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Neurocognitive Functions in Bipolar Disorder in Relation to Comorbid ADHD

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ABSTRACT

Introduction: Bipolar disorder (BD) and attention deficit hyperactivity disorder (ADHD) often co-occur in adult population. Both conditions present various neurocognitive and behavioral problems. We aimed to examine neurocognitive functions in adult patients with comorbid BD and ADHD (BD+ADHD) in comparison to patients with only BD, only ADHD and healthy controls (HCs).

Method: An extensive cognitive battery which evaluates verbal learning and memory, visual memory, processing speed, attention, executive functions, working memory and verbal fluency, was used to assess neurocognitive functions respectively in adult (age 18–65 years) patients with BD (n=37), ADHD (n=43), BD+ADHD (n=20) in comparison to HCs (n=51). The Multivariate Analysis of Covariance models, where age, level of education and total BIS-11 scores were included as covariates, were used for comparing neurocognitive scores among groups.

Results: Both BD and BD+ADHD groups showed significantly poorer performance than HCs in processing speed, attention, executive functions, and verbal fluency domains. The BD group had additional significant deficits in executive functions, verbal learning and memory domains. There were no significant differences between BD and BD+ADHD groups with regards to verbal learning and memory, visual memory, processing speed, attention, executive functions, working memory and verbal fluency domains. Patients with only ADHD showed significantly poorer performance than HCs in verbal fluency domain.

Conclusions: Our results show similarities in the neurocognitive functions of adults with BD and BD+ADHD across a wide range of cognitive domains. The findings point to the need for further exploration of diverging and converging neurodevelopmental trajectories of BD and ADHD.

Keywords: Bipolar disorder, attention deficit hyperactivity disorder, neurocognitive functions

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INTRODUCTION

Bipolar Disorder (BD) is a chronic psychiatric disorder, characterized by relapsing and remitting mood episodes, which effects approximately 2–4% of the population (1). Attention-deficit/hyperactivity disorder (ADHD) is the most common childhood psychiatric disorder, and about half of those diagnosed with ADHD in childhood also meet the diagnostic criteria for ADHD in adulthood (2). Both disorders present with an early age of onset, neurodevelopmental background, and high prevalence (3). BD is three to six times more common in people with ADHD than in those without (4). The comorbidity of ADHD in children and adolescents with BD (BD+ADHD) range between 38 and 98%. In adults, the comorbidity decreases to 9–35% (2).

BD and ADHD have such common clinical features as talkativeness, distractibility, and motor hyperactivity. However, increased self-esteem, decreased need for sleep and increase in goal-directed activity is unique to manic episodes. On the other hand, it has been shown that neurocognitive impairment in BD is not unique to mood episodes, but it can also be seen in inter-episodic periods (5). It has been shown that patients with BD+ADHD have greater affect regulation problems, earlier onset of the mood symptoms, a greater number of depressive and mixed episodes, fewer euthymic periods, and more frequent comorbidities, such as alcohol and substance abuse and anxiety disorders (2). Evidence indicates that comorbid ADHD in youth with BD negatively effects the clinical features, as well as neurocognitive and global functioning of BD (6). Although epidemiologic studies show that these two disorders may be related, the nature of this relationship yet to be clarified (7).

Neurocognitive functions are mental activities or functions of information acquisition, thought, experience and perception. These activities consist of areas such as attention, memory, executive functions, language, visual-perceptual functions, and motor functions. All these functions are thought to emerge as a result of complex pathways in the brain and the interrelationships of these pathways (8). Both patients

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with BD or ADHD reveal neurocognitive deficits (9, 10) and it is well-known that neurocognitive functions are highly related to psychosocial functioning (11). Findings of the studies investigating the impacts of ADHD comorbidity on cognitive performances of patients with BD are not consistent. While one study showed poorer results on executive functions in the comorbid BD+ADHD group compared to ADHD group, and healthy controls (HCs) (12), another found no significant difference in the cognitive domain of functionality scale (FAST) between the BD+ADHD and BD patients (13). Comparison of cognitive functions in adolescents with comorbid BD+ADHD, BD only, ADHD only and HCs revealed that BD+ADHD and ADHD groups had significantly poorer performances on processing speed, working memory and response inhibition tests compared to the patients with BD and HCs (14). The only study focusing on neurocognitive functions in adult patients with BD+ADHD, BD and ADHD showed that there was no significant difference between patients with BD+ADHD and BD in any of cognitive domains, and both patient groups with BD showed poorer performance on executive functions compared to the patients with ADHD (15). In line with this finding, in a recent study, neurocognitive profiles of BD patients with and without childhood ADHD were found similar (16).

