

Article

Biological Rhythms and Psychosocial Functioning in Depression: An Exploratory Analysis Informed by a Mediation Model

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Abstract

Background. Major Depressive Disorder (MDD) is a highly prevalent and disabling condition frequently accompanied by cognitive deficits, impaired psychosocial functioning, and biological rhythm disturbances. Despite extensive literature on individual associations between depression and circadian disruptions, the mediating role of biological rhythms in the functional outcomes of MDD remains underexplored. **Objectives.** This study aimed to explore the associations between depression severity, biological rhythms, sleep quality, and psychosocial functioning, and to assess whether biological rhythm disturbances mediate the impact of depression on functioning. **Methods.** Sixty-one inpatients diagnosed with moderate-to-severe MDD were assessed using standardized instruments: BDI-II for depressive symptoms, BRIAN for biological rhythms, PSQI for sleep quality, and FAST for global functioning. Group comparisons, non-parametric correlations, and a mediation analysis were conducted to test direct and indirect effects. **Results.** Participants showed severe depressive symptoms, impaired functioning, disrupted biological rhythms, and poor sleep. Women reported more depressive episodes, reduced autonomy, and worse sleep than men. Depression severity was associated with circadian and sleep disturbances, which in turn related to functional impairment. Mediation analysis suggested that biological rhythms partially mediate the impact of depression on functioning. **Conclusions.** Findings from this preliminary analysis suggest that biological rhythm disturbances may play a mediating role in the relationship between depressive symptoms and daily psychosocial functioning. While not conclusive, these results highlight the potential relevance of chronobiological factors in understanding functional outcomes in MDD. Further research using longitudinal and controlled designs is needed to clarify these associations and their clinical implications.

Keywords: depression; major depressive disorder; sleep disturbances; biological rhythms; functional impairment; mediation model



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1. Introduction

Major Depressive Disorder (MDD) is a prevalent and debilitating psychiatric condition characterized by persistent low mood, anhedonia, and cognitive impairment [1,2]. With an estimated global prevalence of approximately 5.79% among adults [3], MDD is recognized as a leading cause of disability worldwide, contributing to increased morbidity and mortality [4]. In addition to its impact on emotional and cognitive functioning, MDD is frequently comorbid with various medical conditions, including cardiovascular diseases, neurodegenerative disorders, and metabolic syndromes [5,6]. Moreover, a growing body of research highlights the role of biological rhythms and sleep disturbances in the pathophysiology of MDD [7,8].

Sleep alterations, including insomnia and hypersomnolence, are highly prevalent among individuals with MDD, affecting 60–90% of patients during depressive episodes [9–12]. These disturbances, characterized by dissatisfaction with sleep amount or quality, can impair daytime functioning and increase stress levels [1]. Not only do they exacerbate depressive symptomatology, but they also negatively affect daily functioning, treatment response, and long-term prognosis [13]. Insomnia, in particular, plays a dual role in MDD as both a diagnostic criterion [1] and a critical risk factor for its onset and recurrence, with evidence suggesting that persistent sleep disturbances increase the likelihood of relapse even after remission [14]. Moreover, patients with MDD who experience severe insomnia tend to show poorer global functioning compared to those without sleep disturbances [15].

Beyond sleep disturbances, disruptions in biological rhythms have been identified as a core feature of depression. Patients with MDD often display reduced daytime motor activity and significant irregularities across various biological domains [16]. These disruptions include alterations in endogenous and exogenous rhythms such as sleep–wake cycles, appetite, social interactions, and daily activity levels [17], and have been associated with greater depression severity and higher relapse risk [18].

Although biological rhythm disturbances are widely acknowledged in mood disorders, their specific contribution to psychosocial functioning in MDD remains underexplored. While several studies have examined distinct domains of biological rhythms—such as sleep, activity, eating, and social patterns—in relation to depressive symptom severity, the potential impact of these disturbances on functional outcomes has received comparatively little attention. Most of the existing literature has focused on symptom associations, often overlooking the broader implications for patients' daily functioning. In addition, the use of analytical approaches that go beyond simple associations—such as models exploring potential intermediary links—remains limited [16,17,19]. Addressing this gap is particularly relevant given the growing interest in functional recovery and the emergence of chronobiological interventions in clinical practice. Advances in assessment tools (e.g., actigraphy, chronotype measures) and treatments (e.g., light therapy, behavioral activation) further highlight the need to better understand how disruptions in biological rhythms may contribute to the everyday challenges faced by individuals with MDD [20].

In this context, the present study aimed (1) to explore how depressive symptom severity, biological rhythms, and sleep quality relate to psychosocial functioning in a clinical sample of inpatients with moderate-to-severe MDD. While the primary goal was to describe the associations among these dimensions, we also included a mediation model as an exploratory tool to examine whether self-reported biological rhythm disturbances might partially account for the relationship between depressive symptoms and functional impairment. Given the cross-sectional design, the absence of a control group, and reliance on self-report measures, all analyses were conducted with hypothesis-generating intent.

