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Comparison of cognitive functions in bipolar disorder patients with and without comorbid borderline personality disorder

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ABSTRACT

Objective: The aim of this study was to compare patients with bipolar disorder type I (BD) with and without comorbid borderline personality disorder (BPD), in euthymic period, in terms of cognitive functions. The main hypothesis of this study was that cognitive functions would be more impaired in patients with BD with comorbid BPD (BD + BPD).

Methods: The structured clinical interviews for diagnostic and statistical manual of mental disorders-IV axis I disorders (SCID-I and SCID-II) were administered to 105 patients and the patients were separated into two groups as 79 BD patients and 26 BD plus BPD patients. Young Mania Rating Scale, Hamilton Depression Rating Scale, California verbal learning test, Wisconsin card sorting test, trail-making test (TMT), and stroop test were administered to the both groups.

Results: BD with comorbid BPD group showed statistically significantly lower performance in the average scores of TMT-A seconds and errors, and TMT-B seconds scores than the BD group (respectively $t = -3.449$, $p = .001$; $t = -3.431$, $p = .001$; $t = -2.331$, $p = .022$).

Conclusions: The processing speed, set shifting, and selective attention in BD with comorbid BPD group is more disturbed than the BD group. We suggest that when evaluating the cognitive functions, evaluation of comorbid psychiatric diagnosis, especially BPD, is crucial in BD.

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Bipolar disorder; borderline personality disorder; cognitive function; comorbidity

Introduction

It is known that the patients diagnosed with bipolar disorder (BD) experience cognitive dysfunctions and these dysfunctions also persist in the euthymic period [1–4]. In a 27.3 months follow-up study, Ferrier et al. found that cognitive dysfunctions in patients with BD persist even at the full inter-episode recovery period [5]. Martinez-Aran et al. reported cognitive dysfunctions in verbal memory and executive functions in patients with BD in the euthymic period [6]. Quraishi and Frangou suggested that, in addition to verbal memory dysfunctions, the number of perseverative errors and deficits in verbal fluency and planning are present [7]. In a two-year follow-up study, Mur et al. reported that impairment in executive functions were present in patients with BD in the euthymic period and cognitive impairment is one of the most important features of BD [8].

Subsequently, it was reported that even in the euthymic period of BD, medium- to large-sized cognitive impairments in verbal memory, attention, and executive functioning are present [9,10]. There are a number of studies, which report a correlation between cognitive and occupational, and psychosocial functioning

impairments [11–13]; however, the existence of patients with BD with good occupational and psychosocial functions, despite their disorder, reveals a contradiction on that subject [14,15]. The fact that the comorbid diagnoses, especially personality disorders, have not been studied enough so far could be one of the key elements which can explain contradicting results.

Borderline personality disorder (BPD) is a continuous clinical condition which usually begins during young adulthood period and is characterized by unstable interpersonal relationships, self-perception, and affect, along with significant impulsivity [16]. Recent studies reported that the individuals with BPD could also have cognitive dysfunctions [17–19]. O’Leary et al. compared 16 BPD patients and 16 healthy controls in terms of cognitive functions and detected attention, memory, and cognitive flexibility impairments in BPD patients in comparison to healthy controls [20]. Dinn et al. reported visual-spatial function, non-verbal memory, and trail-making test (TMT) performance impairments in BPD patients in comparison to healthy controls [21]. In their study which evaluates cognitive functions, Haaland and Landro pointed to the attention, memory, and executive function impairments [22].

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The presence of comorbid psychiatric conditions in patients with BD changes the observed symptoms, masks, and intensifies the disease, adversely effects response to the treatment, complicates the diagnosis, and increases cognitive function impairments [23,24]. It could be expected that BD patients with comorbid BPD have cognitive function impairments more than BD patients without comorbid BPD. The aim of this study is to compare BD patients with and without comorbid BPD, in the euthymic period, in terms of cognitive functions.