To date, only one study has examined neurocognitive functions of adult patients with BD+ADHD, BD, and ADHD compared to the HCs, and there is no consensus about the impacts of ADHD comorbidity on the neurocognitive functioning in BD. Therefore, the aim of this study was to examine the neurocognitive functions of adult BD patients with comorbid lifelong ADHD diagnosis, in comparison to patients with only BD, patients with only ADHD, and HCs.

METHODS

This is a cross-sectional, observational study, involving patients with BD+ADHD (n=20), patients with BD only (n=37) and patients with ADHD only (n=43), who were being followed at the general outpatient and bipolar outpatient units of Dokuz Eylül University, Faculty of Medicine, Department of Psychiatry and outpatient unit of Maltepe University, Faculty of Medicine, Department of Psychiatry. Participants were included in the study between March 2013 – July 2015. Patients and HCs group (n=51) were recruited via physician referral or posted flyers at psychiatry outpatient clinics. The study protocol was approved by the Ethics Committee for Non-Interventional Clinical Trials of Dokuz Eylül University. All participants provided signed written informed consent.

Participants

All patients were interviewed with SCID-I by a trained clinician in order to confirm 'bipolar disorder' diagnosis. Subsequently, the ADHD clinical interview, in which detailed ADHD DSM-IV-TR criteria were presented to the participants with examples, was applied to each patient to identify ADHD. The ADHD diagnosis was supported with Adult Attention Deficit Hyperactivity Disorder Self-Reported Questionnaire (ASRS), which indicates the present symptoms of ADHD, and Wender Utah Rating Scale-25 (WURS), which describes childhood experiences related to ADHD. Hamilton Depression Scale (HAM-D 17), Young Mania Rating Scale (YMRS) and Barratt Impulsiveness Scale (BIS-11) were applied to all participants. The same process was conducted for HCs.

All participants were between 18–65 years of age. All BD and BD+ADHD patients were euthymic for at least six months prior to the study enrollment with no subclinical symptoms, scoring 7 or less both on YMRS, and on HAM-D 17.

The following participants were excluded from the study: Individuals who had a degenerative neurological disorder, mental retardation (diagnosed during the clinical interview), epilepsy, cerebral tumor or cerebrovascular disease, history of head trauma with loss of consciousness, a diagnosis of alcohol or substance dependence. Also excluded were those who were given electroconvulsive therapy (ECT) within the last six months, and those who used any medication (i. e. benzodiazepines or psychostimulants) with a potential effect on neurocognitive performance 24 hours prior to the neurocognitive assessment. For the ADHD group, exclusion criteria were having a diagnosis of comorbid schizophrenia, schizophreniform disorder, schizoaffective disorder, brief psychotic disorder, psychotic disorder NOS and for HCs, and having any Axis I diagnosis according to DSM-IV-TR.

Neurocognitive Assessment

The neurocognitive test battery was completed in a standard sequence in one session by a formally trained psychologist or a psychiatrist. Participants were evaluated with Wisconsin Card Sorting Test (WCST) (17), Rey Auditory Verbal Learning Test (RAVLT) (18, 19), Visual Copy Test (20, 21), Trail Making Test A and B (TMT-A, TMT-B) (22, 23), Digit Symbol Test (20, 21), Auditory Consonant Trigrams (24) (ACT), Stroop Color and Word Test (25, 26), Digit Span Test (20, 21), Controlled Oral Word Association Test (COWAT) (27, 28) and Word List Generation Test (28, 29). Table 1 summarizes the neurocognitive tests used in this study and the corresponding cognitive parameters measured by each test.