This study does not aim to establish causal mechanisms, but rather to contribute preliminary insights that may inform future longitudinal and clinically oriented investigations.

2. Materials and Methods

2.1. Recruitment and Participants

A total of 61 participants diagnosed with Major Depressive Disorder (MDD) were recruited for the study from April 2022 to December 2024. The sample had a mean age of 45.75 years ($SD = 13.32$) and included 39 females and 22 males. All participants were inpatients at the Psychiatric Clinic Villa dei Gerani in Catania, Sicily (Italy), where they were hospitalized at the time of assessment. Patients were assessed by clinical psychologists in an individual setting at the time of admission, prior to the initiation of inpatient pharmacological treatment or psychotherapeutic interventions. Prior to enrollment, participants received comprehensive oral and written information regarding the study's objectives and data use, and each provided written informed consent. The study was conducted in accordance with the ethical standards of the Declaration of Helsinki.

Crucially, the decision to include a participant in the study—following informed consent—was made independently of any clinical treatment decisions. The study was non-interventional in nature and did not interfere with the clinical practice or prescribing behaviors of the treating psychiatrists. Participation in the study did not involve additional appointments, procedures, or deviations from routine clinical care.

No control group was included in this study, as the primary objective was to explore the role of biological rhythms within a clinical sample of inpatients with MDD. This design choice allowed us to focus on the variability and interrelations of depressive symptoms, biological rhythms, and functioning specifically within the MDD population.

2.2. Inclusion Criteria

- A diagnosis of moderate to severe Major Depressive Disorder (MDD) according to DSM-5 criteria, with a Hamilton Depression Rating Scale (HAM-D) score > 17 .
- Age between 18 and 65 years.
- Provision of written informed consent.

2.3. Exclusion Criteria

- A history of intellectual disability or any condition that could significantly impair cognitive performance.
- Comorbidity with a psychotic disorder.
- Electroconvulsive therapy (ECT) within the 12 months prior to the neuropsychological assessment.

2.4. Neuropsychological Assessment

A trained clinical psychologist evaluated all participants in an individual setting through the following neuropsychological tests:

2.5. Affective Domain

- Beck Depression Inventory-Second Edition (BDI-II), Italian Version [21]: It is a 21-item self-administered instrument to detect the severity of depression in adults and adolescents from age 13 onward. Scores 0–13 indicate no depressive content; scores 14–19: mild depression; scores 20–29: moderate depression; scores 30–63: severe depression. The Italian validation data confirm the existence of two sides of depression, the mental and the somatic, as in the original edition. The internal consistency calculated through Cronbach's alpha results in 0.86 for the first factor and 0.65 for the second factor.

2.6. Psychosocial Domain

- Functioning Assessment Short Test (FAST) [22]: It was used as a primary outcome of psychosocial risk at the study endpoints to identify predictors for specific domains of function, such as autonomy, occupational functioning, cognitive functioning, financial issues, interpersonal relationships, and leisure. The higher the score, the worse the patient's functional impairment. The cut-off scores for the FAST scale derived from this equation were as follows: scores from 0 to 11 included patients with no impairment. Scores from 12 to 20 represented the category of mild impairment. Moderate impairment comprised scores from 21 to 40. Finally, scores above 40 represented severe functional impairment [23]. Cronbach's alpha for the five components was 0.96, 0.88, 0.88, 0.91, 0.92, respectively, and for the total was 0.93.

2.7. Sleep Domain

- Pittsburgh Sleep Quality Index (PSQI) [24] is a self-assessment scale about sleep quality that can be easily compiled by the subject. It consists of 19 items that can be summarized into seven evaluation domains: (1) subjective quality of sleep, (2) sleep latency, (3) duration of sleep, (4) usual efficiency of sleep, (5) sleep disorders, (6) drugs used for sleep, and (7) daytime malfunction. A PSQI score >5 highlights sleep quality problems.
- Biological Rhythms Interview of Assessment in Neuropsychiatry (BRIAN) [25] is a self-report questionnaire consisting of 21 items, referring to the 15 days immediately preceding completion. The subject is asked to report how often he or she experienced sleep disturbances at different times during that time period. The four domains considered, which are related to circadian rhythm disorders, are (1) sleep, (2) general activity, (3) social rhythms, and (4) nutrition. The fifth scope (items 19–21), not included in the total score, involves the evaluation of the subject's chronotype. Each of these domains represents a potential factor in the onset and worsening of affective states, psychosocial functioning, and clinical functioning. Each item is evaluated on a 4-point Likert scale (from "no difficulty" to "severe difficulty") the sum of the final score (18 to 72), where the highest intervals indicate a more serious subjective impairment of the circadian rhythm. The Italian clinical mean score is 22.22 (SD = 11.19) [25]. In this sense, the BRIAN scale offers a rapid self-reported measurement of the biological rhythm dysregulation in individuals with depression.

