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INVESTIGATION OF APRAXIA IN PATIENTS WITH SCHIZOPHRENIA AND BIPOLAR DISORDER TYPE I

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SUMMARY

Background: *Almost 50% of patients with schizophrenia experience problems in their praxia performance, whereas executive function losses can be seen in patients with bipolar disorder. Although schizophrenia and bipolar disorder can be categorized as different disorders, in patient groups with similar symptom clusters, we aimed to determine whether there are common or disorder-specific praxia defects and to investigate the relationship between the sociodemographic and clinical features with apraxia.*

Subjects and methods: *52 Schizophrenia and 77 Bipolar Disorder Type I outpatients in remission for at least 6 months were included in our study. Test of Upper Limb Apraxia (TULIA) and Mayo Clinic Praxia Assessment Test (MCPAT) were used to evaluate praxia performance.*

Results: *Patients with Schizophrenia performed poorer on the TULIA and MCPAT than patients with Bipolar Disorder Type I. While impairment in personal and social functioning was higher in the apraxic schizophrenia group compared to the non-apraxic group, the mean age of disease onset was lower. Functioning in the Apraxic Bipolar Disorder Type I group was lower than in the group without apraxia; whereas the patient's age, duration of disease and number of hospitalizations were higher.*

Conclusions: *Although apraxia, which have an important effect on the functioning and quality of life of the patient by causing impairment in daily activities, are seen at higher rates in patients with schizophrenia, might be also seen in patients with bipolar disorder type I. Decreasing diagnostic confusion and developing appropriate treatment strategies, evaluation of apraxia seems to be clinically important in terms of prognosis of diseases and functioning of patients.*

Key words: *apraxia - bipolar disorder - schizophrenia*

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INTRODUCTION

Apraxia is the inability to perform actions that are learned and require skill without impairment in sensory-motor systems, comprehension, cooperation and co-ordination (Leiguarda & Marsden 2000). A classic assessment includes tests on the use of objects, and the recognition and production of meaningful and meaningless movements are tested (Goldenberg 2007). Although there are various classifications of apraxia in the literature, that is associated with the dominant (usually left) hemisphere, apraxia can be divided into six main subtypes: limb-kinetic, ideomotor, ideational, conceptual, conduction and dissociation apraxia (Wheaton & Hallet 2007).

Almost 50% of patients diagnosed with schizophrenia experience problems in upper extremity movement in various areas including timing, movement sequence and spatial hand configuration (Walther et al. 2013a, Walther et al. 2015). In the same manner, studies conducted in a group at risk for the psychosis show that there are timing and content errors and less gesture use in these groups (Millmann et al. 2014, Mittal et al. 2006, Osborne et al. 2017).

As the idea, that Bipolar Disorder and Schizophrenia might be considered as similar disorders, which are on the same spectrum according to DSM-5 and have many common genetic, symptomatic features and show similar response to therapeutics, has gradually gained importance, it leads to the investigation of praxia defects observed in the patient group with schizophrenia also in bipolar patients. Although there is no comprehensive study on praxia defects in patients with bipolar disorder in the literature; there are studies regarding that motor problems of especially patients with bipolar depression may be associated with psychomotor slowing and memory impairment, hypomania may be associated with executive function loss and patients with bipolar disorder can be separated from healthy controls due to mild problems such as poor attention, memory and executive dysfunction that may be observed during the euthymic period (Malhi et al. 2007).

Determining whether there are similar or specific praxis defects in patient groups with common symptoms such as bipolar disorder and schizophrenia, determining subtypes of these praxia defects and determining their relationship with sociodemographic and clinical characteristics of the disease may play an important role in the prognosis of diseases and the functioning of the patients as it may reduce diagnostic confusion in patient groups and help to develop appropriate treatment strategies.

In our study, we aimed to investigate whether there are praxia defects in patients with schizophrenia and bipolar disorder type I. Our hypothesis is that the scores of the Test for the Upper Limb Apraxia (TULIA) and the Mayo Clinic Praxia Assessment Test will differ in patients diagnosed with schizophrenia and bipolar

disorder type I, and that there might be differences in sociodemographic data and clinical characteristics in subgroups with and without praxia in patients with schizophrenia as well as bipolar disorder type I.