Table 1. Cognitive domains measured by neurocognitive tests

Tests	Parameters
Wisconsin Card Sorting Test (WCST)	Executive functions
Rey Auditory Verbal Learning Test	Verbal learning and memory
Visual Copy Test	Visual memory, attention
Trail Making Test A and B (TMT-A, TMT-B)	Attention, processing speed, executive functions
Digit Symbol Test	Attention, processing speed
Auditory Consonant Trigrams	Working memory
Stroop Colour and Word Test	Attention, interference, response inhibition
Digit Span Test	Working memory, attention
Controlled Oral Word Association Test (COWAT)	Verbal fluency, processing speed, executive functions
Word List Generation Test	Verbal fluency, processing speed

Statistical Analyses

The IBM SPSS Statistics 23.0 (Chicago IL, USA) for Windows was used for statistical analyses. Categorical variables were compared with the Chi-square test. Skewness and Kurtosis calculations were used to examine the normality of continuous data. Logarithmic transformations were applied for the non-Gaussian distributed data (RAVLT delayed recall, RAVLT correct recognition, Visual Copy Test scores, WCST completed category number, WCST percentage of perseverative errors, ACT, TMT-A, TMT-B, Stroop Color and Word Test interference) in order to provide normality. Group differences among continuous variables were tested with one-way analysis of variance (ANOVA), post-hoc Bonferroni and independent samples t-test. Multivariate analysis of covariance (MANCOVA) models, where age, level of education and total BIS-11 scores were included as covariates, were used for comparing neurocognitive scores. The significance level was accepted as 0.05 and all test results were presented as mean ± standard deviation (SD) values. All test scores were also converted into z-scores based on mean score and standard deviation of the healthy controls for visualization.

Table 2. Comparisons of demographics and clinical characteristics among the study groups

Demographic characteristics	BD (n=37)	ADHD (n=43)	BD+ADHD (n=20)	HC (n=51)	Analyses F/χ^2	Analyses p
Age (Mean ± SD)	31.86±9.16	28.49±8.33	30.95±7.31	32.29±10.37	1.525	0.210[a]
Education in years (Mean ± SD)	12.41±3.75	13.30±2.98	12.85±3.12	13.61±3.27	1.039	0.377[a]
Sex Male, n (%)	14 (37.8)	20 (46.5)	8 (40.0)	22 (43.1)	0.672	0.880[b]
Occupation status n (%) Employed Unemployed Unable to work	29 (78.4) 6 (16.2) 2 (5.4)	35 (81.4) 6 (14.0) 2 (4.7)	14 (70.0) 3 (15.0) 3 (15.0)	47 (92.2) 4 (7.8) 0 (0.0)	9.534	0.146[b]
Medications: n (%) Mood stabilizers Antipsychotics Psychostimulants Antidepressants	31 (83.8) 22 (59.5) 0 (0.0) 3 (8.1)	2 (4.7) 2 (4.7) 13 (30.2) 14 (32.6)	15 (75.0) 7 (35.0) 2 (10.0) 3 (15.0)	- - - -	57.195 28.116 14.747 7.821	**<0.001[b]** **BD+ADHD>ADHD** **p<0.001** **BD>ADHD** **p<0.001** **<0.001[b]** **BD+ADHD>ADHD** **p=0.003** **BD>ADHD** **p<0.001** **0.001[b]** **ADHD>BD** **p=0.001** **0.020[b]** **ADHD>BD** **p=0.017**
Lifetime history of comorbid psychiatric diagnoses: n (%) Anxiety disorder Alcohol abuse Substance abuse Unipolar depression Others*	 13 (35.1) 0 (0.0) 1 (2.7) NA 0 (0.0)	 15 (34.9) 2 (4.7) 1 (2.3) 18 (41.9) 2 (4.7)	 12 (60.0) 3 (15.0) 1 (5.0) NA 2 (10.0)	 – – – – –	 4.167 6.169 0.353 – 3.464	0.124[b] **0.046[b]** **BD<BD+ADHD** **p=0.039** 0.838[b] – 0.177[b]
Number of suicide attempts (Mean ± SD)	0.57±1.07	0.12±0.45	1.20±2.50	-	4.686	**0.011[a]** **ADHD<BD+ADHD** **p<0.009**
HAMD-17 score Mean ± SD	1.68±2.03	1.72±1.98	2.87±2.10	-	2.117	0.126[a]
YMRS score (Mean ± SD)	0.51±1.22	0.16±0.65	1.53±1.60	-	8.994	**<0.001[a]** **BD<BD+ADHD** **p=0.008** **ADHD<BD+ADHD** **p<0.001**
BIS Total Score (Mean ± SD)	61.05±10.91	79.72±10.66	77.35±11.53	54.37±8.83	55.077	**<0.001[a]** **ADHD>BD p<0.001** **BD+ADHD>BD** **p<0.001** **ADHD>HC p<0.001** **BD+ADHD>HC p<0.001** **BD>HC p=0.018**
BIS Attention score (Mean ± SD)	16.46±3.71	23.19±4.12	22.25±5.54	14.63±2.99	43.418	**<0.001[a]** **ADHD>BD p<0.001** **BD+ADHD>BD p=0.001** **ADHD >HC p<0.001** **BD+ADHD >HC p<0.001**
BIS Motor score (Mean ± SD)	19.73±4.28	26.19±4.59	25.75±4.13	17.80±3.73	37.778	**<0.001[a]** **ADHD>BD p<0.001** **BD+ADHD>BD p<0.001** **ADHD>HC p<0.001** **BD+ADHD>HC p<0.001**
BIS Non-planning score (Mean ± SD)	24.95±5.04	30.35±4.74	29.35±4.46	21.94±4.27	32.778	**<0.001[a]** **ADHD>BD p<0.001** **BD+ADHD>BD p=0.005** **ADHD>HC p<0.001** **BD+ADHD>HC p<0.001** **BD>HC p=0.019**