2.8. Data Analysis

The study adopted an integrated methodological approach, combining descriptive statistics, group comparisons, non-parametric correlations, and formal mediation modeling. This methodological plurality enabled us to move beyond simple symptom description and explore the functional relationships among clinically relevant constructs, as well as the underlying psychological mechanisms that may link them.

All analyses were performed using *R* (version 2024.12.1). To assess the presence of extreme values in the main study variables (depression severity, biological rhythms, and psychosocial functioning), univariate outlier detection was performed using standardized z-scores. Specifically, z-scores were computed for BDI-II, BRIAN, and FAST scores. Values exceeding ± 3 standard deviations from the mean were considered potential outliers, based on conventional thresholds for extreme values in small samples [26]. This procedure was applied prior to conducting correlational and mediation analyses. No data were excluded on the basis of this criterion. See Figure S1 in the Supplementary Materials. Moreover, all variables included in the model were complete, with no missing data.

Descriptive statistics were calculated using the "*psych*" package [27] to evaluate central tendency, dispersion, and distributional characteristics of the study variables. The "*dplyr*"

and “*tidyr*” packages were used to create descriptive tables [28,29]. To assess normality, we applied the Shapiro–Wilk test (via the “*rstatix*” package [30]) to all continuous variables. Given that several distributions significantly deviated from normality ($p < 0.05$), we relied on non-parametric statistical methods for subsequent analyses.

To explore bivariate associations, a Spearman correlation matrix—appropriate for non-normally distributed data—was computed and visualized using “*corrplot*” and “*Hmisc*” packages [31,32]. Spearman’s rank correlations were computed to examine associations among all study variables. To increase robustness, 95% confidence intervals were estimated using non-parametric bootstrap resampling (1000 iterations). The full correlation matrix, including coefficients, confidence intervals, and p -values for all variable pairs, is provided as Supplementary Table S1.

Group comparisons between male and female participants were conducted using the Wilcoxon rank-sum test (also known as the Mann–Whitney U test), a non-parametric alternative to the independent samples t -test. To enhance interpretability, boxplots were generated with “*ggplot2*” [33], visually illustrating the distribution of scores across sex groups and complementing the statistical results of the Wilcoxon test. Effect sizes for this test were computed using the “*rcompanion*” package [34].

Formal mediation analysis was carried out with the “*mediation*” package [35]. In clinical psychology, such models can be useful for exploring whether an independent variable may be statistically linked to an outcome through an intermediate construct. In this study, the analysis was included as an exploratory extension to examine whether disruptions in biological rhythms (as measured by BRIAN) might partially account for the association between depression severity (BDI-II) and psychosocial functioning (FAST). This model follows the mediation framework proposed by Baron and Kenny (1986) [36] and further refined by Preacher and Hayes (2008) [37] through nonparametric bootstrapping techniques. To account for potential confounding effects, sex was included as a covariate in both the mediator and outcome models of the mediation analysis. This decision was based on previous research showing that sex differences influence biological rhythms, sleep patterns, and functional outcomes in individuals with MDD [38,39]. In contrast, age was not included as a covariate because prior evidence regarding age effects on these associations is less consistent. Including sex as a covariate allowed us to control for gender-related variability while preserving model parsimony.

The model estimated four key effects: the indirect effect (ACME), representing the pathway from BDI-II to FAST through BRIAN; the direct effect (ADE), indicating the effect of BDI-II on FAST independent of the mediator; the total effect, capturing the overall association between BDI-II and FAST; and the proportion mediated, reflecting the percentage of the total effect accounted for by the mediator. Confidence intervals were estimated using 10,000 nonparametric bootstrap simulations with the bias-corrected and accelerated (BCa) method, offering improved accuracy in the presence of non-normal sampling distributions. Given the cross-sectional nature of the data, the mediation analysis should be interpreted as exploratory and hypothesis-generating; no causal inferences can be drawn from the observed associations. To visualize the path diagram of the mediation analysis, the “*DiagrammeR*” package [40] was used.

A threshold of $p < 0.05$ was used to determine statistical significance.

3. Results

Descriptive analysis (Table 1) showed that the sample had a mean age of 45.75 years ($SD = 13.32$), with an average of 3.02 previous depressive episodes ($SD = 1.15$) and 0.38 suicide attempts ($SD = 0.80$). The group exhibited moderate to severe depression (BDI-II mean = 34.33, $SD = 10.20$) and signs of cognitive impairment (MoCA mean = 23.23,

SD = 4.63). Additionally, they experienced moderate global functioning impairment (FAST.tot mean = 36.57, SD = 14.66), disruptions in biological rhythms (BRIAN.tot mean = 49.74, SD = 9.28), and poor sleep quality (PSQI.tot mean = 11.20, SD = 4.33).

Table 1. Descriptive analysis ($n = 61$).

