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BRIEF REPORT



The effect of bright light therapy on irritability in bipolar depression: a single-blind randomised control trial

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ABSTRACT

Objective: The symptom-complex irritability, widely used in descriptions of bipolar patients' manic and mixed states, also represents a common feature in depressive phases. Irritability negatively affects the clinical course of depression, leading to a higher risk of treatment non-adherence, violence, and suicide attempts. Nevertheless, proportional attention from the scientific literature seems to be scarce. We conducted the first randomised controlled trial with the aim of evaluating BLT as a possible therapeutic strategy for irritability in bipolar depression.

Methods: 180 inpatients were randomly assigned to: Group A exposed to bright light therapy (BLT) daily, or Group B treated with pharmacotherapy only. A qualitative assessment of irritability was performed after a 4-week program.

Results: Group A showed about one-third fewer cases of irritability compared to Group B, this reduction was not related to the overall remission of depressive symptoms.

Conclusions: The present study supports the usefulness of BLT in irritability in bipolar depression.

KEYPOINTS

- Irritability is an underestimated feature of bipolar depression.
- Irritability is related to higher suicide risk and lower quality of life.
- Bright light therapy is an effective strategy to reduce irritability in bipolar depression.

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Irritability; bipolar disorder; bipolar depression; bright light therapy; mood disorders; chronotherapy

Introduction

Despite the lack of clinical research on this matter conducted in the last decades, irritability represents an important symptom in many psychiatric disorders.

The term irritability, widely used in descriptions of patients' behaviour, has many different definitions, all sharing the negative valence of physical and psychological tension and excessive sensitivity to external stimuli (Born & Steiner, 1999).

There is a strong association between irritability and bipolar disorders since the early 1900s. Emil Kraepelin described irritability as 'a vulnerability to manic-depressive illness' (Kraepelin, 1921). Irritability is not only a key symptom in manic and mixed states but also a common feature during depressive phases being present in half of the depressed patients (Balbuena et al., 2016; Fava et al., 2010).

Irritability is a major source of distress in depressed patients and their carers, as well; studies have linked it to social and family dysfunction, treatment non-adherence (Pugh, 1983), suicide attempts (Akiskal et al., 2005), violence (Asnis et al., 1994), depressive recurrences, and poor quality of life (Orri et al., 2018). Although irritability represents a key symptom of bipolar depression in clinical practice, proportional attention from the scientific literature seems to be scarce.

Bright light therapy (BLT) represents an efficacious and well-tolerated therapy in depression therapeutic programs. Well documented is the positive effects of BLT on depressive symptoms and sleep quality, less explored is the effect on irritability. Only

a few studies explored the use of BLT for irritability and agitation in patients affected by neurocognitive disorders (Brasure et al., 2016).

Our study represents a first step to fill the large gap in the knowledge of irritability in bipolar depression. A better understanding of this symptom-complex, from clinical assessment to possible therapeutic strategies, could provide an important improvement in the clinical management of depressive phases in bipolar disorder.

For our investigation, we chose a broad definition of irritability as it allows us to include diverse conceptions of a largely subjective symptom, excluding the component of aggression that denotes an intention to cause harm. We considered irritability as persistent anger, a tendency to respond to events with angry outbursts or blaming others, and an exaggerated sense of frustration over minor matters, in line with the definition of irritability adopted by the American Psychiatric Association (American Psychiatric Association, 2022).

We conducted the first single-blind randomised controlled trial with the aim of evaluating the effect of BLT as a possible therapeutic strategy for irritability in bipolar depression.

Materials and methods

We enrolled 180 depressed inpatients with a diagnosis of bipolar disorder (BD) according to DSM-5 criteria. Exclusion criteria were contraindications to BLT (retinal disease, photophobia, and

medications that cause light sensitivity), the use of any other augmentation strategy, psychotic features, major psychiatric co-diagnosis, cognitive decline, or any other severe neurological comorbidity.

Participants were randomly assigned to a group with a 1:1 ratio through computer-scheduled randomisation. Group A in addition to pharmacotherapy was daily exposed to 10.000-Lux BLT through two CoeLux 45 LC artificial windows for 30min at an individualised time in the morning according to the Morningness-Eveningness Questionnaire (Wirz-Justice et al., 2009); Group B was treated with pharmacotherapy only. Every participant was hospitalised and followed a four-week program. All patients were on a stable and equivalent dose of antidepressants (fluoxetine equivalent dosage from 20 to 40mg/die). Low doses (equivalent diazepam dosage of 5–10mg) of short half-life benzodiazepines were allowed as hypnotics. Every patient was under a stable dosage of lithium or sodium valproate for at least 2 months.

