Original article

The Relationship Between Cognitive Impairment And Functionality In Euthymic Bipolar Patients: A Case Controlled Study

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ABSTRACT

Objective: We sought to compare differences in cognitive function between patients with bipolar disorder type 1 (BPD-1) and healthy controls (HC) and to investigate the relationship between cognitive functions and functional areas of patients with BPD-1.
Methods: This study included 93 euthymic patients with BPD-1 and 64 healthy age- and sex-matched individuals. All participants completed a sociodemographic form; took the Beck Anxiety Inventory (BAI), Beck Depression Inventory (BDI), and Montreal Cognitive Assessment Scale (MoCA) assessments; and underwent a neuropsychometric battery. Results pertaining to the Structured Clinical Interview for Diagnostic and Statistical Manual of Mental Disorders, fourth revision Axis I Disorders (SCID-I), Young Mania Rating Scale score, and Bipolar Disorder Functioning Questionnaire score were obtained for the patients; the HC group was investigated using the SCID nonpatient version.
Results: All of the cognitive domain scores were significantly lower in the BPD-1group than in the HC group ($p < 0.05$). A statistically significant positive correlation was observed between the neurocognitive domains of attention, verbal memory, visual memory, and BPD-1 total functioning ($p < 0.05$).
Discussion: Impairments in verbal memory, visual memory, and attention among euthymic patients with BPD-1 may cause impaired functionality.

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Keywords: bipolar disorder, cognitive function, funcionality

Introduction

Bipolar disorder (BPD) might affect the quality of life and psychosocial functioning negatively [1]. According to the World Health Organization, BPD is one of the top 10 causes of disability worldwide. Previous research has documented that patients with BPD may not be able to return to a predisease psychosocial functioning state even after recovering from mood attacks and/or residual symptoms [2]. After an attack, only 40% of patients may achieve premorbid functionality during their euthymia period [3].

Impairment in functioning has been reported in remission period patients with BPD[4].Factors such as poor predisease functionality, early onset, total disease duration, number of hospitalizations, the presence of subclinical symptoms, education level, psychiatric comorbidities, substance/alcohol abuse, and poor social support may affect functionality in BPD [4]. Moreover, several publications have been released on the impact of cognitive deficits on the functionality of patients with BPD [1,5]. Impairments in executive functions, attention, verbal learning, and memory, which may persist in the euthymic period, are reported to be strong predictors of psychosocial dysfunctionality in BPD [6-8].

Studies indicate that cognitive functions, especially executive functions and verbal memory, are associated with psychosocial functionality [8]. In a study by Baldessarini et al. reviewing 13 studies—including eight studies with euthymic and five studies with noneuthymic populations—a positive correlation was reported between cognitive impairment and decreased psychosocial functioning [9]. Although several studies have suggested the relationship between cognitive impairment and functionality in BPD-1, little attention has been paid to date to the relationship between subtypes of cognitive impairment and functionality.

The first aim of this study was therefore to compare the cognitive functions of euthymic BPD-1 patients and healthy controls, while the second aim was to investigate the relationship between cognitive functions and functional areas of euthymic patients with BPD-1. We hypothesized that subjects suffering from BPD-1 (in the euthymic period) would differ in terms of cognitive functions from healthy controls. Our second hypothesis is that the functionality level would be associated with cognitive functions in the domains of attention, executive function, and memory in BPD-1 patients.

Methods

Sample

The study sample consisted of BPD-1 patients, who visited the outpatient treatment unit of the Bakirkoy Research and Training Hospital for Psychiatry, Neurology, and Neurosurgery (Istanbul, Turkey) between April 2019 and September 2019. A psychiatrist from the research team interviewed the patients in euthymic states who had been diagnosed with BPD-1 based on the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5)

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criteria. Medical histories and past hospital records of the patients were examined. Patients who agreed to participate in the study were included. In addition, healthy participants, who matched the patient group in terms of age, gender, and educational status, were included as a control group. They were selected among volunteer hospital workers. The volunteers were also interviewed by the researcher. None of these volunteers had past or current personal history of any psychiatric disorder according to the DSM-5.