SUBJECTS AND METHODS

52 patients with schizophrenia and 77 patients with Bipolar Disorder type I in remission matched for age were included in this study. Patients were recruited from the outpatient units of Bakirkoy Mazhar Osman Mental Health and Neurology Training and Research Hospital, Turkey between February-April 2020. All subjects were right handed as determined by the Edinburgh handedness inventory (Oldfield 1971). Exclusion criteria included pregnancy and lactation, any other psychiatric comorbidities, substance abuse or dependence other than nicotine, any neurological condition impairing movements, such as tremor, dystonia, idiopathic Parkinsonism or stroke, history of head trauma, any motor abnormalities and history of electroconvulsive treatment in the previous year. All subjects were interviewed with the Clinical Interview for DSM-V (SCID-5). All patients received antipsychotic pharmacotherapy. Clinical and demographic data are given in Table 1. All participants provided written informed consent. The protocol was approved by the local ethics committee.

In the clinical interview, Schizophrenia and Bipolar Disorder Type I diagnoses were confirmed according to SCID-5, and patients with any other psychiatric comorbidity was excluded. Patients with Bipolar Disorder Type I in remission according to the Young Mania Rating Scale (YMRS) and the Hamilton Depression Rating Scale (HAM-D) scores and patients with schizophrenia in remission according to the Positive and Negative Syndrome Scale (PANSS) and the Negative Symptoms Rating Scale (SANS) scores were applied Sociodemographic and Clinical Data Form.

Table 1. Comparison of the sociodemographic and clinical features of apraxic and non-apraxic patients according to the Test for Upper Limb Apraxia (TULIA) scores among patients diagnosed with Schizophrenia and Bipolar Disorder Type I

	Patients with Schizophrenia				Patients with Bipolar Disorder Type I				p	p	p	p
	TULIA≥210 (I)		TULIA<210 (II)		TULIA ≥210 (III)		TULIA<210 (IV)		(I-II)	(III-IV)	(I-III)	(II-IV)
	n	%	n	%	n	%	n	%				
Gender									*0.048*	0.362	0.719	*0.004*
Male	5	38.5	27	69.2	22	44	9	33.3				
Female	8	61.5	12	30.8	28	56	18	66.7				
Marital Status									0.567	0.831	0.662	*0.015*
Single	6	46.2	25	64.1	19	38	8	29.6				
Divorced	2	15.4	4	10.3	5	10	3	11.1				
Married	5	38.5	10	25.6	26	52	16	59.3				
Personal and Social Functioning									*0.021*	*0.007*[a]	0.186[a]	*0.010*[a]
Fair	1	7.7	2	5.1	1	2	0	0.0				
Good	11	84.6	16	41.0	48	96	21	77.8				
Poor	1	7.7	21	53.8	1	2	6	22.2				
Smoking									0.165	0.765	0.707	*0.014*[a]
No	6	46.2	10	25.6	26	52	15	55.6				
Yes	7	53.8	29	74.4	24	48	12	44.4				
ECT									0.259	0.023	0.405	0.732
Yes	4	30.8	19	48.7	10	20	12	44.4				
No	9	69.2	20	51.3	40	80	15	55.6				
Suicide attempt									0.685	0.076	0.123	0.668
No	10	76.9	32	82.1	46	92	21	77.8				
Yes	3	23.1	7	17.9	4	8	6	22.2				
Family History of Psychiatric Illness									0.678	0.686	0.357[a]	0.23
No	8	61.5	28	71.8	36	72	17	63.0				
Yes	3	23.1	8	20.5	12	24	4	14.8				
Unknown	2	15.4	3	7.7	2	4	6	22.2				
	Mean	SD	Mean	SD	Mean	SD	Mean	SD				
Age	43.92	8.99	41.62	9.46	39.66	10.16	46.7	13.35	0.403	*0.018*	0.227	0.075
Year of Education	9.92	4.39	6.62	3.06	9.62	3.21	7.48	4.33	*0.028*	*0.018*	0.931	0.588
Age of Onset of Psychiatric Disorder	30.62	8.43	24.00	7.97	25.96	8.45	26.37	9.37	*0.011*	0.843	0.077	0.323
Number of Hospitalisations	2.08	1.38	4.33	4.95	1.70	1.88	3.11	2.50	0.179	*0.002*	0.191	0.751

Chi-squared test results; [a]Fisher's exact test results. Data presented with mean and standard deviation (SD) were compared with Mann-Whitney U test; Statistical significance with $p<0.05$

Test of Upper Limb Apraxia (TULIA) was applied to patients with schizophrenia and Bipolar Disorder Type I. Mayo Clinic Praxia Assessment Test was applied to 39 patients with schizophrenia and 27 with bipolar disorder type I who were found to have significant apraxia like errors by getting less than 210 points according to the cut off value specified for an average age of 42 years in TULIA test (Walther et al. 2013b).

