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Review article

Bright light therapy for nonseasonal depression: Meta-analysis of clinical trials

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ABSTRACT

Background: Bright light therapy (BLT) is a well-established treatment for seasonal depression. In the last two decades, the interest in BLT has expanded to involve other nonseasonal types of depression. The role of BLT for nonseasonal depression remains unsettled. In view of the growing number of studies in this area, this review aimed to assess the efficacy of BLT in nonseasonal depression.
Methods: We searched Pubmed; Scopus; PsychINFO; Evidence Based Medicine Guidelines and Cochrane Library until December 2015. The Standardized mean difference was calculated to assess the efficacy of BLT in nonseasonal depression. Data were subgrouped according to different study characteristics. Heterogeneity was assessed by examining the I^2 index.
Results: Nine trials met the inclusion criteria. After employing the more conservative random-effects model, the overall model showed a significant reduction of depressive symptoms after BLT administration (SMD = −0.62, $P < 0.001$, $I^2 = 37\%$). In particular, BLT appears to be efficacious when administered for 2-5 weeks (SMD = −0.78, $P < 0.001$, $I^2 = 0\%$), and as monotherapy (SMD = −0.71, $P < 0.001$, $I^2 = 18\%$). Studies of BLT for perinatal depression have found statistically insignificant improvement (SMD = −0.17, $P > 0.05$, $I^2 = 44\%$).
Limitations: The overall heterogeneity of the included trials was moderate. The participants were not adequately blinded to the intervention. The sample size was small for certain subgroups. The long-term effect of BLT on depression was not explored.
Conclusions: BLT appears to be efficacious, particularly when administered for 2–5 weeks' duration and as monotherapy. There is an obvious need to optimize the duration and intensity of exposure, the timing and the duration of treatment sessions.

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1. Introduction

The description of light therapy as a treatment option was first mentioned in association with the syndrome of seasonal affective disorder/winter type (SAD) (Rosenthal et al., 1984). This syndrome is characterized by episodes of major depression which follow a seasonal pattern, mostly occurring in winter and fall with full remission during spring and summer seasons (Even et al., 2008). Since these seasonal changes in mood are mediated by alterations in melatonin, which is a central hormone secreted by the pineal gland in a circadian pattern and regulated by the light-dark cycle (day and night) and the seasonal cycle, the exposure to bright light was proposed as the treatment of choice (Lewy et al., 1980). Several mechanisms were suggested to explain how bright light therapy (BLT) may alleviate depressive symptoms. First, early animal studies showed that light is able to shift the circadian and seasonal rhythms (De Coursey, 1960; Pittendrigh, 1960), thus modulating the chronobiological cycle (Murray et al., 2005). Second, it is believed that extending the duration of daylight during the winter season will modulate these rhythms by regulating the master clock, the suprachiasmatic nucleus (SCN), resulting in an antidepressant effect (Rosenthal et al., 1984). Afterwards, these hypotheses were supplanted by the phase shift hypothesis which attributed depression in SAD patients to phase delay in circadian rhythms relative to the sleep/wake cycles, with a smaller subgroup of these patients becoming depressed due to a phase advance (Lewy et al., 1987). However, the exact mechanism of action of BLT in the treatment of depression remains unclear (Pail et al., 2011).

The interest in BLT has expanded beyond SAD; many clinical trials reported conflicting conclusions about whether BLT is effective as a treatment modality in nonseasonal depression (Even et al., 2008). Earlier meta-analyses of trials on the efficacy of BLT revealed that it is efficacious in the treatment of the seasonal type of depression (Golden et al., 2005; Martensson et al., 2015). However, its application in nonseasonal depression is less clear as recent reviews have refrained from meta-analytically pooling data, due to the heterogeneity of studies (Even et al., 2008; Martensson et al., 2015). Because new trials on the efficacy of BLT in nonseasonal depression have been recently published, we decided to conduct a meta-analysis in order to assess the clinical efficacy of such treatment in nonseasonal depression.

2. Methods

2.1. Literature search

This systematic review protocol was registered at Prospero International Prospective Register of Systematic Reviews (Registration ID= CRD42015032297). We have systematically searched the following online databases: Pubmed; Scopus; PsycINFO; Evidence Based Medicine (EBM) Guidelines; JAMA evidence and the Cochrane library. Several MeSH terms were used to identify relevant literature: bright light therapy OR phototherapy AND depression OR major depressive disorders OR nonseasonal depression AND clinical trials AND efficacy OR effect. The search was restricted to trials published in English language only. The references mentioned in the identified trials were also scanned for relevant publications. The guidelines as described in the *Preferred Reporting Items for Systematic Reviews and Meta-analysis*, the PRISMA statement, were followed during the identification and selection of relevant studies (Moher et al., 2009). The initially-identified studies were imported into the EndNote reference management software to screen for duplication. Initially, we screened the titles and abstracts against the inclusion criteria, then the full-text of the relevant articles was retrieved for further assessment and scrutiny.

2.2. Inclusion criteria

For a trial to be considered in this meta-analysis, it had to meet the following criteria; *Criterion A:* has to be a controlled trial with intervention and control arms; *Criterion B:* must have enrolled only patients with nonseasonal depression who have been diagnosed by standardized depression scales; *Criterion C:* must have bright light therapy as primary independent intervention; *Criterion D:* must have a valid placebo as control (such as dim light or in case of negative air ions; the low-density type was assumed acceptable); *Criterion E:* must have quantified the improvement in depression as the key outcome variable by standardized depression scales; *Criterion F:* if the trial administered BLT as adjunctive to another intervention (such as antidepressant medication or sleep deprivation therapy), it must be equally administered in both intervention and control arms to be able to rule out the effect of the adjunct treatment; and *Criterion G:* must have at least "moderate" final global rating by a quality assessment tool. The literature search was independently conducted by the authors. The summary of the literature search process is depicted as PRISMA flow chart (Fig. 1).

2.3. Data abstraction and quality assessment

Two reviewers (DA and LJ) independently abstracted data from the identified trials by utilizing a pre-piloted data form. Relevant information about the age of participants, gender, the use of psychotropic medication, past medical history, the presence of other comorbidities, the study design and setting, sample size, the diagnostic criteria of depression and the assessment of seasonality, the type and the intensity of intervention, the duration of treatment, the type of study control, and the major findings reported were all retrieved. The extracted data were matched and discussed in a consensus meeting. Inconsistencies or disagreements were resolved by discussion and referring back to the original trials.

We employed the Quality Assessment Tool for Quantitative Studies to evaluate the quality of the included trials (Effective Public Health Practice Project, 2008). This tool offers a standardized method to appraise the quality of the evidence which is presented as an overall rating of strong, moderate or weak in eight areas: selection bias; study design; adjustment for confounders; blinding; data collection method; withdrawals and dropouts; intervention integrity; and the appropriateness of the analysis to the question. The final global rating for each study is quantified according to the number of "weak" ratings in each of the above-mentioned areas with a final score of "strong" rating (no weak rating), "moderate" rating (one weak rating) or "weak" rating (two or more weak ratings) (Effective Public Health Practice Project,