Ninety-three patients who visited to Bakirkoy Training and Research Hospital Outpatient Clinic aged 18 to 65 years and recently diagnosed and/or followed up with for a diagnosis of euthymic BPD-1 according to Young Mania Rating Scale (YMRS) score of less than 8 points and a Beck Depression Inventory (BDI) score of less than 10 points were included. Diagnoses were ascertained using the Structured Clinical Interview for Diagnostic and Statistical Manual of Mental Disorders, fourth revision (DSM-IV) Axis I Disorders criteria [10]. Individuals who were uncooperative or cognitively impaired due to mental retardation; who had a Montreal Cognitive Assessment Scale (MOCA) score of less than 21 points; who had a neurological disease; who had undergone electroconvulsive therapy in the last six months; and those with a history of psychosurgery or other brain surgery, head trauma, alcohol/drug addiction, comorbid psychiatric disease other than specific phobia presenting with psychotic symptoms were excluded from this study. Serum levels of mood stabilizers were measured in all patients and were revealed to reside in the normal range (i.e., 0.6–1 mEq/L for lithium; 60–100 mg/L for valproic acid, and 6–10 mg/L for carbamazepine). Sixty-four healthy subjects without any psychiatric disease (except specific phobia) according to the DSM-IV and evaluation using the Structured Clinical Interview non-patient edition [11], without neurological disease or alcohol/drug use and matched to the patient group in terms of age, gender, and education were included as a control group. Written informed consent was obtained from all subjects prior to enrolment and approval for the study was secured from the ethics committee of the İstanbul Training and Research Hospital for the study protocol (March 15th, 2019, protocol no. 1748).

Instruments

The YMRS, BDI, Beck Anxiety Inventory (BAI), and MOCA were used before the neuropsychometric battery was applied to the patient group considering that the latter might affect the neuropsychometric test results; additionally, the BDI, BAI and MOCA were applied to the control group. Then, neuropsychometric battery was applied to those patients with YMRS score of less than eight points, BDI score of less than 10 points, and MOCA score of more than 21 points. The Bipolar Disorder Functionality Questionnaire (BDFQ) was also administered to the patient group.

In addition to interviews with patients and their relatives, the medical documents and hospitalization files of the patients were examined. Missing information was gathered where possible.

Sociodemographic Data Form: The researchers prepared this form to evaluate from the participants' sociodemographic and clinical aspects. The researchers completed the form during interviewing with the participants.

SCID-1 (The Structured Clinical Interview for DSM-IV Axis I Disorders): It was developed by First et al. in 1997 in order to diagnose major DSM-IV Axis I disorders. Turkish validity and reliability study was conducted by Özkürkçügil et al. [12].

Young Mania Rating Scale (YMRS): This scale was developed by Young et al. [13]. It consists of 11 items, each measuring the severity of a symptom on a scale of 0-4. The total score varies between 0 and 60. A score of <8 indicates a remission of manic symptoms. The items in the scale encompass the core symptoms of manic episodes. Validity and reliability studies for the Turkish version of the scale were conducted by Karadag et al. [14].

Beck Depression Inventory (BDI): The BDI was developed by Beck to determine the severity of depressive symptoms [15]. Validity and reliability studies for the Turkish form were conducted by Hisli [16].

Beck Anxiety Inventory (BAI): This scale was developed by Beck et al. [17]. It measures the frequency of anxiety symptoms experienced by the individual. Turkish validity and reliability studies were conducted by Ulusoy et al. [18].

Montreal Cognitive Assessment (MoCA): It was developed by Nasreddine et al[19]. MOCA assesses the different cognitive dimensions of attention and concentration, executive functions, memory, language, visual-spatial skills, abstract thinking, calculation and orientation. It is a rapid instrument especially for the detection of mild cognitive impairment. Currently, it is successfully used as a screening method with evidence based validity and reliability [20]. A score of 21 points and above is considered as normal.

