

ORIGINAL ARTICLE

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Biological rhythm, sleep quality and functionality in the euthymic period in patients diagnosed with bipolar disorder

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Abstract

In our study, sleep quality, biological rhythm disorders and functionality were examined in euthymic patients diagnosed with Bipolar Disorder. 60 patients diagnosed with Bipolar Disorder and 50 healthy controls were included in the study. All participants were administered the Biological Rhythm Assessment Interview (BRAI), Functioning Assessment Short Test (FAST), and Pittsburgh Sleep Quality Index (PSQI). No statistically significant difference was found between the patient and control groups in the BRAI scores ($p=0.063$). The patient group's FAST total score ($p<0.001$), FAST-autonomy score ($p<0.001$), FAST-Occupational functioning score ($p<0.001$), FAST-Cognitive Functioning score ($p<0.001$), FAST-Financial Issues score ($p<0.001$), FAST-Free Time Activities score ($p=0.001$), FAST-Interpersonal Relationships score ($p<0.001$), and PSQI total score ($p<0.001$) were found to be statistically significantly higher than the control group. In the patient group, a negative significant correlation was found between the total score of the BRAI and FAST-Cognitive Functioning ($r=-0.339$, $p=0.008$) and FAST-Free Time Activities ($r=-0.329$, $p=0.010$). Even in the euthymic phase, patients diagnosed with Bipolar Disorder may experience sleep disturbances, disruption of biological rhythms, and decreased functionality. Continuing the treatment and follow-up of patients during this phase, detailed evaluation and treatment arrangement for symptoms are important for the positive prognosis of the disease.

Keywords: Bipolar disorder, euthymia, sleep quality, biological rhythms

Introduction

Bipolar Disorder (BD) is a mental disorder characterized by manic-depressive episodes and leading to significant disability. Although its etiology has not yet been fully elucidated, it is known that genetic factors play an important role. This mental disorder, which affects a significant portion of society, begins especially in young adults. Many areas of life such as daily living activities, biological rhythm such as sleep and appetite, family relationships, and professional life are negatively affected by the disease process. Especially during manic episodes, patients experience significant disability. In BD, in addition to manic and depressive episodes, there are intermediate periods when no symptoms of the disease are observed [1]. These intermediate periods are called euthymic phase and it is thought that patients reach a state of well-being during these phase. However, there are recent studies reporting that patients have disease-related loss of functionality

even during euthymic phase. In many studies comparing patients in the attack period and healthy controls, it has been reported that patients in the euthymic phase experience losses especially in the cognitive area and a decrease in executive functions such as memory and attention. In addition to the cognitive losses of the patients, residual symptoms similar to those in the active periods of the disease are observed in their functionality, biological rhythms and other areas of life. Biological rhythm plays an important role in regulating activities such as eating, drinking and sleeping patterns. This cyclical order, which encompasses the basic physiological functions of living things, is necessary for living things to survive. Biological disorders may develop along with mental illnesses such as BD [2]. In our study, it was hypothesized that there was a loss of functionality in patients during the euthymic phase, sleep disorders were observed, and there was a disruption in biological rhythm, in line with the literature. When looking at the literature, there are few studies

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investigating biological rhythm, functionality and sleep patterns in the euthymic phase. Our study will contribute to the literature on this subject. The idea that patients may have symptoms of the disease in their euthymic phases as well as in their mood episodes periods offers a different perspective in terms of the follow-up of BD with a chronic course.

