



Short Communication

Evaluating the impact of adjunct bright light therapy on subjective sleep quality in major depressive disorder

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ABSTRACT

Background: Sleep disturbances are a fundamental feature of depression, with their persistence after remission serving as a key risk factor for recurrence of depressive episodes, suicide, and hypnotics abuse. Though Adjunct Bright Light Therapy (BLT) has shown efficacy in treating depression by improving sleep duration and timing, its impact on subjective sleep quality remains underexplored.

Objective: This study investigates the effect of adjunct BLT on the subjective experience of sleep quality of Major Depressive Disorder (MDD) inpatients.

Methods: A randomized controlled trial was undertaken with 100 MDD consecutively admitted inpatients on consistent antidepressant regimens. Participants were divided into two groups; Group A, received pharmacotherapy augmented with BLT, Group B, received pharmacotherapy alone. The Hamilton Depression Rating Scale assessed depressive symptoms, while the Pittsburgh Sleep Quality Index (PSQI) evaluated subjective sleep quality.

Results: While both groups displayed enhanced depressive symptomatology, only Group A manifested significant improvement in perceived sleep quality (PSQI scores: A T0 8.05 ± 5.07 vs. T1 5.64 ± 3.64 , $p < 0.001$; B T0 7.11 ± 3.17 vs. T1 6.50 ± 3.04 , $p = 0.072$).

Limitations: Study limitations include its single-site design, lack of objective sleep measurement, and exclusive SSRI use, suggesting caution in generalizing findings. Further, the absence of placebo control and unmeasured expectancy effects may influence treatment outcomes.

Conclusions: These findings underscore the criticality of subjective sleep quality in clinical evaluations and highlight the potential of adjunct BLT as an augmentation therapeutic strategy to ameliorate sleep perception in MDD patients, emphasizing its potential role in enhancing therapeutic outcomes.

1. Introduction

There is a strong bidirectional association between sleep disturbances and mood disorders. Sleep alterations are recognized as a fundamental feature of depression to such an extent that a diagnosis of depression should be made with caution in the absence of sleep complaints (Jindal and Thase, 2004).

There is ample evidence documenting alterations in sleep architecture during depressive episodes. However, the subjective experience of sleep, or how an individual perceives their sleep, has not been studied as thoroughly, particularly in psychiatric populations.

A growing body of research indicates that an individual's subjective

perception of sleep, obtained through self-administered questionnaires, may diverge from objective sleep metrics assessed through polysomnography (PSG). While the gold standard for measuring sleep parameters, PSG may not fully encapsulate the subjective experience of sleep, leading to instances where individuals report wakefulness that is not reflected in the objective recording of sleep (Hsiao et al., 2018; Stephan et al., 2021).

Within the context of major depressive disorder, a limited body of research indicates that subjective sleep quality often deteriorates preceding a depressive episode (Perlis et al., 1997) and may be a predictive factor of early recurrence (Dombrovski et al., 2007). Additionally, poor subjective sleep quality is associated with increased risk of suicide

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(Bernert et al., 2014), diminished quality of life (Matsui et al., 2021), hypnotic abuse (Kapil et al., 2014) and, albeit inconsistently, cognitive decline (Jelicic et al., 2002; Mayers and Baldwin, 2006), highlighting the clinical importance of addressing subjective sleep disturbances in the effective management of depression.

Over the past four decades, BLT has been studied and applied as an adjunctive treatment for depression, primarily due to its ability to resynchronize circadian rhythms and restore neurotransmitter dysfunction, thereby accelerating and improving the reduction of depressive symptoms. It is well-documented that exposure to light of appropriate intensity and timing can positively affect sleep duration and timing (Pail et al., 2011; van Maanen et al., 2016; Wirz-Justice et al., 2009). However, the specific impact of adjunct BLT on subjective sleep quality is less explored (Dietzel et al., 1986; Rutten et al., 2019).

In response, we designed a randomized controlled trial to evaluate the effects of adjunct BLT on subjective sleep quality in MDD. Our hypothesis posits that BLT, by directly influencing sleep mechanisms, may attenuate subjective sleep disturbances which often persist despite depressive symptoms amelioration.