Methods

Study participants

A total of 156 patients who consecutively presented in the Department of Psychiatry, Mood Disorders Clinic between February 2013 and July 2014 were evaluated using the structured clinical interview for diagnostic and statistical manual of mental disorders (DSM)-IV axis I disorders (SCID-I), were diagnosed with BD type I according to DSM IV-TR criteria, and were included in this study. While 51 patients who refused to take neuropsychological tests and did not meet inclusion criterias were excluded from the study, the study has been completed with 105 patients who met the inclusion criteria. Inclusion criteria consisted of being between 18 and 65 years old, being at least an elementary school graduate, not having any other comorbid axis I psychiatric diagnoses, having a score of 8 and below from the Hamilton Depression Rating Scale (HDRS), and having a score of 5 and below from the Young Mania Rating Scale (YMRS). Subjects with intellectual disability and patients who had loss of consciousness as a result of head trauma in the past were excluded from the study. SCID-II was administered to 105 patients who were included in the study and the patients were separated into two groups as BD patients ($n = 79$) and BD comorbid BPD patients (BD + BPD) ($n = 26$).

Neuropsychological evaluation was carried out by a clinical psychologist specialized in the psychometrics, who was blind to the group label of included patients. The study was approved by the Eskisehir Osmangazi University's Ethics Committee. Written informed consents from all participants were obtained prior to inclusion in the study.

Materials

Socio-demographics data form: This form was developed by researchers in order to gather research data. It includes questions about included patients' socio-demographic features (age, sex, education, and marital status), clinical disorder characteristics, and drug utilization.

Structured clinical interview for DSM-IV axis I disorders: It was developed by First et al. [25]. Turkish

version of SCID-I has been validated and shown as reliable [26].

Structured clinical interview for DSM-III-R axis II disorders: It was developed by Spitzer et al. according to DSM-III-R classification and was administered to diagnose Axis II personality disorders [27]. Turkish version of SCID-II has been validated and shown as reliable [28].

Young Mania Rating Scale: This scale was developed by Young et al. to measure the severity and the change of the manic situation and is administered by the interviewer [29]. The Turkish version's validity and reliability were tested [30].

Hamilton Depression Rating Scale: This scale was developed by Hamilton to evaluate the severity of the depression and is administered by the interviewer [31]. The 17-item version is used in this study. The Turkish version's validity and reliability were measured [32].

California verbal learning test: It was developed by Delis et al. to evaluate verbal learning and memory [33]. Unlike other verbal tests, California verbal learning test (CVLT) allows the evaluation of numerous cognitive verbal memory elements. A CVLT form was translated into Turkish for adults and it was used in a study by Tukel et al. [34].

Wisconsin card sorting test: It was developed by Heaton [35]. It is mainly related to dorsolateral prefrontal cortex functions [36]. The test is administered with two decks of cards including 4 stimulus card and 64 reaction cards. There is no time limitation. The adaptation of Wisconsin card sorting test (WCST) into Turkish was conducted by Karakas et al. [37]. Completed category, perseverative reaction, and perseverative error number scores were used in our study.

Trail-making test: It is a widely used, easily administered neurocognitive test [38]. It is a test of complex visual scanning with a motor component, which can evaluate the flexibility in shifting the course of an ongoing activity. It consists of two sections: Part A and Part B. Part A measures processing speed, and Part B measures processing speed together with set shifting and selective attention. In this study, we determined the test durations and the number of errors. The Turkish version of TMT has been validated and shown as reliable [39].

Stroop test: It is a neurocognitive test, which was developed to assess the capacity of resistance to interference by reading the names of colors that are printed in colors different than that which they denote [40]. In order to do the test, only one visual characteristic shall be marked as a selector and the others shall be blocked. It consists of four parts; reading the names of colors written in black, telling the color of the colourful squares or dots, reading the names of colors that are printed in colors different than that which they denote, and not to read colored color names and just telling

their colors. The test has several adaptations different from each other in terms of colors utilized, item number, part order, and scoring. In the subsequent years, the part of telling the colors of the words which are not word names was added to test. Adaptation studies into Turkish were conducted by Karakas et al. [41].