Bipolar Disorder Functioning Questionnaire (BDFQ): It was prepared by Psychiatric Association of Turkey Mood Disorders Work Unit. The scale consists: emotional functioning, intellectual functioning, sexual functioning, feelings of stigmatization, social withdrawal, household relations, relations with friends, participation to social activities, daily activities and hobbies, taking initiative and self-sufficiency and occupation. Validity and reliability study was developed by Aydemir et al. [21]. In this scale, higher score demonstrates better global functioning.

Neuropsychometric battery

All test were performed in a silent room at around 9.00 a.m. The duration for completing the test battery was approximately 60 minutes. The standard guidelines were given to all participants. Before the test, the participants were asked whether they had glasses or hearing aids, and it was made sure that they were used throughout the assessment process. The participants who were found to have insomnia the night before the examination were not tested. They were also asked to refrain from stimulant substances for two hours before the application.

A battery of neurocognitive functions was designed to assess the following domains: attention, verbal memory, visual memory, and executive functions. Attention was assessed with the Stroop Colour–Word Test, the Wechsler Memory Scale—Revised (WMS-R) Digit Span Subtest, and the Trail-making Test (TMT). Verbal memory was assessed with Rey's Auditory Verbal Learning Test (RVALT). Visual memory was evaluated using the WMS-R Visual Memory Subtest. Executive functions were evaluated using the Wisconsin Card Sorting Test (WCST). While higher scores indicated better performance, neurocognitive test scores that had inconsistent metrics were revised. The scores on each test were converted to z-scores based on the scores of the control group. Subsequently, the following neurocognitive domains were calculated: attention, verbal memory, executive functioning, and visual memory. In addition, an overall cognition score was generated based on the average of all the z-scores. This method was designed based on previous research [22].

Further explanations of the tests in the battery are included as follows.

Öktem Verbal Memory Test (ÖVMT), RVALT: This test is a word list learning test developed by Rey in 1964 for the purpose of evaluating verbal learning and memory functions [23]. Standardization research was carried out in 1992 by Öktem [24] .

Wisconsin Card Sorting Test (WCST): This is one of the tests used in the evaluation of the integrity of the frontal complex attention system including conceptualization, abstraction, and

the ability to maintain the subjective installation and change this installation if necessary. It was developed by Berg in 1948 and modified into a handbook by Heaton and colleagues in 1981 and 1993 [25]. Valid Turkish adaptation studies have also been conducted [26].

Stroop Color Word Test: First developed by J. R. Stroop in 1935, several versions of Stroop Test have since been introduced. The essential assessment here is the evaluation of concentration and attention sustainment based on a time period and the task that is given. The Stroop Test is one of the best evaluations to assess one's ability to withstand interfering stimuli, to block the improper stimuli, and to suppress inappropriate reaction tendencies. The Turkish validity and reliability study of the test was performed by Karakaş et al. [27].

WMS-R Digit Span Subtest: The WMS-R is an improved version of the original test first developed by Wechsler in 1945 [28]. The Digit Span Subtest was utilized in this study, which is used to evaluate simple attention. According to various sources, the straight-line range is also referred to as short-term memory. The Backward Span Test can be used to measure complex attention. The test consists of two parts: the Forward Span Test and the Backward Span Test. The Turkish reliability and validity study was conducted by Karakaş et al.[27].

WMS-R Visual Memory Subtest: Another subtest of WMS-R can be used to demonstrate learning, immediate memory, and long-term memory regarding figures [28].

Trail Making Test (TMT): This is a neuropsychological test of visual attention and task-switching assessing domains such as visuomotor scan, motor speed, planning, inhibition of response tendency, task change, abstract thinking, concentration, and inhibition tolerance [29]. The Turkish standardization research was performed by Türkeş et al. [30].