Variable	Mean	SD	Shapiro–Wilk Value
Age	45.75	13.32	0.94 *
Previous episodes	3.02	1.15	0.80 ***
Suicide attempts	0.38	0.80	0.54 ***
BDI-II	34.33	10.20	0.97
MoCA	23.23	4.64	0.94 **
FAST.tot	36.57	14.66	0.98
BRIAN.tot	49.75	9.28	0.98
PSQI.tot	11.20	4.33	0.98

BDI-II = Beck Depression Inventory-II; MoCA = Montreal Cognitive Assessment; FAST.tot = Functioning Assessment Short Test, total score; BRIAN.tot = Biological Rhythms Interview of Assessment in Neuropsychiatry, total score; PSQI.tot = Pittsburgh Sleep Quality Index, total score. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$.

Applying the Mann–Whitney U test, statistically significant differences between females (group 1) and males (group 2) were detected (Table 2, Figure 1). Females had more previous depressive episodes ($W = 585$, $r = 0.323$, $p < 0.01$) and greater impairment in functional autonomy ($W = 576$, $r = 0.284$, $p < 0.05$). Additionally, they reported poorer overall sleep quality ($W = 560$, $r = 0.252$, $p < 0.05$), more difficulties with sleep duration ($W = 559$, $r = 0.273$, $p < 0.05$), and lower sleep efficiency ($W = 545.5$, $r = 0.254$, $p < 0.05$).

Table 2. Mann–Whitney U test grouping by sex (n group 1 = 39; n group 2 = 22).

Variable	Groups	Mean (DS)	W	$r_s b$	p Value
Previous episodes	1	3.31 (0.98)	585	0.323	<0.01
	2	2.50 (1.26)			
F.Autonomy	1	6.87 (3.40)	576	0.284	<0.05
	2	4.68 (3.80)			
PSQI.tot	1	12.00 (4.80)	560	0.252	<0.05
	2	9.77 (2.93)			
P.Duration	1	1.26 (1.27)	559	0.273	<0.05
	2	0.55 (0.96)			
P.Efficiency	1	1.10 (1.31)	545.5	0.254	<0.05
	2	0.41 (0.80)			

Mann–Whitney U test grouping by sex. Group 1 = female; Group 2 = male. F.Autonomy = Functioning Assessment Short Test, Autonomy subscale; PSQI.tot = Pittsburgh Sleep Quality Index, total score; P.Duration = Pittsburgh Sleep Quality Index, Sleep Duration; P.Efficiency = Pittsburgh Sleep Quality Index, Sleep Efficiency.

Moreover, Spearman's correlation was computed (Figure 2, Table S1). The correlation analysis revealed significant associations between BDI-II, BRIAN, and PSQI with various clinical and functional variables. Higher BDI-II scores were moderately and positively associated with greater functional impairment (FAST.tot, $\rho = 0.48$, $p < 0.05$), particularly in autonomy (F.Autonomy, $\rho = 0.43$, $p < 0.05$), interpersonal relationships (F.Interpersonal, $\rho = 0.45$, $p < 0.05$), and leisure activities (F.Leisure, $\rho = 0.38$, $p < 0.05$). Additionally, BDI-II was associated with increased circadian rhythm dysregulation (BRIAN.tot, $\rho = 0.52$,

$p < 0.05$) and poor sleep quality (PSQI.tot, $\rho = 0.34$, $p < 0.05$), reflecting moderate to large effect sizes. These findings reinforce the established link between mood disorders and disruptions in both biological rhythms and sleep regulation. BRIAN.tot was also moderately significantly associated with sleep disturbances (PSQI.tot, $\rho = 0.38$, $p < 0.05$). The relationship between circadian rhythm dysregulation and poor sleep quality was also confirmed (BRIAN.tot and PSQI.tot, $\rho = 0.38$, $p < 0.05$), indicating a moderate effect size. The complete correlation matrix, including Spearman's coefficients, 95% bootstrap confidence intervals, and p -values for all variable pairs, is provided as Supplementary Table S2.