Material and Methods

Our research was conducted between 01.03.2023 and 01.06.2024 at the mental health and diseases clinic of Recep Tayyip Erdoğan University Training and Research Hospital. The study included 60 patients diagnosed with BD in the euthymic phase for the last 3 months and 50 healthy controls consisting of patients' relatives and healthcare professionals matched with the patients' sociodemographic characteristics. The sample of the study was determined with the Gpower program version 3.1. The minimum number of each sample to be taken into the study planned to be conducted with 0.5 alpha value, 0.66 effect size and 80% power was calculated and the number of samples was determined in accordance with the data [3]. The patient group consists of patients who have been diagnosed with BD and have been receiving treatment for at least 2 years. Patients were clinically interviewed and evaluated according to fifth version of the Statistical and Diagnostic Manual of Mental Disorders (DSM-5) diagnostic criteria. The patients' current mental status examinations were conducted by a psychiatrist and their past medical records were reviewed. As a result of the clinical interview, patients with current BD I and II diagnoses were included in the study. Other mental diagnoses such as substance use disorder and personality disorders were determined through the interview, and patients with comorbid mental disorder diagnoses were not included in the study. Additionally, patients with chronic internal diseases were excluded from the study. The euthymic phases of the patients were evaluated clinically, and the Hamilton Depression Rating Scale (HAM-D) and the Young Mania Scale were applied, and it was determined that they were in the euthymic period. Patients with HAM-D <7 and young mania scale score <7 were included in the study [4-7]. In the study, euthymic period criteria were determined by scale scores and clinical interviews. Based on the history and medical records obtained from the patients, patients who had no symptoms of illness in the last 3 months were included in the study. As a result of the evaluation, 12 patients were excluded from the study due to showing mood symptoms and 4 patients were excluded due to not being able to comply with the scale forms. All participants were administered the Biological Rhythm Assessment Interview (BRAI), Functioning Assessment Short Test (FAST), and Pittsburg Sleep Quality Index (PSQI). In addition, detailed information about the purpose and method of the research was given, and written and verbal approvals were obtained. Ethical principles were followed during the research process and the ethics committee approval of the research was received from the Recep Tayyip Erdoğan University Non-Interventional Ethics Committee (Ethics Committee Approval No: 2022/225).

Scales Used in the Study

Biological Rhythm Assessment Interview (BRAI): The scale was developed by Giglio et al. in 2009 to evaluate biological systems such as sleep and appetite. The 21-item scale consists of 5 sub-dimensions: chronotype, sleep, activity, social life and eating habits. It is a Likert-type scale, and as the scores obtained from the scale increase, it is thought that there is a disruption in the biological rhythm. The Turkish validity and reliability of the scale was made by Aydemir et al. and was found to be valid and reliable in a Turkish sample. In the validity and reliability analysis of the scale, Cronbach alpha value was found to be 0.899. In our research sample, Cronbach's alpha value was calculated as 0.78 and the total score of the scale was used [8,9].

Pittsburg Sleep Quality Index (PSQI): It is a Likert-type scale that evaluates sleep disorders especially in the last month. It was developed by Buysse et al. in 1989 and was found to have a valid and sufficient internal consistency. It is thought that sleep disturbance increases as the scores obtained from the scale increase. It has 7 sub-dimensions: sleep quality, time spent asleep, time to fall asleep, sleep patterns, sleep disorders, medication use and daytime sleepiness. There is a total scale score calculated with sub-dimensions and the total scale score was used in our research. The Turkish validity and reliability of the scale was made by Ağargün et al. and a sufficient Cronbach value was found. In our sample, the Cronbach value of the scale was calculated as 0.82 [10,11].

Functioning Assessment Short Test (FAST): It is a scale developed by Rosa et al. for the evaluation of functionality. It has 6 sub-dimensions: Autonomy, occupational functioning, Cognitive Functioning, Financial Issues, Free Time Activities and Interpersonal Relationships. While the sub-dimensions of the scale can be calculated individually, the total score is also calculated. In our research, both the sub-dimensions and the total score were calculated separately. It is thought that functionality deteriorates as the scores obtained from the scale increase. The Turkish validity and reliability of the scale was made by Aydemir et al. The scale has a valid and sufficient internal consistency value. In our research sample, the Cronbach value was calculated as 0.89 [12,13].

Statistics

Statistical analysis of the research data was done with SPSS program 25th version. Descriptive statistics were presented as minimum, maximum, mean and standard deviation. Chi square and Fisher exact tests were used in the analysis of categorical data. The normality of the data was assessed with the Kolmogorov test, skewness and kurtosis values, and histogram visuals. In normally distributed data, the independent sample t test was used to compare the means of two independent groups. The Mann Whitney U test was used to compare the means of two groups in data that were not normally distributed. The correlation of the groups was evaluated with the Spearman correlation test. Statistical significance was taken as $p < 0.05$.