A qualitative assessment of irritability was performed by two trained psychiatrists, blind to treatment conditions; data were collected using items derived from spontaneous descriptions of irritability (annoyance, anger, tension, hostility, sensitivity to noise and touch). Two clinicians asked patients a series of questions to globally evaluate their irritability at that moment as compared with their usual premorbid state, how severe the patient's irritability was at the presentation, and how much irritability may be considered normal for the patient. Raters and patients were blind to study structure and treatment assignment.

Depressive symptoms were weekly assessed with the 21-item version of the Hamilton depression rating scale (HDRS). Response was defined as $\geq 50\%$ reduction of the HDRS score from the baseline.

Every participant had the opportunity to attend a post-hospitalisation follow-up visit after two months.

The study was approved by the Ethical Committee of the Hospital. Written informed consent was obtained from all participants.

Results

No participants voluntarily withdrew from the study, and no relevant side effects occurred. 180 inpatients were enrolled and randomised. 16.11% of the original sample (29 participants, 24 in Group A and 5 in Group B) was excluded from the final analysis, due to a change in medication protocol, failure to comply with the BLT schedule, or discharge before the end of the trial.

The mean age was 56.49 ± 11.89 and 56.28 ± 14.57 in groups A and B, respectively ($p=0.925$, T-test). Females were 40 in Group A and 57 in Group B ($p=0.412$, Chi-squared test (χ^2)).

At the end of the study, 36.42% of the sample (55 subjects) reported irritability.

We observed a significant association between Group variable and irritability. 27.27% (18 subjects) of Group A and 43.53% (37 subjects) of Group B displayed irritability ($p=0.039$, χ^2 , Figure 1).

No significant effect of BLT on response rate was observed. 73.49% and 83.08% of Group A and B, respectively, achieved clinical response ($p=0.131$, χ^2).

No significant differences between groups were observed for psychomotor agitation (Group A 15.15% and Group B 24.71%, $p=0.149$, χ^2), suicidal thoughts (Group A 7.58% and Group B 8.23%, $p=0.882$, χ^2) and post-discharge visits adherence (Group A 80.0% and Group B 79.76%, $p=0.971$, χ^2).

No association between response rate and irritability was observed ($p=0.142$, χ^2).

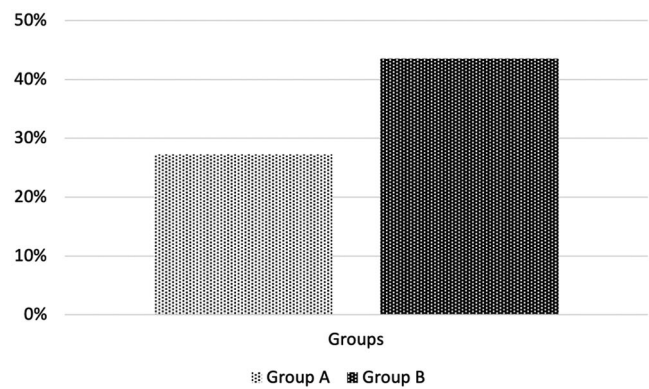


Figure 1. Prevalence of irritability between groups after 4-week BLT exposure protocol.

We found no significant association between groups, irritability symptom, and other clinical and socio-demographic variables (e.g., age, gender, menopause, family history of psychiatric disease, length of hospitalisation, number of illness episodes, duration of the episode, severity of the episode, past psychotic manifestations).

Discussion

The results of this preliminary study, consistent with the little previous literature available (Balbuena et al., 2016; Fava et al., 2010), suggest that irritability is not only a key feature of manic and mixed phases, but it is also widely represented during depressive episodes in bipolar disorder. At the end of the study, one-third of the depressed sample showed irritability.

Despite its high prevalence, the severe impact on clinical practice and quality of life, little consideration is given to this symptom to date.

Our results showed a potent effect of morning BLT in reducing irritability during a depressive episode. After a 4-week BLT program, Group A showed about one-third fewer cases of irritability when compared to Group B. Unexpectedly this result appeared to be not related to symptomatic remission, which is in favour of a positive effect of BLT on irritability.

We also explored the known consequences of irritability described in the literature, but we did not find a direct effect of BLT on agitation, suicide ideation, and follow-up adherence, which should be explored in future research.

The present study represents a first step towards the clinical management of irritability in bipolar depression, supporting the usefulness of BLT in reducing internal tension and the subjective experience of irritability. The reduction of the symptom-complex irritability may lead to an improvement in the global subjective illness perception by the patient, so indirectly reducing suicidal risk, and preventing secondary over-prescription of tranquilisers, drug misuse, and low treatment adherence.

A limitation of this study could be represented by the lack of a quantitative assessment of irritability. To the best of our knowledge, no scales are available to specifically measure irritability in a clinical sample of bipolar-depressed inpatients with an Italian validation. Therefore, according to our experience, a qualitative rate of the symptom irritability through clinical interview represented the best approach to conduct this study and minimize confounding factors.

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