function occurred. ERG parameters in the summer and melatonin concentrations in fall/winter were not significantly different between groups. CONCLUSIONS: Depressed patients with SAD demonstrate ERG changes in the winter compared with healthy comparison subjects with lower rod retinal sensitivity and lower cone maximal amplitude. These changes normalized following 4 weeks of light therapy and during the summer, suggesting that ERG changes are state markers for SAD.

A Controlled Trial of the Litebook Light-Emitting Diode (LED) Light Therapy Device for Treatment of Seasonal Affective Disorder (SAD).


BACKGROUND: Recent research has emphasized that the human circadian rhythm system is differentially sensitive to short wavelength light. Light treatment devices using efficient light-emitting diodes (LEDs) whose output is relatively concentrated in short wavelengths may enable a more convenient effective therapy for Seasonal Affective Disorder (SAD). METHODS: The efficacy of a LED light therapy device in the treatment of SAD was tested in a randomized, double-blind, placebo-controlled, multi-center trial. Participants aged 18 to 65 with SAD (DSM-IV major depression with seasonal pattern) were seen at Baseline and Randomization visits separated by 1 week, and after 1, 2, 3 and 4 weeks of treatment. Hamilton Depression Rating Scale scores (SIGH-SAD) were obtained at each visit. Participants with SIGH-SAD of 20 or greater at Baseline and Randomization visits were randomized to active or control treatment: exposure to the Litebook LED treatment device (The Litebook Company Ltd., Alberta, Canada) which delivers 1,350 lux white light (with spectral emission peaks at 464 nm and 564 nm) at a distance of 20 inches or to an inactivated negative ion generator at a distance of 20 inches, for 30 minutes a day upon awakening and prior to 8 A.M. RESULTS: Of the 26 participants randomized, 23 completed the trial. Mean group SIGH-SAD scores did not differ significantly at randomization. At trial end, the proportions of participants in remission (SIGH-SAD less than 9) were significantly greater (Fisher’s exact test), and SIGH-SAD scores, as percent individual score at randomization, were
significantly lower (t-test), with active treatment than with control, both in an intent-to-treat analysis and an observed cases analysis. A longitudinal repeated measures ANOVA analysis of SIGH-SAD scores also indicated a significant interaction of time and treatment, showing superiority of the Litebook over the placebo condition. CONCLUSION: The results of this pilot study support the hypothesis that light therapy with the Litebook is an effective treatment for SAD.

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The Can-SAD Study: A Randomized Controlled Trial of the Effectiveness of Light Therapy and Fluoxetine in Patients With Winter Seasonal Affective Disorder.


Lam RW, Anthony, Levitt J, Levitan RD, Enns MW, Morehouse R, Michalak EE, Tam EM.

OBJECTIVE: Light therapy and antidepressants have shown comparable efficacy in separate studies of seasonal affective disorder treatment, but few studies have directly compared the two treatments. This study compared the effectiveness of light therapy and an antidepressant within a single trial. METHOD: This double-blind, randomized, controlled trial was conducted in four Canadian centers over three winter seasons. Patients met DSM-IV criteria for major depressive disorder with a seasonal (winter) pattern and had scores ≥ 23 on the 24-item Hamilton Depression Rating Scale. After a baseline observation week, eligible patients were randomly assigned to 8 weeks of double-blind treatment with either 1) 10,000-lux light treatment and a placebo capsule, or 2) 100-lux light treatment (placebo light) and fluoxetine, 20 mg/day. Light treatment was applied for 30 minutes/day in the morning with a fluorescent white-light box; placebo light boxes used neutral density filters. RESULTS: A total of 96 patients were randomly assigned to a treatment condition. Intent-to-treat analysis showed overall improvement with time, with no differences between treatments. There were also no differences between the light and fluoxetine treatment groups in clinical response rates (67% for each group) or remission rates (50% and 54%, respectively). Post hoc testing found that light-treated patients had greater improvement at 1 week but not at other time points. Fluoxetine was associated with greater treatment-emergent adverse events (agitation, sleep disturbance, palpitations), but both treatments were generally well-tolerated with no differences in overall number of adverse effects. CONCLUSIONS: Light treatment showed earlier response onset and lower rate of some adverse events relative to fluoxetine, but there were no other significant differences in outcome between light therapy and antidepressant medication. Although limited by lack of a double-placebo condition, this study supports the effectiveness and tolerability of both treatments for seasonal affective disorder and suggests that other clinical factors, including patient preference, should guide selection of first-line treatment.