Results

A total of 110 participants were included in the study, 60 patients and 50 controls. The youngest age of the patients was 27 and the oldest was 61, with a mean age of 42.77±9.7. Of the patient group, 27 (45.0%) were male, 33 (55.0%) were female. 34 (56.7%) were primary school graduates, 13 (21.7%) were secondary school graduates, and 13 (21.7%) were university graduates. 22 (36.7%) were single, 30 (50.0%) were married and 8 (13.3%) were separated from their partners. No statistically significant difference was found in the comparison of sociodemographic data of the patient and control groups (p>0.05) (Table 1). Scale scores of the patient and control groups were compared and presented in Table 2. No statistically

significant difference was found between the patient and control groups' scores on BRAI (p=0.063). The patient group's FAST total score (p<0.001), FAST-autonomy score (p<0.001), FAST-occupational functioning score (p<0.001), FAST-Cognitive Functioning score (p<0.001), FAST-Financial Issues score (p<0.001), FAST-Free Time Activities score (p=0.001), FAST-Interpersonal Relationships score (p<0.001), and PSQI total score (p<0.001) were statistically significantly higher than the control group (Table 2). When the relationship between scale scores in the patient group was examined, a negative significant relationship was found between the BRAI total score and FAST-Cognitive Functioning (r=-0.339, p=0.008) and FAST-Free Time Activities (r=-0.329, p=0.010) (Table 3).

Table.1. Sociodemographic data of the patient and control group

	Patient (n=60)		Control (n=50)		p
	Min-Max	Mean±SD	Min-Max	Mean±SD	
	n	%	n	%	
Age	27-61	42.77±9.7	20-63	39.2±9.8	0.620
Gender					
Male	27	45.0	27	54.0	0.444
Female	33	55.0	23	46.0	
Education					
Primary school	34	56.7	11	22.0	0.122
High school	13	21.7	35	70.0	
University	13	21.7	4	8.0	
Marital status					
Single	22	36.7	20	40.0	0.096
Married	30	50.0	29	58.0	
Divorced	8	13.3	1	2.0	

Independent Sample T Test, chi square, fisher exact

Table 2. Comparison of scale scores of patient and control group

	Patient (n=60)		Control (n=50)		Test stat.	p
	Min-Max	Med (IQR)	Min-Max	Med (IQR)		
BRAI total score	18-58	31 (13)	22-54	36 (9)	1191.000	0.063
FAST total score	11-56	35 (11)	0-36	9 (9)	116.000	<0.001**
FAST-autonomy	0-12	6 (4)	0-4	0 (2)	197.000	<0.001**
FAST-occupational functioning	0-14	7 (5)	0-5	0 (1)	95.500	<0.001**
FAST-cognitive functioning	1-13	8 (4)	0-11	3 (3)	343.000	<0.001**
FAST-financial issues	0-5	2 (3)	0-5	0 (0)	835.000	<0.001**
FAST-free time activities	0-6	2.5 (2)	0-6	1 (3)	974.000	0.001**
FAST-interpersonal relationships	3-17	8 (6)	0-10	1 (3)	266.500	<0.001**
PSQI total score	1-16	8 (4)	1-14	3 (2)	580.500	<0.001**

Mann Whitney U, **p<0.01; BRAI: biological rhythm assessment interview, FAST: functioning assessment short test, PSQI: Pittsburg sleep quality index, IQR: interquartile range

Table 3. Correlation of scale scores of the patient group

		1	2	3	4	5	6	7	8
1. BRAI total score	r	-	-	-	-	-	-	-	-
	p	-	-	-	-	-	-	-	-
2. FAST total score	r	-0.217	-	-	-	-	-	-	-
	p	0.096	-	-	-	-	-	-	-
3. FAST-autonomy	r	-0.094	0.805	-	-	-	-	-	-
	p	0.475	0.000**	-	-	-	-	-	-
4. FAST-occupational functioning	r	-0.076	0.834	0.747	-	-	-	-	-
	p	0.563	0.000**	0.000**	-	-	-	-	-
5. FAST-cognitive functioning	r	-0.339	0.680	0.483	0.545	-	-	-	-
	p	0.008**	0.000**	0.000**	0.000**	-	-	-	-
6. FAST-financial Issues	r	-0.059	0.574	0.431	0.407	0.233	-	-	-
	p	0.654	0.000**	0.001**	0.001**	0.073	-	-	-
7. FAST-free time activities	r	-0.329	0.348	0.162	0.268	0.299	0.027	-	-
	p	0.010*	0.006**	0.216	0.039*	0.020*	0.837	-	-
8. FAST-interpersonal relationships	r	-0.215	0.776	0.566	0.485	0.414	0.389	0.359	-
	p	0.098	0.000**	0.000**	0.000**	0.001**	0.002**	0.005**	-
9. PSQI total score	r	0.146	0.041	-0.113	-0.032	0.035	0.019	-0.034	0.080
	p	0.267	0.757	0.391	0.807	0.791	0.887	0.797	0.543

