ORIGINAL ARTICLE

Comparison of Neuropsychological Functioning among Individuals Diagnosed with Bipolar Disorder with and without Childhood ADHD

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Abstract

Background: Bipolar mood disorder (BMD) with a lifetime history of Attention-deficit hyperactivity disorder (ADHD) characterized by a particularly neuropsychological profile. This study aimed to clarify whether there is a difference between BMD patients with ADHD and BMD patients without ADHD in terms of neuropsychological functioning.

Methods: This is a cross-sectional study with 68 samples (24 patients had BMD with ADHD and 44 patients had BMD) selected based on the target sampling during a year (March 2014 to March 2015). Tower of London (ToL) task, Conners' Continuous Performance Test (CPT), and Wisconsin Card Sorting Test (WCST) were used for assessing neuropsychological functioning in participants. All statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS) version 16 software.

Results: The results revealed that the BMD with ADHD group was not more impaired than the BMD group on two measures of executive functioning TOL and CPT. The BMD in the ADHD group was more impaired than the BMD group on WCST.

Conclusion: This study will be effective in understanding whether the cognitive flexibility impairments often detected in adult BMD are partially the result of lifetime ADHD.

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Introduction

Bipolar mood disorder (BMD) is a recurrent and chronic disorder characterized by fluctuations in the mood state and energy and affects around 2.4% of the global population.[1] As a lifelong and recurrent illness, BMD is associated with functional decline, cognitive impairment, and a reduction in quality of life (QoL).[2]

Attention-deficit hyperactivity disorder (ADHD) is a chronic disorder characterized by symptoms of inattention, hyperactivity, and impulsivity.[3] ADHD is the most common neurodevelopmental disorder in childhood, affecting approximately 5–8% of children. Persistence of symptoms into adulthood occurs in two-thirds of early-diagnosed patients, with an estimated worldwide prevalence of 3–5% for affected adults.[4]

BMD individuals tend to suffer from comorbid disorders, with the highest prevalence rate found for anxiety disorders (54%), ADHD (48%), disruptive behavior (31%), and substance use (SUD) (31%) disorders.[5] Set shifting, or cognitive flexibility, is a core executive function involving the ability to quickly and efficiently shift back and forth between mental sets.[6] ADHD is often characterized by underdeveloped behavioral inhibition, working memory, temporal organization, and regulation of emotions, which are traditionally ascribed to deficient executive functioning.[7]

Several studies have proposed that symptoms of ADHD arise from a primary deficit in a specific

executive function domain such as response inhibition, working memory, or a more general weakness in executive control.[7] However, moderate effect sizes and lack of universality of executive function deficits among individuals with ADHD suggest that executive function weaknesses are neither necessary nor sufficient to cause all cases of ADHD.[8]

One study compared the adults with BMD, ADHD, BMD with ADHD, and healthy controls across a broad spectrum of cognitive domains but found no significant differences between BMD and BMD with ADHD.[9] Working memory and concentration/focused attention (measured by CPT, TOL) did not differ between those in the BMD with childhood ADHD group who only had a history of childhood ADHD and those who still met the criteria for ADHD in adulthood. The results of this study showed that both patient groups performed worse than the controls on several tests.[10]

The results of the study that compared children with BMD, ADHD, and BMD with ADHD showed that all three groups were impaired in general executive function and metacognition; only the two BMD groups revealed more extensive executive dysfunction, in both cognitive and emotional control domains, compared to the ADHD group.[11]

Another study used only the Wisconsin Card Sorting Test and found that BMD patients with ADHD showed set-shifting difficulties compared with the ADHD and healthy controls.[12] One study comparing patients with BMD, ADHD, BMD with ADHD, and healthy controls found that the BMD group in general performed similarly to the controls, whereas BMD with comorbid ADHD was associated with cognitive impairment. The greatest deficits in the BMD with the ADHD group were found in verbal memory and inhibitory control.[13]

BMD with a lifetime history of ADHD is associated with a particularly severe clinical profile characterized by an early onset of mood symptomatology, a greater frequency of mood episodes, multiple comorbidities, and a poor response to psychotropic medication. BMD with a history of ADHD is also associated with poor functional outcomes. Some authors have suggested that BMD with lifetime ADHD may represent a distinct BMD phenotype.[7]

At present, it is still unclear whether ADHD comorbidity in BMD leads to a more severe profile of cognitive dysfunction or not, and whether the comorbid phenotype is just a more severe form of BMD or altogether a distinct clinical phenotype.[11] Therefore, we aimed to investigate the comparison of neuropsychological functioning among individuals with a diagnosis of bipolar disorder with and without childhood ADHD.

