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Circadian Dysregulation in Bipolar Disorder and Schizophrenia

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ABSTRACT

Sleep and circadian rhythms are fundamental to the proper functioning of emotions, cognitive processes, and behaviors. Dysregulations in those rhythms are a core feature of severe mental illnesses, particularly bipolar disorder (BP) and schizophrenia (SZ). Moreover, diverse changes in sleep architecture have been consistently reported throughout various illness stages and are associated with symptom severity, relapse risk, cognitive impairment, and psychosocial functioning. This review attempts to aggregate existing evidence on circadian rhythm disruption and sleep abnormalities in BP and SZ. It focuses on shared and disorder-specific mechanisms, clinical correlates, and therapeutic implications. The authors searched the literature using PubMed and Scopus, including papers published mainly in the last decade. Sleep patterns in those two disorders are not identical, but there are overlapping biological pathways, such as dysregulation of clock genes, neurohormonal alterations, and dopaminergic transmission. In this review, the authors will also discuss interventions targeting circadian rhythms, such as melatonin, chronotherapy, light-based interventions, and digitally supported monitoring. Studying the impact of circadian dysregulation on SZ and BP can support early detection, monitoring, and treatment for patients with those disorders.

Keywords: circadian rhythm; sleep disturbances; bipolar disorder; schizophrenia; chronobiology

1. INTRODUCTION

Circadian rhythms are endogenous approximately 24-hour cycles that regulate sleep–wake patterns, hormonal secretion, and metabolism. The central role in the circadian system is played by the suprachiasmatic nucleus (SCN). It synchronizes peripheral clocks throughout the organism in response to environmental stimuli, most importantly the light–dark cycle. In recent years, disruption of circadian rhythms in the pathophysiology of mental disorders has been a topic of discussion. The evidence shows that the relation between mental disorders and disturbances of sleep is bilateral. Circadian dysfunction may contribute directly to psychiatric vulnerability, and the disorders themselves can cause secondary problems with sleep (Walker et al., 2021; Dollish et al., 2024).

Growing evidence shows that alterations in sleep and circadian phase have been noticed in both bipolar disease (BP) and schizophrenia (SZ), even during phases of

symptomatic remissions (Meyer et al., 2020; Freeman and Waite, 2025). In BP exists a strong link between different mood phases and accompanying changes in the sleep–wake patterns (Ahmad et al., 2021; Marchetti et al., 2025). Patients with this disorder often present with an evening chronotype or irregular social rhythms (Melo et al., 2017; Tonon et al., 2024). There is evidence that the connection between circadian rhythms and BP or SZ exists at the molecular level as well: in dysregulation of clock genes and circadian-related transcriptional pathways (Chung et al., 2024; Courtin et al., 2023).

Similarly, disturbances of sleep and circadian rhythms are part of the clinical picture of SZ. Patients with it exhibit sleep fragmentation and disruptions in sleep–wake cycles (Ferrarelli, 2021; Matsui et al., 2021). Cognitive deficits and negative symptoms, which are core features of the disorder, can partly result from alterations in circadian signaling pathways, including clock gene function and melatonin regulation (Lee et al., 2021; Boiko et al., 2024). Patients with SZ who exhibit circadian rhythm disturbances are more likely to show impaired memory consolidation and increased suicidality (Demirlek and Bora, 2023; Rogers et al., 2023).

The connection between circadian rhythms and BP or SZ extends to the molecular level, as evidenced by studies of clock genes and circadian-related transcriptional pathways (Chung et al., 2024; Courtin et al., 2023).

The aim of this review is to discuss the relationship between sleep, circadian rhythms, and affective disorders, in particular, BP and SZ. Our goal is to highlight shared as well as disorder-specific mechanisms and briefly discuss possibilities for precise interventions.