Spearman correlation, *p<0.05, **p<0.01; BRAI: biological rhythm assessment interview, FAST: functioning assessment short test, PSQI: Pittsburg sleep quality index

Discussion

In our study, the sleep, biological rhythm and functionality levels of BD patients in the euthymic phase were compared with healthy controls. According to our research results, the patient group's scores on all scales except the BRAI were higher than the control group. However, there was no difference between the total BRAI scores of the patient and control groups. When we look at the findings, although the patients were in the euthymic phase, their functionality and sleep quality were worse than healthy controls. These results were also consistent with the main hypothesis of our research. When we look at the literature, there are studies that find similar results. In a study conducted by Rosa et al., euthymic patients with BD were compared with a healthy control group, and although the BD patients were in the euthymic phase, their functionality was found to be worse than the healthy group. It has been stated that factors such as the number of previous hospitalizations and the presence of depressive episodes were more likely to cause functional deterioration and may be a predictor. It is also important to know and investigate risk factors in order to reduce the loss of functionality of patients during the euthymic phase [14]. Although the data on the clinical characteristics of the patients in our study were not evaluated as risk factors, it is important to investigate the factors that will negatively affect functionality in the euthymic phase with large sample studies. In a study conducted with euthymic patients with

BD, factors such as family history of illness, the total number of mood episodes, and the number of depressive episodes were found to be risk factors that impair functionality during the euthymic phase [15]. In a meta-analysis conducted during the euthymic phase of BD, similar to our study, all sub-dimensions of functionality were found to be worse in the patient group than in the healthy control group [16]. Even though patients are in the euthymic phase, the damage caused by the disease, especially in the neurocognitive area, can lead to functional deterioration along with the course of the disease. Studies have shown that neurocognitive loss continues in patients during the euthymic phase. This situation negatively affects the cognitive functions and quality of life of patients. Residual depressive symptoms and sleep disorders of the patients negatively affect their daily life functions. Most studies report that patients' functioning is negatively affected during the euthymic phase [17]. Patients' cognitive functions, especially memory and attention, are negatively affected. Factors such as advanced age, lack of family support, and irregular treatment increase the risk of cognitive dysfunction in patients. A decrease in the functionality of patients is observed with all these factors [18]. In a study, patients in the euthymic phase were examined with neuropsychological tests. According to research results, cognitive impairment in patients leads to deterioration in psychosocial functioning and a decrease in quality of life. In this case, it is an important factor that cognitive

losses due to bipolar disorder continue in the euthymic phase [19]. At this point, there are actually confounding factors such as family support, previous functioning, medication use, age of onset, and individual characteristics. This condition is not only due to neurocognitive losses, many factors affect the course of the disease [20]. Another hypothesis of our research was that in addition to functionality, sleep quality would be poor in patients. Although sleep disturbance and insomnia are actually observed more in mania and hypomania attacks and are considered as a distinguishing feature in terms of the period between attacks, there is data indicating that sleep quality deteriorates and sleep disorders can be seen in the euthymic period [21-23]. In a study, it was found that euthymic BD patients had worse sleep quality than healthy controls [24]. In a similar study, it was found that euthymic bipolar patients had poor functionality and poor sleep quality [25]. Sleep disorders, poor quality sleep and circadian rhythm disruptions can also negatively affect the functionality of patients.

In our study, no difference was found between the BRAI scores of the patient group and the control group. In this patient group, biological rhythm is significantly disrupted, especially during the attack periods of the disease. Symptoms such as insomnia and disruption of the day-night cycle also negatively affect the biological rhythm. In this case, biological rhythm disturbances are possible in the euthymic phase in the patient group. However, when we look at the literature, although there are relatively fewer studies on the biological rhythms of BD patients during the euthymic phase, there are studies showing that the biological rhythm is also disturbed during the euthymic phase [26,27].]. When the pathophysiology of the disease is examined, disruption in biological rhythm paves the way for disease development. Circadian rhythm abnormalities have been demonstrated in many studies. Factors such as 24-hour hormone levels and sleep-wake cycles are disrupted during the disease process and may persist in remission periods as residual symptoms [28-30]. There are studies showing that biological rhythm is disrupted in BD. Disruption in biological rhythm also leads to a decrease in the quality of life. In a study, a positive relationship was found between biological rhythm and quality of life in a patient group in the euthymic phase. Sleep quality and adaptation to daily life can be found with disruption in biological rhythm [31]. In our study, in addition to the difference in scale scores of the patient and control groups, the relationship between the scale scores were also examined. A negative significant correlation was found between the patients' BRAI and FAST sub-dimensions cognitive function and free time activity scores. In fact, what is expected is that there will be a positive correlation between biological order and functionality in patients. However, in some cases, patients may experience increased functionality, especially due to decreased sleep or subsyndromal hypomanic symptoms [32].

