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ARAŞTIRMA / RESEARCH

Relationship between theory of mind and metabolic parameters and functioning in patients with bipolar I disorder

Bipolar I bozukluk tanılı hastalarda zihin kuramının, metabolik parametreler ve işlevsellik ile ilişkisi

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Abstract

Purpose: We aimed to investigate the relationship theory of mind abilities with functionality and metabolic alteration in patients with bipolar disorder-1 (BD-1) during the remission period.
Materials and Methods: This cross-sectional study is consisted of 68 patients with bipolar disorder-1 and 45 healthy controls. Sociodemographic form, Reading the Mind in the Eyes Test (RMET), Bipolar Disorder Functioning Questionnaire (BDFQ) were administered to the participants. Body mass index (BMI), waist circumference (WC), fasting plasma glucose (FG), high density lipoprotein cholesterol (HDL), low density lipoprotein cholesterol (LDL), total cholesterol (TC), triglyceride (TG) levels were recorded.
Results: There were significant differences between the patient group and healthy control group in terms of WC, BMI, HDL, LDL, TG. The results of independent samples t-test indicated a statistically significant difference in RMET score between the two groups with control group significantly higher than patient group.
Conclusion: Patients with BD-1 during the remission period have lower performance on theory of mind abilities and more alteration in metabolic parameters than healthy controls. Metabolic alteration and theory of mind impairment should be potential treatment target for BD
Keywords: Theory of mind, bipolar disorder, metabolic dysfunction

Öz

Amaç: Bu çalışmada bipolar bozukluk-1 (BB-1) tanılı hastaların remisyon dönemlerindeki zihin kuramı becerileri ile, işlevsellik ve metabolik değişimleri arasındaki ilişkiyi araştırmayı amaçladık.
Gereç ve Yöntem: Bu kesitsel çalışma, remisyonda BB-1 tanılı 68 hasta ve 45 sağlıklı kontrolden oluşmaktadır. Katılımcılara sosyodemografik form, Gözlerden Zihin Okuma Testi, Bipolar Bozukluk İşlevsellik Anketi uygulandı. Katılımcıların beden kitle indeksi (BKİ), bel çevresi (BÇ), açlık plazma glukozu (PG), yüksek yoğunluklu lipoprotein kolesterol (HDL), düşük yoğunluklu lipoprotein kolesterol (LDL), toplam kolesterol, trigliserit (TG) seviyeleri kaydedildi.
Bulgular: Hasta grubu ile sağlıklı kontrol grubu arasında BÇ, BKİ, HDL, LDL, TG düzeyleri açısından anlamlı farklılıklar vardı. Bağımsız örnekler t-testi sonuçlarına göre kontrol grubunda hasta grubuna göre Gözlerden Zihin Okuma Testi'nde istatistiki olarak anlamlı daha yüksek skorlar elde edilmiştir.
Sonuç: Remisyon döneminde BB-1 tanılı hastalar, sağlıklı kontrollere göre zihin kuramı becerilerinde daha düşük performansa ve metabolik parametrelerde daha fazla değişikliğe sahiptir. Metabolik değişiklik ve zihin bozukluğu teorisi, BD için potansiyel tedavi hedefi olmalıdır.
Anahtar kelimeler: Zihin kuramı, bipolar bozukluk, metabolik disfonksiyon

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INTRODUCTION

Bipolar disorder (BD) is a chronic disorder and characterized with recurrent mood swings. It affects about 2% of the general population. Mood episodes are linked with impairments in cognition, functionality, and lower quality of life. During their lifetime, the patients with BD may have lower functioning due to the subsyndromal symptoms. Subsyndromal symptoms are related to lower social adjustment[1]. Deficits in the process of learning knowledge and senses are referred to as cognitive impairment. Patients with BD were shown to have cognitive abnormalities regardless of the phase of disorders, and this problem has gotten a lot of attention in the last several decades. Previous studies suggest that cognitive performance, especially verbal memory and executive function are impacted in BD and lower cognitive performance is related to poor psychosocial outcomes[2-4].

