



Light therapy in the treatment of patients with bipolar depression: A meta-analytic study



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Abstract

Light therapy (LT) has been widely used in the treatment of seasonal affective disorder. Recently some evidence indicated that LT may play a role in bipolar depression, either as monotherapy or in combination with total sleep deprivation (TSD). However, the studies examining the treatment effect of LT in bipolar depression resulted in inconsistent findings. To clarify the role of LT in the disorder, we conducted a meta-analysis to compare the efficacy of LT in the treatment of bipolar depression. The results of individual studies were synthesized by a random effects model. Nine studies including 489 patients with bipolar depression were included in this current meta-analysis. We found that disease severity was significantly decreased after LT, in both with and without TSD, and with concomitant medication ($p < 0.001$). Augmentation treatment with LT significantly decreased disease severity compared to treatment without LT ($p = 0.024$). Our results highlight the significant efficacy of LT, either as monotherapy or in combination with TSD, in the treatment of bipolar depression. However, the

Abbreviations: LT, light therapy; BD-D, bipolar disorder, depressive episode; TSD, total sleep deprivation; CI, confidence interval; HAM-D, Hamilton depression rating scale; SIGH-SAD, structured interview guide for the Hamilton depression rating scale, seasonal affective disorder; POMS-B, profile of mood states, brief; BDI, Beck depression inventory; ESs, effect sizes; PRISMA, preferred reporting items for systematic reviews and meta-analyses

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detailed mechanism of LT still remains elusive. Further well-designed controlled trials are required to investigate the optimal intensity and frequency of LT in the treatment of bipolar depression.

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1. Introduction

Bipolar disorder, depressive episode (BD-D) is a complicated psychiatric illness which can lead to high rates of morbidity and the risk of suicide (Wulsin et al., 1999), with a reported 30% increase in suicide attempts with about 20% of such attempts resulting in death (Chen and Dilsaver, 1996; Jamison, 1986; Leverich et al., 2003; Osby et al., 2001). The primary goal of treatment for BD-D is to rapidly alleviate the severity of illness and prevent the risk of suicide. However, the response to traditional treatment for BD-D is slow, at an average of 2 to 8 weeks (Jick et al., 2004; Machado-Vieira et al., 2008; Walsh et al., 2002). In addition, the response rate to antidepressant treatment is also poor. At least 40% of depressive patients respond poorly to initial antidepressant therapy, and most of them respond unsatisfactorily to several types of antidepressants (Crown et al., 2002). In addition, the usage of antidepressants can induce iatrogenic phase-switching to manic episodes in patients with BD-D. Although some studies have proposed clinical guidelines for the treatment of BD-D such as augmentation with lithium or valproate, these strategies may lead to complications such as renal toxicity or hepatic damage (Baldessarini et al., 2003; Castellani et al., 2015; Grunze et al., 2010; Kendall et al., 2014).

Light therapy, also called phototherapy, involves the use of a bright artificial light, either white or other colors, with or without total sleep deprivation (TSD). It has been used in psychiatric practice for a long time (Mueller, 1989), and it has been widely used for the treatment of seasonal affective disorder (Avissar et al., 1999; Terman et al., 1989). The main mechanism by which light therapy regulates mood is unclear. It has been suggested to have a modulating effect on 5-HT function (Benedetti et al., 2003a), melatonin regulation (Lewy et al., 1980), and on the synchronization of the circadian rhythm (Terman et al., 2001; Wehr et al., 2001; Wever et al., 1983). Therefore, light therapy is frequently combined with TSD in clinical practice (Benedetti et al., 2010; Colombo et al., 2000). Abnormalities in melatonin secretion and circadian rhythm have been reported in patients with bipolar disorder (Bhattacharjee, 2007; Neumeister et al., 1997, 1998; Plante and Winkelman, 2008), and modification of circadian rhythm has been reported to rapidly improve the symptoms of mood disorder (Benedetti et al., 2007a; Bunney and Potkin, 2008).

Most previous clinical trials and studies on light therapy have focused on seasonal affective disorder (Avissar et al., 1999; Bauer et al., 1994; Pjrek et al., 2004). However, light therapy has attracted increasing attention for the treatment of other affective disorders, especially BD-D and major depressive disorder (MDD). Most studies on the efficacy of light therapy for BD-D or MDD have combined

light therapy with TSD or psychotropic agents (Benedetti et al., 2010, 2003a, 2014), of which only a few have involved a case-control design for clinical trials (Colombo et al., 2000; Kripke et al., 1992; Wu et al., 2009). Therefore, in order to clarify the role of light therapy in BD-D, we performed this meta-analysis to investigate whether light therapy, either in the form of monotherapy or in combination with other treatment, can alleviate the severity of depression.

2. Experimental procedures

2.1. Literature search and screening

A systematic article search using the PubMed electronic platform at the National Library of Medicine and the ClinicalTrials.gov website (<https://clinicaltrials.gov>) was conducted by two independent authors (Yen-Wen Chen and Ping-Tao Tseng). When there was inconsistent selection or lack of agreement, another senior psychiatrist (Ching-Kuan Wu) would make the final judgment and decision. The search was performed using the key words “(Phototherapy OR light therapy) AND (bipolar disorder)” for all articles available in PubMed and “(light therapy) AND (bipolar disorder)” on the ClinicalTrials.gov website until October 29, 2015. The limitation was articles written in English. The search process in this meta-analysis was divided into two subgroups. Initially, all articles that included the keywords and were written in English were collected, and the titles and abstracts of all these articles were screened by Kun-Yu Tu to determine whether they were potentially eligible for inclusion in this meta-analysis. When there was disagreement on eligibility, we reached agreement through consensus. All reports that were not related to the application of light therapy in bipolar disorder were excluded. We then screened all of the selected articles using the following inclusion criteria: (1) articles discussing changes in disease severity before and after light therapy, either in terms of a cohort only or case-control study, and (2) articles on clinical trials in humans with BD-D. The exclusion criteria were (1) case reports, (2) non-clinical trials, (3) studies not performed on human subjects, and (4) those including patients with seasonal affective disorder.

Finally, we subdivided and regrouped the articles into two categories: (i) studies relevant to comparisons of disease severity before and after light therapy, and (ii) studies comparing treatment effect with or without light therapy. In addition, we further researched the reference articles listed in the review studies. The screening and search protocol are depicted in Figure 1.

2.2. Data extraction

The primary outcome was the severity of depression, as assessed by the Hamilton Depression rating scale (HAM-D), Structured Interview Guide for the Hamilton Depression Rating Scale, Seasonal Affective Disorder (SIGH-SAD), Profile of Mood States, Brief (POMS-B), and Beck Depression Inventory (BDI). All other clinical variables were also extracted where possible. When data were not available in the

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