TULIA gesture assessment

Test for Upper Limb Apraxia (TULIA), which has proven to be sensitive to detect upper extremity movement disorders in schizophrenia, allows comprehensive evaluation of motion performance in two main areas: imitation and pantomime (Vanbellingen et al. 2010, Walther et al. 2013a,b, 2015, 2016). Each impact area contains three categories containing elements representing intransitive (symbolic, communicative), transitive (object related) and meaningless movements. Performance ratings ranging from 0 to 5 focus on content and temporospatial errors. High scores indicate superior performance. Total TULIA scores range from 0 to 240. The cut off value of apraxia-like defects is 210 in studies conducted with middle-aged individuals (Walther et al. 2013b). The Turkish standardization, validity and reliability study of TULIA was conducted in 2019 (Cegil 2019).

Mayo Clinic Praxia Assessment Test

In our study, praxia performances were assessed also with the Mayo Clinic Praxia assessment test, which was developed by Kökmen et al., and of which the validity and reliability were previously shown in the Turkish population and Parkinson's patients (Kokmen et al. 1998, Uluduz et al. 2010). This test provides an understanding of the presence of apraxia and the type of apraxia by evaluating a total of 55 items in seven subsections: ideomotor apraxia, which is evaluated under three sub-headings (upper extremity, axial and lower extremity), ideational apraxia, oral-facial apraxia, imitation and real tool use. Patients are asked to perform the gestures, and for each gesture, 2 points are given when done correctly, 1 when slow or incompetent, and 0 when not done or wrong.

Statistical analyses

All statistical analyses were conducted with the Statistical Package for Social Sciences for Windows (SPSS) version 22.0. Demographic information was analyzed through descriptive statistics. Proportional data among participants diagnosed with schizophrenia and Bipolar Disorder I were compared using Pearson Chi-Square Analysis. In addition, Fisher's Exact Chi-Square Analysis was used in cases where the percentage of proportional data was below 5. Among the participants with Schizophrenia and Bipolar Disorder Type I, the Independent Samples t test was used in cases where the numerical demographic, clinical and psychometric properties were met with the normal distribution hypothesis and the number of cases exceeded 30, in cases where these criteria were not met, the Mann-Whitney U test was used. Correlation analysis was performed by Pearson or Spearman correlation tests. The normal distribution hypothesis was tested with the coefficient of kurtosis and skewness in the range of ± 1.5 in the study. A p value <0.05 was accepted as statistically significant.