Statistical Analysis

Statistical analysis was performed using SPSS 22.0 for Windows statistical software. P value<0.05 was considered to be statistically significant. Descriptive statistical methods including mean, standard deviation, frequency and ratio values were used. Distribution of the variables was detected with the Kolmogorov simirnov test. Independent samples t-test; in addition to mann-whitney u test were used for the quantitative independent data. The chi-square test was used for the analysis of qualitative independent data and the fischer test was used when the chi-square test conditions were not met. Spearman correlation analysis was used for correlation analysis.

High and low functionality were determined on the basis of median values. A 103 median value was calculated for total functionality. Fourty five of the patients were in low functionality group (BDFQ total functionality score≤ 103) and 48 were in the high fuctionality (103< BDFQ total functionality score) group.

Results

The mean age of the BPD-1 group was 37.23 ± 9.58 years while that was 34.53 ± 8.10 years in the control group. The mean education level of the BPD-1 group was 11.31±3.71 years while that was 11.22±3.84 years in the control group. There was no statistically significant difference between the ages, gender and education levels of BPD-1 and HC groups (p>0.05). In BPD-1 group, the employment rate was significantly lower in the HC group (p<0.05). The ratio of single-divorced individuals in BPD-1 group was significantly higher than the HC group (p<0.05) (Table 1).

The mean age at onset of the disease was 22.6 ± 6.5 years in the BPD-1group. Average duration of episodes was 15.72 ± 7.05 days. Mean YMRS score was 0.8 ± 1.5. Mean BAI score was 7.5±8.4 and mean BDI score was 5.6 ±3.3. The mood stabilizers of choice were as follow: 48 lithium (51.6%), 24 valproic acid (25.8%), 2 carbamazepine (2.20%), lamotrigine 1 (1.10%), 10 lithium and valproic acid (%10.8), 2 lithium and carbamazepine (2.20%), 1 valproic acid and carbamazepine (1.10%), 1 valproic acid and lamotrigine 1 (1.10%) and 4 (4.30%) none. The additional treatments were listed as: 62 (66.7%) atypical antipsychotics (quetiapine, risperidone, olanzapine, aripiprazole, paliperidone), 1 (1.10%) antidepressant (bupropion), 1 (1.10%) atypical antipsychotic and long acting injectable antipsychotic (risperidone oral and injectable form), 6 (6.50%) atypical antipsychotic and antidepressant (olanzapine and fluoxetine), 1 (1.10%) antidepressant and long acting injectable antipsychotic (sertraline and aripiprazole long acting injectable form) and 1 (1.10%) atypical antipsychotic (haloperidole) and atypical antipsychotic (quetiapine).

All of the cognitive domains scores were significantly lower in theBPD-1 group than the HC group (p<0.05). MOCA scores were statistically significantly lower the BPD-1 group than the HC group (p<0.05) (Table 3). The BAI scores of the groups showed no statistically significant difference BPD-1 (7.5±8.4) and HC (9.0±9.3), and there was also no significant difference in BDI scores BPD-1 (5.6±3.3) and HC (5.0±2.9) (Table 3).

A statistically significant positive correlation was observed between the neurocognitive domains of attention and BPD-1 total functioning (p:0.041, r:0.229), intellectual functioning (p:0.023, r:0.254), taking initiative and self-sufficiency (p:0.024, r:0.251) scores (p<0.05). A statistically significant positive correlation was observed between the neurocognitive domains of verbal memory

Table 1: Comparison of Sociodemographic Variables Between BPD-1 Group and HC Group