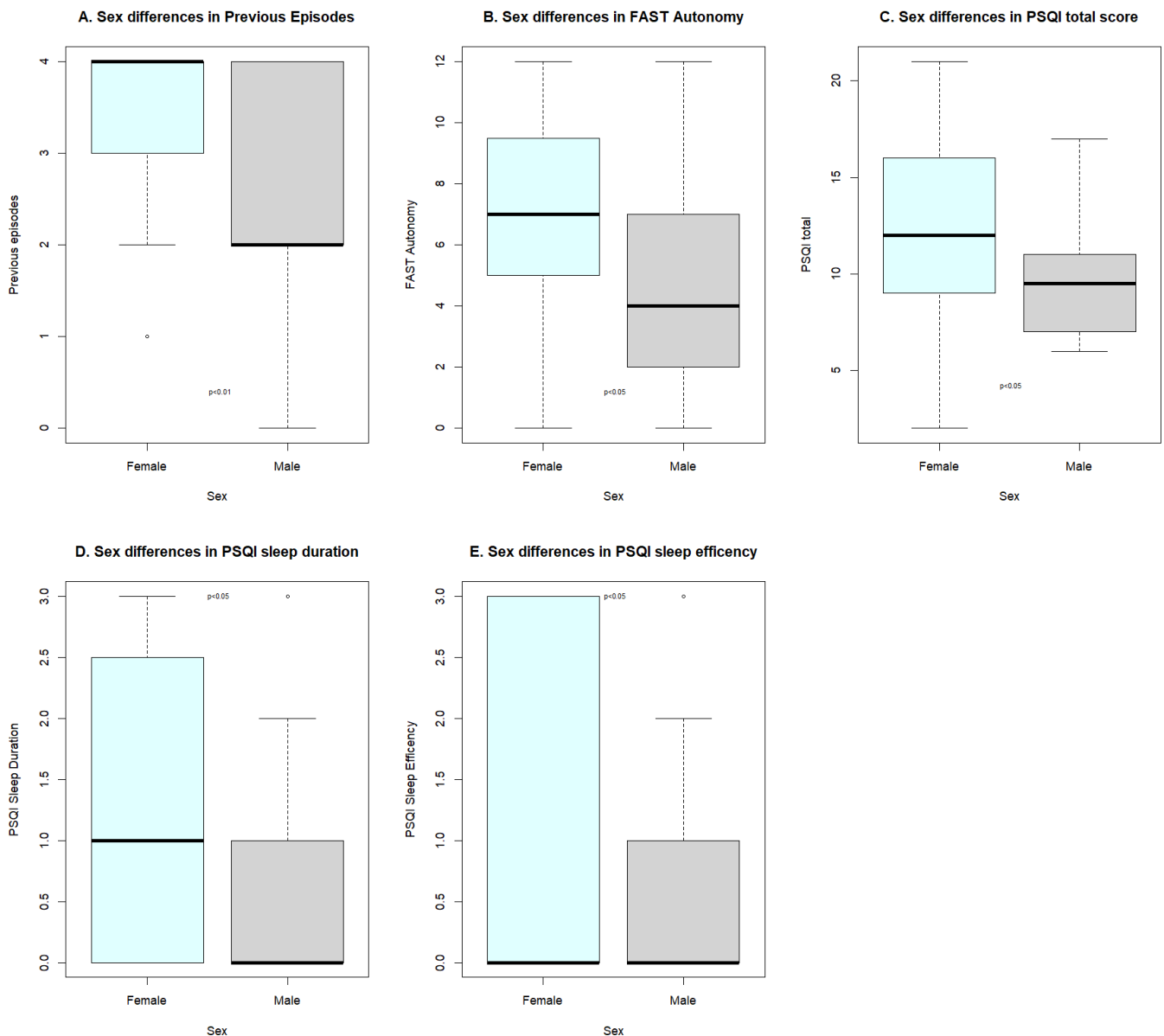


Figure 1. Boxplots illustrating sex differences in (A) number of previous depressive episodes, (B) FAST Autonomy scores, (C) PSQI total scores, (D) PSQI Sleep Duration, and (E) PSQI Sleep Efficiency. Female participants reported more previous episodes (mean) (A), greater functional autonomy (B), and higher overall sleep disturbance (C) compared to male participants. In addition, women showed significantly poorer sleep in specific domains, including shorter sleep duration (D) and lower sleep efficiency (E). All group comparisons were statistically significant ($p < 0.05$), based on Mann–Whitney U tests reported in Table 2. Boxplots show the median (horizontal line), interquartile range (boxes), and range (whiskers). Abbreviations: FAST = Functioning Assessment Short Test; PSQI = Pittsburgh Sleep Quality Index.