BMD is associated with impairment in various domains of cognitive function, including executive function, verbal memory, verbal memory, and attention. However, the performance of some of these individuals is in the normal range. For this reason, these disorders may be due to coexistence with other disorders such as ADHD. People with ADHD show several cognitive impairments. This study aimed to clarify whether there is a difference between BMD patients with ADHD and BMD patients without ADHD. This study could be effective in understanding whether the neurocognitive impairments often detected in adult BP are partially the result of lifetime ADHD.

Methods

This cross-sectional study was conducted at Hafez and Ebnesina hospitals affiliated to Shiraz University of Medical Sciences (SUMS), Shiraz, Iran. During a year (March 2014 to March 2015), the researchers explained the purpose of the study in the clinic and asked the samples to register and participate in the psychiatric interview based on Diagnostic Interview for ADHD in Adults (DIVA) to rule out any psychiatric problems. According to this method, about 87 subjects visited, and, finally, 68 (24 patients had BMD with ADHD and 44 patients had BMD) selected based on the target sampling participated in the study. All participants were in remission.

Inclusion criteria were: 1) having received a diagnosis of BMD type I or II by a psychiatric, 2) having a normal IQ (clinical), 3) being in the age range of 18 to 65, 4) having Individual willingness to participate in the study and complete the evaluation form by the end of the study, and 5) having at least primary school education. The exclusion criteria included 1) unwillingness to participate in the study and complete the evaluation form by the end of the study, 2) uncontrolled serious neurological disease such as seizures, 3) drug abuse, 4) medical illnesses known to affect the neurological function of the patients, and 5) mental retardation. Diagnosing the disorders and examining the entry and exit criteria were done by a psychiatrist and a clinical psychologist.

Ethical Consideration

The Ethics Committee of Shiraz University of Medical Sciences approved this study (Ir.sums.rec.6359). All participants signed informed consent forms to participate in the study. Patients were assured that their data would be kept confidential and the withdrawal from the study at any time would not influence their treatment process.

Instruments

Demographic Checklist: We used it to evaluate the age, education, place of living and marital status, occupation.

Tower of London (ToL) task: This test was made by Shallice (1982). The computerized versions of the WCST were created using the Colorado Assessment Tests software package (CATs; Keller & Davis, 1998), and the appearance, setup, and ordering of all stimulus and key cards were identical to the manual version.[14] It evaluates the planning ability. The task is composed of a wooden platform with three vertical rods and three colored spheres (red, green, and blue). The participant must transpose the three spheres, starting from an initial position, to reach various final positions. The task comprises 12 problems (i.e., target positions), the difficulty level of which increases as a function of the number of moves necessary to reach the final position, with a variation of two to five moves, with unlimited time to solve the task. The measure used is the total score. For each problem, the participant obtains three points if a solution is reached in only one attempt, two points if the solution is reached in two attempts, one point if the solution is reached in three attempts, and zero points if the solution is not reached in three attempts. Therefore, the total score can range from 0 to 36 points.[15] The Persian version was used in this study. The reliability of all subscales was more than 0.70 in the Persian version.[16]

Conners' Continuous Performance Test (CPT): It is a computer-administered test that is designed to assess problems with attention. The Conners CPT-2 presents 360 stimuli trials (i.e., individual letters) on the screen, with 1, 2, or 4 s between the presentation of letters (ISI: Inter-Stimulus Interval). The 360 trials are divided into 18 blocks of 20 trials each. The ISIs are counterbalanced across these blocks. Respondents are instructed to press the spacebar or the appropriate key on the mouse for any letter that appears, except the letter "X." The CPT takes fourteen minutes to administer excluding the recommended practice test. Throughout the test, 324 non-X stimuli (i.e., targets) appear, and the letter "X" (nontarget) appears 36 times.[17] The Persian version was used in this study. The reliability of this test was 0.90.[18]

