NÖRO PSİKİYATRİ ARŞİVİ
ARCHIVES OF NEUROPSYCHIATRY

RESEARCH ARTICLE

Arch Neuropsychiatry 2021;58:41–47
https://doi.org/10.29399/npa.25056

Seasonality in Bipolar Disorder: Impact on Mood Symptoms, Psychosocial Functioning, Neurocognition, and Biological Rhythm

Fikret Poyraz ÇÖKMÜŞ[1], Kadir AŞÇIBAŞI[2], Didem SÜCÜLLÜOĞLU DİKİCİ[1], Emine Özge ÇÖLDÜR[3], Emin AVCI[4], Ömer AYDEMİR[4]

[1]Manisa Mental Health and Disease Hospital, Psychiatry Clinic, Manisa, Turkey
[2]Tepecik Training and Research Hospital, Department of Psychiatry, İzmir, Turkey
[3]Kuşadası State Hospital, Psychiatry Clinic, Aydın, Turkey
[4]Manisa Celal Bayar University Hospital, Department of Psychiatry, Manisa, Turkey

ABSTRACT

Introduction: Even though an increase in the number of hospital admissions for manic and depressive periods at certain times of the year is reported in bipolar disorder (BD), mood symptoms do not show a seasonal variation. We aimed to find out the possible causes of increased hospital admissions of BD patients in certain periods of the year.

Methods: The study was carried out in four centers in Turkey. The patient group consisted of 41 persons with a diagnosis of BD in remission. The healthy control (HC) group consists of 37 persons. The selected evaluation times are fall equinox (September 23), spring equinox (March 21), summer solstice (June 21) and winter solstice (December 21). For mood symptoms, Hamilton Depression Rating Scale and Young Mania Rating Scale; for functioning Functioning Assessment Short Test; for neurocognition Stroop Test (ST) and Rey Auditory Verbal Learning Test (RAVLT), for biological rhythm Biological Rhythms Interview of Assessment in Neuropsychiatry, and Seasonal Pattern Assessment Questionnaire were used.

Results: In terms of mood symptoms no seasonal variation was found. Across all four periods of assessment of BD group, statistically significant variation was only observed in the instant recall, learning and recognition domains of RAVLT and word test and color test domains of ST; however, it was not sufficient to distinguish the BD group separating from the control group.

Conclusions: In terms of mood symptoms, psychosocial functionality, biological rhythm, neurocognition, no seasonal variation was demonstrated that could distinguish the BD group from the HC group.

Keywords: Biological rhythm, bipolar disorder, neurocognition, psychosocial functionality, seasonality

Cite this article as: Çökmüş FP, Aşçıbaşı K, Sücüllüoğlu Dikici D, Çöldür EÖ, Avcı E, Aydemir Ö. Seasonality in Bipolar Disorder: Impact on Mood Symptoms, Psychosocial Functioning, Neurocognition, and Biological Rhythm. Arch Neuropsychiatry 2021; 58:41-47.

INTRODUCTION

Bipolar disorders (BD) are severe psychiatric disorder, with heterogeneous clinical presentations and multifactorial origins (1). The circadian rhythm system plays a major role in the regulation of important physiological processes such as hormone secretion and the sleep-wake cycles, which have been implicated in the pathophysiology of BD (2). One of the main features of BD is rhythm disruption (3). In the etiologic background of the disease, it has been hypothesized that disturbances of the circadian rhythm system play a major role (4). Patients with BD have a disrupted circadian rhythm, which changes with the seasons and affects their sleeping efficiency and mood (5).

"Seasonality" refers to the seasonal variations of several environmental factors, such as photoperiod (day length), light intensity, outdoor temperature, and food availability (6). On an individual level, seasonality was shown to influence the clinical course of mood episodes and is profoundly affected in one-quarter of patients with BD (7). As a result of many studies, it has been shown that there is an increase in the number of hospital admissions for manic and depressive periods at certain times of the year (7–10), yet neither manic nor depressive symptoms do not show a seasonality pattern (11,12).

In light of these data, we aimed to determine the possible causes of increased hospital admissions of patients with BD in certain periods of the year. In our study, it was aimed to monitor and determine the changes in mood symptoms, psychosocial functionality, neurocognitive function, biological rhythm, and seasonality of patients with BD and healthy control (HC) volunteers. We planned to perform this study because we think that seasonality may be effective on mood symptoms in patients with BD and on functionality, biological rhythm, and neurocognitive function. This present study hypothesized that in winter, patients with BD would have increased depressive symptoms, which might cause impairment and withdrawal in psychosocial functionality, biological rhythm, and neurocognitive functions, whereas in the spring and summer period, there would be an increase in manic symptoms and psychosocial functionality, impairing biological rhythm, and neurocognitive functions are impaired. The other hypothesis of the study was that in seasonal

Correspondence Address: Fikret Poyraz Çökmüş, Manisa Mental Health and Disease Hospital, Psychiatry Clinic, Manisa, Turkey • **E-mail:** fikretpoyrazcokmus@hotmail.com
Received: 04.02.2020, **Accepted:** 18.08.2020, **Available Online Date:** 19.11.2020

measures, the BD group would be more symptomatic and shows more impairment in psychosocial functionality, biological rhythm, and neurocognitive functions.