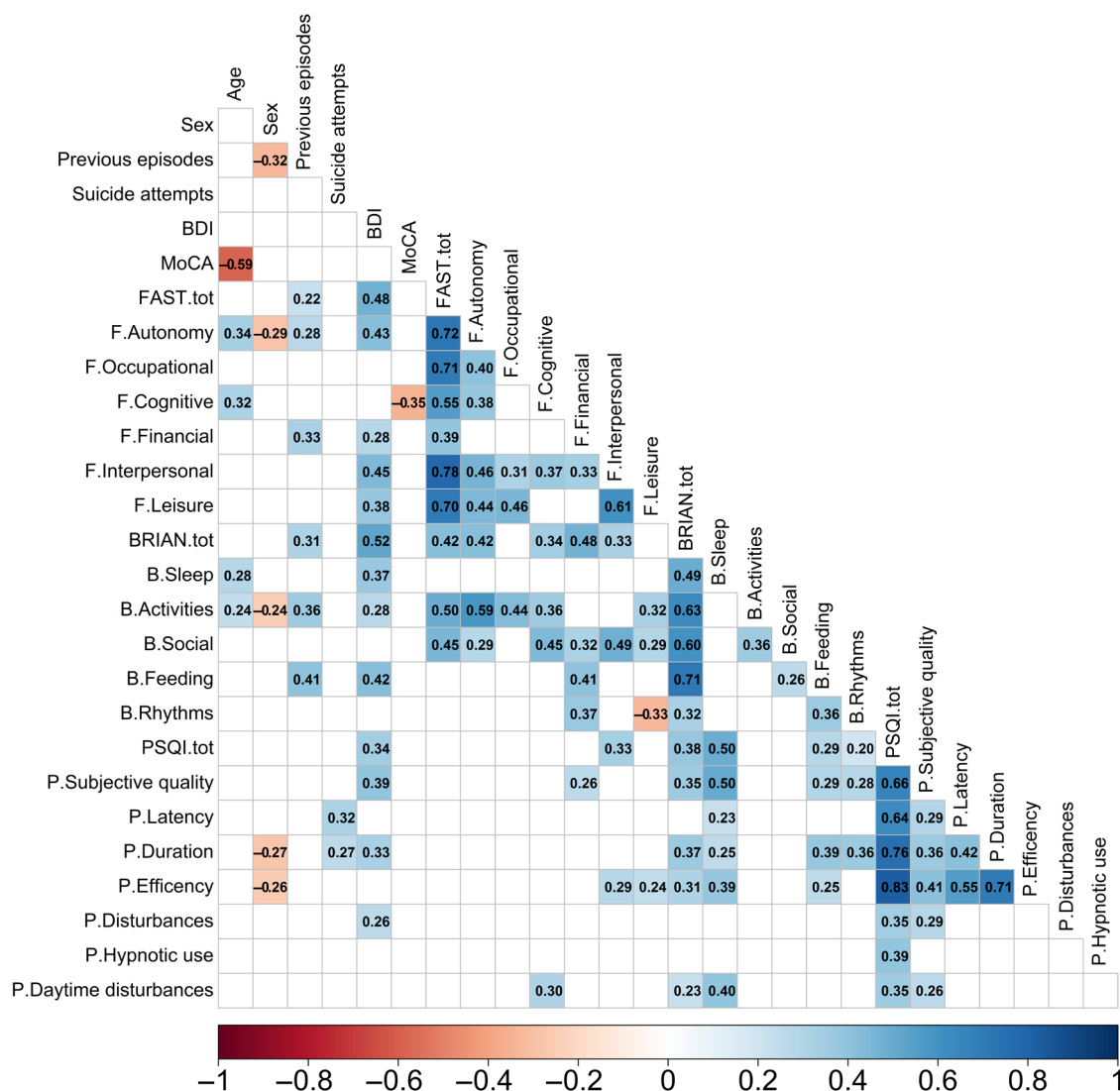


Figure 2. Correlation matrix of all study variables. Spearman's correlation coefficients are displayed for each pair of variables, with color intensity reflecting the strength and direction of the correlation (blue = positive correlations; red = negative correlations). Darker colors represent stronger associations. Abbreviations: BDI = Beck Depression Inventory-II; MoCA = Montreal Cognitive Assessment; FAST.tot = Functioning Assessment Short Test total score; F.Autonomy = FAST Autonomy subscale; F.Occupational = FAST Occupational subscale; F.Cognitive = FAST Cognitive subscale; F.Financial = FAST Financial subscale; F.Interpersonal = FAST Interpersonal Relationships subscale; F.Leisure = FAST Leisure Time subscale; BRIAN.tot = Biological Rhythms Interview of Assessment in Neuropsychiatry total score; B.Sleep = BRIAN Sleep subscale; B.Activities = BRIAN Activities subscale; B.Social = BRIAN Social Rhythm subscale; B.Feeding = BRIAN Feeding Rhythm subscale; B.Rhythms = BRIAN Rhythms Regularity subscale; PSQI.tot = Pittsburgh Sleep Quality Index total score; P.Subjective quality = PSQI Subjective Sleep Quality component; P.Latency = PSQI Sleep Latency component; P.Duration = PSQI Sleep Duration component; P.Efficiency = PSQI Sleep Efficiency component; P.Disturbances = PSQI Sleep Disturbances component; P.Hypnotic use = PSQI Hypnotic Medication Use component; P.Daytime disturbances = PSQI Daytime Dysfunction component.