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Terman M, Terman JS.

Bright light therapy for seasonal affective disorder (SAD) has been investigated and applied for over 20 years. Physicians and clinicians are increasingly confident that bright light therapy is a potent, specifically active, nonpharmaceutical treatment modality. Indeed, the domain of light treatment is moving beyond SAD, to nonseasonal depression (unipolar and bipolar), seasonal flare-ups of bulimia nervosa, circadian sleep phase disorders, and more. Light therapy is simple to deliver to outpatients and inpatients alike, although the optimum dosing of light and treatment time of day requires individual adjustment. The side-effect profile is favorable in comparison with medications, although the clinician must remain vigilant about emergent hypomania and autonomic hyperactivation, especially during the first few days of treatment. Importantly, light therapy provides a compatible adjunct to antidepressant medication, which can result in accelerated improvement and fewer residual symptoms.
The Efficacy of Light Therapy in the Treatment of Mood Disorders
A Review and Meta-Analysis of the Evidence


Objective: The purpose of this study was to assess the evidence base for the efficacy of light therapy in treating mood disorders.

Method: The authors systematically searched PubMed (January 1975 to July 2003) to identify randomized, controlled trials of light therapy for mood disorders that fulfilled predefined criteria. These articles were abstracted, and data were synthesized by disease and intervention category.

Results: Only 13% of the studies met the inclusion criteria. Meta-analyses revealed that a significant reduction in depression symptom severity was associated with bright light treatment (eight studies, having an effect size of 0.84 and 95% confidence interval [CI] of 0.60 to 1.08) and dawn simulation in seasonal affective disorder (five studies; effect size=0.73, 95% CI=0.37 to 1.08) and with bright light treatment in nonseasonal depression (three studies; effect size=0.53, 95% CI=0.18 to 0.89). Bright light as an adjunct to antidepressant pharmacotherapy for nonseasonal depression was not effective (five studies; effect size=−0.01, 95% CI=−0.36 to 0.34).

Conclusions: Many reports of the efficacy of light therapy are not based on rigorous study designs. This analysis of randomized, controlled trials suggests that bright light treatment for seasonal affective disorder and bright light for nonseasonal depression are efficacious, with effect sizes equivalent to those in most antidepressant pharmacotherapy trials. Adopting standard approaches to light therapy’s specific issues (e.g., defining parameters of active versus placebo conditions) and incorporating rigorous designs (e.g., adequate group sizes, randomized assignment) are necessary to evaluate light therapy for mood disorders.

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Psychic and Somatic Anxiety Differentially Predict Response to Light Therapy in Women with Seasonal Affective Disorder.
J of Affect Disord 2005;88:163–166

MacKenzie B, Levitan RD.

Objective: To examine whether psychic and/or somatic anxiety predict responsiveness to light therapy in women with winter Seasonal Affective Disorder (SAD).

Design: Eighty-one women with SAD were administered a standard 10-day trial of light therapy administered for one-half hour in the early morning. Using a multiple regression model, baseline somatic and psychic anxiety item scores were used to predict percentage change scores on the 29-item SIGH-SAD post treatment. Baseline scores for weight gain, hypersomnia and the total SIGH-SAD were also included as predictor variables.

Results: The regression model was highly significant (F =4.63, df =5, 75; p =.001; model R2=.236), with both psychic anxiety and somatic anxiety contributing significantly to the model. Consistent with prior work using antidepressant medication in non-seasonal depression, psychic anxiety was positively correlated with outcome, while somatic anxiety negatively predicted outcome.