METHODS

Participants

The study was approved by the Scientific Research Ethics Committee of Manisa Celal Bayar University Faculty of Medicine (Date: 12/04/2017–20.478.486). All participants gave written informed consent for participation in the study.

Two groups of volunteers were included in the present study. The patient group consisted of 41 patients with BD. The patients met the Diagnostic and Statistical Manual Mental Disorders, Fourth Edition (DSM-IV-TR) criteria for BD as determined by medical records, and the diagnosis was confirmed using the Structured Clinical Interview for DSM-IV-Patient Edition (SCID-IV). The inclusion criteria were being aged 18–65 years, being in remission for at least 6 months (remission criteria: YMRS <5, HDRS <7) and willing to participate in the study. The exclusion criteria were determined as the presence of additional psychiatric illness including substance use disorders, presence of electroconvulsive therapy (ECT) in the last six months, presence of neurologic disease, and mental retardation. The HCs consisted of 37 volunteers who had no psychiatric diagnosis (based on clinical SCID interview by an experienced psychiatrist). HCs were matched with the BD group according to their demographic features such as age, sex, and education level.

At the beginning of the study, 56 patients diagnosed with BD were included in the study. Fifteen patients were excluded from the study; three moved to another city and did not attend follow-up visits, two wanted to get pregnant and stopped the medication, three stopped the medication of their own will, and seven did not attend the follow-up meetings at the planned date. A total of 41 patients diagnosed with BD (39 BD-I, 2 BD-II) completed the research.

The selected evaluation times were fall equinox (September 23), spring equinox (March 21), summer solstice (June 21), and winter solstice (December 21). For all four interviews, both groups tolerated one week before and after these dates. In the first evaluation interview, a sociodemographic data form and the Seasonal Pattern Assessment Questionnaire (SPAQ) were administered to both groups. Additionally, in all evaluation visits, the Hamilton Depression Rating Scale (HDRS), Young Mania Rating Scale (YMRS), Functioning Assessment Short Test (FAST), Biological Rhythms Interview Assessment Short Test (BRIAN), Stroop Test (ST), and Rey Auditory Verbal Learning Test (RAVLT) were performed in both groups.

Data Collection Tools

Sociodemographic data form

The sociodemographic data form included sex, age, occupation, marital status, financial status, years of education, duration of illness, medicine use, number of hospitalizations, presence of ECT in the last six months, family history of psychiatric disorder, comorbid disease, and comorbid medicine use.

Hamilton Depression Rating Scale (HDRS)

The HDRS, which has 17 items, was used in this study. Each item is rated on a 5-point scale (0–4).

Young Mania Rating Scale (YMRS)

The YMRS comprises 11 items that encompass the main symptoms of the manic episodes.

Functioning Assessment Short Test (FAST)

FAST was developed to evaluate the functions of patients with BD more quickly. FAST is a 24-item interviewer-rated scale with 4-point Likert-type rating (0=no difficulty, 3=severe difficulty). FAST consists of six dimensions: autonomy, occupational functioning, cognitive functioning, financial issues, interpersonal relations, and leisure time. Higher scores indicate poorer functionality of patients with BD. Aydemir and Uykur performed the reliability and validity study for the Turkish version (13).

Rey Auditory Verbal Learning Test (RAVLT)

The purpose of RAVLT is to evaluate verbal learning and memory. The RAVLT was performed as a part of a larger neuropsychological battery in a standard style of five learning trials, presentation of a distractor list, recall after the distractor list, long delay, and recognition as measured through circling of target words from a paragraph read by the patient. Karakaş performed the validation study for the Turkish version (14).

Stroop Test (ST)

This neuropsychological test, which is extensively used for experimental and clinical purposes, evaluates the ability to prevent cognitive interference that occurs when processing a stimulus feature, which affects simultaneous processing of another attribute of the same stimulus. In the test, the time for the subject to complete both stages, the difference between these stages, and the number of correct and incorrect responses are calculated. Especially, the interference time is considered to be an indicator of the ability to suppress a response. Karakaş performed the validation study for the Turkish version (15).

Biological Rhythms Interview of Assessment in Neuropsychiatry (BRIAN)

BRIAN, as an interviewer-rated instrument, contains 21 items designed to assess five areas related to biologic rhythms: sleep, activity, social aspect, diet, and predominant rhythm (chronotype). All items are evaluated on a four-point scale (1–4), higher scores denote greater disturbance in the corresponding biologic rhythm. Aydemir et al. (16) performed the reliability and validity of the Turkish version.

