

Perseveration is not Related with Functionality in Bipolar I Disorder with a Psychotic Mood Episode

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ABSTRACT

Aim: The aim of this study was to assess perseverative errors and responses as measured by the Wisconsin Card Sorting Test (WCST) in remitted bipolar I disorder patients having at least one previous psychotic mood episode and investigated the relationship between perseveration, areas of functionality, and clinical features.

Methods: In the current study 48 remitted patients with bipolar I disorder diagnosed with DSM-IV criteria, and 45 socio-demographically matched healthy controls were consecutively enrolled. Socio-demographic and clinical characteristics form, Young Mania Rating Scale, Hamilton Depression Rating Scale, Bipolar Disorder Functioning Questionnaire (BDFQ), the Wisconsin Card Sorting Test (WCST), the DSM-IV Structured Clinical Interview for axis I Disorders, Montreal Cognitive Assessment Scale were used.

Results: The distribution of age, gender and years of education between the patient and the control group was similar. In the patient group scores of perseverative errors in WCST was found to be higher than controls but there were no significant association between the total BDFQ scores of patients and the number of perseverative errors or responses.

Conclusion: Perseverative errors and responses on the WCST was significantly higher in the remitted patients with bipolar I disorder who had at least one psychotic mood episode, when compared with the healthy controls, but this impairment did not have any impact on functioning.

Keywords: Bipolar disorder, executive function, functionality

ÖZET

Psikotik Duygudurum Atağı Olan Bipolar Hastalarda Perseverasyon ve İşlevsellik İlişkisi

Amaç: Bu çalışmada, en az bir psikotik duygudurum atağı geçirmiş olan, remisyon dönemindeki bipolar I bozukluk hastalarında Wisconsin Kart Eşleme Testi (WKET) ile perseverasyon hataları değerlendirildi ve bunlarla işlevsellik alanları ve klinik özellikler arasındaki ilişki araştırıldı.

Yöntem: Bu çalışmada, DSM-IV ölçütlerine göre Bipolar I Bozukluğu tanısı konulan remisyon dönemindeki 48 hasta ile sosyo-demografik açıdan eşleştirilmiş 45 sağlıklı kontrol ardışık olarak çalışmaya alındı. Çalışmada, sosyo-demografik ve klinik veri formu, Young Mani Derecelendirme Ölçeği, Hamilton Depresyon Derecelendirme Ölçeği, Bipolar Bozukluk İşlevsellik Ölçeği (BDFQ), WKET, Eksen I Bozuklukları için Yapılandırılmış DSM-IV Klinik Görüşme Formu (SCID-I) ve Montreal Bilişsel Değerlendirme Ölçeği kullanıldı.

Bulgular: Hasta ve kontrol grubu arasında yaş, cinsiyet ve eğitim yılı dağılımı benzerdi. Hasta grubunda WKET'deki perseveratif hata puanları kontrollerden yüksek olmakla beraber, hastaların toplam BDFQ puanları ile perseveratif hata veya cevap sayısı arasında anlamlı bir ilişki bulunmamıştır.

Sonuç: Sağlıklı kontrol grubu ile karşılaştırıldığında, en az bir psikotik duygudurum atağı geçirmiş remisyondaki bipolar I bozukluğu hastalarında perseverasyon değerleri yüksek olmasına karşın, bu perseveratif hatalar ile işlevsellik arasında bir bağlantı saptanmadı.

Anahtar sözcükler: Bipolar bozukluk, yönetici işlevler, işlevsellik

INTRODUCTION

Bipolar disorder is the sixth most frequent disease causing loss of functioning among all medical illnesses, according to the World Health Organization.¹ The impairment in functioning of patients with bipolar disorder was found to be associated with factors such as presence of low functioning before illness, early onset, total duration of illness, prominent major or minor depressive symptoms, psychotic features, number of hospitalizations, total duration of education, substance or alcohol abuse, weak social support, and low socio-economic level.² Also, cognitive deterioration in bipolar patients are strong predictors of loss of functioning in psychosocial area.³

information processing speed in the cognitive area were detected in bipolar patients with a history of psychosis, in comparison with those without a history of psychosis.¹³ Perseveration is one of the important executive dysfunctions which is known to be impaired in bipolar disorder and considered as main WCST measure.¹⁴

We evaluated perseveration in the remitted patients with a diagnosis of bipolar I disorder having history of psychotic mood episode, and assessed its effects on the clinical features and areas of functioning. The hypothesis was that perseveration would be more pronounced in the patients than healthy controls and this impairment would have negative effects on the clinical course and functioning.