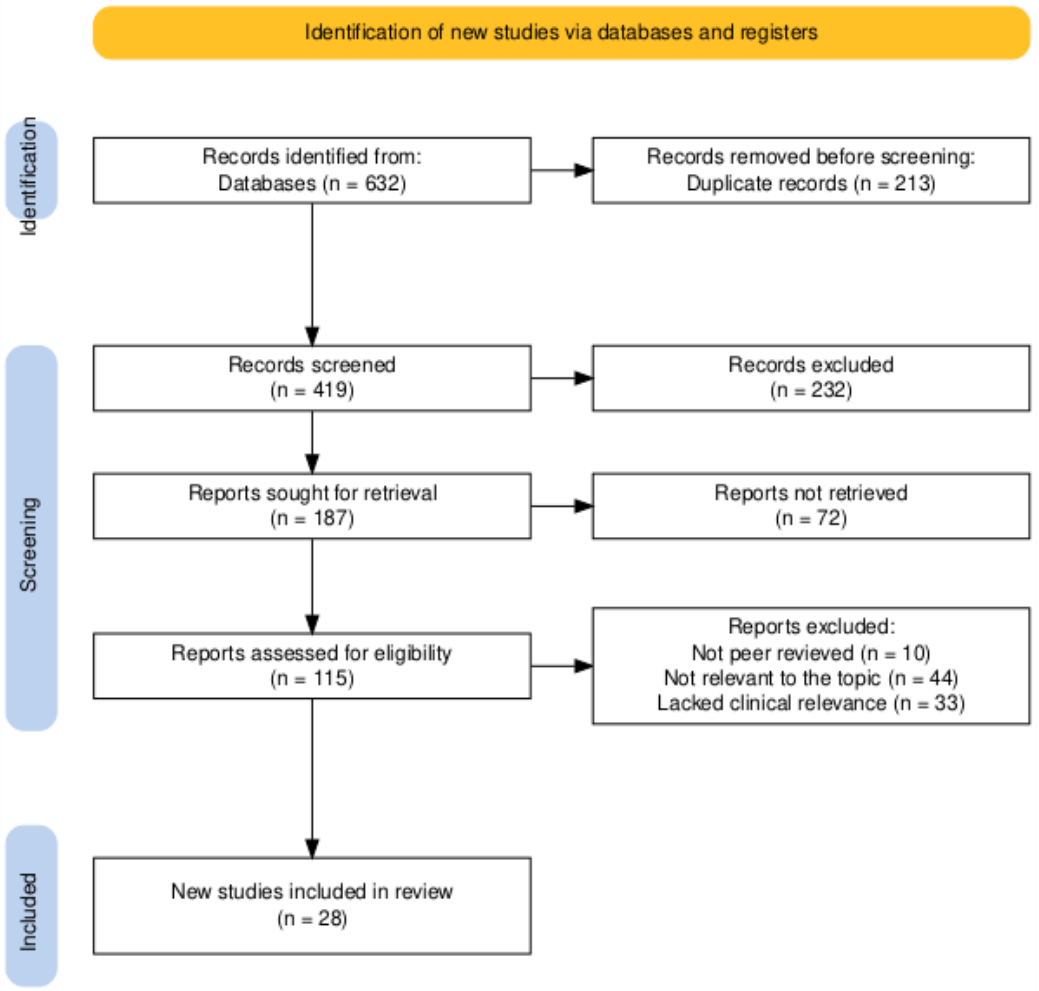

Figure 1. PRISMA flowchart for the article selection process.

2. REVIEW METHODS

A structured literature search was performed using the PubMed database as the primary source of biomedical literature. Additional relevant articles were identified through manual screening of reference lists of key review articles to guarantee comprehensive coverage of the topic.

The search strategy that was implemented included combinations of the following keywords and Medical Subject Headings (MeSH): bipolar disorder, schizophrenia, sleep disturbances, circadian rhythm, chronotype, melatonin, clock genes. The authors used Boolean operators ("AND", "OR") to refine the selection.

Articles were included based on their relevance to the topic, publication in peer-reviewed journals, and availability in English. Both clinical studies and reviews were considered. The reference lists of selected articles were also reviewed to uncover any additional relevant sources. The exclusion criteria included content that was non-peer-reviewed, lacked clinical relevance, or was unrelated to the topic. Case reports and conference abstracts were excluded (Figure 1).