Seasonal Pattern Assessment Questionnaire (SPAQ)

Noyan et al. (17) performed the reliability and validity of the Turkish version. SPAQ is used to determine patterns of mood and behavior changes in different seasons. Using this questionnaire, one can learn the severity of seasonal changes of patients, in terms of sleep, social activity, mood, weight, appetite, and energy level. Changes are assessed between 0 as no change and 4 as extremely marked change with a global seasonality score between 0–24. Changes in feelings, changes in weight, socialization, eating and sleeping; in different months of the year can also be assessed using the questionnaire. The questionnaire also assesses weight changes during the year, approximate sleeping times during a day, and food preference changes. Also, a person's feelings and whether the seasonal changes were problematic for them. If the participant scores 11 (or higher) in the global seasonality score, it can be deduced that the seasonal changes may be problematic to a moderate degree. If they feel the worst in the winter, then that person is classified as probably having winter seasonal affective disorder as suggested by SPAQ.

Statistical Analysis

Statistical analyses were performed with 78 participants (41 with BD and 37 HCs). The analyses of distribution plots and Shapiro-Wilks tests were conducted for the parametric statistical testing. The independent samples *t*-test and Chi-square tests were executed to estimate the differences in the socio-demographic variables. For the four consecutive assessments performed during the equinox times and the winter and summer solstices, all data concerning mood symptoms, neurocognitive abilities, psychosocial functions, biological rhythm variations, and seasonality

patterns were subjected to the non-parametric Friedman test for the comparison of multiple means.

RESULTS

Sociodemographic and Clinical Variables in Both Groups

The mean ages of the BD and HC groups were 38.10 and 37.9 years, respectively. Males constituted 56.1% (n=23) of the BD group and 48.6% (n=18) of the HCs. The mean education years of the BD group was 10.42 years, and for the HC group it was 11.78 years. There were no statistical differences between the BD and HC groups in terms of age (p=0.94), education (p=0.10), and sex (p=0.51). Eleven (26.8%) of the BD group had seasonality, 2.7% (n=1) of the HC group showed seasonality. There was a statistically significant difference between the groups (p=0.003). The mean duration of illness in the BD group was 8.76 years. Seventy-eight percent of the BD group had previously been treated in psychiatric inpatient services and the number of hospitalizations was two. Data are shown in Table 1.

Medical Treatment in the BD Group

In the BD group, only one patient was not receiving any mood stabilizer treatment, and the most commonly used treatment at all four periods of assessment was mood stabilizer + antipsychotic drug combination.

Table 1. Sociodemographic and clinical variables in patients with BD and HCs

	BD n=41		HC n=37		p
Age (mean±SD)	38.10±11.31		37.90±11.27		0.94
Education (years) (mean±SD)	10.42±3.9		11.78±3.37		0.10
	n	%	n	%	
Sex					
Female	18	43.9	19	51.4	0.51
Male	23	56.1	18	48.6	
Marital Status					
Married	24	58.5	23	62.2	
Single	16	39.1	10	27	0.22
Divorced	1	2.4	4	10.8	
Seasonality pattern					
Yes	11	26.8	1	2.7	**0.003**
No	30	73.2	36	97.3	
Family history of psychiatric disorders					
Yes	29	70.7	7	18.9	**<0.001**
No	12	29.3	30	81.1	
Comorbid disease					
Yes	10	24.4	6	16.2	0.37
No	31	75.6	31	83.8	
Continuous medicine use					
Yes	14	34.1	6	16.2	0.07
No	27	65.9	31	83.8	
Hospitalization					
Yes	32	78			
No	9	22			
No. of hospitalizations (mean±SD)	2±3.01				
Duration of illness (years) (mean±SD)	8.76±7.12				

BD, bipolar disorder; HC, healthy control; SD, standard deviation.

Table 2. Medical treatment in BD group

	June	September	December	March
MS	3	6	6	5
MS+MS	5	5	5	5
MS+MS+AP	1	1	2	1
MS+MS+AD	1	1	1	1
MS+AP	19	18	16	17
MS+AP+AP	8	6	7	8
MS+AD	1	-	-	-
MS+AP+AD	1	2	2	1
AP	1	1	1	1
MS+MS+AP+AD	-	-	-	1
MS+MS+AP+AP	1	1	1	1

BD, bipolar disorder; MS, mood stabilizer; AP, antipsychotic; AD, antidepressant.

The second most commonly used treatment was mood stabilizer + two antipsychotic drugs in combination. The medications used by the BD group at all four periods of assessment are shown in Table 2.

Mood Symptoms

In terms of HDRS, the BD group had significantly higher scores than the HC group at all four periods of assessment (Table 3). Except for the measure of YMRS in December (p=0.07), significantly higher scores were observed at all of the other three measures in the BD group compared with the HC group (Table 3).

When the measures of depressive symptoms as assessed using HDRS across all four periods for the BD group were taken into consideration, there were no statistically significant differences (p=0.21). Similarly, there was no statistically significant difference in HDRS scores across the four periods of assessment of the HC group (p=0.19) (Table 3). In terms of manic symptoms assessed with YMRS, both the BD group (p=0.49) and the HC group (p=0.87) showed no significant differences across all four measures (Table 3).