Social cognition (SC) is a multidimensional domain that includes a complex range of processes such as the representation of the internal physical state, awareness of others' self-perception, and interpersonal motivation[5,6]. Social knowledge, emotion processing, social perception, attributional bias, and theory of mind (ToM) are the five core domains of SC that have been identified by The National Institute of Mental Health (NIMH)[7]. ToM is the ability to infer oneself and other people's mental states, such as desires, beliefs, knowledge, feelings, and intention. Emotional (social perceptual) and cognitive aspects (mental state decoding) are two main accounts of ToM. A deficit in ToM has been shown as an important feature for schizophrenia and autism spectrum disorder[8,9]. However, there has been an increasing interest in emotional perception in BD.

According to two meta-analyses conducted by Samame et al., the performance of patients with BD was significantly lower than healthy controls (HC) during the three episodes (manic, depressive, euthymic) of the BD, and higher impairments were reported in cognitive performance related to affective tasks[10,11]. In other meta-analyses conducted by Bora et al., ToM performance was assessed in patients with BD during the acute, subsyndromal, and euthymic episodes, and compared with healthy control (HC). According to the results of these meta-analyses, ToM performance was significantly impaired in bipolar group and this deficit was found more severe during acute episodes of BD[12]. Both emotional and cognitive aspects of ToM were found impaired in remitted patients with BD[12]. Recently, Neerven et al. conducted a systemic review on ToM impairment in psychotic and affective disorders. According to this systematic review, severe impairments in ToM were found in mania or psychosis, and milder deficits were found with major depression. However, results show decreased impairments in patients with schizophrenia or BD during remission, unaffected first-degree relatives of patients, and clinical high-risk groups. This finding suggests that the ToM is a part of a larger developmental phenotype associated to BD and schizophrenia[13]. 'Reading the mind in the eyes test (RMET)' was used in most of the searches to evaluate the emotional ToM[14]. Although there are studies that showed lower scores of RMET scores in remitted BDs compared to healthy controls[15,16], there are also studies showed no differences between two groups in RMET test[17,18]. According to a recent study investigated RMET abilities in remitted BD-1, BD-2, unipolar depression, and control groups, both BD and unipolar depression groups scored lower than the control group[19].

The ability to carry out tasks and activities related with various life domains is referred to as functionality. It has been known that deficits in everyday functioning is observed in many patients with BD. This situation is also observed even in the absence of acute symptoms[20]. It encompasses a wide range of abilities, including the ability to socially interact with others, as well as the ability to work independently and participate in activities. According to Goswami et al, 54% of patient with BD during remission had mild to moderate deficit in functionality[21]. It has been suggested that deficits in ToM ability may also be related with everyday functioning in BD. Thus, it has been suggested that ToM deficits may be a potential treatment target for functionality rehabilitation in patients with BD.

Patients with BD have a higher risk of developing metabolic alteration, type 2 diabetes mellitus, cardiovascular diseases and obesity than the general population. There have been several factors contributing to the development of metabolic alteration in BD such as disease treatment, environmental exposure, social factors, lifestyle[22]. It has been known that obesity and metabolic syndrome are related with cognitive impairments in general population[23,24]. The link between cognitive impairment and metabolic syndrome was also found in psychiatric disorders. According to a recent meta-

analysis, a modest but significant relationship was found between obesity and cognitive impairments (especially executive functions and processing speed) in BD[25]. Although there are many studies that reported cognitive impairment in patient with BD with metabolic dysfunction, the studies that investigated the relation between social cognition and metabolic alteration in BD are very rare. To our knowledge, no study has addressed yet the relationship between ToM abilities, functionality, and metabolic alteration in a sample of remitted BD. In this study, we aimed to investigate metabolic risk factors on social cognition and our main hypothesis was that we would find a negative relationship between metabolic alteration, social cognition, and functionality.

MATERIALS AND METHODS:

Sample

In this cross-sectional study, the participants aged between 18-65, were selected from among the individuals who applied to Erenkoy Training and Research Hospital for Mental Health and Neurological Diseases psychiatry outpatient clinic between June 2021- December 2021. Participants who were subsequently assessed by two psychiatrists and met Diagnostic and Statistical Manual of Mental Disorders (DSM-5) criteria for BD-I who had been in remission period for at least six months (a) Young Mania Rating Scale (YMRS)<7, b) Hamilton Depression Rating Scale (HDRS) < 10) were admitted to study. Out of these 87 patients, 9 patients were excluded from the study due to additional substance use disorder, 5 patients were excluded since they did not finish the RMET, and 5 patients were excluded since their blood sample results were uncompleted. Finally, 68 patients were included to the study. Healthy controls were selected from hospital workers. The exclusion criteria of both groups were lack of education, being illiterate or mental retardation, having cognitive weakening, comorbid psychiatric diseases (i.e., substance-alcohol use disorder, personality disorder, anxiety disorder), neurological disease (i.e., dementia, organic brain disorder), pregnancy or breastfeeding, having inflammatory and chronic diseases, being heavy smoker (>20 cigarettes per day).