Conclusions: In SAD, psychic and somatic anxiety scores at baseline appear to be independent and opposite predictors of light therapy response. These effects were independent of baseline scores for weight gain and hypersomnia, two previously established predictors of response to light. These findings may be an important consideration in the design and interpretation of light therapy studies of SAD.

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Decreasing Tsh Levels in Patients with Seasonal Affective Disorder (SAD) Responding to 1 Week of Bright Light Therapy.

Martiny K, Simonsen C, Lunde M, Clemmensen L, Bech P.
**BACKGROUND:** Seasonal Affective Disorder (SAD) is characterised by lowered mood and atypical depressive symptoms such as hypersomnia, weight gain and fatigue. These symptoms seem associated with hypothyroidism, but the results of evaluations of the thyroid function in SAD patients have been conflicting, most likely due to the very small number of observations. **METHODS:** In total, 83 patients fulfilling the DSM-III-R criteria for SAD were treated with bright light for 1 week in an open trial. Thyroid function was evaluated by TSH (thyroid-stimulating hormone), T(4) (thyroxine) and T(3) (triiodothyronine) levels at baseline and after 1 week of bright light treatment. **RESULTS:** The response rate in terms of a 50% reduction of pre-treatment scores on the Hamilton Depressions Rating Scale (HAM-D(17)) was 61%. The TSH levels in all 83 patients decreased significantly from 1.57 at baseline to 1.30 at endpoint. In the group of responders (n=52) the TSH levels decreased significantly from 1.71 to 1.37, while in the group of non-responders (n=31) the decrease in TSH levels was not statistically significant. **CONCLUSIONS:** During 1 week of bright light therapy the TSH levels in SAD patients were reduced, with the highest reduction in the group of patients responding to light therapy.

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**A Comparison of Open Treatment of Seasonal Major and Minor Depression with Light Therapy.**


Levitt AJ, Lam RW, Levitan R.

**BACKGROUND:** Although several investigators have described a milder form of seasonal affective disorder (SAD), called subsyndromal SAD, little is known about the effect of light therapy in this group. The current study evaluates 3 weeks of open treatment with light therapy in SAD and subsyndromal SAD patients. **METHODS:** Subjects with major or minor depression according to DSM-IV with a seasonal pattern were recruited during the winter of 1998-1999 from clinic patients and media advertising. Subjects were commenced on open treatment of morning light therapy, for 30 min daily using a new fluorescent light therapy unit that produced approximately 5,000 lux at a distance of 12 inches. The treatment lasted 3 weeks and at the end of the first and second week of treatment the duration of exposure could be increased to a maximum of 60 min at the discretion of the clinician. The Structured Interview Guide for the Hamilton Depression Rating Scale-SAD version (SIGH-SAD) was administered weekly to evaluate outcome. Response was defined in a variety of ways to reflect the fact that subsyndromal SAD subjects had milder symptoms. **RESULTS:** Forty-six subjects entered treatment and 44 (SAD, n = 29, subsyndromal SAD, n = 15) completed at least 2 weeks. Response rates were generally similar in SAD subjects (64-69%) and subsyndromal SAD (40-67%) patients. There was a trend for longer exposure to be associated with better outcome. **CONCLUSIONS:** Light therapy may be an effective treatment for subjects with both major and minor depression with a seasonal pattern. Optimal duration, for the light therapy unit used in this study, is likely 45-60 min daily.

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**Bright Light Therapy of Subsyndromal Seasonal Affective Disorder in the Workplace: Morning vs. Afternoon Exposure.**


Avery DH, Kizer D, Bolte MA, Hellekson C.

