

Bright light therapy for bipolar depression



ANDRZEJ WOJCIK

Suhayl J. Nasr, MD

Professor of Psychiatry
Indiana University School
of Medicine
Indianapolis, Indiana
Chief of Behavioral
Health Services
Beacon Health System
South Bend, Indiana

Ahmed Z. Elmaadawi, MD

Adjunct Assistant Professor
of Psychiatry
Indiana University School
of Medicine
Indianapolis, Indiana
Director of Interventional
Psychiatry Division
Beacon Health System
South Bend, Indiana

**Rikinkumar Patel, MD,
MPH**

Department of Psychiatry
Griffin Memorial Hospital
Norman, Oklahoma

Evidence suggests efficacy as an adjunctive treatment

Bright light therapy (BLT) refers to the use of bright light to treat symptoms of depression. BLT was initially prescribed as a treatment for patients with seasonal affective disorder.¹ It was later found helpful for nonseasonal depression,² premenstrual dysphoric disorder, postpartum depression, and phase shift circadian disorders, including for patients with dementia whose cognitive function improved after treatment with BLT.³ More recent studies suggest year-round benefit for nonseasonal depression.² The American Psychiatric Association practice guidelines for the treatment of depression list BLT as an alternative and/or addition to pharmacologic and psychological treatment.⁴ BLT also may be beneficial for patients who are in the depressive phase of bipolar illness.

This article describes the evidence, rationale for use, mechanism of action, benefits, and safety profile of BLT for treating patients with bipolar depression.

Circadian rhythm disruption in bipolar disorder

Clinical manifestation. Patients with bipolar disorder (BD) spend more time in depression than in mania.⁵ Sleep disturbance is a core symptom of BD; patients typically have little need for sleep during a manic episode, and excess sleepiness during a depressive episode. Sleep complaints can be both precipitating factors and consequences of mood disorders. Patients with seasonal depression have excess sleepiness and weight gain in the winter followed by hypomanic-like symptoms in the spring, including decreased need for sleep and weight loss with psychomotor activation. In a recent review of sleep

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problems in patients with BD, Steinar et al⁶ reported that 20% of patients with euthymic mood in bipolar disorder experience a sleep disorder. Circadian disruption and “eveningness” (being more active during the evening) have been associated with mood episodes, functional impairment, poor quality of life, and treatment resistance.⁷⁻¹⁰

Pathophysiology. Existing hypotheses for the biological mechanism underlying dysregulation of circadian rhythm in BD include changes in melatonin levels, expression of melatonin receptors in the CNS, and daily cortisol profiles.¹¹ Genetic evidence also links circadian rhythm dysregulation with BD. Two polymorphisms on the circadian locomotor output cycles kaput (CLOCK) gene that control circadian rhythm—aryl hydrocarbon receptor nuclear translocator-like (ARNTL) and timeless circadian clock (TIMELESS)—have been linked to lithium responsiveness in BD.¹² In addition, *Per2*, *Cry1*, and *Rev-Erb α* expression—all components of the circadian clock—have been found to increase individual susceptibility to the therapeutic effects of lithium in mice.¹³ In addition, circadian rhythm dysregulation is associated with metabolic problems encountered by patients with BD, including weight gain, diabetes mellitus, and cardiovascular disease.¹⁴

Rationale for use

Regulation of a patient’s circadian rhythm disruption is a potential treatment for BD. Hashimoto et al¹⁵ demonstrated that mid-day bright light exposure can phase advance and increase the amplitude of nocturnal melatonin production in healthy individuals. Morning light therapy has been shown to increase blood serotonin throughout the day in both healthy individuals and in patients with nonseasonal depression; the effect was apparent with light intensities as low as 50 lux.¹⁶ Lithium may exert its therapeutic effect through its influence on the retino-hypothalamic-pineal tract and thus its effect on melatonin secretion.¹⁷

BLT is a logical choice to treat the depression phase of BD when exposure to sunlight is not feasible due to geographical location,

season, or other factor. For patients who live in areas that receive frequent sunshine, an outside stroll for half an hour will likely achieve similar benefit to BLT.

The precise mechanism of action of BLT for bipolar depression has not yet been determined. It may be attributed to a phase-resetting effect via melanopsin and the suprachiasmatic nucleus (*Box*,¹⁸⁻²⁴ page 30).

BLT for BD: What’s the evidence?

Several studies and case reports have evaluated the use of BLT for bipolar depression. The number of participants in these studies is small, and there is no uniformity of methodology or patient selection.