Statistical analysis

The data analysis was performed using SPSS for Windows Version 21.0 (SPSS Inc., Chicago, IL, USA). The distribution of normality for continuous variables was evaluated with the Shapiro-Wilk test. Independent samples *t*-test was used to compare continuous variables that were normally distributed. Mann-Whitney U test was used to compare outcomes between two independent groups, who were not normally distributed. The relationship between categorical variables was compared by Chi-Square test. A *p*-value less than 0.05 was considered statistically significant.

Results

The study group consisted of 105 patients diagnosed with BD of which 63 (60%) were female and 42 (40%) were male. Patients diagnosed with BD were divided into two groups as without comorbid BPD (*n* = 79) and with comorbid BPD (*n* = 26).

The average age of the group with comorbid diagnosis was statistically significantly lower compared to the group without comorbid diagnosis ($z = -3.567$ and $p < .001$). The rate of the single/divorced in the group with comorbid diagnosis was statistically significantly higher compared to the group without additional diagnosis ($\chi^2 = 7.726$ and $p = .005$). The family history and suicide attempts in the group with comorbid diagnosis were statistically significantly higher in comparison to the group without comorbid diagnosis ($\chi^2 = 4.452$, $p = .035$; $\chi^2 = 4.152$, $p = .042$, respectively). There were no statistically significant differences between the groups in terms of the education period, gender, employment, socio-economic situation, age of onset, number of episodes, number of hospitalizations, and total duration of the disease ($p > .05$). Using only mood satabilizer rate was statistically significantly lower in the group with comorbid diagnosis ($p = .039$) (Table 1).

When the two groups were compared in terms of cognitive functions, patients with comorbid diagnosis showed statistically significantly lower performance in the average scores of CVLT free delayed recall, TMT-A duration and number of errors, TMT-B duration and number of errors, and Stroop Color Word duration (respectively $z = -2.684$, $p = .007$; $z = -2.458$, $p = .014$; $z = -3.213$, $p < .001$; $z = -2.376$, $p = .018$; $z = -1.983$, $p = .047$; $t = -2.486$, $p = .019$). However, a statistically significant difference was observed between groups in terms of age, mean YMRS, and HDRS scores

Table 1. Demographic characteristics of patients with bipolar disorder with and without BPD.

	BD (<i>n</i> = 79) Median (25%–75%)	BD + BPD (<i>n</i> = 26) Median (25%–75%)	<i>z</i>	<i>p</i>
Age (years)	37 (28–48)	28.50 (25–35)	–3.567	<.001
Education (years)	11 (11–15)	12 (11–15)	–0.612	.540
Age of onset	23 (19–32)	20.50 (18–25)	–1.787	.074
Number of epizodes				
Depression	2 (1–3)	2.50 (1–4.25)	–1.252	.211
Manic/hypomaniac	2 (1–3)	2.50 (2–5.25)	–1.715	.086
Mix	0 (0–1)	0 (0–2)	–1.397	.162
Total	5 (3–8)	6 (4–9.25)	–1.662	.096
Number of hospitalizations	2 (1–3)	2 (0.75–4.25)	0.189	.850
Duration of disorder (year)	9 (3–17)	3.50 (2–12.50)	–0.787	.074
YMRS	3 (2–5)	5 (4.75–5)	4.551	<.001
HDRS	4 (2–6)	5.50 (3.75–6.25)	2.016	.044
	<i>n</i> (%)	<i>n</i> (%)	χ^2	<i>p</i>
Gender			3.240	.072
Male	36 (45.6)	6 (23.1)		
Female	43 (54.4)	20 (79.9)		
Employment			2.628	.105
Unemployed	21 (26.5)	12 (46.1)		
Employee	58 (73.4)	14 (53.8)		
Marital status			7.726	.005
Single/divorced	36 (45.6)	20 (76.9)		
Married	43 (54.4)	6 (23.1)		
Socio-economic status			2.850	.240
Low	8 (10.1)	6 (23.1)		
Moderate	67 (84.8)	19 (73.1)		
High	4 (5.1)	1 (3.8)		
Family history			4.452	.035
Positive	28 (35.4)	16 (61.5)		
Negative	51 (64.6)	10 (38.5)		
Attempts of suicide			4.152	.042
Positive	18 (22.8)	12 (46.2)		
Negative	61 (77.2)	14 (53.8)		
Drug ^a				.039
MS	17 (21.5)	1 (3.8)		
MS + AP	62 (78.5)	25 (96.2)		