A mediation analysis was conducted to explore whether disruption of biological rhythms (BRIAN.tot) mediates the relationship between depressive symptom severity (BDI-II) and functional impairment (FAST.tot) (Figure 3). The analysis used nonparametric bootstrapping with 10,000 simulations and bias-corrected and accelerated (BCa) 95% confidence intervals. Sex was included as a covariate to control for gender-related effects. As

shown in Table 3 and Figure 3, the results revealed that depressive symptoms (BDI-II) were associated with psychosocial impairment (FAST.tot) both directly and indirectly through circadian rhythm dysfunction (BRIAN.tot). The indirect effect was statistically significant and of small-to-moderate magnitude ($\beta = 0.142$, 95% BCa CI [0.017, 0.380], $p < 0.05$), indicating that disruptions in biological rhythms partially mediated the relationship between depression severity and functional outcomes. The direct effect of BDI-II on FAST.tot, controlling for BRIAN.tot, remained statistically significant and showed a moderate effect size ($\beta = 0.309$, 95% BCa CI [0.048, 0.510], $p < 0.05$), suggesting that depressive symptoms independently contribute to impaired functioning beyond the influence of circadian factors. The total effect of BDI-II on FAST.tot was robust and of moderate-to-large magnitude ($\beta = 0.450$, 95% BCa CI [0.260, 0.630], $p < 0.001$), supporting a strong overall association between depression severity and psychosocial dysfunction. Notably, the proportion of the total effect mediated by BRIAN.tot was estimated at 31.5% (95% BCa CI [0.045, 0.930], $p < 0.05$), indicating that nearly one-third of the effect of depressive symptoms on functioning may operate through circadian rhythm disruption.

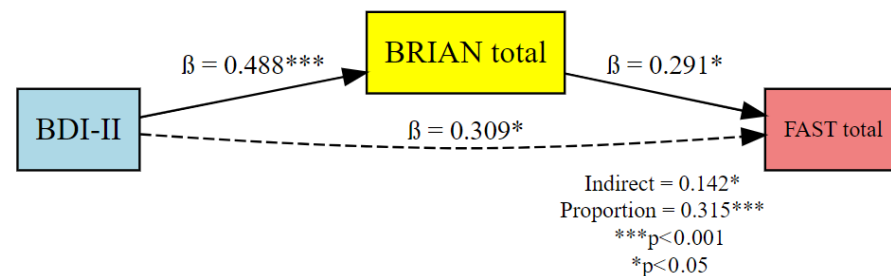


Figure 3. Conceptual mediation model illustrating the indirect effect of depressive symptoms on psychosocial functioning through biological rhythm disturbances. The model depicts the proposed relationships between depression severity (BDI-II), biological rhythms (BRIAN total), and functioning (FAST total). Solid arrows indicate significant associations between variables, while the dashed arrow represents the direct effect of depressive symptoms on functioning after accounting for the mediator. Indirect effect and proportion mediated are also reported. Abbreviations: BDI-II = Beck Depression Inventory-II; BRIAN = Biological Rhythms Interview of Assessment in Neuropsychiatry; FAST = Functioning Assessment Short Test. * $p < 0.05$, *** $p < 0.001$.

Table 3. Mediation analysis of BRIAN.tot between BDI-II and FAST.tot.

Effect	Predictor (X)	Mediator (M)	Outcome (Y)	β (Standardized)	95% CI (Lower)	95% CI (Upper)	p-Value
Indirect Effect (ACME)	BDI-II	BRIAN.tot	FAST.tot	0.142	0.017	0.38	<0.05
Direct Effect (ADE)	BDI-II	—	FAST.tot	0.309	0.048	0.51	<0.05
Total Effect	BDI-II	—	FAST.tot	0.451	0.260	0.63	<0.001
Proportion Mediated	BDI-II	BRIAN.tot	FAST.tot	0.315	0.045	0.93	<0.05

BDI-II = Beck Depression Inventory-II; FAST.tot = Functioning Assessment Short Test, total score; BRIAN.tot = Biological Rhythms Interview of Assessment in Neuropsychiatry, total score.

4. Discussion

This study mainly aimed to explore how depressive symptom severity, biological rhythms, and sleep quality were related to psychosocial functioning in a clinical sample of inpatients with moderate-to-severe MDD.

The clinical profile of the sample is consistent with the literature describing MDD as a condition characterized by marked emotional, cognitive, and psychosocial impairments [1]. Participants showed elevated depressive symptoms alongside notable cognitive deficits and diminished overall functioning. The mean MoCA score indicates partial cognitive impairment, reflecting prior evidence that cognitive deficits often accompany depression—even outside of acute episodes—and significantly affect daily life [41]. Combined with disturbances in sleep and biological rhythms, these cognitive impairments play a well-recognized role in the pathophysiology and course of depression [42–45], likely contributing to the observed global functional reductions, as measured by the FAST scale.

Moreover, sex differences emerged: female participants reported a greater number of previous depressive episodes, more severe functional impairment, and poorer sleep quality compared to males, aligning with prior evidence suggesting that depression in women tends to be more chronic and severe, particularly regarding biological rhythms and sleep [46–48].