	BPD1		HC		P	
	Mean±SD/n-%		Mean±SD/n-%			
Age	37.23 ± 9.58		34.53 ± 8.1		0.128	t
Gender						
Female	46	49.50%	34	53.10%	0.652	X^2
Male	47	50.50%	30	46.90%		
Education (years)	11.31 ± 3.71		11.22 ± 3.84		0.947	m
Employment Status						
Employed	41	44.10%	59	92.20%	p<0.001	X^2
Unemployed	52	55.90%	5	7.80%		
Marital						
Single	39	41.90%	20	31.30%	0.038	X^2
Married	40	43.00%	40	62.50%		
Divorced/Widow	14	15.10%	4	6.30%		

BPD1: Bipolar Disorder type 1, HC: Healthy Control, SD: Standart deviation, n: number of participiants
In BPD-1 group, the employment rate was significantly lower in the HC group (p<0.05). The ratio of single-divorced individuals in BPD-1 group was significantly higher than the HC group (p<0.05) t: independent t test, X^2: Chi-square test, m: Mann-Whitney u test

and BPD-1 total functioning (p<0.001, r:0.410), emotional functioning (p<0.001, r:0.355), intellectual functioning (p:0.001, r:0.343), social withdrawal (p:0.006, r:0.281), household relations (p:0.002, r:0.321), relations with friends (p<0.001, r:0.370), participation to social activities (p:0.014, r:0.255), daily activities and hobbies (p:0.002, r:0.316), and taking initiative and self-sufficiency (p<0.001, r:0.356), scores (p<0.05). A statistically significant positive correlation was observed between the neurocognitive domains of visual memory and BPD-1 total functioning (p<0.001, r:0.268), emotional functioning (p:0.004, r:0.299), intellectual functioning (p:0.006, r:0.285), social withdrawal (p:0.031, r:0.224), and daily activities and hobbies (p:0.043, r:0.211), scores (p<0.05) (Table 4).

MOCA, verbal memory and attention of the cognitive domains scores were significantly lower in the low functionality BPD-1 group than the high functionality BPD-1group (p<0.05). BAI and BDI scores were significantly higher in the low functionality BPD-1 group than the high functionality BPD-1 group (p<0.05) (Table 5).

The univariate model revealed statistically significant effects for the MOCA, BAI, BDI, attention, and verbal memory values (p < 0.05) (Table 6). The multivariate model revealed a significant and independent effect for the BAI value (Table 6).

Table 2: Clinical Characteristics of BPD-1 Group

		Mean±SD/n-%
Age of onset (years)		22.61 ± 6.5
Number of hospitalizations		2.15 ± 2.13
Duration of episode(days)		15.72 ± 7.05
YMRS		0.8 ± 1.5
BAI		7.5 ± 8.4
BDI		5.6 ± 3.3
		N %
Mood Stabilizator of choice	Li	48 51.60%
	VPA	24 25.80%
	CBZ	2 2.20%
	Lamotrigine	1 1.10%
	Li+VPA	10 10.80%
	Li+CBZ	2 2.20%
	VPA+CBZ	1 1.10%
	VPA+Lamotrigine	1 1.10%
	None	4 4.30%
Additional treatment	Absent	21 22.60%
	Present	72 77.40%
Additional medication	AAP	62 66.70%
	AD	1 1.10%
	AAP+LAI	1 1.10%
	AAP+AD	6 6.50%
	AD+LAI	1 1.10%
	TypicalAP+AAP	1 1.10%

YMRS: Young Mania Rating Scale, Li: Lithium, VPA: Valproic acid, CBZ: Carbamazepine, AP: Antipsychotic, AAP: Atypical antipsychotic, AD: Antidepressant, LAI: Long –acting injectable antipsychotic n: number of patients

The mean age at onset of the disease was 22.6 ± 6.5 years in the BPD-1group. Average duration of episodes was 15.72 ± 7.05 days. Mean YMRS score was 0.8 ± 1.5. The mood stabilizers of choice were shown in the table

Table 3: Comparison of Cognitive Functions, MoCA, BAI and BDI Scores Among BPD-1 Group and HC Group