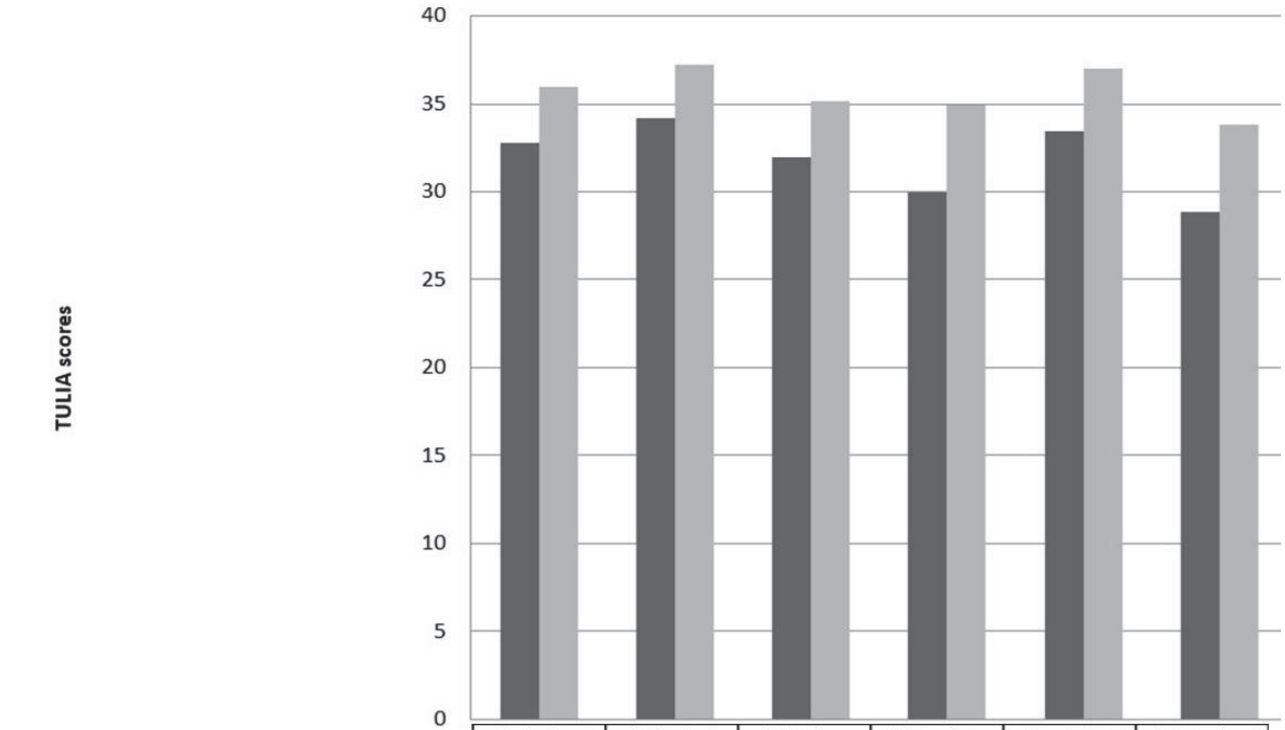
RESULTS

Patients with schizophrenia performed poorer on the TULIA and Mayo Clinic Praxia Assessment Test than patients with Bipolar Disorder Type I (Table 2, Figure 1).

Table 2. Comparison of Mayo Clinic Praxia Assessment Test (MCPAT) scores between patients with Schizophrenia and Bipolar Disorder Type I

	Patients with Schizophrenia (n=39)		Patients with Bipolar Disorder Type I (n=27)			
	Mean	SD	Mean	SD	Z	p
MCPAT Oral-Facial	17.28	1.49	17.78	1.42	-1.37	0.172
MCPAT Upper Extremity	31.00	3.78	34.15	3.05	-3.58	*<0.001*
MCPAT Upper Extremity (Transitive)	12.10	2.99	14.56	2.95	-3.23	*0.001*
MCPAT Upper Extremity (Intransitive)	18.90	2.46	19.59	0.64	-1.61	0.108
MCPAT Lower Extremity	7.08	1.58	8.04	1.13	-2.52	*0.012*
MCPAT Axial	8.67	0.96	8.86	1.17	-1.34	0.179
MCPAT Ideational	4.38	2.16	6.07	2.13	-3.04	*0.002*
MCPAT Imitation	7.05	1.57	7.74	1.72	-2.03	*0.042*
MCPAT Use Actual Objects	9.95	0.32	10.00	0.00	-0.83	0.405
MCPAT Ideomotor	56.95	4.89	60.78	4.41	-3.28	*0.001*
MCPAT Total	85.41	8.76	92.63	7.56	-3.49	*0.001*

Data presented with mean and standard deviation (SD) were compared with Mann-Whitney U test;
Statistical significance with p<0.05



	Imitation Meaningless	Imitation Intransitive	Imitation Transitive	Pantomime Meaningless	Pantomime Intransitive	Pantomime Transitive
Patients with Schizophrenia	32,75±2,58	34,17±2,78	31,98±2,85	29,94±3,80	33,46±3,42	28,87±4,20
Patients with Bipolar Disorder Type I	35,95±3,00	37,19±2,63	35,17±2,76	34,96±3,28	36,99±2,93	33,84±3,71
t value	-6,27	-6,26	-6,35	-8,00	-6,27	-7,09
p value	<0,001	<0,001	<0,001	<0,001	<0,001	<0,001

Figure 1. Comparasion of TULIA scores between patients with schizophrenia and Bipolar Disorder Type I

Table 3. Relationship between PANSS and SANS scores and Test for Upper Limb Apraxia (TULIA) Scores of Patients with Schizophrenia (n=52)

		PANSS Positive	PANSS Negative	PANSS General	PANSS Total	SANS Affective Flattening	SANS Alogia	SANS Apathy	SANS Anhedonia	SANS Attention	SANS Total
TULIA	r	-0.442	-0.761	-0.699	-0.764	-0.692	-0.704	-0.429	-0.586	-0.444	-0.698
	p	*0.001*	*<0.001*	*<0.001*	*<0.001*	*<0.001*	*<0.001*	*0.002*	*<0.001*	*0.001*	*<0.001*
TULIA Imitation	r	-0.404	-0.671	-0.624	-0.680	-0.611	-0.661	-0.476	-0.581	-0.439	-0.658
	p	*0.003*	*<0.001*	*<0.001*	*<0.001*	*<0.001*	*<0.001*	*0.000*	*<0.001*	*0.001*	*<0.001*
TULIA Pandomime	r	-0.442	-0.779	-0.711	-0.779	-0.708	-0.693	-0.369	-0.554	-0.421	-0.685
	p	*0.001*	*<0.001*	*<0.001*	*<0.001*	*<0.001*	*<0.001*	*0.007*	*<0.001*	*0.002*	*<0.001*

Pearson Correlation Analysis Results

The demographic and clinical characteristics of patients diagnosed with schizophrenia and bipolar disorder type I with and without apraxia according to the TULIA scores are compared in Table 1.