**OBJECTIVE:** Bright light therapy in seasonal affective disorder (SAD) has been studied extensively. However, little attention has been given to subsyndromal seasonal affective disorder (SSAD) or the use of bright light in the workplace. Many patients using bright light boxes complain of the inconvenience of use. Much of this inconvenience involves the often-recommended early timing of the bright light therapy. Patients, who already have difficulty awakening, often have difficulty using the bright light therapy soon after awakening before going to work. If bright light could be used effectively in the workplace, the treatment would be more convenient; the improved convenience would probably improve compliance. In
this study, we studied the effectiveness of bright light therapy in subjects with SSAD in the workplace, comparing morning bright light with afternoon bright light. **METHOD:** Morning and afternoon bright light treatment (2500 lux) were compared in 30 subsyndromal seasonal affective disorder patients using the bright light therapy in the workplace. Hamilton Depression Ratings and subjective measures of mood, energy, alertness and productivity were assessed before and after 2 weeks of light therapy. **RESULTS:** Both morning and evening bright light significantly decreased the depression ratings and improved the subjective mood, energy, alertness and productivity scores. However, there were no significant differences between the two times of administration of the bright light treatment. Both bright light treatments were well tolerated. **CONCLUSION:** Bright light given in the workplace improves subjective ratings of mood, energy, alertness and productivity in SSAD subjects. Morning and afternoon bright lights resulted in similar levels of improvement.
Early Response to Light Therapy Partially Predicts Longterm Antidepressant Effects.


Sher L, Matthews JR, Turner EH, Postolache TT, Katz KS, Rosenthal NE.

OBJECTIVE: To determine if the antidepressant effect of 1 hour of light therapy is predictive of the response after 1 and 2 weeks of treatment in patients with seasonal affective disorder (SAD).

PATIENTS: Twelve patients with SAD. SETTING: National Institutes of Health Clinical Center, Bethesda, Md.

INTERVENTIONS: Light therapy for 2 weeks. OUTCOME MEASURES: Scores on the Seasonal Affective Disorder Version of the Hamilton Depression Rating Scale (SIGH-SAD) on 4 occasions (before and after 1 hour of light therapy and after 1 and 2 weeks of therapy) in the winter when the patients were depressed. Change on typical and atypical depressive scores at these time points were compared.

RESULTS: Improvement of atypical depressive symptoms after 1 hour of light therapy positively correlated with improvement after 2 weeks of therapy. CONCLUSION: In patients with SAD, the early response to light therapy may predict some aspects of long-term response to light therapy, but these results should be treated with caution until replicated.

An Open Trial of Light Therapy for Women with Seasonal Affective Disorder and Comorbid Bulimia Nervosa.


Lam RW, Lee SK, Tam EM, Grewal A, Yatham LN.

OBJECTIVE: Many patients with seasonal affective disorder (SAD) have dysfunctional eating behaviors. Conversely, many women with bulimia nervosa have marked winter worsening of mood and bulimic symptoms. Controlled studies of light therapy in SAD and in bulimia nervosa have shown beneficial effects on mood and binge/purge symptoms. We explored the clinical use of light therapy in women with SAD who also had comorbid bulimia nervosa.

METHOD: Twenty-two female patients diagnosed using DSM-IV criteria with both bulimia nervosa and major depressive disorder with a seasonal (winter) pattern were treated with an open design, 4-week trial of light therapy (10,000 lux fluorescent light box with an ultraviolet filter, 30 to 60 minutes per day in the early morning). Patients were assessed before and after treatment with depression scales and with binge/purge diaries.

RESULTS: Light therapy resulted in significant improvement in mood, with a mean 56% reduction in 29-item Hamilton Rating Scale for Depression scores following treatment (p < .001). The frequency of binges and purges per week also significantly decreased (p < .001) from baseline by a mean of 46% and 36%, respectively. Two (9%) of 22 patients became abstinent of binge/ purge episodes, compared with 10 (45%) of 22 patients who met criteria for remission of depressive symptoms. The light therapy was well tolerated by patients.

CONCLUSION: These results suggest that therapeutic effects of light therapy on mood and bulimic symptoms in patients with SAD and comorbid bulimia nervosa are sustained over at least 4 weeks. However, the low abstinence rate in bulimic symptoms indicates that light therapy may be most effectively used as an adjunctive treatment to medications and/or psychotherapy for bulimia nervosa.