	BPD-1				HC			p	
	Mean±SD				Mean±SD				
Attention	-0.09	±	0.47		0.24	±	0.58	p<0.001	m
Excutive Function	0.08	±	0.52		0.38	±	0.57	0.004	m
Verbal Memory	-0.25	±	0.61		0.33	±	0.54	p<0.001	m
Visual Memory	-0.2	±	0.91		0.29	±	0.87	p<0.001	m
MOCA	24.5	±	2.2		26.6	±	1.7	p<0.001	m
BAI	7.5	±	8.4		9.0	±	9.3	0.283	m
BDI	5.6	±	3.3		5.0	±	2.9	0.180	m
mMann-whitney u test									

[m]Mann-whitney u test

BPD-1: Bipolar Disorder type 1, HC: Healthy Control, MOCA: Montreal cognitive assessment scale,BAI: Beck anxiety inventory, BDI: Beck depression inventory, SD: Standard deviation

All of the cognitive domains scores were significantly lower in the BPD-1group than the HC group (p<0.05).

Table 4: Correlation of BDFQ Scores and Cognitive Functions in BPD-1 Group

		Attention	Executive Function	Verbal Memory	Visual Memory
Total	r	0.229	0.098	0.410	0.268
Functioning	p	0.041	0.429	p<0.001	p<0.001
Emotional	r	0.240	0.233	0.355	0.299
Functioning	p	0.320	0.058	p<0.001	0.004
Intellectual	r	0.254	0.033	0.343	0.285
Functioning	p	0.023	0.794	0.001	0.006
Sexual	r	0.145	0.101	0.004	0.194
Functioning	p	0.199	0.418	0.973	0.063
Feelings of	r	0.097	0.033	0.194	0.149
Stigmatization	p	0.394	0.792	0.062	0.154
Social	r	0.026	0.106	0.281	0.224
Withdrawal	p	0.817	0.392	0.006	0.031
Household	r	0.115	0.129	0.321	0.184
Relations	p	0.312	0.299	0.002	0.77
Relations with	r	0.41	0.110	0.370	0.123
Friends	p	0.719	0.377	p<0.001	0.240
Participation to	r	0.119	0.40	0.255	0.065
Social Activities	p	0.295	0.749	0.014	0.533
Daily Activities	r	0.117	0.152	0.316	0.211
And Hobbies	p	0.300	0.219	0.002	0.043
Taking Initiative	r	0.251	0.137	0.356	0.187
And Self-sufficiency	p	0.024	0.268	p<0.001	0.072
Occupation	r	0.212	0.097	0.019	0.038
	p	0.059	0.437	0.857	0.716
Spearman correlation					

Spearman correlation
A statistically significant positive correlation was observed between the neurocognitive domains of visual memory and BPD-1 total functioning, emotional functioning, intellectual functioning, social withdrawal and daily activities and hobbies scores (p<0.05)

Table 5: Comparison of Cognitive Functions, MoCA, BAI and BDI Scores and clinical variables Among Low and High Functionality BPD-1 Groups

	Low Functionality				High Functionality			p	
	Mean±SD				Mean±SD				
Attention	-0.21	±	0.53		0.04	±	0.35	0.013	m
Excutive Function	-0.02	±	0.48		0.16	±	0.53	0.170	m
Verbal Memory	-0.45	±	0.62		-0.06	±	0.53	0.001	m
Visual Memory	-0.33	±	0.86		-0.09	±	0.94	0.117	m
Age	36.27	±	9.72		38.24	±	9.43	0.268	m
Education	11.97	±	3.64		10.60	±	3.68	0.068	m
Age of onset	21.54	±	5.81		23.82	±	7.06	0.103	m
Number of hospitalizations	2.25	±	2.04		2.04	±	2.23	0.321	m
Duration of episode(days)	15.93	±	7.17		15.52	±	7.00	0.231	m
MOCA	23.9	±	2.12		24.9	±	2.19	0.021	m
BAI	10.6	±	9.92		4.58	±	5.35	p<0.001	m
BDI	7.20	±	2.65		4.10	±	3.13	p<0.001	m
mMann-whitney u test,									

[m]Mann-whitney u test,
MOCA: Montreal cognitive assessment scale, BAI: Beck anxiety inventory, BDI: Beck depression inventory, SD: Standard deviation
Attention and verbal memory of the cognitive domains and MOCA scores were significantly lower in the low functionality group than the high functionality group, while BAI and BDI scores were significantly higher in the low functionality group than the high functionality group (p<0.05).