Dauphinais et al (2012)²⁵ randomly assigned 44 patients with bipolar depression to BLT or a high-density or low-density negative ion generator for 8 weeks. They reported no difference in outcome between the various groups (50% vs 55.6%, remission and response rate). Only one patient in each group showed a switch to hypomania.

Carmadese et al (2015)²⁶ reported an open-label study of adjunctive BLT in 31 difficult-to-treat patients with depression (16 unipolar and 15 bipolar). Significant improvement was noted within 3 weeks and was sustained in 1 patient with bipolar depression 5 weeks after cessation of BLT.

Papatheodorou and Kutcher (1995)²⁷ treated 7 adolescents with bipolar depression with adjunctive BLT (10,000 lux twice per day). Three patients showed a marked response (>70% decrease from baseline Beck Depression Inventory and Symptom Check List scores). Two patients had a moderate response (40% to 47% decrease) and 2 patients obtained mild to no response. There were no reported adverse effects.

Benedetti et al (2014)²⁸ studied 141 patients with treatment-resistant bipolar depression. Approximately one-quarter (23%) had a history of attempted suicide, and 83% had a history of drug resistance. The authors found a combination of total sleep deprivation, BLT, and lithium rapidly decreased suicidality and improved patients’ depressive symptoms.

Liebenluft et al (1995)²⁹ administered 13 trials of BLT to 9 patients with rapid-cycling

Clinical Point

Circadian rhythm dysregulation is associated with metabolic problems in patients with bipolar disorder



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BLT for bipolar depression

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BLT can be used to treat bipolar depression when exposure to sunlight is not feasible due to geographical location or season

Box

Bright light therapy: How it works

The mechanism of action of bright light therapy is yet to be elucidated. The suprachiasmatic nucleus (SCN) in the hypothalamus is the center of circadian rhythm regulation and receives direct input from the retina through the retinohypothalamic tract.¹⁸ Melanopsin, a short-wavelength, light-sensitive G-protein-coupled receptor located in human retinal ganglion cells, is known to transduce short-wavelength light signals into neural signals.¹⁹ Since melanopsin is primarily responsible for resetting the timing of the SCN, suppressing pineal gland melatonin secretion and improving alertness and electroencephalogram-derived correlates of arousal,²⁰ short-wavelength light with a low light intensity might be a better stimulator for melanopsin-containing retinal ganglion cells and the behaviors mediated via this photoreceptor system.^{21,22} Whether the antidepressant effect of light is also related to its alerting property is unclear.²³ However, the acute alerting and performance-enhancing effects of light are increasingly taken into account for the design of indoor light standards in office environments.²⁴ Response to light therapy is thus attributed to its phase-resetting effect.

BD during a 3-month period. Five patients received the treatment in the morning, 5 around midday, and 3 in the evening. Patients who received BLT at midday had the best outcome, while 3 of the 5 patients who received morning BLT developed unstable mood. The authors recommended titrating the duration of light exposure so that patients could skip a treatment if their mood was trending toward hypomania.

Sit et al (2007)³⁰ evaluated BLT in a case series of 9 women with bipolar I or II disorder in the depression phase. Patients were exposed to 50 lux of red light for 2 weeks, and then they received 7,000 lux BLT for 15, 30, and 45 minutes daily for 2 weeks (4 patients received morning light and 5 received midday light). Mood was assessed using the Structured Interview Guide for the Hamilton Depression Rating Scale with Atypical Depression Supplement and the Mania Rating Scale. Of the 4 patients receiving morning BLT, one patient had a full response and the other 3 developed hypomania. Of the 5 patients who received

midday BLT, 2 achieved full response, 2 showed early improvement but required a dose increase, and one remained depressed but had a full response when she was switched to morning BLT.

Tseng et al (2016)³¹ reported a meta-analysis of BLT for bipolar depression that included a total of 567 patients from 11 studies. They reported significant improvement with BLT alone or in combination with antidepressants or total sleep deprivation. They also reported significant improvement with BLT in 130 patients who were not receiving other treatments. There was no difference in the frequency of mood shifts between patients on BLT alone or in combination with other modalities. The authors reported no mood shift in any of the patients receiving concurrent mood stabilizers. They also reported no difference with the color of light, gender, or duration of illness.