2. Methods

We recruited 100 inpatients diagnosed with MDD according to DSM-5-TR criteria (American Psychiatric Association, 2022), with episodes ranging in severity from mild to severe, consecutively admitted to our unit. Exclusion criteria included contraindications to BLT (retinal disease, photophobia, and medications inducing photosensitivity), psychotic features, major psychiatric comorbidities, intellectual disabilities, cognitive decline, or severe neurological conditions.

All participants were admitted and followed a program spanning four weeks. We randomly assigned participants to groups in a 2:1 ratio using computer-generated randomization. Group A participants received pharmacotherapy and daily exposure to 10,000-Lux BLT from two CoeLux® 45 LC artificial windows for 30 min each morning at a time personalized based on the Morningness-Eveningness Questionnaire (Wirz-Justice et al., 2009); Group B participants received only pharmacotherapy.

At the study's commencement, all patients had been on a stable SSRI dose for a minimum of two weeks, which we maintained throughout the study (fluoxetine equivalent dose ranging from 20 to 40 mg/day). To prevent direct influence on nighttime sleep, only low doses of short half-life benzodiazepines (equivalent diazepam dosage of 2.5–5 mg) were allowed during the day.

Assessment was conducted by two trained psychiatrists, blinded to treatment conditions, ensuring high interrater reliability (Intra-Class Correlation Coefficient for HDRS = 0.95). We evaluated depressive symptoms weekly using the 21-item version of the Hamilton Depression Rating Scale (HDRS), defining clinical response as a ≥ 50 % reduction in HDRS score from the baseline.

Subjective sleep quality was assessed at the start (T0) and end (T1) of the study using the Pittsburgh Sleep Quality Index (PSQI). This patient-completed tool evaluates sleep over a 4-week period with scores from 0 to 21, where higher scores indicate poorer sleep quality (Buysse et al., 1989).

Various clinically observable sleep features and indicators of sleep disturbances — such as time of lights-out, duration in bed, instances of lights turned on during the night, in-bed movements, frequency of nocturnal awakenings, nighttime ambulation or restroom visits, periods of wakefulness during the night, and early morning awakenings — were continually evaluated by the department staff throughout the study. These characteristics were meticulously transcribed into daily logs. This process provided a foundation based on clinical observational ratings for the compilation of the sleep disturbance factors (HDRS-S) (O'Brien, 2000) within HDRS (items 4, 5, and 6), parameters that have also been correlated with objective sleep measures obtained through PSG (Hejazi et al., 2022).

We performed a preliminary sample size calculation based on our unit's previous PSQI and HDRS-S data before initiating the trial. The Hospital's Ethical Committee approved the study, which complied with the most recent version of the Declaration of Helsinki. Written informed consent was acquired from all participants after thoroughly explaining the research procedures and aims.

2.1. Statistical analyses

To investigate clinical and demographic variables, changes in sleep quality and sleep differences between groups, upon normality distribution check, we performed Student T, Friedman, Mann-Whitney U tests and two-way repeated analysis of variance (RMANOVA) for continuous variables, Chi-square for categorical ones.

Power analyses based on the collected data were performed to evaluate the chances of detecting a statistical significant group difference in HDRS, HDRS-S and PSQI scores ($\alpha = 0.05$, $\beta = 0.20$).

3. Results

During the study, there were no dropouts or significant side effects associated with the use of pharmacotherapy or BLT. Of the 100 participants enrolled (66 in Group A and 34 in Group B), 84 achieved a clinically validated response on the HDRS—55 from Group A and 29 from Group B. We analyzed data from these 84 responders.

The clinical and demographic characteristics of the sample are shown in Table 1.

Improvements in depressive symptoms during the study, as assessed by the HDRS, were noted for both groups, as detailed in Table 2. No HDRS differences were recorded between groups throughout the study ($p = 0.285$, $\eta^2 0.002$, RMANOVA).

The Friedman test revealed a significant improvement in subjectively perceived sleep quality (PSQI) for Group A during the study, while Group B demonstrated no significant changes over the same timeframe. Data presented in Table 2.

