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Medicine

Circadian Cycle in Patients with Bipolar Disorder

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Abstract		Original Research Article

Objective: To examine the distribution of chronotypes (morning, evening, intermediate) in patients with bipolar disorder and their associations with sociodemographic factors, clinical history, and comorbidities. *Results:* Chronotype. *Distribution:* Morning 74%, Evening 15%, Intermediate 11%. Bipolar type I: Morning 34.6%, Evening 8.6%, Intermediate 32.1%. Bipolar type II: Morning 11.1%, Evening 0%, Intermediate 13.6%. Significant associations: Morning chronotype linked to fewer suicide attempts (p = 0.034). Fewer depressive episodes in morning chronotype vs. evening/intermediate (p < 0.001). No significant associations: Chronotype vs. gender, age, marital status, education, occupation, medical comorbidities, number of manic/hypomanic episodes. *Discussion:* Unexpected. *Finding:* Predominance of morning chronotype, contrary to literature which often finds evening preference in bipolar disorder. *Possible Explanations:* Lithium and mood stabilizers' effect on circadian genes, Long-term psychiatric follow-up and structured daily routines, Social/work constraints in an urban population. Low evening chronotype proportion: May reflect stable/post-acute phase, prior hospitalization routines, or underreporting.
Keywords: Bipolar disorder, chronotype, circadian rhythm, morning chronotype, lithium.

INTRODUCTION

Bipolar disorder is a chronic psychiatric condition characterized by alternating manic, hypomanic, and depressive episodes, interspersed with periods of euthymic mood. Beyond this affective variability, numerous studies have highlighted underlying biological disturbances, among which circadian rhythm abnormalities play a central role.

The circadian rhythm regulates many physiological and behavioral processes over a 24-hour period, including the sleep-wake cycle, hormonal secretion, body temperature, and cognitive functions. It is primarily synchronized by the light-dark cycle via the suprachiasmatic nucleus of the hypothalamus. In bipolar disorder, this circadian regulation system appears to be altered, contributing not only to the frequent sleep disturbances observed but also to vulnerability to mood episodes.

Chronobiological studies have shown that bipolar patients present alterations in circadian rhythmicity, such as phase delay or advance, instability of sleep-wake cycles, variability in daily motor activity, and atypical morning-evening typology. These dysfunctions can precede decompensation episodes, persist during euthymic phases, and are sometimes correlated with greater disorder severity.

Understanding these disturbances paves the way for innovative therapeutic strategies, including chronotherapy, light therapy, and stabilization of the sleep-wake rhythm through targeted psychoeducational interventions.

In this perspective, our work aims to explore the characteristics of the circadian rhythm in patients with bipolar disorder, through a review of current data and an analysis of their clinical and therapeutic implications.

PATIENTS AND METHODS

This cross-sectional, descriptive, and analytical study was conducted at the Ar-Razi Psychiatric Hospital in Salé between October 2024 and April 2025. It included patients diagnosed with bipolar disorder, in the euthymic phase, followed in outpatient psychiatric consultations. Data were collected using an anonymous questionnaire administered by a resident physician.

Participants were patients over 18 years old, diagnosed with bipolar disorder according to DSM-5-TR criteria, and who had given their free and informed

consent. Anonymity and confidentiality of data were strictly maintained throughout the study.

Exclusion Criteria
- Presence of a severe neurological or somatic disorder
- Major psychiatric comorbidity such as schizophrenia or delusional disorder
- Use of medications strongly disrupting sleep
- Refusal to participate in the study

Data Collection Tools and Evaluation
Data were collected during psychiatric consultations through a structured interview administered by the physician. The questionnaire consisted of two main parts:
1. **First part (14 questions):** Sociodemographic data (sex, age), clinical characteristics (type of bipolar disorder, history of suicide attempts, number and type of mood episodes per year, age at onset of the disorder), psychiatric comorbidities (anxiety disorders, substance use disorders, other psychiatric disorders), and somatic comorbidities (hypertension, migraine, asthma, obstructive sleep apnea syndrome, or any other somatic illness).
2. **Second part (13 questions):** The *Composite Scale of Morningness* (CSM), a validated tool measuring individual circadian preferences.