n, number; [a]ANOVA, post-hoc Bonferroni; [b]Chi Square Test; SD, standard deviation
*Conversion disorder, adjustment disorder, oppositional defiant disorder, specific learning disorder or personality disorder

RESULTS

Comparison of Demographics and Clinical Characteristics Among the Study Groups

Table 2 presents comparisons of demographics and clinical characteristics among study groups. There were no significant differences between the groups in terms of age (p=0.210), years of education (p=0.377), gender (p=0.880) or occupational status (p=0.146).

Alcohol abuse was significantly higher in BD+ADHD patients compared to BD patients (p=0.039). 18 individuals in the ADHD group had a history of at least one major depressive episode. Suicide attempts were more common in BD+ADHD patients compared to ADHD patients (p=0.009). YMRS scores of BD+ADHD patients were significantly higher compared to BD (p=0.007) and ADHD patients (p<0.001).

ADHD and BD+ADHD groups had significantly higher attention, motor, non-planning subscale scores and total score of BIS-11 than BD and HCs groups. The BD group had significantly higher scores on non-planning and BIS-11 total scores compared to HCs.

There was a significant difference between BD and BD+ADHD groups in terms of bipolar disorder subtype (p=0.002) and number of mood episodes with psychotic features (p=0.036). In both patient groups, BD type I was the most common diagnosis, however, the rate of BD type II was significantly higher in BD+ADHD group (35%) in comparison to BD group (2.7%) (p=0.002). For the BD group, the number of mood episodes with psychotic features was significantly higher than BD+ADHD group (p=0.036). The clinical characteristics and comparison of these groups are shown in Table 3.

Table 3. Clinical characteristics of bipolar disorder in BD and BD+ADHD groups

Clinical Characteristics	BD (n=37)	BD+ADHD (n=20)	F/χ^2	p value
BD type: BD I n (%) BD II n (%)	 36 (97.3) 1 (2.7)	 13 (65.0) 7 (35.0)	11.224	**0.002**[b]
Total number of episodes Mean ± SD	5.65±3.35	6.55±7.69	6.578	0.623[a]
Number of depressive episodes Mean ± SD	2.16±2.13	3.40±4.17	7.570	0.226[a]
Number of Mania+hypomania+mixed episodes Mean ± SD	3.49±2.74	3.15±3.90	0.301	0.734[a]
Number of mood episodes with psychotic features Mean ± SD	1.30±1.97	0.45±1.00	4.107	**0.036**[a]
Duration of BD (month) Mean ± SD	127.70±74.18	119.40±89.42	0.849	0.725[a]
Age of onset of BD Mean ± SD	21.27±6.98	20.90±6.61	0.017	0.844[a]
Remission time (month) Mean ± SD	30.14±31.36	20.25±18.27	3.884	0.139[a]
Number of hospitalization Mean ± SD	1.43±1.54	0.90±1.07	1.130	0.132[a]
Number of suicide attempt Mean ± SD	0.57±1.07	1.20±2.50	4.115	0.293[a]

n, number; [a]Independent Sample T Test; [b]Chi Square test

ADHD and BD+ADHD groups did not differ significantly in terms of ADHD subtypes (inattentive, impulsive/hyperactive, and combined types) (χ^2=0.36, p=0.84). All patients in the ADHD only group met the current adult ADHD diagnostic criteria, whereas 17 participants in the BD+ADHD group met the current adult ADHD diagnostic criteria. The remaining three patients in BD+ADHD group met ADHD diagnostic criteria only in childhood.