Table 6: Regression Analysis of Test Scores in the Differentiation of Low Functionality from High Functionality in BPD1 Group

	Univariate Model					Multivariate Model				
	OR	0.95			p	OR	0.95			p
MOCA	0.60	-0.14	-	0.08	p<0.001					
BAI	1.94	-0.22	-	0.00	p<0.001	1.67	1.02	-	2.72	0.041
BDI	0.94	-0.09	-	-0.02	p<0.001					
Attention	0.39	-0.10	-	0.38	0.002					
Verbal Memory	0.10	-0.06	-	0.30	p<0.001					

Lineer Regression, OR:odds ratio
MOCA: Montreal cognitive assessment scale, BAI: Beck anxiety inventory, BDI: Beck depression inventory,
The univariate model revealed statistically significant effects for the MOCA, BAI, BDI, attention, and verbal memory values ($p < 0.05$). The multivariate model revealed a significant and independent effect for the BAI value..

Discussion

We hypothesized that cognitive functions in the domains of attention, executive functions, and memory may differ among patients with BPD-1 and may be related to functionality. We tested these hypotheses by comparing euthymic patients with BPD-1 and healthy controls across a range of cognitive functions as well as examined the relationships between functionality and cognitive functioning in patients with BPD-1. From this, we determined that patients with BPD-1 displayed higher cognitive impairments across nearly all domains relative to the control subjects. Besides, as the impairment in memory functions increased in patients with BPD-1, there was a corresponding dysfunctionality. These findings were in line with our hypothesis.

In previous studies, it has been suggested that patients with BPD-1 have impairment in verbal memory, even in the euthymic period [6,31]. Other studies also suggest that impairment in verbal memory was correlated with dysfunction [8,32].The results of the current study additionally demonstrated a statistically significant positive correlation between verbal memory and total functioning; emotional functioning; intellectual functioning; social withdrawal; household relations; relations with friends; participation in social activities, daily activities, and hobbies; and taking the initiative and self-sufficiency scores. Likely the ISBD Task Force suggests facial expression recognition, implicit emotion regulation, and reward processing as most affected parts of the neurocognitive profile and possible treatment targets in bipolar disorder [33].

With remarkable similarity to the findings of previous studies [34,35], we observed visual memory impairment in patients with BPD-1, even in the euthymic period. Furthermore, statistically significant positive correlations were observed between visual memory and total functioning, emotional functioning, intellectual functioning, social withdrawal, and daily activities and hobbies scores. Although several studies have attempted to explain the relationship between verbal memory and functionality in BPD-1, little attention has been paid to date to the association between visual memory and functionality. One of the most compelling aspects of the current study's results is that, due to the relationship between impairment in visual memory and functionality, the evaluation of visual memory may be a key aspect in the follow-up of BPD-1 patients.

The available literature indicates a possible impairment in executive functions in patients with euthymic BPD-1 [6,36]. Similarly, the results of this study demonstrated that the patient group experienced worse executive functioning, which was evaluated by WCST, than the healthy controls. Several studies have argued that executive functions like category disruption and—in particular—response inhibition may be endophenotypes for BPD-1 [36]. Despite some studies not detecting an impairment of executive functioning in patients with BPD-1, we found that executive functions such as the ability to change categories showed a significant deterioration in the BPD-1 group when compared with healthy subjects [37]. This discrepancy might be explained by differences in sample sizes and IQ levels. Sanchez Moreno et al. in 2009 and Altshuler et al. in 2008, revealed a statistically significant relationship between cognitive functions, particularly verbal memory and executive functions, and functionality [7,32]. However, we could not establish a definitive relationship between executive function and functionality. This difference may be related to the variability of the tests used to evaluate executive functions and functioning. Further studies are needed to examine the relationship between executive functions and functioning.