Consistent with prior studies, our results highlight a moderate to strong association between depressive severity and functional impairment across autonomy, interpersonal relationships, and leisure activities [12,49–54]. These findings underscore the need to assess psychosocial outcomes alongside symptom severity in clinical practice. Depression severity also moderately correlated with greater circadian rhythm disruption and poorer sleep quality, supporting hypotheses about the close interconnection between mood, biological rhythms, and sleep [55,56]. Notably, the moderate relationship between circadian disruption and sleep disturbances highlights their intertwined roles in contributing to overall dysfunction in MDD [57,58].

Additionally, as previously stated, while the primary aim of this study was to describe the associations among depressive symptoms, biological rhythms, and psychosocial functioning, we also included a mediation model as an exploratory extension to examine whether self-reported circadian rhythm disturbances might partially account for the relationship between depression severity and functional impairment. The results indicated that biological rhythm disruption partially mediated this association. Although previous research has highlighted the relevance of circadian dysregulation in mood disorders [14,59], our findings extend this evidence by quantifying the indirect effect and showing that approximately one-third of the total impact of depressive symptoms on functioning may operate through circadian rhythm disturbance. By replicating this association within an inpatient sample and applying a mediation framework, the study contributes to the growing empirical support for the role of circadian dysfunction in psychosocial impairment. However, given the cross-sectional design, the absence of a control group, and reliance on self-report measures, the findings should be interpreted as preliminary and hypothesis-generating, rather than indicative of causal mechanisms. Future longitudinal and clinically grounded studies are needed to confirm and further clarify these pathways.

Clinically, these results suggest that targeting biological rhythm disruptions—through interventions such as sleep hygiene, light therapy, behavioral activation, and pharmacological approaches—may help alleviate not only mood symptoms but also functional impairments associated with depression [13,60]. Importantly, beyond confirming prior findings, our results point toward underexplored directions and challenge some assumptions in the literature. The partial mediating role of biological rhythms suggests that chronotherapeutic interventions may differentially impact functional domains, such as autonomy or interpersonal functioning, which are often overlooked in routine care. Future research should investigate these possibilities using longitudinal or experimental designs to clarify temporal dynamics, causal pathways, and potential differential effects across functional areas.

Limitations and Future Directions

Despite the relevance of these findings, several limitations should be acknowledged. First, the cross-sectional design limits the ability to infer causality; longitudinal research is essential to confirm whether biological rhythms genuinely mediate the relationship between depressive symptoms and functioning over time. Second, the small sample size and the absence of a comparison group (such as individuals with mild MDD, outpatients with anxiety, or healthy controls) restrict the external validity and generalizability of our findings. While this study deliberately focused on a homogeneous inpatient sample with moderate-to-severe MDD, future research should include diverse groups to clarify whether the observed associations are unique to severe depression or extend to broader clinical and nonclinical populations. Third, although we applied a statistical mediation model [57], it is important to underline that the mediation findings represent statistical associations rather than evidence of causal or temporal relationships. Only longitudinal or experimental designs can determine whether biological rhythms act as a true mediator over time. Another notable limitation is the absence of an examination of potential moderating variables. Factors such as age, medication use, illness duration, or comorbid conditions might affect the strength or direction of the identified relationships. Investigating these moderators in future research would offer valuable insights into whether the mediating role of biological rhythms varies across demographic or clinical subgroups and could help design more personalized interventions. Furthermore, the exclusive reliance on self-report measures raises concerns about perception biases and shared method variance, which may artificially inflate the associations between depressive symptoms, biological rhythms, and functioning. This issue should be carefully considered when interpreting the mediation results. To strengthen future investigations, objective assessments—such as actigraphy, polysomnography, or biological markers—should be incorporated alongside self-reported data to provide a richer, multimodal understanding of circadian disruptions in MDD, considering also the possibility of conducting multi-center studies. Finally, this study did not control for seasonal variations, which are known to influence biological rhythms and sleep patterns. The lack of seasonal consideration may have affected the measurements obtained and potentially limits the generalizability of the findings across different times of year.

5. Conclusions

This study underscores the association between depressive symptoms, biological rhythm disruption, and psychosocial functioning in individuals with Major Depressive Disorder. The findings confirm that greater depression severity is linked to increased circadian dysregulation and poorer functioning across multiple domains. While the primary focus was descriptive, an exploratory mediation model was included to preliminarily examine whether circadian disruption might partly account for the relationship between depression and functioning. Results suggested a partial mediation, indicating that biological rhythms may represent one of several pathways linking mood symptoms to daily life impairment. Although limited by its cross-sectional design and reliance on self-report, the study contributes novel evidence from an inpatient sample and highlights the potential relevance of chronobiological factors in understanding and managing functional outcomes in depression. Future longitudinal and clinically oriented research is needed to clarify directionality and causal mechanisms.

Supplementary Materials: The following supporting information can be downloaded at: <https://www.mdpi.com/article/10.3390/psychiatryint6030085/s1>, Figure S1—Boxplots and dotplots of out-

liers analysis of FAST, BDI and BRIAN; Table S1—Spearman correlation matrix; Table S2—Spearman correlations with CI values.

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