Table 1. Comparison of the Sociodemographic Data of Patient (n = 48) and Control Groups (n = 45)

		Patient Group	Control Group	t	P
*Age		36.71±7.71	35.07±6.96	1.075	0.285
*Education		11.94±4.86	11.91±4.26	0.028	0.978
**Gender	Female	23(%47.9)	21(%46.7)	0.015	0.904
	Male	25(%52.1)	24(%53.3)		
***Marital Status	Married	25(%52.1)	32(%71.1)	4.053	0.150
	Divorced/Widow	6(%12.5)	2(%4.4)		
	Bachelor	17(%35.4)	11(24.4)		
***Employment Status	Unemployed	20(%41.7)	0(%0)	23.887	0.001**
	Employed	28(%58.3)	45(%100)		
Living With	Spouse – children	27(%56.2)	31(%68.9)	10.550	0.005
	Mother – Father	19(%39.6)	6(%13.3)		
	Alone	2(%4.2)	8(%17.8)		
Monthly Income (TL)	500-1000	5(%10.4)	2(%4.4)	3.683	0.323
	1000-2000	21(%43.8)	14(%31.1)		
	2000-3000	14(%29.2)	17(%37.8)		
	3000 <	8(%16.7)	12(%26.7)		

*Student t test **Chi-Square ***Fisher's Exact Test

Findings of a meta-analysis support the hypothesis that impairment is present in areas of specific neuro-cognitive domains such as executive functions, memory, information processing speed, and attention in the euthymic period.⁴ The main impairment in the euthymic period occurs in executive functions.^{5,6} Some authors claim that the impairment in learning and memory is secondary to the impairment in the executive functions.⁷ Studies have shown that the impairment in executive functions cause a decrease in academic success, professional and social functioning areas and quality of life.⁸⁻¹¹ There is no conclusive data on the etiology of cognitive impairment which continues in the asymptomatic period in bipolar patients. Although residual mood symptoms and drug side effects contribute to the cognitive impairment in bipolar patients, this impairment cannot be explained with only these factors. The presence of psychotic symptoms during episodes may also affect the cognitive impairment in patients in remission. The cognitive deficits of bipolar patients with psychotic episodes are associated with the severity of illness.¹² A higher number of hospitalizations, earlier onset and more use of antipsychotics as well as more impairment in planning, verbal memory, working memory and

with mental retardation, those having substance addiction (apart from smoking), and patients with a mental illness due to a general medical condition were excluded.

Scales

Sociodemographic and Clinical Characteristics Data Form, is a form consisting of questions on sociodemographic – clinical characteristics which was developed by the investigators, taking into consideration the characteristics of the study. There were items on age, gender, marital status, education, employment, income, age of onset of bipolar disorder, drug intake, and family history of psychiatric illness in this form.

DSM-IV Structured Clinical Interview for axis I Disorders (SCID-I); This is a semi-structured clinical interview form which was developed by First et al in order to investigate the presence of first axis diagnosis according to DSM-IV diagnostic criteria.¹⁸ It consists of six modules on mood disorders, psychotic disorders, psychotic symptoms, anxiety disorders, substance abuse disorders and other disorders. This was adapted to Turkish by Çorapçıoğlu et al and its reliability and validity for Turkish was investigated.¹⁹

Young Mania Rating Scale (YMRS); This scale is developed by Young et al in 1978, in order to measure the severity and changes in the manic status.²⁰ The validity and reliability of this scale was investigated by Karadağ et al. It consists a total of 11 items. It consists subgroups such as increased mood, increased movement and energy, sexual attention, sleep, irritability, speech velocity and amount, impaired ideation structure, ideation content, aggressive and destructive behavior, outer appearance, and insight.²¹

Table 2. Distribution of the Clinical Characteristics of the Patient Group (n=48)