Our findings also indicated that the attention scores of BPD-1 patients were significantly lower than those in the healthy group. There exists conflict as to whether psychomotor speed and attention are affected in the euthymic period in bipolar patients. Despite some studies reporting no deterioration in psychomotor speed or attention [38], other studies demonstrated that bipolar patients might be affected in such a manner [39]. This difference in results might be related to the variability of the tests used to evaluate attention functions. When we examined the BPD-1 group, a statistically significant positive correlation was observed between the neurocognitive domains of attention and total functioning, emotional functioning, intellectual functioning, taking the initiative, and self-sufficiency. Similarly, Wingo et al. found that there were impairments in attention, attention concentration, and processing speed among euthymic patients with BPD-1 and a positive correlation between this impairment and decreased psychosocial functioning [9].

Cognitive dysfunction is an important factor affecting functionality along with clinical variables and environmental factors [7]. Although there are studies indicating a relationship exists between cognitive functions and functionality in BPD-1, there are also those that have not detected a relationship. Malhi et al. investigated the correlation between cognitive functions and functionality in 25 euthymic, depressive, and hypomanic patients followed up with after BPD-1 diagnosis, ultimately finding no relationship between cognitive functions and functionality in the euthymic period. However, these authors stated that there was a relationship between executive functions and functionality in the depressive and hypomanic period [40]. According to this, in our study, it seems contradictory that there was a relationship between impairment in cognitive functions and dysfunctionality among patients with euthymic BPD-1. Since our sample was larger than that of Malhi et al., the relationship between cognitive functions and functionality might be determined.

Cognitive impairments are present in a significant percentage of BPD patients, even during euthymic periods [41]. There are many studies indicating that cognitive dysfunctions and functional impairment are correlated. In a four-year follow-up study conducted by Bonnin et al. involving BPD-1 and BPD-2 patients, long-term memory performance and subsendromal depressive symptoms were reported to be important factors capable of predicting long-term psychosocial functioning in patients with bipolar disorder. Solé B et al. also suggested that subsyndromal symptomatology and cognitive performance may play an important role in psychosocial functioning in patients with bipolar disorder [42]. It is stated that working memory is a predictor of professional functionality [8]. Martinez Aran et al. also stated that verbal memory performance was one of the predictors of psychosocial functioning and reported that spontaneous memory was the most predictive factor in achieving success during verbal memory testing [43]. Similarly, we found a positive correlation between verbal memory performance and functionality.

Our study has some limitations. First, our research is cross-sectional. Also, these results cannot be generalized for all BPD subgroups of patients, since only BPD-1 patients in a euthymic period are included in this study. The hospital where the study was conducted serves a more difficult group of patients who may undergo frequent hospitalizations, and BPD-1 patients constitute the majority of individuals with BPD admitted to this hospital. Therefore, only BPD-1 patients were included in this study. Third, since we receive information about the disease from patients and their relatives, some information may be missing or incorrect due to the influence of recall. The level of situational anxiety experienced by the participants during the neuropsychometric evaluation may also affect their neurocognitive performance. Moreover we did not control for the possible effects on cognition of medications. Finally, factors arising from the tester and different cultural structures of the sample can be considered to have an effect on the test results.

Overall, our study results that verbal memory, visual memory, and attention impairments in euthymic patients with BPD-1 may cause impaired functionality. These findings can be considered of importance as they have implications for the neurobiology of BPD-1, its treatment considerations, and the course of the disease.

Conflict of Interest

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors. The authors are responsible for the content and writing of the paper.

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