Bright Light Improves Vitality and Alleviates Distress in Healthy People.

J Affect Disord 2000;57:55–61

Partonen T, Lönnqvist J.

BACKGROUND: The relative shortage of light during the decreasing photoperiod may compromise well-being. Earlier studies suggest that bright-light exposure may be of help to alleviate winter-bound symptoms.

METHODS: We carried out a field study with exposure to bright light on office employees
during winter. **RESULTS:** Repeated bright-light exposure improved vitality and reduced depressive symptoms. The benefit was observed not only in healthy subjects with season-dependent symptoms but also in those not having the seasonal variation. **CONCLUSIONS:** Bright-light exposure during winter appears to be effective at improving the health-related quality of life and alleviating distress in healthy subjects. **CLINICAL IMPLICATIONS:** Administration of bright light is a useful option to improve vitality and mood among subjects working indoors in wintertime. **LIMITATIONS OF STUDY:** Our field setting used self-reports, not interviews, for the assessment of outcome.

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**Morning vs Evening Light Treatment of Patients with Winter Depression.**


**BACKGROUND:** According to the phase-shift hypothesis for winter depression, morning light (which causes a circadian phase advance) should be more antidepressant than evening light (which causes a delay). Although no studies have shown evening light to be more antidepressant than morning light, investigations have shown either no difference or morning light to be superior. The present study assesses these light-exposure schedules in both crossover and parallel-group comparisons. **METHODS:** Fifty-one patients and 49 matched controls were studied for 6 weeks. After a prebaseline assessment and a light/dark and sleep/wake adaptation baseline week, subjects were exposed to bright light at either 6 to 8 AM or 7 to 9 PM for 2 weeks. After a week of withdrawal from light treatment, they were crossed over to the other light schedule. Dim-light melatonin onsets were obtained 7 times during the study to assess circadian phase position. **RESULTS:** Morning light phase-advanced the dim-light melatonin onset and was more antidepressant than evening light, which phase-delayed it. These findings were statistically significant for both crossover and parallel-group comparisons. Dim-light melatonin onsets were generally delayed in the patients compared with the controls. **CONCLUSIONS:** These results should help establish the importance of circadian (morning or evening) time of light exposure in the treatment of winter depression. We recommend that bright-light exposure be scheduled immediately on awakening in the treatment of most patients with seasonal affective disorder.

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**A Controlled Trial of Light Therapy for the Treatment of Pediatric Seasonal Affective Disorder.**


**OBJECTIVE:** To evaluate the efficacy of light therapy for the treatment of pediatric seasonal affective disorder (SAD). **METHOD:** 28 children (aged 7 to 17 years) at two geographically distinct sites were enrolled in a double-blind, placebo-controlled, crossover trial of bright-light treatment. Subjects initially entered a week-long baseline period during which they wore dark glasses for an hour a day. They were then randomly assigned to receive either active treatment (1 hour of bright-light therapy plus 2 hours of dawn simulation) or placebo (1 hour of clear goggles plus 5 minutes of low-intensity dawn simulation) for 1 week. The treatment phase was followed by a second dark-glasses phase lasting 1 to 2 weeks. After this phase, the children received the alternate treatment. Response was measured using the parent and child versions of the Structured Interview Guide for the Hamilton Depression Rating Scale, Seasonal Affective Disorders version (SIGH-SAD). **RESULTS:** Data were analyzed as change from baseline. SIGH-SAD-P total depression scores were significantly decreased from baseline during light therapy compared with placebo (one-way analysis of variance, rho = .009), and no differences were found between the placebo and control phases. Subscores of atypical and typical depression were also significantly decreased during the active treatment (rho = .004 and .028, respectively). A similar trend was noted with the SIGH-SAD-C, but this did not reach significance. At the end of the study, 78% of the parents
questioned and 80% of the children questioned rated light therapy as the phase during which the child "felt best." **CONCLUSION:** Light therapy appears to be an effective treatment for pediatric SAD.