3. RESULTS & DISCUSSION

Physiology of Circadian Rhythms and Clock Genes

The previously mentioned SCN is located in the anterior part of the hypothalamus and controls circadian rhythms according to the external light-dark cycle. It does so by registering light stimuli from the environment. Those stimuli are delivered to the SCN core via pathways that start in retinal photoreceptors. From the SCN, this information is transferred to various regions of the brain (Dollish et al., 2024). Several publications study clock genes. Their expression regulates circadian rhythms at the molecular level (Chung et al., 2024; Meyer et al., 2024).

Signals sent by SCN stimulate the pineal gland to produce melatonin. Its secretion increases in the absence of light, creating an endogenous signal for night. Alterations in melatonin's secretion or responsiveness to light can cause sleep disturbances (Moon et al., 2022; Palaghini et al., 2021). It has been shown that evening chronotype and reduced circadian amplitude are associated with vulnerability to sleep disruption and mood instability, indicating a role for circadian physiology in shaping behavioral and emotional regulation (Zou et al., 2022; Melo et al., 2017). These physiological characteristics provide a foundation for understanding why circadian dysregulation may represent a shared mechanism across mood and psychotic disorders.

Together, these findings underscore that normal sleep depends on the accurate coordination of circadian timing, molecular clock function, and neurohormonal signaling. Disruption at any level of this system can result in clinically meaningful alterations of sleep and behavior.

Circadian Disruption in Bipolar Disorder

The most consistent clinical manifestations of BP are sleep irregularities that often precede manic or depressive episodes. In the first one, patients typically suffer from reduced need for sleep, whereas depression frequently involves hypersomnia or insomnia (Ahmad et al., 2021; Marchetti et al., 2025; Scott and McClung, 2023).

Importantly, circadian and sleep disturbances often stay with patients during remission. Euthymic individuals with BP continue to exhibit irregular sleep–wake rhythms, increased variability in sleep timing, and reduced rhythm integrity compared with healthy controls (Meyer et al., 2020; Laskemoen et al., 2019)

A predominance of evening chronotype in BP has been consistently reported, with associations with a higher risk of mood instability. Patients complain of delayed sleep timing and impaired social rhythm regularity (Melo et al., 2017; Zou et al., 2022). Dysregulation of melatonin secretion may cause irregular sleep-wake patterns and mood instability (Moon et al., 2022). In the future, we could use this knowledge about melatonin to form new therapeutic approaches for patients with BP (Palagini et al., 2021; Moon et al., 2022). Looking at the molecular level, growing evidence implicates dysregulation of clock genes in the pathophysiology of BP. When one or more CLOCK 3111C/T gene alleles were present in patients with BP, the evening chronotype was more prominent. There are many other genes related to BP disorder and circadian rhythm, among which BMAL1, PER3, and CRY2 are worth mentioning (Chung et al., 2024; Courtin et al., 2023).

Patients with BP who suffer from circadian disturbances have been associated with a higher risk of suicidal attempts (Ahmad et al., 2021; Scott and McClung, 2023). Pharmacological and behavioral interventions may partially exert their therapeutic effects by modulating circadian rhythms. Lithium has been shown to influence circadian timing and rhythm stability (Xu et al., 2021).

Circadian Dysregulation in Schizophrenia

Sleep and circadian rhythm disturbances are highly prevalent in SZ and are recently more frequently recognized as integral components of the disorder rather than consequences of the nature of SZ and antipsychotic treatment (Ferrarelli, 2021; Meyer et al., 2020).

Sleep characteristics in patients with SZ can be objectively assessed using electroencephalography (EEG). In the past, publications mostly focused on sleep architecture, delayed sleep onset, alterations in rapid eye movement sleep, and non–rapid eye movement sleep. However, those characteristics were heavily influenced by factors such as the duration of SZ. Recently, studies have focused on alterations in sleep-specific EEG oscillations such as sleep spindles and slow waves. Those abnormalities have been present in patients with different stages of SZ (Ferrarelli, 2021; Freeman and Waite, 2025).