Regarding the results of evaluation scales in terms of symptom severity; in the schizophrenia group, a statistically significant negative correlation was found between the PANSS and SANS subscale scores and the TULIA, TULIA *Imitation* and TULIA *Pantomime* scores (Table 3), and between Young Mania Rating Scale (YMRS) scores and TULIA *Pantomime* scores in the Bipolar Disorder Type I group, there was a statistically significant negative correlation between Hamilton Depression Rating Scale (HAM-D) scores and TULIA, TULIA *Imitation*, and TULIA *Pantomime* scores (Table 4).

A weak negative correlation was found between mean 5-year Chlorpromazine (CPZ) dosage and praxia performance (Table 5).

TULIA scores in the Bipolar Disorder Type I group using Long Acting Antipsychotics were found to be statistically significantly lower than the group not using Long Acting Antipsychotics (TULIA (p=0.001), TULIA *Imitation* (p=0.003), TULIA *Pandomime* (p=0.001)), whereas there was no significant difference in the schizophrenia group (p>0.05).

Table 4. Relationship between Young Mania Rating Scale (YMRS), Hamilton Depression Rating Scale (HAM-D) scores and Test for Upper Limb Apraxia (TULIA) scores of patients with Bipolar Disorder Type I (n=77)

		YMRS	HAM-D
TULIA	r	-0.220	-0.543
	p	0.054	*<0.001*
TULIA	r	-0.200	-0.535
Imitation	p	0.081	*<0.001*
TULIA	r	-0.225	-0.521
Pandomime	p	*0.049*	*<0.001*

Pearson Correlation Analysis Results

Table 5. Relationship between mean 5 year Chlorpromazine dosage and Test for Upper Limb Apraxia (TULIA) Scores in Patients with Schizophrenia and Bipolar Disorder Type I

		Patients with Schizophrenia (n=52)	Patients with Bipolar Disorder Type I (n=77)
TULIA	r	-0.279	-0.371
	p	*0.045*	*0.001*
TULIA	r	-0.271	-0.374
Imitation	p	0.052	*0.001*
TULIA	r	-0.293	-0.380
Pandomime	p	*0.035*	*0.001*

Spearman Correlation Analysis Results

Table 6. Comparison of Test for Upper Limb Apraxia (TULIA) Scores between Patients with Schizophrenia and Bipolar Disorder Type I with or without Valproate or Lithium Treatment

		Patients with Schizophrenia Valproate Use				Patients with Bipolar Disorder Type I Lithium Use				Valproate Use			
		n	Mean	SD	p	n	Mean	SD	p	n	Mean	SD	P
TULIA	No	39	190.95	17.37	0.941[a]	40	211.73	18.43	0.196[b]	38	214.82	15.30	0.738[b]
	Yes	13	191.85	18.14		37	216.66	14.40		39	213.41	18.14	
TULIA	No	39	99.00	7.70	0.816[a]	40	107.20	8.81	0.197[b]	38	108.82	6.93	0.937[b]
Imitation	Yes	13	98.62	7.38		37	109.51	6.52		39	107.82	8.69	
TULIA	No	39	91.95	10.40	0.832[a]	40	104.53	10.03	0.219[b]	38	106.00	8.93	0.540[b]
Pandomime	Yes	13	93.23	11.08		37	107.16	8.50		39	105.59	9.89	

Data presented with mean and standard deviation (SD) were compared with [a]Mann-Whitney U test and [b]independent t-test.
Statistical significance with p<0.05

It was found that the use of Valproate in the schizophrenia group and the use of lithium and valproate in the bipolar disorder type I group did not create a statistically significant difference in the TULIA scores (Table 6).

In patients with schizophrenia and bipolar disorder type I, it was found that the Mayo Clinic Praxia Assessment Test scores between men and women were not statistically significantly different (p>0.05).