Note: BD, bipolar disorder; BPD, borderline personality disorder; YMRS, Young Mani Rating Scale; HDRS, Hamilton Depression Rating Scale; MS, mood satabilizer; AP, antipsychotic.

^aFisher's exact test.

(respectively $z = -3.567$, $p < .001$; $z = -4.551$, $p < .001$; $z = 2.016$, $p = .044$). Subsequently, Rank Analysis of Covariance Test (Quade's test) was performed for correction of the effect of age, YMRS, and HDRS scores on the verbal memory and executive function in which age, YMRS, and HDRS scores were controlled as a covariate [42]. The impairment on TMT-A duration and number of errors, and TMT-B duration were statistically significant after correction in patients with comorbid diagnosis (respectively $t = -3.449$, $p = .001$; $t = -3.431$, $p = .001$; $t = -2.331$, $p = .022$) (Table 2).

Discussion

In the studies evaluating the BD patients in the euthymic period, at least one comorbid personality disorder was reported to be present at the rate of 45–62% [43]. While Kay et al. reported the rate of comorbid personality disorder in BD as 38% [44]; Rosso et al. reported

Table 2. Comparison of test scores between BD and BD + BPD groups.

	BD Mean \pm SD/median (25–75%)	BD + BPD Mean \pm SD/median (25–75%)	Statistical analysis	Statistical analysis after Quade's test
<i>CVLT</i>				
Total 1–5	49.74 \pm 10.65	45.73 \pm 14.09	$t = 1.533, p = .128$	$t = 0.106, p = .916$
Free short recall	10.54 \pm 3.41	9.23 \pm 3.76	$t = 1.657, p = .101$	$t = 0.534, p = .594$
Free delayed recall	11 (9–13)	8.50 (6–13.25)	$z = -2.684, p = .007$	$t = 0.687, p = .494$
<i>WCST</i>				
Categories achieved	3 (2–6)	2 (1–5)	$z = -1.504, p = .133$	$t = 1.733, p = .086$
Perseverative reaction	29 (13–46)	36.50 (23.75–46)	$z = -1.177, p = .239$	$t = -0.437, p = .663$
Perseverative errors	28 (13–47)	32 (22.50–38.50)	$z = -0.683, p = .494$	$t = -0.387, p = .699$
<i>TMT A</i>				
Seconds	47 (33–63)	52 (43.75–135.5)	$z = -2.458, p = .014$	$t = -3.449, p = .001$
Errors	0 (0–0)	0.50 (0–2.25)	$z = -3.213, p < .001$	$t = -3.431, p = .001$
<i>TMT B</i>				
Seconds	98 (65–124)	128.50 (84–222)	$z = -2.376, p = .018$	$t = -2.331, p = .022$
Errors	1 (0–2)	2 (0–3.25)	$z = -1.983, p = .047$	$t = -1.431, p = .156$
<i>Stroop color word</i>				
Seconds	27.05 \pm 8.22	34.53 \pm 14.61	$t = -2.486, p = .019$	$t = -1.535, p = .128$
Errors	1 (0–3)	2 (0–3)	$z = -0.517, p = .605$	$t = 0.062, p = .950$
Corrections	1 (0–3)	2 (0–3)	$z = -1.319, p = .187$	$t = -0.698, p = .487$

Note: BD, bipolar disorder; BPD, borderline personality disorder; SD, standart deviation; CVLT, California verbal learning test; TMT, trail-making test; WCST, Wisconsin card sorting test.

this rate as 43.7% [45]. In the present study, we found the rate of BPD comorbidity to be 24.8%.