	Min-Max	Mean±SD	
Age of Onset of Disease	12-44	23.40±8.13	
Duration of Disease (Years)	1-31	13.50±8.22	
Total Number of Episodes	1-13	5.43±3.02	
Number of Depressive Episodes	0-9	2.16±1.92	
Number of Manic Episodes	1-10	3.18±2.20	
Number of Mixed Episodes	0-1	0.10±0.30	
Number of Psychotic Manic Episodes	0-8	1.93±1.44	
Number of Psychotic Depressive Episodes	0-4	0.97±1.26	
Number of Psychotic Mixed Episodes	0-1	0.08±0.27	
Number of ECTs	0-25	3.04±5.62	
Number of Hospitalizations	0-10	2.22±2.28	
	n	%	
Longest Duration of Remission	2-6 Months	2	4.2
	6-12 Months	5	10.4
	12-24 Months	5	10.4
	24 Months and Over	36	75.0
History of Psychiatric Disease in First-degree Relative	None	21	43.8
	Bipolar disorder	18	37.5
	Schizophrenia-Psychosis	3	6.3
	Anxiety – Depression	6	12.5
Rapid Cycle	None	48	100
Ultra Rapid	None	48	100
Seasonality	No	16	33.3
	Yes	32	66.7
History of ECT	No	33	68.8
	Yes	15	31.3
Alcohol – Substance in Family	No	39	81.3
	Yes	9	18.8
Smoking	No	25	52.1
	Yes	23	47.9
Alcohol	No	42	87.5
	Yes	6	12.5
Medical Illness	No	47	97.9
	Yes	1	2.1
Suicide Attempts	None	38	79.2
	Once	6	12.5
	Twice	3	6.3
	3 and more times	1	2.1

Table 3. Comparison of WCST Scores of Patient (n=48) and Control (n=45) Groups

WISCONSIN CARD SORTING TEST (WCST)	Patient Group	Control Group	T	p
	Mean±SD	Mean±SD		
Number of Perseverative Responses	17.27±9.08	13.24±7.85	2.280	0.025
Perseverative Errors	14.95±6.59	11.62±6.44	2.464	0.016
Percent of Perseverative Errors	23.34±10.30	18.14±10.06	2.462	0.016
MOCA	26.54±2.06	27.65±1.84	-3.147 ^a	0.002

* Student t test ** Mann-Whitney U test, ^aZ value, ^bp<0.05 **p<0.01

Hamilton Depression Rating Scale (HAM-D); This scale is developed by Hamilton in order to evaluate the severity of depression in patients with a diagnosis of depression.²² The validity and reliability of the Turkish form was investigated by Akdemir et al in 1996.²³

Bipolar Disorder Functioning Questionnaire (BDFQ); This is a reliable and valid tool developed by the Turkish Psychiatric Association Task Force on Mood Disorders for the evaluation of functioning in bipolar disorder. It consists 58 scales and also 11 subscales on sentimental functioning, mental functioning, sexual functioning, feeling of being marked, introversion, household relationships, relations with friends, attendance to social activities, daily activities and hobbies, acting on own initiative and use of self-potential and work. Bipolar Disorder Functioning Questionnaire was developed by the Turkish Psychiatric Association Task Force on Mood Disorders. Six items were removed after reliability analysis, and Mood Disorder Functioning Questionnaire containing 52 items was shown to be a valid and reliable tool in evaluating functioning in bipolar disorder.²⁴

Table 4. Relationship Between WCST and Functioning Scale Scores in the Patient Group (n=48)

	WCST 1	WCST 2	WCST 3
*Emotional Functioning	r:0.235 p:0.109	r:0.206 p:0.160	r:0.204 p:0.168
*Mental Functioning	r:0.115 p:0.435	r:0.102 p:0.489	r:0.098 p:0.509
*Sexual Functioning	r:0.000 p:0.999	r:0.021 p:0.887	r:0.024 p:0.873
Feeling of being stigmatized	r:-0.043 p:0.774	r:-0.025 p:0.867	r:-0.025 p:0.867
Introversion	r:0.084 p:0.568	r:0.089 p:0.548	r:0.094 p:0.526
Household Relations	r:-0.191 p:0.194	r:-0.193 p:0.188	r:-0.192 p:0.190
Friendship Relations	r:0.134 p:0.364	r:0.170 p:0.248	r:0.173 p:0.238
Social Activity	r:-0.062 p:0.676	r:-0.056 p:0.707	r:-0.053 p:0.718
Daily Activity	r:0.156 p:0.290	r:0.193 p:0.188	r:0.194 p:0.186
*Initiative taking	r:0.057 p:0.700	r:0.039 p:0.792	r:0.046 p:0.754
*Employment	r:-0.154 p:0.350	r:-0.123 p:0.457	r:-0.121 p:0.462
*Total	r:0.007 p:0.960	r:-0.025 p:0.867	r:-0.023 p:0.877