Psychosocial Functionality

The total score and the scores of the domains of FAST were statistically significantly higher in the BD group than in the HC group in all four periods of assessment (Table 3). In the BD group, the total score and the scores of the domains of FAST were not statistically different across all periods of assessment. However, in the HC group, the score of the leisure time domain was higher in the September assessment than in the other three assessments (p=0.04), whereas the total score and the other domains of FAST were not statistically different across all periods of assessment.

Biologic Rhythm

In the comparison of the scores of BRIAN and its domains of the BD and HC groups in four periods of assessment, there was a statistically significant difference in the total score in the March assessment (p=0.01), and in the social domain in the September (p=0.05) and March assessments (p=0.004), and the eating domain in the December assessment (p=0.05). The other measures were not statistically significantly different between the groups.

When the four periods of assessment were compared within the BD group, there was no statistically significant difference in terms of total score and domain scores of BRIAN. However, the HC group showed significantly higher scores in the activity (p=0.02) and eating (p=0.03) domains in the September assessment than in the other three assessments. All the other assessments in the four periods were not statistically different within the HC group (Table 3).

Table 3. Mood symptoms, biological rhythms, psychosocial functionality and neurocognitive functions of the BD and HC groups across seasonal assessments

	June			September			December			March			BD	HC
	BD n=41	HC n=37		BD n=41	HC n=37		BD n=41	HC n=37		BD n=41	HC n=37			
	Mean±SD	Mean±SD	p*	Mean±SD	Mean±SD	p*	Mean±SD	Mean±SD	p*	Mean±SD	Mean±SD	p*	p**	p**
HDRS	4.51±4.68	0.92±1.62	**<0.001**	3.41±3.40	0.97±1.85	**<0.001**	3.22±6.56	0.7±1.49	**0.02**	3.76±4.64	0.73±1.74	**<0.001**	0.21	0.19
YMRS	1.29±1.90	0.11±0.4	**<0.001**	1.76±3.4	0.05±0.23	**<0.001**	2.85±8.93	0.16±0.69	0.07	2.15±4.42	0.14±0.42	**0.01**	0.49	0.87
BRIAN Total	42.59±11.95	38.86±10.32	0.15	42.46±15.51	38.59±10.12	0.20	40.93±12.02	36.14±9.44	0.06	42.85±12.46	36.22±8.58	**0.01**	0.77	0.35
Sleep	11.34±3.51	10.73±3.3	0.43	11.66±7.5	10.24±3.09	0.29	10.66±3.4	9.65±3.08	0.17	11.27±4.59	9.73±3	0.09	0.77	0.23
Activity	9.63±3.87	8.6±3.71	0.23	9.54±4.38	9.11±3.87	0.65	9.29±3.78	8.27±3.89	0.24	9.49±4	7.92±3.06	0.06	0.75	**0.02**
Social	7.37±3.04	6.49±2.55	0.17	7.59±3.34	6.27±2.23	**0.05**	7.2±3.21	6.03±1.98	0.06	7.61±2.56	10.43±2.4	**0.004**	0.52	0.54
Eating	8.24±3.49	7.32±2.15	0.17	7.68±3.47	7.43±2.44	0.72	7.95±3.26	6.73±2.09	**0.05**	8.15±3.25	6.92±2.17	0.06	0.29	**0.03**
Chronotype	6±1.64	5.73±1.26	0.42	6±1.66	5.54±1.39	0.19	5.83±1.5	5.46±1.32	0.25	6.32±2.21	5.68±1.4	0.13	0.58	0.58
FAST Total	17.1±12.66	4.05±6.41	**<0.001**	16.34±13.1	4.62±5.72	**<0.001**	16.46±15.17	4.22±5.61	**<0.001**	17.24±12.06	3.46±5.31	**<0.001**	0.10	0.54
Autonomy	2.9±2.83	0.38±0.79	**<0.001**	2.93±2.82	0.41±0.96	**<0.001**	2.88±3.36	0.43±0.96	**<0.001**	2.51±2.62	0.3±0.81	**<0.001**	0.46	0.87
Occupational functioning	3.27±3.6	0.38±1.28	**<0.001**	3.32±4.19	0.35±0.75	**<0.001**	3.32±4.44	0.3±0.97	**<0.001**	4.05±4.27	0.27±1.17	**<0.001**	0.29	0.59
Cognitive functioning	4.76±3.4	1.57±2.57	**<0.001**	4.2±3.53	1.76±2.62	**<0.001**	4.4±4.12	1.49±2.18	**<0.001**	4.8±3.65	1.51±2.39	**<0.001**	0.35	0.92
Financial issues	0.78±1.35	0.05±0.32	**<0.001**	0.78±1.46	0.19±0.52	**0.02**	0.93±1.66	0.22±0.63	**0.02**	0.95±1.32	0.05±0.23	**<0.001**	0.22	0.15
Interpersonal relationships	3.41±3.79	0.89±1.97	**<0.001**	3.44±3.52	1.03±1.64	**<0.001**	3.56±3.81	1.24±1.71	**<0.001**	3.24±3.1	0.86±1.64	**<0.001**	0.98	0.09
Leisure time	1.98±1.96	0.84±1.36	**<0.001**	1.87±1.7	0.97±1.38	**0.03**	1.61±1.51	0.59±0.98	**<0.001**	1.63±1.46	0.46±0.96	**<0.001**	0.35	**0.04**
RAVLT Total			**<0.001**						**<0.001**					
Instant recall	5.76±1.76	7.84±1.77	**<0.001**	6.83±1.95	8.51±1.97	**<0.001**	7.39±2.39	9.57±2.15	**<0.001**	7.66±1.98	10.16±2.25	**<0.001**	**<0.001**	**<0.001**
Trial 1-5 (learning)	39.37±9.48	50.27±9.79	**<0.001**	42.71±11.73	53.81±10.91	**<0.001**	44.22±12.42	57.08±10.41	**<0.001**	43.44±11.34	58.43±10.28	**<0.001**	**0.001**	**<0.001**
Short delay	8.1±2.91	10.84±2.7	**<0.001**	8.78±2.95	11.08±2.7	**<0.001**	8.73±3.17	11.35±3.14	**<0.001**	8.56±2.65	11.32±2.93	**<0.001**	0.67	**0.03**
Long delay	7.34±3.05	10.19±2.69	**<0.001**	7.93±3.06	10.65±2.96	**<0.001**	7.78±3.3	11.73±2.43	**<0.001**	7.61±2.56	10.43±2.4	**<0.001**	0.23	**<0.001**
Recognition	11±2.97	13.32±1.11	**<0.001**	11.49±2.88	13.81±1.29	**<0.001**	12±2.59	14.08±1.09	**<0.001**	12.07±2.4	14.22±1.13	**<0.001**	**0.002**	**<0.001**
Stroop Test														
Word test (s)	12.32±3.6	10.43±2.4	**0.009**	11.13±3.25	9.74±1.6	**0.02**	11.68±3.82	9.37±1.48	**0.001**	11.43±3.39	9.3±1.47	**0.001**	**0.003**	**0.006**
Color test (s)	29.02±11.55	21.43±4.18	**<0.001**	26.32±9.77	20.66±4.67	**0.002**	27.61±13.68	20.08±4.16	**0.002**	27.97±11.5	20.42±5.04	**<0.001**	**0.003**	**0.001**
Interference (s)	16.70±9.9	11±4.5	**0.002**	15.19±7.92	10.91±4.41	**0.005**	15.94±10.8	10.69±4.12	**0.007**	16.54±9.23	11.15±4.85	**0.002**	0.17	0.82