Scale Used: Composite Scale of Morningness (CSM)
The CSM is a self-administered questionnaire designed to assess an individual's chronotype—i.e., whether they are more active in the morning, evening, or intermediate times. Developed by Smith *et al.,* (1989) and translated into French by Caci *et al.,* (1999), the scale contains 13 items scored on 4- or 5-point Likert scales, depending on the question.

The total score ranges from 13 to 55, classifying individuals into three chronotypes:
- **Evening chronotype:** score 13–26
- **Intermediate chronotype:** score 27–43
- **Morning chronotype:** score 44–55

Statistical Analyses
Statistical analyses were performed using Jamovi software (version 2.6.26.0).

RESULTS
The study involved 625 patients who consulted during this period at the hospital emergency department; among them, a total of 62 patients hospitalized for suicide attempts were recruited (32 women and 30 men).

Sociodemographic Characteristics
The mean age in our study was 25 ± 8 years (Table 1).

Bipolar Disorder and Chronotype
The distribution of chronotypes in the sample (N = 81) was as follows: 45.7% morning chronotype (n = 37), 45.7% intermediate chronotype (n = 37), and 8.6% evening chronotype (n = 7).

Among type I bipolar patients (n = 61), 34.6% were morning chronotype, 32.1% intermediate chronotype, and 8.6% evening chronotype. Among type II bipolar patients (n = 20), 11.1% were morning chronotype, 13.6% intermediate chronotype, and none were evening chronotype (Tables 1 and 2).

Statistical Analysis
The Chi² test showed no significant association between chronotype and type of bipolar disorder (χ^2 = 2.80; df = 2; p = 0.246). Fisher's exact test, used due to small cell sizes, confirmed this result (p = 0.296).

Chronotype and Sociodemographic Characteristics
Analysis of associations between chronotype and various sociodemographic and clinical characteristics revealed no significant differences for most variables studied. Chronotype distribution was comparable between men and women (χ^2 = 0.91; df = 2; p = 0.635), across marital statuses (χ^2 = 10.8; df = 8; p = 0.216), education levels (χ^2 = 7.75; df = 6; p = 0.257), and employment status (χ^2 = 4.47; df = 4; p = 0.346). No significant age difference was found according to chronotype (Kruskal–Wallis, χ^2 = 1.11; df = 2; p = 0.573).

Chronotype and Comorbidities
No statistically significant differences were found in the distribution of chronotypes between patients with or without hypertension (χ^2 = 0.73; p = 0.696), migraine (χ^2 = 1.06; p = 0.589), asthma (χ^2 = 0.73; p = 0.692), or obstructive sleep apnea syndrome (χ^2 = 1.55; p = 0.461). Fisher's exact tests confirmed these results (all p > 0.5).

Chronotype and Psychiatric History
In contrast, a statistically significant association was found between chronotype and history of suicide attempts (χ^2 = 6.75; df = 2; p = 0.034). Post-hoc analysis showed that morning chronotype patients had significantly fewer suicide attempts than expected (residual = −2.53), suggesting a potentially protective effect.

The Kruskal–Wallis test also showed a significant difference in the number of depressive episodes by chronotype (χ^2 = 16.2; df = 2; p < 0.001; ε^2 = 0.211). Post-hoc analyses revealed that morning chronotype differed significantly from both evening (p = 0.027) and intermediate chronotypes (p < 0.001), while no difference was found between evening and intermediate chronotypes (p = 0.961).

No significant differences were observed for the number of hypomanic episodes ($\chi^2 = 3.06$; p = 0.216) or manic episodes ($\chi^2 = 3.64$; p = 0.162) across chronotypes.