WCST 1: Mean Score for Total Number of Perseverative Responses, WCST 2: Mean Score for Total Number of Perseverative Errors, WCST 3: Mean Score for Percentage of Perseverative Errors, *p<0.05, Pearson correlation ^aSpearman test

Wisconsin Card Sorting Test (WCST); This is one of the tests evaluating the executive functions.²⁵ This test evaluates the individual's decision making, flexibility, change of response in accordance with the feedback, as well as problem solving abilities.²⁶ The computer form of this test was used in the present study. A key card and four response cards similar to the key card, but in different color, geometric form and numbers are seen on the screen. The interviewer is asked to match the response cards with one of the key cards. A feedback of "right" or "wrong" is obtained

after each matching. After 10 consecutive right responses, the principle of matching without stimulus is changed. And the individual is expected to match according to this change. There is no time limit in this test. It continues until six categories or 64 trials are completed.

Montreal Cognitive Assessment Scale (MOCA); This scale was developed for mild cognitive disorder as a fast screening test and it evaluates different cognitive functions. These are attention and concentration, executive functions, memory, language, visual structuring skills, abstract thoughts, calculation and orientation. MOCA is administered in approximately 10 minutes. The maximum total score is 30 and a score of 21 points and above is considered as normal.¹⁷ It was adapted to Turkish by Selekler et al and its validity and reliability was shown.²⁷

number of perseverative responses, number of perseverative errors and the percentage of perseverative errors were significantly lower for controls ($p<0.05$).

Investigating the relationship of Bipolar Functioning Scale and WCST in the patient group, no significant correlation was found between BDFQ and mean scores for total number of perseverative responses, total number of perseverative errors, and percentage of perseverative errors ($p>0.05$) (Table 4).

In the evaluation of WCST and some clinical data of the patients; a negative significant association was found between the total number of episodes, the total number of perseverative responses ($p<0.01$) and total number of perseverative errors ($p<0.05$).

Table 5. Clinical Characteristics of the Patient Group (n = 48) and Their Relationships With WCST Scores

	AOI	DD	TNE	^a NDE	^a NME	^a NME	^a NPM	^a NPD	^a NMPE	^a NECT	^a NH
WCST1	r:-0.171 p:0.245	r:0.040 p:0.787	r:0.308 p:0.008**	r:0.105 p:0.476	r:0.129 p:0.383	r:-0.104 p:0.484	r:0.076 p:0.610	r:0.186 p:0.205	r:-0.079 p:0.593	r:-0.021 p:0.888	r:-0.089 p:0.546
WCST2	r:-0.161 p:0.273	r:0.040 p:0.787	r:0.356* p:0.013	r:0.101 p:0.493	r:0.149 p:0.312	r:-0.118 p:0.423	r:0.096 p:0.516	r:0.177 p:0.228	r:-0.079 p:0.593	r:0.025 p:0.866	r:-0.085 p:0.566
^a WCST3	r:-0.135 p:0.360	r:-0.005 p:0.975	r:0.214 p:0.144	r:0.097 p:0.511	r:0.150 p:0.309	r:-0.106 p:0.473	r:0.097 p:0.512	r:0.174 p:0.236	r:-0.065 p:0.659	r:0.035 p:0.813	r:-0.089 p:0.545

AOI: Age of onset of illness, DD: Duration of Disease, TNE: Total Number of Episodes, NDE: Number of Depressive Episodes, NME: Number of Manic Episodes, NME: Number of Mixed Episodes, NPM: Number of Psychotic Mania, NPD: Number of Psychotic Depressions, NMPE: Number of Mixed Psychotic Episodes, NECT: Number of ECTs, NH: Number of WCST 1: Mean Score for Total Number of Perseverative Responses WCST 2: Mean Score for Total Number of Perseverative Errors, WCST 3: Mean Score for Percentage of Perseverative Errors, * $p<0.05$ ** $p<0.01$, Pearson correlation ^aSpearman test

Statistical Analysis

Statistical analysis was carried out with SPSS 16 for Windows. Descriptive statistics were used to describe the basic features of the data (mean, standard deviation, frequency). Pearson Correlation Coefficient was used when variables were normally distributed, Spearman's rho was used when variables were not normally distributed. The comparisons of the two groups' parameters with a normal distribution was done with Student t test, and those not with normal distribution were compared with Mann Whitney U test. Chi-square test was used in the comparison of qualitative data, and Fisher's Exact test was used when the expected frequencies were not found. Significance was evaluated at $p<0.05$ and $p<0.01$ levels.