* students-t independent test
** Friedman test
BD, bipolar disorder; HC, healthy control; SD, standard deviation; HDRS, Hamilton depression rating scale; YMRS, Young mania rating scale; FAST, functioning assessment short test; BRIAN, biological rhythms interview of assessment in neuropsychiatry; RAVLT, Rey auditory verbal learning test; instant recall.
Trial 1: Trial 1–5 indicates the sum of the correctly recalled words in trials 1 to 5.

Neurocognitive Tests

Both RAVLT domain scores and ST domain scores were statistically worse in the BD group than in the HC group in every period of assessment (Table 3).

Across all four periods of assessment of the BD group, a statistically significant difference was found in instant recall (p<0.001, M >D >S >J), learning (p=0.001, D >M >S >J), and recognition (p=0.002, M>D>S>J) domains of RAVLT, whereas short delay and long delay domains were not statistically different. In the HC group, a statistically significant difference was found in all domain scores of RAVLT across all four assessments (Table 3).

In the BD group, a statistically significant difference was found in the word test (p=0.003, J>D>M>S) and color test (p=0.003, J>M>D>S) domains of the ST across all four periods of assessments, whereas the interference domain was not statistically different. When we evaluated the four periods of assessments of the HC group, a statistically significant difference was found in the word test (p=0.006, J>S>D>M) and color test (p=0.001, J>S>D>M) domains, but the interference domain was not significantly different (Table 3).

DISCUSSION

Although many studies in the literature reported that hospital admissions and hospitalization rates increased in certain seasons in BD (7–10), not all results have been consistent with the notion that mood symptoms vary across seasons (11,12), like our findings. In this present study, the effects of seasonality on patients with BD were investigated, for mood symptoms, and for psychosocial functionality, biologic rhythm, and neurocognitive functions to examine unapparent causes of increased hospital admissions of bipolar disorder in certain seasons. It was found that although there were differences in biological rhythm and neurocognitive function across seasons in bipolar disorder, the HC group also showed variability in the same aspects.

Comparison of the BD and HC groups in terms of mood symptoms, psychosocial functioning, neurocognition, and biologic rhythm

In previous studies and meta-analyses, it is well-demonstrated that patients with BD have worse psychosocial functioning, higher impairment in neurocognition, and more mood symptoms even in remission than control subjects. Due to the residual symptoms in remitted bipolar patients, it is widely known that mood symptoms persist throughout the course of the illness. In every period of assessment, both manic and depressive symptoms were more prevalent in the BD group than in the HC group in this present study. The only assessment period where manic symptoms did not differ between the BD and HC groups was in December, which had the least likelihood for the manic episodes to emerge (18).