Neurocognitive Tests

Comparison of the four study groups using MANCOVA adjusting for age, level of education and BIS-11, and with post-hoc Bonferroni correction, revealed significantly lower performance of BD and BD+ADHD groups compared to HCs in five tests: TMT-A completion time (p<0.001, p=0.030 respectively), TMT-B completion time (p=0.017, p=0.028 respectively), Digit Symbol Test total number (p=0.003, p=0.025 respectively), COWAT total word number (p<0.001, p<0.001 respectively) and Word List Generation Test total word number (p=0.003, p=0.014 respectively). The BD group showed significantly poorer performance compared to the HCs group, in three additional tests: RAVLT number of words delayed recall (p=0.016), WCST completed category number (p=0.002) and percentage of perseverative errors (p=0.021). Patients with only ADHD showed poorer performance only in COWAT total word number (p<0.001) compared to HCs. The significance between groups in RAVLT number of words recalled between trial 1 to 5 disappeared after post-hoc Bonferroni (p=0.061). Neurocognitive test scores are given in Table 4. Z-scores of neurocognitive tests are given in Figure 1.

DISCUSSION

In the present study, we compared neurocognitive performance of individuals with only BD, only ADHD, BD+ADHD and HCs. Our findings showed that both BD and BD+ADHD groups underperformed HCs on tasks associated with processing speed, attention, executive functions, and verbal fluency. The BD group showed impairment in a wider range of cognitive domains than the BD+ADHD group including tasks associated with executive functions, verbal learning and memory in comparison to HCs.

Our findings indicating no significant difference in any of the cognitive domains between the BD+ADHD and BD patients, is in line with a previous study (15). In addition, a more recent study revealed no significant difference in neurocognitive performances between BD patients with and without childhood ADHD (16).

Despite no significant difference was found between BD and BD+ADHD groups in any of the neurocognitive tests, compared to HCs, the BD group showed impairment in a wider range of cognitive domains than the BD+ADHD group. A number of factors might have played a role in the current findings. First, BD and BD+ADHD groups showed a significant difference in terms of BD subtype. Although the number of patients with BD type I was higher in both groups, the proportion of the patients with BD type II in the BD+ADHD group was higher. A meta-analysis study reported that BD type II patients were shown to exhibit impairments similar to BD type I patients, on executive functions, working memory,

Table 4. Comparisons of neurocognitive test scores of all groups

	Mean ± SD					
	BD n=37	**ADHD n=43**	**BD+ADHD n=20**	**HC n=51**	**F**	**p***
Number of words recalled between Rey 1 to 5 trial	55.14±8.35	59.49±8.04	60.30±8.25	60.49±7.05	3.023	**0.032 post-hoc significance disappears**
Rey delayed recall	11.35±2.72	12.84±2.06	12.75±2.02	13.14±2.10	3.242	**0.023 BD <HC p=0.016**
Rey correct recognition	13.54±1.92	13.93±1.53	13.70±1.69	14.14±1.23	0.034	0.578
Visual copy and memory immediate recall	35.62±5.86	37.23±4.53	38.40±4.84	37.22±4.63	1.598	0.184
Visual copy and memory delayed recall	31.97±8.96	36.02±5.76	34.85±7.62	36.45±6.26	1.510	0.244
Wisconsin completed category number	4.97±1.48	5.56±0.98	5.30±1.26	5.78±0.83	5.168	**0.003 BD <HC p=0.002**
Wisconsin percentage of perseverative errors	15.43±7.51	11.28±5.86	12.95±7.15	10.68±4.85	2.821	**0.030 BD >HC p=0.021**
Auditory Consonant Trigrams	49.14±8.77	50.98±6.35	51.75±6.58	53.45±5.38	1.876	0.169
Completion time in Trail Making Test A (second)	42.38±14.03	33.77±13.31	38.90±15.17	28.63±10.77	8.282	**<0.001 BD >HC p<0.001 BD+ADHD >HC p=0.030**
Completion time in Trail Making Test B (second)	92.08±49.04	74.94±27.52	89.55±42.92	65.75±32.80	4.393	**0.008 BD >HC p=0.017 BD+ADHD >HC p=0.028**
Digit Symbol Test total number	50.57±13.35	57.79±13.18	50.65±13.88	62.33±14.12	6.780	**<0.001 BD <HC p=0.003 BD+ADHD <HC p=0.025**
Digit Span Test forwards	7.57±2.56	6.95±1.85	7.85±2.68	7.69±2.19	2.287	0.068
Digit Span Test backwards	6.84±2.29	7.14±2.23	7.60±2.78	8.25±2.62	2.248	0.085
COWAT total word number	36.08±13.10	43.14±14.26	37.20±17.01	48.65±13.99	4.983	**<0.001 BD <HC p<0.001 ADHD <HC p<0.001 BD+ADHD <HC p<0.001**
Word List Generation total word number	21.03±5.39	23.81±5.82	21.15±5.17	24.80±3.78	4.791	**0.001 BD <HC p=0.003 BD+ADHD <HC p=0.014**
Stroop Colour and Word Test interference (second)	41.72±20.49	43.28±20.26	44.10±16.23	38.31±17.93	1.479	0.575