Circadian disruption not only influences poor sleep quality but also the daytime activity of patients (Adan et al., 2024; Purple et al., 2023). Moreover, alterations in sleep patterns are associated with exacerbation of positive symptoms and increased affective instability, although the relationships remain incompletely understood (Freeman and Waite, 2025; Ferrarelli, 2021).

The evidence suggests that genetic factors may also play a role in the circadian rhythm disturbances observed in SZ (Boiko et al., 2024). One recent study shows that disrupted-in-schizophrenia 1 (DISC1), a gene implicated in SZ susceptibility, stabilizes circadian rhythms and is regulated by BMAL1, providing evidence that circadian abnormalities are at least partly driven by genetic and molecular mechanisms (Lee et al., 2021). In addition to molecular clock dysfunction, abnormalities in melatonin secretion have been reported in SZ. The secretion of melatonin in SZ is reduced due to a smaller volume and enlarged calcification of the pineal gland (Moon et al., 2022).

Sleep disturbances in SZ have significant clinical implications, including deficits in memory consolidation, which can lead to cognitive impairment observed in the disorder (Demirlek and Bora, 2023). Furthermore, circadian abnormalities have been linked to increased risk of suicidality in SZ (Rogers et al., 2023). After recognizing circadian dysfunction in SZ as an important feature, the interest in new chronotherapeutic and rhythm-stabilizing interventions has grown. Those interventions target light exposure, daily activity patterns, and regularity of sleep (Faulkner et al., 2023). Some publications support the cautious use of melatonin for the management of insomnia in neuropsychiatric populations, including SZ (Palagini et al., 2021; Moon et al., 2022).

New possible strategies to reduce side effects and bring more therapeutic successes involve aligning treatment schedules with individual circadian profiles. Further research is needed to establish evidence-based guidelines in SZ (Colita et al., 2024). Disorders discussed in this review are summarised in Table 1. It includes the main circadian and sleep disturbances, the biological mechanisms behind it and possible clinical implications

Table 1. Summary of circadian rhythm and sleep abnormalities observed in bipolar disorder and schizophrenia.

Circadian rhythm and Sleep abnormalities	Bipolar Disorder	Schizophrenia
Main circadian abnormalities	Evening chronotype, irregular social rhythms, reduced circadian stability, phase shifts	Irregular sleep–wake cycles, reduced rhythm amplitude, circadian rhythm sleep–wake disorders
Sleep disturbances	Reduced need for sleep in mania; insomnia or hypersomnia in depression; persistent sleep irregularity during euthymia	Fragmented sleep, reduced sleep efficiency, abnormal sleep spindles, delayed sleep phase
Biological mechanisms	Clock gene dysregulation, altered melatonin secretion, circadian–dopaminergic interactions	DISC1-related circadian instability, melatonin dysregulation, impaired circadian synchronization
Clinical implications	Increased risk of mood episode relapse, mood instability, functional impairment, increased suicidality	Cognitive impairment, poorer psychosocial functioning, increased suicidality

4. CONCLUSION

Psychiatric disorders studied in this review share some possible circadian rhythm disturbances, but each condition has features specific to it. In BP, circadian instability is closely connected to changes in mood phase, and clock gene expression plays a prominent role. In contrast, SZ is characterized by more persistent and severe disruptions of sleep architecture and circadian organization, which are strongly associated with cognitive impairment, functional disability, and adverse clinical outcomes. From a clinical perspective, circadian dysregulation is a promising, potentially modifiable treatment target. Standard pharmacological treatment or psychotherapy can be supported by new forms of interventions, such as those targeting chronotypes or clock genes. However, further research is required to determine which patients are most likely to benefit from circadian-based therapies.

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Authors' Contributions

The author performed the literature search, analysis, manuscript drafting, and approved the final version of the manuscript.

Informed consent

Not applicable.

Ethical approval

Not applicable. This article does not contain any studies with human participants or animals performed by any of the authors.

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Conflict of interest

The authors declare that they have no conflicts of interest, competing financial interests or personal relationships that could have influenced the work reported in this paper.

Data and materials availability

All data associated with this study will be available based on the reasonable request to corresponding author.

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