The FAST-total score and the scores of subdomains were statistically higher in the BD group compared with HC group in all four periods. It was reported in a review article that even in remission, the functional outcome of bipolar disorder was negatively affected (19).

Biologic rhythm as a whole and the 'social' domain were more impaired in the BD group than in the HC group in the equinox assessments. It has been shown previously that patients with BD have a more disrupted circadian rhythm, and eveningness is predominant as the chronotype (20). However, the 'eating' domain of BRIAN in the BD group was only separated from the HC group in the December assessment. In winter, the atypical depression features tend to increase and the prevalence of binge eating in seasonal affective disorders may exceed simply overeating during winter depressive episodes (21).

As previously shown (22), the ST and RAVLT scores were found to be statistically significantly different between the groups in all four periods.

Mood symptoms in the BD and HC groups across seasonal assessments

In this present study, no change across the four seasonal assessments was observed in the manic and depressive mood symptoms in both the BD and HC groups. By contrast, in previous studies, it has been suggested that in terms of hospital admissions, manic episodes peaked in spring/summer, while depressive episodes were predominant in autumn (7–10). In a study that evaluated 60.607 patients with BD between 2001 to 2014 in Austria, for males, there was only a significant seasonal pattern for mania evident in summer months, and for females, there were more symptoms of mania in summer and autumn months and symptoms of depression in winter months (8). In a cohort study (9) conducted in 2016, when more than 24.000 hospital admissions in Denmark between 1995 and 2012 were examined, hospital admissions for manic episodes were observed to peak in May and August, most of the time they were in summer. Aguglia et al. (10) recruited all patients admitted to the psychiatric inpatient unit of a large hospital in Turin, Italy, over 2 years (n=730). Patients with BD experiencing (hypo) manic episodes exhibited significant peaks in admissions between May and July.

According to one study (11), in which 429 patients with BD were followed for 1–5 years in Canada, coordinated variation in BD symptoms was not affected by seasonal changes. In another study (12), participants with 12 consecutive months of data were assessed for the seasonality of symptoms in BD (n=212 patients from multiple sites within 5 climate zones) and no seasonal variation was observed in the self-reported mood data in any climate zone.

In this study, we also failed to show mood symptom fluctuations indicating seasonal patterns. However, it must be kept in mind that the volunteers of this present study were on medication throughout the four assessment periods.

Psychosocial functionality of BD and HC groups affected by seasonality

In the BD group, psychosocial functionality was not changed across the four assessment periods and showed no seasonal patterns. It is shown that patients with BD had impaired functionality, even in remission (23). As far as we know, this is the first study to evaluate the fluctuations of functionality in terms of seasonal patterns. Functionality was impaired in the BD group and remained stable across the seasonal assessments. Similarly, in all domains of functionality except leisure time, the HC group had no change across the seasonal assessments. However, the HC group experienced better functionality in leisure time activities in March than in the other assessment periods. When vitality was taken into consideration in the general population concerning seasonal patterns, in a study (24) on 5085 adult individuals, leisure-time physical activity was found to be higher in spring and summer months. This reflects the fact that healthy individuals tend to make use of their leisure-time mostly in spring, whereas individuals with BD are invariably throughout the year.

Biologic rhythms of BD and HC groups across seasonal assessments

The BRIAN total score and domain scores show that the BD group had no fluctuations in biologic rhythms across seasonal assessments. However, it has been shown that biologic rhythm deterioration in bipolar disorder occurs both during episodes and in the remission period (25). In the HC group, significantly lower scores were observed in the 'activity' and 'eating' domains in the March assessment. In a study conducted on healthy volunteers (26), it was shown that most of the physical activities were performed in summer, followed by spring, autumn, and winter. In our study, 'activity' was found as the highest in spring equinox. Like in

'leisure time activities' detected with FAST, healthy individuals tended to participate in activities in their leisure time especially in spring. Also, 'eating' habits did not change with a seasonal pattern and the lowest score was observed in December. However, in a community-based study in Norway, it was reported that individuals showed the greatest dissatisfaction with their eating behaviors in January and December (27). By contrast, in our study the HC group seemed to have fewer problems with eating in winter, which could be related to the patients eating regularity in winter as assessed according to the BRIAN scale.

Neurocognitive functions of the BD and HC groups across seasonal assessments

Both in the BD and HC groups, neurocognitive impairment was most evident in the June assessment. It is demonstrated that bipolar patients are slower in neurocognitive tests and thus, perform worse during winter (28). In this same study, the control group had no seasonal variation in neurocognition. However, in a study conducted on mice under laboratory conditions, it was shown that although during summer male subjects adopted quicker against predator-stimulus, it took more time for them to find shelter compare with subjects tested during winter (29). It is obvious that during winter, individuals tend to perform slower in neurocognitive tests, but this does not mean they perform accurately. In our sample, as a whole, neurocognition was worse in the June assessment.