n, number; *MANCOVA, post-hoc Bonferroni

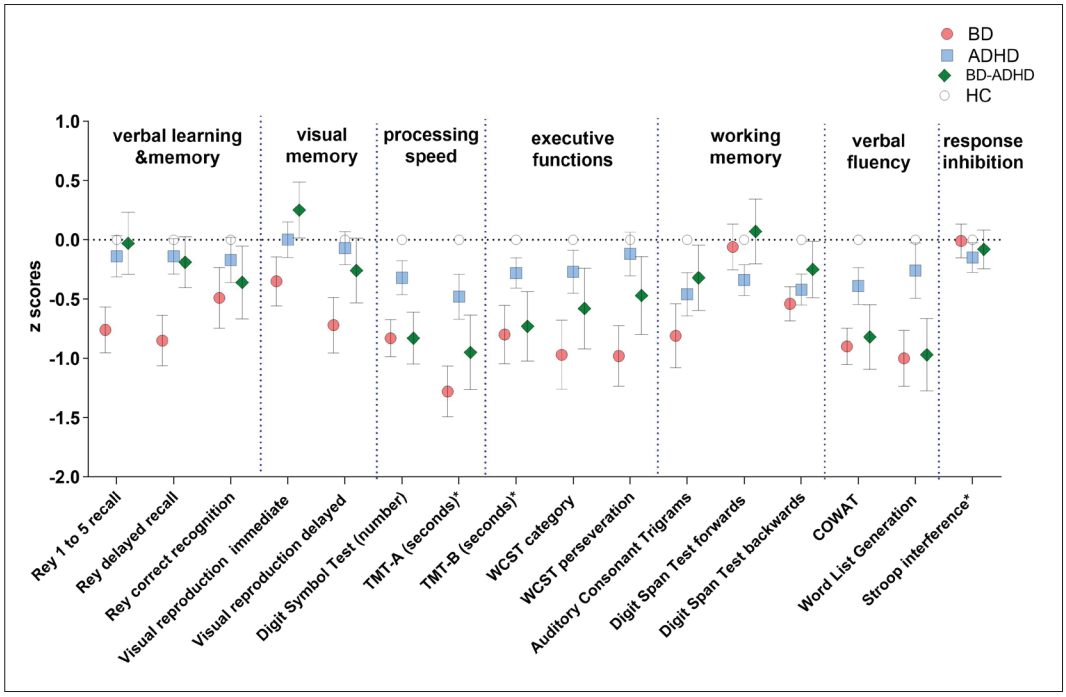

Figure 1. Comparison of all groups in terms of Z-Scores of neurocognitive tests (*Z-scores are multiplied by -1 for visuality).

attention and processing speed; but the impairments on verbal learning and memory were more specific to patients with BD type I (30). In our study, the verbal learning and memory performance of the BD only group, in which the proportion of BD type I was higher, was significantly lower than that of the HCs, while BD+ADHD group, which had a much lower BD type I diagnosis rate, showed no such difference compared to HCs on this cognitive domain. In accordance with the literature, BD and BD+ADHD groups performed similarly in tests such as attention, processing speed, and verbal fluency.