Yorguner et al (2017)³² conducted a 2-week randomized, single-blind study of BLT as an add-on treatment for 32 patients with bipolar depression. Patients were randomly assigned to BLT or dim light, which they were administered each morning for 30 mins for 2 weeks. Sixteen patients who received BLT showed a significantly greater reduction in Hamilton Depression Rating Scale scores (mean score of 24 at baseline down to 12) compared with 16 patients who received dim light (mean score of 24 at baseline down to 18). The authors also reported remission in 4 out of 4 patients who had seasonal depression, compared with 3 out of 12 who did not have seasonal depression (the other 9 showed response but not remission).

Zhou et al (2018)³³ conducted a multicenter, randomized, single-blind clinical trial of 63 patients with bipolar depression. Thirty-three patients received morning BLT, and 30 received dim red light therapy (control group). The authors reported a significantly higher response rate in the BLT group (78%) compared with the control group (43%).

Sit et al (2018)³⁴ conducted a 6-week randomized, double-blind, placebo-controlled trial of BLT vs dim red light in patients with bipolar I or II depression. Twenty-three patients were administered 7,000 lux

bright white light, and 23 patients received 50 lux dim red light, at midday 5 days a week. The light dose was increased by 15 minutes every week up to 60 minutes by Week 4, unless the patient achieved remission. Patients were maintained on their usual medications, which included mood stabilizers and/or antidepressants. At Week 6, the group randomized to BLT had a significantly higher remission rate (68%) compared with patients who received dim red light (22%). Improvement was noted by Week 4. Patients receiving BLT also had significantly fewer depressive symptoms, and no mood polarity switch was noted.

Prescribing bright light therapy

Light box selection criteria. When selecting a light box or related BLT treatment apparatus, the Center for Environmental Therapeutics recommends consideration of the following factors³⁵:

- clinical efficacy
- ocular and dermatologic safety
- visual comfort.

The intensity of the light hitting the cornea depends on the distance from the light. In our experience, when the patient is facing the box it should provide 10,000 lux when he or she is 1 foot away at approximately a 45° angle (1 lux = 1 lumen per square meter). The light box selected should emit full spectrum white light with UV filter. The newest filters use LED, which is less expensive and more durable. Typically, we've found that it is most convenient for patients to use the light box in the morning before 9 AM, but around noon is preferred for patients with BD. If using a light box is not feasible, we suggest the use of dawn light by the bedside before waking in the morning. Again, it is preferable to get some sunshine outdoors while taking a walk as long as geographical location and weather conditions permit.

Bottom Line

Evidence suggests that bright light therapy is an effective, well tolerated, and affordable adjunct treatment for bipolar depression. Exposure to 5,000 to 7,000 lux around noon for 15 to 60 minutes will enhance the remission rate.

Related Resource

• Mostert M, Dubovsky S. When bipolar treatment fails: what's your next step? *Current Psychiatry*. 2008;7(1): 39-46.

Drug Brand Name

Lithium • Eskalith, Lithobid

Selecting a dose. The dose received is determined by the intensity emitted from the light source, distance from the light box, and duration of exposure.³⁶ Begin with midday light therapy between 12 noon and 2 PM at a daily dose of 15 minutes, and increase by 15 minutes every 2 weeks until the patient has achieved a euthymic mood.³⁴ Patients need not stare directly into the light source as long as the light is able to meet the eye at an angle of 30° to 60°.³⁵ The upper limit of midday light is 45 to 60 minutes, beyond which patients are more likely to have difficulty with adherence. Because morning BLT also may be effective, consider a change to morning light at a starting dose of 15 minutes for patients who respond partially or minimally to 45 to 60 mins of midday light, then increase it every week by an additional 7 to 15 mins.³⁵ For patients who respond to BLT, it is reasonable to continue light therapy for 12 months after remission to prevent relapses, similar to the recommendations for antidepressant therapy.³⁴

Monitor for adverse effects. Generally, BLT is well tolerated.³⁷ Adverse effects are rare; the most common ones include headache, eyestrain, nausea, and agitation.³⁸ One study found no adverse ocular effects from light therapy after 5 years of treatment.³⁹ Adverse effects tend to remit spontaneously or after dose reduction.³⁵ Evening administration of BLT may increase the incidence of sleep disturbances.⁴⁰ Like other biologic

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Use of BLT around noon is preferred for patients with bipolar depression



BLT for bipolar depression

Clinical Point

Exposure to 5,000 to 7,000 lux for 15 to 60 minutes may enhance remission rates

treatments for bipolar depression, BLT can precipitate manic/hypomanic and mixed states in susceptible patients, although the light dose can be titrated against emergent symptoms of hypomania.⁴¹

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