Wisconsin Card Sorting Test (WCST): It was used as an established version of the computer WCST.[19, 20] Stimuli were presented against the white background of a 15.3-inch notebook screen. Participants were required to match the cards according to one of three possible sorting rules (color, shape, number), with the valid sorting rule changing after a variable number of trials. Target displays consisted of four key cards which appeared invariantly above one stimulus card, all configured around the center of the computer screen. Stimulus cards varied on three dimensions (color: red, green, yellow, blue; shape: triangle, star, cross, circle; the number of objects: one, two, three, four), and these dimensions equaled the three viable task rules. As each stimulus card shared exactly one unique stimulus feature with three out of the four key cards, the applied sorting rule could unambiguously be identified. Cronbach's alpha was at least 0.73 in all subscales. The discriminant validity could separate people with anxiety disorder from healthy control.[20]

We used ANOVA to compare the differences of the variables in the two groups. All statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS) version 16 software. The significance level was $P<0.05$.

Results

The present study was conducted on 68 patients aged 19 and 63 years, with a mean age of 33.70±10.93 years old. Patients without a history of ADHD had a mean age of 33.56±10.68, duration of disorder of 7.81±7.08, and patients without a history of ADHD had a mean age of 33.95±11.63 years, and duration of disorder of 6.18±7.49. Patients were evaluated for age (t=0.13,

Table 1: Demographic characteristics of the participants

Variables	Level	Patients BMD without ADHD		Patients BMD with ADHD		P
		N	F (%)	N	F (%)	
Sex	Female	5	11.36	4	16.66	0.26
	Male	39	88.63	20	83.33	
Marital Status	Single	20	45.45	14	58.33	0.41
	Married	23	52.27	9	37.50	
	Missing	1	2.27	1	4.16	
Occupation	Unemployed	7	15.90	6	25	0.69
	Employed	6	13.63	4	16.66	
	Self-Employment	20	45.45	10	41.66	
	Pensionary	5	11.36	1	4.16	
	Missing	6	13.63	3	12.50	
Education	Under Diploma	14	31.81	6	25	0.71
	Diploma	17	38.63	13	54.16	
	Academic	13	29.54	4	16.66	
	Missing	0	0	1	4.16	
Place of Living	Village	9	20.45	6	25	0.11
	City	32	72.72	14	58.33	
	Missing	3	6.81	4	16.66	

Table 2: T-test of the variables between the groups

Variables		Groups	Mean±SD	t	P
Tower of London Test		Patients BMD without ADHD	27.46±6.67	1.63	0.10
		Patients BMD with ADHD	24.60±7.00		
Continuous Performance Test	Error Commission	Patients BMD without ADHD	2.23±3.68	0.20	0.83
		Patients BMD with ADHD	2.41±2.21		
	Omission Error	Patients BMD without ADHD	2.41±4.07	0.03	0.92
		Patients BMD with ADHD	2.46±3.48		
	Categories Achieved	Patients BMD without ADHD	1.46±0.72	0.11	0.73
		Patients BMD with ADHD	1.43±1.37		
Wisconsin Card Sorting Test	Categories Achieved	Patients BMD without ADHD	7.40±6.17	2.84	0.006
		Patients BMD with ADHD	1.86±1.54		
	Perseverative Errors	Patients BMD without ADHD	7.40±6.17	2.78	0.0006
		Patients BMD with ADHD	12.26±7.63		
	Other Errors	Patients BMD without ADHD	24.64±10.44	2.46	0.01
		Patients BMD with ADHD	31.21±10.01		
	Time of Necessary for Succeeds on the First Category	Patients BMD without ADHD	17.26±17.08	2.29	0.02
		Patients BMD with ADHD	28.60±22.20		

P=0.89) and duration (t=0.85, P=0.39) of disorder using ANOVA, and the difference between the two groups was not significant. The demographic characteristics of the participants in the two groups (sex, education, place of living and marital status, occupation) are displayed in Table 1.