According to the Spearman Correlation Analysis performed between the patient's age, disease onset age, duration of the disorder, number of hospitalizations and MCPAT sub-scores, in the patient group with Bipolar Disorder Type I, it was observed that the age of the patient was statistically significantly negatively correlated with the MCPAT *Ideomotor* (r=-0.419, p=0.030) and MCPAT *Total* (r=0.442, p=0.021) scores; also in the schizophrenia patient group, disease duration and the MCPAT *Lower Limb* (r=-0.369, p=0.021), MCPAT *Axial* (r=-0.353, p=0.027) and MCPAT *Ideational* (r=-0.336, p=0.037) scores were found to be statistically significantly negatively correlated.

Among people diagnosed with Bipolar Disorder Type I, a statistically significant negative correlation was found between the number of manic episodes and TULIA (N=77, r=-0.380, p=0.001), T *Imitation* (N=77, r=-0.344, p=0.002), T *Pantomime* (N=77, r=-0.391, p<0.001) scores.

It was found that TULIA and MCPAT scores were not statistically significantly different (p>0.05) according to the Mann-Whitney U test between Bipolar Disorder Type I patients with and without a history of depressive episodes.

DISCUSSION

In our study, which is the first study investigating the praxia defects in patients with Bipolar Disorder Type I, the TULIA scores and the MCPAT scores were found to be statistically significantly lower in the schizophrenia group compared to the bipolar disorder type I group. In apraxic patients, significant impairment in functioning is observed in both schizophrenia and bipolar disorder type I patient groups compared to non-apraxic patients. Both schizophrenia and bipolar disorder are lifelong disorders that occur with remission and relapses. Considering that as they are similar in many respects and are assessed on the same spectrum, causing a heavy burden on the individual, family and society, it's expectable that praxia defects in the patient group with schizophrenia might also be observed in the bipolar disorder group.

In our study, the ratio of males and impairment in functioning in the apraxic subgroup of patients with schizophrenia were found to be significantly higher than in the non-apraxic subgroup. In addition, in the apraxic schizophrenia group, it was found that the mean

years of education and the mean age of disease onset were found to be lower than in the non-apraxic schizophrenia group. In schizophrenia, male gender, younger age of disease onset and poor functioning are among the negative prognostic indicators (Sadock et al. 2015), and our study findings also suggest that apraxia may not be a good prognostic factor in schizophrenia. In our study, we found that 96% of patients with bipolar disorder type I without praxia defects had good functioning and 77.8% of the apraxic bipolar group had good functioning, functioning ratios were found to be statistically significantly higher (p=0.007) in the non-apraxic bipolar disorder type I. It was found that the mean age, duration of illness, and number of hospitalizations of the individuals in the apraxic bipolar disorder I group were found to be higher than in the non-apraxic bipolar disorder I group and the years of education were lower (Table 1). Poor functioning and the high number of hospitalizations, which are among the clinical characteristics of poor prognosis (Sadock et al. 2015), are seen at higher rates in the apraxic group according to our study data, and it draws attention that the presence of praxia defects might also be a poor prognostic indicator in bipolar disorder. In a study included patients with schizophrenia spectrum and other psychotic disorders disorder, it was emphasized that a history of multiple episodes affected TULIA scores negatively (Stegmayer et al. 2016a). In another study, no significant relationship was found between the gender, age and disease duration and praxia defects of the patients, and the number of episodes was found to be significantly higher in the apraxic group (Walther et al. 2013b). Similar to our results, Rapaic et al found out that gender, age and education level may affect praxia performance (Rapaic et al. 2014), whereas Kamm et al. have revealed that apraxia was correlated with advanced age (Kamm et al. 2012). Further comprehensive studies are needed to clarify whether the difference is due to praxia defects or clinical course of the psychiatric disorder. It is also remarkable that Stegmayer et al. have found out that impairment in gesture performance was linked to volume loss in the praxis network in schizophrenia, and they have found the behavioral similarities between apraxia and schizophrenia in parallel with the structural changes that showed destruction. The decrease in the gray matter in the left inferior frontal gyrus draws attention in the group of patients with gesture defects, the results of patients with praxia defects differed from patients with no change in gray matter volume. They emphasized that brain changes in schizophrenia are typically localized in areas damaged in apraxia, and that non-verbal communication defects in schizophrenia are associated with changes in brain structure (Stegmayer et al. 2016b). It is said that the changes detected by neuroimaging in the examinations performed in the first episode patient groups are mostly seen in male patients which indicates a negative prognosis (Ucok 2008). Motor problems are more common in early-onset schizophrenia, which is associated with problems in the brain development process and a poor prognosis (Flashman et al. 1996) and motor problems are more prominent in patients with poor prognosis also in patients with bipolar disorder (Goswami et al. 1998).