One of the limitations of this study is that patients were receiving drug therapy in all of the four assessments, even though the influence of drug therapy on functioning in patients with BD is controversial. Another limitation is the small size of the sample group that fulfilled all four assessments per protocol. Another limitation is the fact that it is impossible to exclude the learning effect of neurocognitive tests, which are repeated every three months, but the same condition applies to the control group also. One of the inclusion criteria in patient selection was being in remission for at least six months (equivalent to two seasons). This time could be shorter and this may have caused bias in patient selection. On the other hand, the location of the study centers in the same geographical region (Aegean Region 38° 57 43 58 ″ Latitude to 28° 43 57 14 Longitude), the implementation of the structured clinical interview for diagnosis, including the age, sex, and education matched groups for BD and HC, keeping the evaluation period short, and removing patients who do not comply with the study procedure from all assessments can be considered as the strengths of our study.

As a conclusion, similar to previous findings where no seasonal variation was detected in patients with BD in terms of mood symptoms (11,12), in this present study, no seasonal variation was demonstrated in psychosocial functionality, biological rhythm, and neurocognition, that could distinguish the patients from the HC group. It was hypothesized in this study that even though patients with BD had no seasonal variation in mood symptoms, to explain the variability in hospital admissions, functioning as a whole would vary across seasonal assessments. The hypothesis was not demonstrated, and the question of why hospital admissions of patients with BD peaked in certain seasons awaits an answer. With the fact that the HC group also showed almost the same seasonal variation, because patients with BD are taught to be alert regarding rhythm instability and seasonal changes (30), they may overestimate the disturbances and present to hospitals easily too readily. In psychoeducation, besides cautioning patients with BD against seasonal disturbances, it is also crucial to describe seasonal variation that occurs in healthy individuals.

Ethics Committee Approval: The study was approved by the Scientific Research Ethics Committee of Manisa Celal Bayar University Faculty of Medicine (Date: 12/04/2017–20.478.486).

Informed Consent: All participants gave written informed consent for participation in the study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept-FPÇ, ÖA; Design-FPÇ, KA, DSD, EÖÇ, EA, ÖA; Supervision-FPÇ, KA, EÖÇ, ÖA; Resource-FPÇ, KA, DSD, EÖÇ, EA; Materials-FPÇ, KA, DSD, EÖÇ, EA; Data Collection and/or Processing-FPÇ, KA, DSD, EÖÇ, EA; Analysis and/or Interpretation-FPÇ, ÖA; Literature Search-FPÇ, KA, DSD, EÖÇ, EA, ÖA; Writing-FPÇ, KA, DSD, EÖÇ, EA, ÖA; Critical Reviews-FPÇ, EA, DSD, EÖÇ, ÖA.

Conflict of Interest: All the authors declared that they have no conflict of interest.

Financial Disclosure: This study was supported by the Turkish Psychiatric Association (Research Project Encouragement Prize, 2018).