Between-group comparisons of the change in PSQI scores from T0 to T1 (Δ PSQI) revealed a statistically significant difference indicating a greater improvement in group A (Δ PSQI, A 2.418 ± 4.429 vs B: 0.517 ± 2.707 , $p = 0.038$, Cohen's $d = 0.484$, independent samples t -test).

Between-group comparisons of PSQI scores at the end of the study using the Mann-Whitney U test did not show a significant difference ($p = 0.207$), with a Rank-Biserial Correlation coefficient of 0.168.

Improvements in sleep quality during the study, as assessed by the HDRS-S scale based on clinical observations, were noted for both groups, as detailed in Table 2.

At study completion (T1), Group A exhibited a significantly lower

Table 1
Clinical and demographic characteristics of the sample according to Groups.

	Group A (N = 55)	Group B (N = 29)	p-Value
Age (y)	56.84 ± 11.22	59.65 ± 14.86	0.363 ^a
Gender (F)	33	18	0.301 ^b
Onset (y)	34.51 ± 14.65	39.29 ± 16.47	0.170 ^c
Duration of the episode (w)	6.60 ± 7.33	5.95 ± 8.08	0.618 ^c
Number of episodes lifetime (N)	8.06 ± 8.12	8.58 ± 7.03	0.432 ^c
Previous intercritical duration (w)	46.32 ± 98.75	32.47 ± 60.46	0.600 ^c
HDRS T0	20.25 ± 5.87	19.93 ± 5.16	0.804 ^a
PSQI T0	8.05 ± 5.07	7.11 ± 3.17	0.750 ^c
HDRS-S T0	3.51 ± 1.33	3.68 ± 1.49	0.630 ^c
Depression severity distribution (%)	Mild: 30.91 Moderate: 45.46 Severe: 23.64	Mild: 28.57 Moderate: 57.14 Severe: 14.29	0.512 ^b

^a Student t -test.
^b Chi-squared test.
^c Mann-Whitney U test.

Table 2
Comparative analysis of HDRS, PSQI and HDRS-S scores between Group A and Group B at baseline (T0) and at the study conclusion (T1).

	T0	T1	p-Value	Effect size
Group A				
HDRS (mean ± SD)	20.25 ± 5.87	5.08 ± 3.35	<0.001 ^a	η ² 0.884
PSQI (mean ± SD)	8.05 ± 5.07	5.64 ± 3.64	<0.001 ^b	Kendall's W 0.256
HDRS-S (mean ± SD)	3.51 ± 1.33	0.89 ± 1.46	<0.001 ^b	Kendall's W 0.733
Group B				
HDRS (mean ± SD)	19.93 ± 5.16	6.68 ± 3.13	<0.001 ^a	η ² 0.912
PSQI (mean ± SD)	7.11 ± 3.17	6.50 ± 3.04	0.072 ^b	Kendall's W 0.116
HDRS-S (mean ± SD)	3.68 ± 1.49	1.88 ± 1.09	<0.001 ^b	Kendall's W 0.529

^a Repeated Measures ANOVA.
^b Friedman's Test.

HDRS-S score in comparison to Group B ($p < 0.001$, Rank-Biserial Correlation coefficient of 0.457, Mann-Whitney U test).
Between-group comparisons of the change in HDRS-S scores from T0 to T1 (Δ HDRS-S) indicated a statistically significant difference, with a greater improvement observed in group A (Δ HDRS-S, A: 2.618 ± 1.716 vs B: 1.786 ± 1.813 , $p = 0.031$, Rank-Biserial Correlation coefficient of -0.285 , Mann-Whitney U Test).