Although apraxia, which makes daily life activities difficult and thus has a significant effect on the deterioration of the patient's functioning, indicates a poor prognosis for both mental disorders, new comprehensive studies are needed to elucidate the neurobiological pathways.

As we compared the sociodemographic and clinical features of apraxic patients with Schizophrenia and Bipolar Disorder Type I according to TULIA scale, we found that the rates of being single or divorced and poor functioning were statistically significantly higher in apraxic patients with schizophrenia compared to the apraxic bipolar disorder type I group. Regarding sociodemographic and clinical features we found no statistically significant difference between patients diagnosed with schizophrenia and bipolar Disorder type I in non-apraxic subgroups. Our study data showed that non-apraxic schizophrenia and bipolar disorder patient groups are similar in terms of sociodemographic and clinical features, it draws attention to the fact that schizophrenia and bipolar disorder (Zhao et al. 2013), which have common neurodevelopmental components, in cases where praxia defects are not detected and therefore a poor prognosis is not considered and neurocognitive impairment is relatively low, may have similar characteristics (Table 1). In a review, it is also stated that apraxia has an important role in the quality of life of the patient, although it is not always obvious, causing disruption in daily activities, and the importance of its clinical evaluation is emphasized (Park 2017).

As we have investigated the effects of residual symptoms on apraxia, we have found that TULIA scores were significantly negatively correlated with PANSS and SANS scores in patients with schizophrenia (Table 3), whereas a statistically significant negative correlation was found between TULIA scores and HAM-D and YMRS scores in patients with Bipolar Disorder Type I (Table 4). In the study of Stegmayer et al. in 2016, praxia defects were found to be independent from negative symptoms (Stegmayer et al. 2016a). In the study of Dutschke et al. in 2017, it was stated that the high levels of hallucinations, motor and negative symptoms negatively affect TULIA performance (Dutschke et al. 2018). Walther et al. found that the PANSS *General Symptoms, Positive Symptoms and Total scores* were significantly higher in the apraxic group compared to the non-apraxic group (Walther et al. 2013b). There are studies reporting that cognitive slowing seen in patients can prevent motor planning (Morrens et al. 2007, 2014) and that psychomotor slowing is associated with negative symptoms, but it is independent from antipsychotic drugs (Morrens et al. 2006, 2007, 2008). In literature there is a study reporting that bipolar depression may be associated with psychomotor slowing and memory impairment, whereas hypomania may be associated with executive function losses (Malhi et al. 2007).

Motor problems such as psychomotor slowing, catatonia and parkinsonism can be seen in antipsychotic-naive patients with first episode psychosis, as well as in chronic patients receiving long-term antipsychotics and in the risk group for psychosis who haven't got a psychiatric diagnosis yet (Walther & Strik 2012). The relationship between motor signs of the disorder and antipsychotics, which can improve motor symptoms, cause an overlook in the clinical presentation of motor problems or worsen the picture, still remains complex (Peralta & Cuesta 2010). In our study, it was found that mean 5 year Chlorpromazine dosage was statistically significantly negatively correlated with TULIA scores among patients with schizophrenia and bipolar disorder Type I (Table 5). In the study that Walther et al. contributed to the literature, the chlorpromazine equivalent dosage averages were found to be significantly different between patients with schizophrenia with and without praxia defects (Walther et al. 2013b). There are studies in which a correlation is found between chlorpromazine dosage and praxia defects (Dutschke et al. 2018), on the other hand there are publications where no relationship is found between gesture performance and dosage (Wüthrich et al. 2020).

Long-acting antipsychotics can reduce relapse, prevent cognitive decline and improve quality of life from the first episode (Viala et al. 2012). In our study in which we have investigated the effect of Long Acting Antipsychotics on praxia performance, we found that the TULIA scores of patients with Bipolar Disorder Type I who did not use Long Acting Antipsychotics were statistically significantly higher than the Bipolar Disorder Type I group who used Long Acting Antipsychotics. The use of Long Acting Antipsychotics in the patient group with schizophrenia does not seem to cause a significant difference in the TULIA scores. Although no similar study was found in the literature, there are publications reporting that the use of Long Acting Antipsychotics may also be advantageous in terms of motor side effects (Fleischhacker 2009, Gharabawi et al. 2005).