REFERENCES

1. Merikangas KR, Akiskal HS, Angst J, Greenberg PE, Hirschfeld RM, Petukhova M, Kessler RC. Lifetime and 12-month prevalence of bipolar spectrum disorder in the National Comorbidity Survey replication. Arch Gen Psych 2007;64:543–552. [Crossref]
2. Buijs RM, van Eden CG, Goncharuk VD, Kalsbeek A. The biological clock tunes the organs of the body: Timing by hormones and the autonomic nervous system. J Endocrinol 2003;177:17–26. [Crossref]
3. Walker WHII, Walton JC, DeVries AC, Nelson RJ. Circadian rhythm disruption and mental health. Transl Psychiatry 2020;10:28. [Crossref]
4. Gonzalez R. The relationship between bipolar disorder and biological rhythms. J Clin Psych 2014;75:e323–e331. [Crossref]
5. McKenna BS, Drummond SPA, Eyler LT. Associations between circadian activity rhythms and functional brain abnormalities among euthymic bipolar patients: a preliminary study. J Affect Disord 2014;164:101–106. [Crossref]
6. Hazlerigg DG, Wagner GC. Seasonal photoperiodism in vertebrates: From coincidence to amplitude. Trends Endocrinol Metab 2006;17:83–91. [Crossref]
7. Geoffroy PA, Bellivier F, Scott J, Etain B. Seasonality and bipolar disorder: a systematic review, from admission rates to seasonality of symptoms. J Affect Disord 2014;168:210–223. [Crossref]
8. Fellinger M, Waldhoer T, König D, Hinterbuchinger B, Pruckner N, Baumgartner J, Vyssoki S, Vyssoki B. Seasonality in bipolar disorder: Effect of sex and age. J Affect Disord 2019;243:322–326. [Crossref]
9. Medici CR, Vestergaard CH, Hadzi-Pavlovic D, Munk-Jørgensen P, Parker G. Seasonal variations in hospital admissions for mania: Examining for associations with weather variables over time. J Affect Disord 2016;205:81–86. [Crossref]
10. Aguglia A, Serafini G, Escelsior G, Canepa G, Amore M, Maina G. Maximum temperature and solar radiation as predictors of bipolar patient admission in an emergency psychiatric ward. Int. J. Environ. Res. Public Health 2019;16:1140. [Crossref]
11. Murray G, Lam RW, Beaulieu S, Sharma V, Cervantes P, Parikh SV, Yatham LN. Do symptoms of bipolar disorder exhibit seasonal variation? A multisite prospective investigation. Bipolar Disord 2011;13:687–695. [Crossref]
12. Bauer M, Glenn T, Grof P, Rasgon NL, Marsh W, Sagduyu K, Alda M, Murray G, Quiroz D, Malliaris Y, Sasse J, Pilhatsch M, Whybrow PC. Relationship among latitude, climate, season and self-reported mood in bipolar disorder. J Affect Disord 2009;116:152–157. [Crossref]
13. Aydemir Ö, Uykur B. Reliability and Validity Study of The Turkish Version of Functioning Assessment Short Test in Bipolar Disorder. Turk Psikiyatri Derg 2012;23:193–200. [Crossref]
14. Karakaş S. Bilnot Bataryası El Kitabı: Nöropsikolojik Testler İçin Araştırma ve Geliştirme Çalışmaları. Ankara: Dizayn Ofset; 2004.
15. Karakaş S, Erdoğan E, Sak L, Soysal Ş, Ulusoy T, Yüceyurt Ulusoy İ, Alkan S. Stroop test TBAG form: standardization for Turkish culture, reliability and validity. J Clin Psychiatry 1999;2:75–88. [Crossref]
16. Aydemir Ö, Akkaya C, Altınbaş K, Kora K, Sücüllüoğlu Dikici D, Akdeniz F, Kalaycı F, Oral T, Vahip S. Biyolojik ritim değerlendirme görüşmesinin Türkçe sürümünün güvenilirliği ve geçerliliği. Anadolu Psikiyatri Derg 2012;13:256–261. [Crossref]
17. Noyan MA, Elbi H, Korukoglu S. The Turkish version of Seasonal Pattern Assessment Questionnaire (SPAQ): A reliability study. Anadolu Psikiyatri Derg 2000;1:69–77.
18. Lee HC, Tsai SY, Lin HC. Seasonal variations in bipolar disorder admissions and the association with climate: a population-based study. J Affect Disord 2007;97:61–69. [Crossref]
19. Chen M, Fitzgerald HM, Madera JJ, Tohen M. Functional Outcome Assessment in Bipolar Disorder, a Systematic Literature Review. Bipolar Disord 2019;21:194–214. [Crossref]

20. Melo MC, Abreu RL, Neto VBL, de Bruin PF, de Bruin VM. Chronotype and circadian rhythm in bipolar disorder: a systematic review. Sleep Med Rev 2017;34:46–58. [Crossref]
21. Donofry SD, Roecklein KA, Rohan KJ, Wildes JE, Kamarck ML. Prevalence and correlates of binge eating in seasonal affective disorder. Psychiatry Res 2014;217:47–53. [Crossref]
22. Bora E, Hıdıroğlu C, Özerdem A, Kaçar ÖF, Sarısoy G, Civil Arslan F, Aydemir Ö, Cubukcuoglu Tas Z, Vahip S, Atalay A, Atasoy N, Ateşci F, Tümkaya S. Executive dysfunction and cognitive subgroups in a large sample of euthymic patients with bipolar disorder. Eur Neuropsychopharmacol 2016;26:1338–1347. [Crossref]
23. Baune BT, Malhi GS. A review on the impact of cognitive dysfunction on social, occupational, and general functional outcomes in bipolar disorder. Bipolar Disord 2015;17:41–55. [Crossref]
24. Pivarnik JM, Reeves MJ, Rafferty AP. Seasonal variation in adult leisure-time physical activity. Med Sci Sports Exerc 2003;35:1004–1008. [Crossref]
25. Harvey AG. Sleep and circadian rhythms in bipolar disorder: Seeking synchrony, harmony, and regulation. Am J Psych 2008;165:820–829. [Crossref]
26. Carr LJ, Dunsinger S, Marcus BH. Long-term Surveillance of Physical Activity Habits of Latinas Enrolled in a 12-Month Physical Activity Intervention. J Phys Act Health 2016;13:740–746. [Crossref]
27. Perry JA, Silvera DH, Rosenvinge JH, Neilands T, Holte A. Seasonal eating patterns in Norway: A non–clinical population study. Scand J Psychol 2001;42:307–312. [Crossref]
28. Rajajärvi E, Antila M, Kieseppä T, Lönnqvist J, Tuulio-Henriksson A, Partonen T. The effect of seasons and seasonal variation on neuropsychological test performance in patients with bipolar I disorder and their first-degree relatives. J Affect Disord 2010;127:58–65. [Crossref]
29. Maille A, Pillay N, Schradin C. Seasonal variation in attention and spatial performance in a wild population of the African striped mouse (Rhabdomys pumilio). Anim Cogn 2015;18:1231–1242. [Crossref]
30. Haynes PL, Gengler D, Kelly M. Social Rhythm Therapies for Mood Disorders: an update. Curr Psychiatry Rep 2016;18:75. [Crossref]