In our study, we found a higher rate of “single/divorced” category in the comorbid diagnosed group. This situation could be a result of the low tolerance threshold to stressors, impulsiveness, and inconsistencies in interpersonal relationships of the patients with comorbid BPD. In BD, the presence of family history is considered as a poor prognostic factor [46]. In the present study, the rate of family history was considerably higher in both groups and was particularly higher in the comorbid diagnosed group. This situation could be interpreted as follows: the presence of family history causes a severe course of disease as well as it is possible to interpret that these patients consult more often in treatment centres or that it is a contribution of social support elements to the treatment.

Comorbid diagnosis in BD increases the risk of suicide [47]. In literature, this rate is known as 25–50% [48]. In the present study, a higher suicide attempt rate was found in the group with comorbid diagnosis compared to the group without comorbid diagnosis, consistent with the current literature. This situation may be related to the fact that these patients commonly experience the hopelessness created by their sense of life that they are not able to find a meaning to it and the anxiety they feel when they face a virtual or real desolation as a result of their impulsive behavior.

It was reported that in comorbid diagnosed BD situations, age of onset is earlier, number of episodes and hospitalizations are higher, and the total duration of the disease is longer [43,49]. In the present study, the age of onset was earlier, consistent with the literature. On the other hand, the total duration of the disease was higher in the group without comorbid diagnosis, not consistent with the literature. This might be related to the fact that patients with comorbid BPD diagnosis were not able to continue to the treatment and that way they remained unrecorded.

Affective instability, which is related with fronto-limbic network dysfunction, is a core feature of both BD and BPD; however its nature may be different as indicated in neuro-imaging studies. BD patients require additional top-down cognitive processing to regulate emotion, while BPD patients have insufficient bottom-up feedback [50]. Also it is indicated that each disorder had specific regions of abnormality in structural magnetic resonance imaging; both cortical and subcortical structures in BD, and confined mainly to fronto-limbic regions in BPD [51].

There were no significant differences between the two groups in their CVLT performance, which measures the verbal memory and learning. We did not find any significant differences when we compared two groups in terms of their WCST and Stroop Test performances. This situation could show that the comorbid BPD diagnosis in BD does not cause any impairments other than BD in complex attention, response inhibition, working memory, and cognitive flexibility which are particularly sensitive for dorsolateral prefrontal cortex function.

In the present study, performances of the BD patients with comorbid BPD were lower than the group of BD patients without comorbid diagnosis in TMT, which measures the processing speed and selective attention that are particularly sensitive for ventral prefrontal cortex function. Consequently, as a result of evaluations made by neuropsychological tests, ventral but not dorsal prefrontal executive functions were found to be impaired by BPD comorbidity in patients with BD. BPD is associated with orbitofrontal cortex (OFC) dysfunction with distinct symptom clusters such as impulsivity. It was reported that dysfunction of medial and lateral regions of the OFC could specifically mediate symptoms of impulsivity in BPD in a perfusion imaging study [52]. Deficits on the processing speed and selective attention might be related to impulsivity that may be the result of dysfunction of the OFC.

This study has certain limitations; the statistically significant difference between the average age of the groups, the lower number of patients, and the lack of a healthy control group are among these limitations. However, as far as we know, our study is one of the rare studies, which evaluate comorbid diagnosis that were not emphasized enough when evaluating cognitive functions in BD. We think that when evaluating the cognitive functions, evaluation of comorbid diagnoses, especially BPD, is crucial. Future studies with larger samples, including all comorbid diagnosis, will increase our knowledge related to the nature of the cognitive dysfunctions in BD.

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No potential conflict of interest was reported by the authors.

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