RESULTS

In the comparison of the patient and control groups, the mean age of patients was 36.71 ± 7.71 , and the mean age of controls was 35.07 ± 6.96 , with no statistically significant difference between the groups regarding their sociodemographic characteristics ($p>0.05$) (Table 1).

In the clinical characteristics of the patients, the mean age of onset of illness of the patients was 23.40 ± 8.13 , and the duration of illness was 13.50 ± 8.22 . The mean number of episodes the patients experienced was 5.43 ± 3.02 , mean number of manic episodes was 3.18 ± 2.20 , mean number of depressive episodes was 2.16 ± 1.92 , mean number of mixed episodes was 0.10 ± 0.30 (Table 2).

In pharmacotherapy, 11 patients (22.9%) were taking only lithium, 26 (54.2%) were taking lithium + antipsychotic, 2 patients (4.2%) lithium + antipsychotic + antidepressants, 3 patients (6.3%) valproic acid + antipsychotic, 1 patient (2.1%) two mood stabilizer, 4 patients (8.3%) two mood stabilizer + antipsychotic, 1 patient (2.1%) two mood stabilizer + antipsychotic + antidepressant.

In the comparison of WCST scores of the patients and controls:

DISCUSSION

This study revealed that BD-I patients who had previously at least one episode with psychotic symptoms display significant perseveration errors and responses as measured by the WCST. The findings of a meta-analysis showed that impairment is present in specific neurocognitive areas such as executive functions, memory, information processing speed, and attention in the euthymic phase in bipolar patients.⁴ The main problem in bipolar disorder in the euthymic phase is in the executive functions, according to the studies by Mur et al.⁵ and Clark et al.⁶ Thompson et al proposed that the impairment in memory is secondary to the deterioration in executive functions.⁷ About the executive function, Bora et al claimed that impairment in the cognitive flexibility area may be a specific marker in patients with a psychotic episode.¹² Glahn et al.²⁸ found prominently lower scores in one non-verbal memory, in spatial working memory measurements in patients with a history of psychosis in comparison with patients without such history. The findings of our study is in accordance with the data that found impairment of cognitive flexibility in BD-I patients with psychosis.

When the relationship between WCST results and clinical variables in the present study is evaluated, there was a positive significant association between the total number of episodes, WCST total number of perseverative responses and total perseverative error scores. When the literature on the relationship between clinical variables and neuro-cognitive functions are reviewed, recurring episodes were found to be associated with progressive cognitive deterioration, and severe cognitive impairment was considered as a sign of poor prognosis for bipolar patients, in accordance with our findings. Additionally, neuro-cognitive impairment was reported to run a more severe course in euthymic patients with a history of psychosis, with symptoms of subsyndromal depression and / or with a rapid cycling course.^{1,29,30}

As to the relation of BDFQ total score with perseverative errors and responses in the patient group, correlation was insignificant.

Perseverative errors which reflect impaired executive functioning may develop during episodes and may have a negative effect on functioning but may subside with clinical improvement. In addition, Aydemir et al have reported that bipolar patients over-estimate their status in subjective cognitive self-evaluation, but that these patients show defects in objective cognitive evaluations in situations requiring them showing an active performance, while they do not show cognitive defects at this level in the absence of such situations.³¹ Thus it can be suggested that evaluation of the cognitive functions and functioning in bipolar disorder should not simply rely on self-reporting.

Main limitations of this study are its cross – sectional design and sample size. Different medications used by the patients and the inability of evaluating their effects on executive functions cause uncertainty of therapeutic effects. Also, comparison of patients with BD-I with different clinical features and in different phases is important in terms of executive functions and functioning.

In conclusion, perseverative errors was significantly higher in the remitted patients with bipolar I disorder with a history of psychotic mood episode, when compared with the healthy controls, but this impairment did not have any impact on functioning. Real life measurement of functioning can be more suitable to draw an exact conclusion.

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