4. Discussion

The results of this randomized controlled trial shed important light on the role of adjunct BLT in improving subjective sleep quality in patients with MDD. Solely pharmacotherapy did not suffice to improve subjective sleep in individuals with MDD, with disturbances persisting even amid symptomatic improvement. In contrast, the incorporation of BLT alongside standard pharmacotherapy resulted in significant enhancements in subjective sleep quality.
Indeed, subjectively perceived sleep quality, as assessed via the PSQI, demonstrated marked differences between the two groups. Only the group receiving BLT reported a significant enhancement in their PSQI scores, whereas the group treated exclusively with pharmacotherapy did not demonstrate any significant improvements in PSQI throughout the study period.
Although the mean PSQI scores at the study's conclusion did not reveal significant differences between the groups—which may be attributed to the small sample size and the non-uniform nature of the sample despite randomization—a significant difference in the delta of improvement favored the BLT-treated group, with a moderate-to-large effect size observed. From a clinical applicability standpoint, the magnitude of improvement observed is of paramount importance as it provides a tangible metric to guide potential therapeutic advancements in the treatment of MDD.
The precise mechanism underpinning the improved subjective sleep quality associated with BLT remains unclear. However, a limited body of literature has hypothesized that the observed improvement in subjective sleep following BLT may be connected to a reduction in cortisol levels (Rutten et al., 2019).
In line with the existing literature on sleep and depression, an improvement in clinically observable sleep parameters was noted in both groups during the study, as assessed by the HDRS-S scale. Furthermore, BLT also demonstrated a beneficial impact on these sleep parameters. At the study's conclusion, the BLT-treated group not only showed a better HDRS-S scores compared to the control group but also exhibited a significantly larger delta of improvement on the HDRS-S scale during the study.

Regarding depressive symptoms, both groups exhibited the expected improvement over the course of the study, without any significant differences between them. Although existing literature suggests a positive effect of light therapy on overall depressive symptoms, this effect was not observed in our study. This may be due to our selective analysis of only those patients who responded to treatment, in an effort to limit confounding factors on sleep—which is the primary focus of this study. However, this selection criterion may also restrict the broader understanding of BLT's impact on global depressive symptoms.
In light of evidence that individuals with MDD may report poor subjective sleep quality even amidst symptomatic recovery, and considering the association of poor subjective sleep with worse disease outcomes and prognosis (Bernert et al., 2014; Dombrowski et al., 2007; Jelcic et al., 2002; Kapil et al., 2014; Matsui et al., 2021; Mayers and Baldwin, 2006; Perlis et al., 1997), it becomes critical to prioritize patients' subjective sleep experiences, as directly reported by patients through self-administered questionnaires, in clinical practice. BLT emerges as a well-tolerated and efficacious intervention for enhancing subjective sleep quality in MDD patients, alongside traditional therapies.
The integration of subjective sleep evaluations is crucial, particularly since objective assessments such as PSG or actigraphy may not be feasible or suitable in routine clinical settings, especially within psychiatric units. This compels a deeper exploration of subjective sleep measures, not only for their inherent significance but also because they often represent the only practical method for assessing sleep in psychiatric inpatient contexts. Understanding how these subjective assessments align with, or reflect, objective sleep metrics is therefore essential, carrying significant weight for clinical decision-making and patient care.
While the results of our study are encouraging, some limitations warrant consideration. The single inpatient setting of the study may affect the generalizability of our findings. Our focus on subjective sleep quality did not extend to an evaluation of adjunct BLT effects on PSG parameters. We opted against using placebo lights, considering the shared inpatient environment and the recognized influence of even dim lighting on circadian rhythms. The study did not formally assess the impact of patients' expectancy effects, which represents a potential area for future research to clarify their influence on treatment outcomes. Finally, it is important to note that, in order to limit confounding factors, we specifically focused on the effect of BLT in combination with SSRI treatment. The applicability of our results to the use of BLT with other therapeutic classes represents an avenue for future research.

5. Conclusion

In conclusion, this study presents preliminary but robust evidence supporting the use of BLT as an adjunctive treatment for improving subjective sleep quality in MDD patients. Given the significant burden that poor sleep quality places on these patients, this is an area that deserves more attention and research. Adjunct BLT represents a safe and non-invasive intervention that could be easily integrated into existing treatment regimens, potentially improving treatment outcomes.

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CRedit authorship contribution statement

Lorenzo Fregna: Conceptualization, Methodology, Investigation, Writing- Reviewing and Editing; Francesco Attanasio: Conceptualization, Investigation, Writing- Original draft preparation, Formal analysis; Cristina Colombo: Project administration, Supervision, Data Curation,

Declaration of competing interest

The authors report there are no competing interests to declare.

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