Several studies have shown that bipolar patients, even outside acute phases, frequently exhibit an evening chronotype, associated with emotional instability, poorer sleep quality, and increased risk of relapse:

- Giglio *et al.,* (2010) found that euthymic bipolar patients had more evening chronotypes than controls, and that these profiles were linked to mood instability, high impulsivity, and circadian phase delay.
- Selvi *et al.,* (2015) observed that both depressive and euthymic bipolar patients scored significantly lower on the CSM than controls, suggesting a persistent evening preference even in stable phases.
- Ritter *et al.,* (2015) highlighted an association between evening chronotype, more severe symptoms, poorer sleep quality, and delayed treatment response.

Thus, the predominance of the morning chronotype in our study stands out as an important divergence from these findings, requiring several explanatory hypotheses.

Interpretative Hypotheses for the Morning Dominance Observed
a) Effect of Medication

Several mood stabilizers, particularly lithium, are known to regulate circadian rhythms. Lithium specifically acts on clock genes (e.g., CLOCK, BMAL1) by lengthening the circadian period, favoring a more stable morning-oriented rhythm (McCarthy et al., 2013). It is therefore possible that prolonged use of mood stabilizers in our sample contributed to this circadian orientation.

b) Long-term psychiatric follow-up and clinical stabilization

In our sample, more than 53% of patients had been followed for over 5 years, which may reflect better therapeutic stability, education on daily routines, and behavioral structuring favoring a daytime rhythm. These factors are known to reinforce a morning chronotype.

c) Adaptation to social constraints

A large majority of our patients live in urban areas (89%), and 68% are employed. These conditions may force adaptation to morning schedules, indirectly influencing chronotype perception. Social pressure (social zeitgeber) is a powerful synchronizer of the circadian rhythm, capable of modifying the sleep-wake cycle over the long term (Roenneberg *et al.,* 2003).

Low Representation of Evening Chronotypes: Possible Meanings

The low proportion of evening chronotypes (15%) in our sample is atypical for bipolar disorder. However, this trend could be explained by:

- **Disease phase**: Patients were likely assessed in a stable or post-acute phase, when rhythms may be less desynchronized.
- **Effect of prior hospitalization**: Hospital stays often impose strict schedules (fixed meal, sleep, and medication times), which can encourage a shift toward morning orientation.
- **Underreporting of evening chronotype**: Some patients may downplay their evening preference, especially if they do not practice it in daily life due to work or family obligations.

Clinical Implications

These results highlight the importance of assessing chronotype in clinical practice for bipolar patients. Morning preference may be an indicator of clinical stability or reflect the beneficial effect of care on circadian regulation. Conversely, identifying evening chronotype patients remains crucial, as they are at greater risk of:

- Sleep disturbances (phase delay, insomnia)
- Mood episode relapses
- Poor treatment adherence
- Psychiatric comorbidities (anxiety, addictions, suicidality)

Targeted interventions such as chronotherapy, light therapy, or interpersonal and social rhythm therapy (IPSRT) could be recommended for these patients.

CONCLUSION

This study highlights the specific circadian profile of patients with bipolar disorder in our sample, with a predominance of the morning chronotype contrasting with most literature reports, which often emphasize evening preference. This difference may be explained by factors such as long-term psychiatric follow-up, stabilization through mood stabilizers like lithium, and adaptation to social and professional constraints.

While morning chronotype may be associated with greater clinical stability and fewer suicide attempts, the identification of patients with an evening chronotype remains essential, as they are at increased risk of sleep disturbances, therapeutic non-adherence, mood episode relapse, and psychiatric comorbidities.

The assessment of chronotype should therefore be integrated into the routine clinical evaluation of bipolar patients. This could guide the implementation of targeted interventions, such as chronotherapy, light therapy, or interpersonal and social rhythm therapy

(IPSRT), aimed at improving circadian regulation and, consequently, the overall prognosis of the disorder.

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