Procedure

Sociodemographic form and RMET were applied to both groups. HDRS, YMRS, Bipolar Disorder Functioning Questionnaire (BDFQ) were applied to the patient group. Ethics committee approval for the study was granted by the Erenkoy Research and Training Hospital for Mental Health and Neurological diseases Ethical Committee with approval numbered 23 dated May 23, 2021.

Metabolic measures

The laboratory results of the last 6 months of the participants were evaluated retrospectively which were obtained in the routine control performed during the period that they have been in remission for at least 6 months. Venous blood samples of the individuals during the euthymic period were obtained after a fasting period of 12 hours. Waist circumference (WC), height and weight were recorded during the interview. Fasting plasma glucose (FG), high density lipoprotein cholesterol (HDL), low density lipoprotein cholesterol (LDL), total cholesterol, triglyceride (TG) levels are recorded. The blood samples of healthy control group were also evaluated retrospectively which were obtained in the last six months for the routine control after a fasting period of 12 hours.

Data collection tools

Sociodemographic data form

This form consists of demographic features including age, gender, marital status, education, occupation, duration of illness, number of hospitalization, number of manic and depressive episodes.

Hamilton Depression Rating Scale (HDRS)

This scale is a structured scale applied by the researcher and developed by Hamilton[26]. It measures the symptoms of depression experienced over the past week. The form consists of 17 items. Items are rated from 0 to 4. The highest point is 51 and higher scores mean higher depression levels. Its Turkish form has been validated by Akdemir et al. The cronbach alpha coefficient was 0.75[27].

Young Mania Rating Scale (YMRS)

This scale measures the severity of manic symptoms. It was developed by Young et al. and consists of 11 items. Items are rated from 0 to 4, and higher scores mean more severe mania. The reliability and validity of the scale has been done by Karadag et al[28]. The cronbach's alpha was 0.79 for that study[28].

Reading the Mind in the Eyes Test (RMET)

This test was first developed by Baron-Cohen et al. in 1997[29] and its revised version was published in 2001[14]. It contains 36 photographs of the eye region with answer options. The participants are asked to select one of the four options given in the picture which describes the best his or her mental state. This test measures the ability to recognize what other people are feeling or thinking. Thus, this test is considered as an indicator of theory of mind ability with recognition. Higher scores mean better ToM capacity. Its Turkish validity and reliability were done by Yildirim et al. and Turkish from is consists of 32 photographs[30].

Bipolar Disorder Functioning Questionnaire (BDFQ)

BDFQ was created by mood disorders working group under Psychiatric Association of Turkey[31]. It contains 52 items and 11 subscales: emotional, intellectual, sexual functionality, feelings of stigmatization, social withdrawal, household relationships, relationship with friends, involvement in social activities, daily activities, occupation and self-sufficiency.

Statistical analysis

SPSS version 23.0 was used to do statistical analyses. The variables were investigated using visual (histograms, probability plots) and analytical methods (Kolmogorov Smirnov test) to determine whether or not they are normally distributed. In the analysis of normally distributed variables, independent samples t-test and Pearson correlation test were performed, while analysis of non-normally distributed variables was used with Mann Whitney-U test and Spearman correlation test. Analysis of covariance (ANCOVA) was used to investigate the differences in RMET between the control and patient groups after controlling for age, gender and education level. Hedge's g value was calculated for the effect size of the difference between the metabolic values of the patient and control groups and reported with 95% CI.

In order to detect an effect size of Cohen's d= 0.608 with %95 power (alpha = 0.05, two-tailed), G*Power suggests we would need 72 participants per group in an independent samples t-test. The smallest effect size of interest was set to d=0.608 based on the study of Donohoe et al[32]. Considering the exclusion criteria determined in this study, a total of 87 patients were interviewed with a 20% margin of error.