Another possible reason for the wider range of neurocognitive deficits in the BD group may be related to the significantly higher number of mood episodes with psychotic features in the BD group compared to the BD+ADHD group. The finding may be associated directly to the effect of psychosis, or attributable to the BD groups' higher rate of BD type I diagnosis, which, by definition, implies the presence of psychotic features. There are studies in the literature which suggest that BD patients who have mood episodes with psychotic features exhibit worse neurocognitive performance than patients not experiencing psychotic features. In a meta-analysis, BD patients with psychotic features showed significantly worse performance on planning, working memory, verbal memory, and processing speed than the BD patients without non-psychotic features (31). In our study, the BD group performed less well on verbal memory compared to HCs, but this result was not found for the BD+ADHD group, perhaps due to the lower number of psychotic mood episodes in this group.

Another explanation for the results may be that patients with BD+ADHD and ADHD alone may have experienced positive aspects of ADHD, such as hyperfocus or divergent thinking. Divergent thinking refers to an ability to create novel and original ideas, while hyperfocus can be defined as an intense concentration on things that produce feelings of enjoyment. This proposition suggests that some aspects of ADHD can be adaptive, and that some adults can compensate for their ADHD-related deficits (32). This may take the form of a neural reorganization that compensates the deficient neural regions affected in ADHD; in response to low activation of the prefrontal cortex, a compensatory network including cerebellum may favorably intervene in the neurocognitive functions (33, 34). This may provide a better cognitive reserve, which may also explain the overall higher level of education in the ADHD group, although this difference was not significant.

Within the same context, in our study, the ADHD group performed worse only in verbal fluency domain compared to HCs group. In a review, poor executive functioning was highlighted as one of the most prominent neurocognitive deficits in adult ADHD patients (35). In addition, studies in the literature show that some aspects of neurocognitive functions are improved with methylphenidate treatment in adult patients (36). In our study, approximately one-third of patients with ADHD had received psychostimulant treatment. Even though there was no significant difference between patients with ADHD only and other patient groups regarding neurocognitive functions, their neurocognitive performance was intermediate between the HCs and the two other patient groups. This may be due to improved neurocognitive performance through psychostimulant treatment.

In the present study BIS total and subscale scores were significantly higher in ADHD and BD+ADHD patients compared to BD patients and HCs. BD patients had significantly higher scores on BIS-11 total and non-planning subscores compared to HCs. Our findings are consistent with data from a number of studies that reported higher subscale and total scores of BIS among ADHD and BD patients than HCs (37, 38). Etain et al. also found a relationship between BIS-10 total scores and alcohol misuse (37). In our study, BD+ADHD group had significantly higher BIS-11 total scores and higher rates of alcohol abuse compared to BD patients. In addition, our findings showed that BD+ADHD group scored the highest YMRS scores, perhaps related to the group's high impulsivity characteristics. Our results suggest that BD+ADHD patients resemble ADHD patients in terms of impulsivity features, which is the core symptom and diagnostic criteria for ADHD.

This study has some limitations to consider while interpreting the results. Small sample size, particularly, in the comorbid BD+ADHD group, is a limitation of the study. Within the same context, the sample size was not large enough to detect the potential effect of the ADHD subtypes on the neurocognitive performance. Another limitation was the diverse pharmacological treatment across the groups. It is well known that, although medications have beneficial effects on providing and maintaining euthymia, they have neurocognitive side effects (39). The majority of patients in the BD and BD+ADHD groups were on antipsychotic or mood stabilizer treatment, and the neurocognitive impairment in these groups may be at least partially attributed to the medication effect. Another point to be considered is that three individuals in the BD+ADHD group did not meet ADHD diagnostic criteria for adulthood, although it is not possible to estimate the exact effect of this on the group's overall neurocognitive performance.

To date, a limited number of studies compared neurocognitive functions of adults with BD+ADHD, BD, ADHD and HCs. Our results show that the performance of adults with BD+ADHD in a wide range of neurocognitive tests is similar to that of the BD patients. In other words, neurocognitive impairment of the BD+ADHD group may be more influenced by the bipolarity rather than ADHD. The findings seem to highlight the need for research on neurodevelopmental aspects of BD and ADHD further exploration of the diverging and converging neurobiological trajectories of both conditions.

Ethics Committee Approval: The study protocol was approved by the Ethics Committee for Non-Interventional Clinical Trials of Dokuz Eylül University.

Informed Consent: All participants provided signed written informed consent.

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