In our study, no significant relationship was found between other scales, but there are studies in the literature that found a relationship between biological rhythm, sleep disorders and

functionality [25,31-34]. In contrast to our study, in a study conducted by Pinho et al., a relationship was found between biological rhythm disorders and functionality, and biological rhythm disturbance was reported as a predictor of poor functionality [30]. Similarly, in a study conducted with BD patients during the euthymic period, a relationship was found between sleep disorders and occupational functioning [35].

In another study, the functionality of patients in the euthymic phase and its relationship with their biological rhythms were examined. When the results of the study were examined, insomnia was found to be associated with poor functioning. However, there are studies reporting that there is no direct relationship between sleep and functionality, and that mood symptoms, especially depressive mood and cognitive dysfunction, have an impact on functionality [25,36]. The reason why no relationship was found between functionality and biological rhythm in our study may be due to the limitations of our study. There are limited studies in the literature on this subject. Studies mostly focus on neurocognitive losses. However, there are many factors that affect the biological order and functionality of patients. Although neurocognitive loss is one of them, many factors such as socioeconomic level, family support, genetic factors may have an effect on this issue. Therefore, more detailed research is needed. Some studies also stated that sleep disturbance and biological rhythm disruption may be predictive of recurrent attacks. For this reason, although the euthymic phase is evaluated as symptom-free or in remission, continuing follow-up and treatment is important for a positive prognosis [28,37-39]. BD, with all its symptoms, causes functional deterioration in patients. Long-term follow-up and treatment of patients is important for the course of the disease. Patients may interrupt treatment during the euthymic phase, which they consider to be symptom-free. Therefore, it is important for clinicians to be aware of this issue and provide psychoeducation to patients [40,41].

Study Limitations

There are some limitations to our study. Since it is a single-center study and includes a patient group from the same region, the data cannot be generalized. A clinical interview scale such as The Structured Clinical Interview for DSM-5 (SCID-5) was not applied while creating the sample group, and diagnosis was made with structured clinical interviews. In addition, the patient group was not divided into BD I and II, and all patients diagnosed with BD were included. The fact that these two diagnostic groups, which show different clinical findings, were not separated from each other is an important limitation. Another limitation of our study is that different factors that may affect functionality, such as family support, economic factors, and regular follow-up, were not evaluated. However, the fact that it was conducted with a specific patient group makes our study valuable. Further detailed studies with larger and multicenter samples are needed.

Conclusion

As a result, patients with BD experience problems such as sleep disorders and functional impairment during the euthymic period. The number of attacks, medication use, regular follow-up and treatment are important in the course of the disease. However, euthymic phases are a risky period in terms of ignoring treatment and symptoms because there are no specific complaints, manic symptoms subside, and it is thought that remission has occurred. However, during this period, sleep disorders, biological rhythm disruption and loss of functionality may occur, reducing the patient's quality of life and negatively affecting the prognosis. In addition, factors such as sleep disorders may further cause functional impairment. It is important to question patients in detail about their symptoms during the euthymic period, as in the attack periods, in terms of situations such as frequent illness, negative response to treatment, and poor prognosis. Further studies in this area will contribute to the literature and bring new perspectives on the course of the disease. Data on the euthymic period, especially on neurocognitive losses, have been increasing in recent years, and research in other areas such as functionality and sleep will contribute to our knowledge of the euthymic period of BD.

Conflict of Interests

The authors declare that there is no conflict of interest in the study.

Financial Disclosure

The authors declare that they have received no financial support for the study.

Ethical Approval

Recep Tayyip Erdoğan University Non-Interventional Clinical Research Ethics Committee approved this study (approval number: 2022/225).

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