Despite the fact that there is no study showing the effect of lithium on praxia performance, which can have central nervous system side effects (Taylor et al. 2018) such as fine tremor at therapeutic dosage and muscle weakness, confusion, ataxia, gross tremor and muscle contractions in toxicity, in the literature, it has been reported that temporary apraxia has occured in a few lithium toxication cases (Frisch et al. 2017, Micheli et al. 1999). Although dose-dependent tremor can be seen in approximately 25% of patients using valproate, parkinsonism may develop with cognitive retardation in a very few of them and the manifestation improves when the drug is discontinued. There is no study in the literature reporting that valproate may cause praxia defects. The effect of mood stabilizers on subtle neurological symptoms has also been rarely investigated. A meta-analysis emphasized that treatment with mood stabilizers did not significantly impair verbal and visual memory, attention, executive function, processing speed and psychomotor performance (Wingo et al. 2009). In our study, in which we wondered the possible effect of lithium and valproate use on praxis, TULIA and MCPAT scores were not found to be statistically significantly different between patients diagnosed with Schizophrenia who used valproate and those who did not and that TULIA scores did not differ significantly among patients with bipolar disorder type I according to the use of lithium and valproate.

In our study, in which we have also investigated the effect of sociodemographic and clinical characteristics among apraxia subtypes, we found that in patients with schizophrenia and bipolar disorder type I, there was no statistically significant difference between men and women in terms of MCPAT scores, that in individuals diagnosed with Bipolar Disorder type I, as the age of the patient increases, the MCPAT Ideomotor and MCPAT Total scores statistically significantly decreeses, and that with the prolonged duration of the disease of patients with schizophrenia the MCPAT Lower Limb, MCPAT Axial, and MCPAT Ideational scores statistically significantly decreases.

Early onset age, male gender, poor functioning, lower socioeconomic level, high number of total episodes, high number of hospitalizations in bipolar disorder are known as clinical characteristics of poor prognosis (Keck et al. 1998), whereas male gender, insidious onset of the disease, early age of onset, absence of precipitating factors, poor premorbid personality traits, being single, living in the city center, low intelligence level, prominent negative symptom, high number of attacks and long-term hospitalizations, disorganized symptoms, irregular treatment history, accompanying comorbidities, presence of neurological pathologies, perinatal trauma history, family history of schizophrenia, weak support systems, high emotion expression in the family are known as poor prognostic factors in schizophrenia (Sadock et al. 2015). Further studies will clarify the impact of sociodemographic and clinical features on apraxia and prognosis of disorders.

According to the analysis we made on the effect of clinical characteristics in the group with Bipolar Disorder type I, we found that the increase in the number of manic episodes significantly affected TULIA scores, and the presence of a depressive episode did not significantly affect the TULIA and MCPAT scores. It is known that the long duration of disease and the high number of previous episodes affect the course of the disease negatively by increasing number and duration of attacks (Ghaemi et al. 1999, Solomon et al. 1995) and it may increase the susceptibility to praxis defects. The fact that depressive episodes, which were suggested to be associated with psychomotor slowing and memory impairment (Malhi et al. 2007) did not predict apraxia in our study may be associated with the small sample size.

Limitations

Since there was no control group in our study, no comparison was made between individuals without a history of psychiatric disorder and patients with schizophrenia and bipolar disorder type I. All patients had been exposed to antipsychotics and mood stabilizers prior to the study, so praxia defects may be partially attributed to both the mental disorder itself and the effects of the treatment. Longitudinal analyzes are obviously needed in the patient groups who are in the first episode and are drug-naive.

CONCLUSION

In conclusion, as apraxic patients experience significantly more problems in daily living activities compared to non-apraxic patients, apraxia, which is considered clinically important, is seen at higher rates in schizophrenia patients, should also be investigated in patients with bipolar disorder type I. Diagnosis is still mainly based on clinical findings due to the absence of a specific diagnostic marker in mental disorders. According to the results of our study with patients with schizophrenia and bipolar disorder type I, although apraxia seems likely to help in the differential diagnosis, it should not be overlooked that praxia defects may also be seen in patients diagnosed with bipolar disorder type I. Accordingly, it should also be taken in consideration that evaluation of apraxia may play an important role in clinical practice in terms of decreasing diagnostic confusion in patient groups, developing appropriate treatment strategies, prognosis of diseases and functioning of patients.

Although there are studies examining praxia defects in patients diagnosed with schizophrenia in the literature, our study is important, as it is the first study investigating praxia defects in patients with bipolar disorder, it will guide future comprehensive and multicenter studies.

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Contribution of individual authors:

Ipek Özönder Ünal recruited participants, performed measurements, analyzed the data and wrote the first draft of the manuscript.

Tonguc D. Berkol wrote the protocol and supervised the study.

Both authors contributed to data interpretation, edited the manuscript and approved the final manuscript.

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