To investigate the difference between the two groups (patients BMD with ADHD and (patients BMD without ADHD) in terms of neuropsychological instruments, we used independent t-test.

The two groups did not have significant differences in terms of the Tower of London Test and Continuous Performance Test, but their function was different in Wisconsin Card Sorting Test. The patients BMD without ADHD compared to patients BMD with ADHD had higher average scores in the categories of Wisconsin Card Sorting Test and lower average scores in perseverative errors, other errors and time required to complete the first category (Table 2).

Discussion

TOL evaluates executive planning[21] and CPT evaluates the process of continuous attention and difficulty in impulse control.[22] The BMD with ADHD group was not more impaired than the BMD group on TOL. The BMD with ADHD group had a weaker performance than the other one on CPT.

There are few previous studies in this area. The results of this study are in line with the results of other studies which show that BMD without ADHD has the same performance as the healthy control and is weaker than BMD with ADHD.[9-13]

BMD has been associated with general cognitive impairment across different cognitive domains.[23] Executive function, verbal memory, and attention/working memory are particularly affected by BMD.[24-27] Cognition in adults with ADHD shows general impairments across multiple cognitive domains, with possible emphasis on impaired attention, inhibition, and verbal memory.[28, 29] A possible explanation is that BMD patients suffering from comorbid conditions like ADHD exhibit varying degrees of cognitive impairment.[30-32]

In this study, executive function was similar in BMD patients with and without ADHD. This means that comorbid ADHD cannot explain the cognitive heterogeneity seen in bipolar disorder patients and that cognitive testing is not likely to be useful for differentiating between BMD with and without ADHD.[9, 10]

Wisconsin Card Sorting Test (WCST) is designed to assess cognitive flexibility. Categories achieved are interpreted as the extent of one's progress during the test and discovery of the laws that govern it. In this test, perseverative errors indicate cognitive inflexibility.[19] In this study, the BMD with ADHD group was more impaired than the BMD group on WCST.

BMD with a lifetime history of ADHD is associated with a severe clinical profile characterized by an early onset of mood symptomatology, a greater frequency of mood episodes, multiple comorbidities, and a poor response to psychotropic medication. The presence of such variables may negatively affect cognitive functioning (Roger, Joseph, 2019).[33]

BMD patients with ADHD exhibited clinically significant deficits only in selected cognitive domains, such as cognitive flexibility, organization, working memory, and monitoring. This pattern is in line with the findings of neurocognitive deficits in attention, working memory, and cognitive flexibility in ADHD, which have also been found to be associated with impaired fronto-striatal circuits.[11]

Some limitations of this study should be considered. The use of mood stabilizers could differ between the two groups. Medication might affect cognitive performance. It is suggested that, in future research, a comparison should be made between these

two groups and the healthy controls. The dose of drugs used can also be considered as a control variable.

Conclusion

This study aimed to clarify whether there is a difference between BMD patients with ADHD and BMD patients without ADHD in terms of neuropsychological functioning. The BMD with ADHD group was similarly impaired as the BMD group in executive planning and process of continuous attention assess by TOL and CPT. The BMD with ADHD group had a weaker performance than the other one in WCST which assesses cognitive flexibility. Therefore, the presence of ADHD throughout life in individuals with a diagnosis of bipolar disorder affects cognitive flexibility. This study is effective in understanding whether the cognitive flexibility impairments often detected in adult BMD are partially the result of lifetime ADHD.

Authors' Contribution

Study concept and design: Arash Mani; collection of the data: Amir Reza Khodaman and Leila Khabir; analysis and interpretation of the data: Arash Mani and Leila Khabir; drafting the manuscript: All authors; critical revision of the manuscript for important intellectual content: Arash Mani and Leila Khabir; statistical analysis: Leila Khabir and Arash Mani.

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Conflict of Interest: None declared.

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