RESULTS

Sociodemographic, clinical variables, and metabolic parameters of the patient group and the healthy controls were shown in Table 1. The average age of patient group was 38.6±10.7 and 33.7±10.1 in the HC group. In the patient group %38.2 (n:26) of the participants were female, %61.8 (n:42) of them were male. In HC group, %62.2 (n: 28) of the participants were female, and %37.8 (n:17) of them were male.

Mean duration of illness was 11.7±8.5, mean number of hospitalizations was 2.4±2.5, mean number of depressive episodes was 3.1±2.6, mean number of manic episodes was 3.8 (SD= ±2.7). When comparing the clinical variables, there were statistically significant differences between the patient group and HC group in terms of WC (p < 0.001), BMI (p < 0.001), HDL (p < 0.001), LDL (p= 0.020), TG (p< 0.001) levels. Differences in metabolic parameters between patient and control groups were shown in Figure 1.

Inter-correlation between sociodemographic and clinical variables, metabolic parameters, BDFQ and RMET scores of patient group were shown in Table-2. Age (r = -.192, p = 0. 041), number of manic episode (r = -.264, p = 0.01), TG (r = -.291, p = 0. 002), fasting glucose levels (r = -.230, p = 0.014), WC (r = -.300, p = 0. 001), BMI (r = -.224, p = 0.017), LDL (r = -.288, p = 0. 002) were statistically negative correlated with RMET scores. Years of education (r =.365, p <0.001) and HDL levels (r =.243, p = 0. 009), BDFQ scores (r = .322, p < 0. 001) were statistically positive correlated with RMET scores.

Inter-correlation between BDFQ subscales and RMET scores of patient group were shown in Table 3. Intellectual functioning (r = .252), sexual functioning (r = .279), participation to social activities (r = .349), and BDFQ (r = .326) sumscores were statistically positive correlated with RMET scores.

The results of independent samples t-test indicated a statistically significant difference in RMET score between the two groups, t (111) = 5.25, p< 0.01. with control group significantly higher than patient group (mean difference = 3.82, SE = 0.72, 95% CI = 2.38 to 5.26). The results were shown in Figure 2. The results of a one-way between-subjects ANCOVA indicated a statistically significant difference in

RMET score between the patient group and healthy control group after adjusting for age, gender and level of education, F=19.78, p<0.05. Adjusted means indicated the healthy control group had significantly higher RMET score than the patient group (23.6 vs 19.7, respectively).

Table 1. Sociodemographic and Clinical Variables of Sample

		Bipolar disorder (n:68)	**Healthy control (n:45)**	
		n (%), Med±SD		p
Age		38.6±10.7	33,7±10,1	0.016
Year of Education		10.8±3.4	12.3±3.2	0.025
Gender	Female	26 (38.2)	17 (37.8)	0.012
	Male	42 (61.8)	28 (62.2)	
Marital status	Married	35 (51.5)	23 (51.1)	0.816
	Single	30 (44.1)	21 (46.7)	
	Divorced	3 (4.4)	1 (2.2)	
Employment	Workers	24 (35.3)	28 (62.2)	0.001
	Unemployed	35 (51.5)	8 (17.8)	
	Student	3 (4.4)	7 (15.6)	
	Retired	6 (8.8)	2 (4.4)	
Duration of illness		11.7±8.5	-	-
Number of hospitalization		2.4±2.5	-	-
Number of Depressive episode		3.1±2.6	-	-
Number of Manic episode		3.8±2.7	-	-
Waist circumference		99.9±10.9	82.4±13.9	<0.001
BMI		29.5±5.2	24.9±4.1	<0.001
Total cholesterol		189.0±39.8	176.5±40.5	0.111
HDL		43.2±11.3	53.1±13.1	<0.001
LDL		121.1±32.3	106.4±32.6	0.020
Triglyceride		165.9±94.0	89.5±35.9	<0.001
Fasting glucose level		96.3±16.3	91.8±14.6	0.135

RMET: reading the mind in the eyes test, BD: Bipolar disorder, BMI:body mass index, HDL:high density lipoprotein, LDL: low density lipoprotein

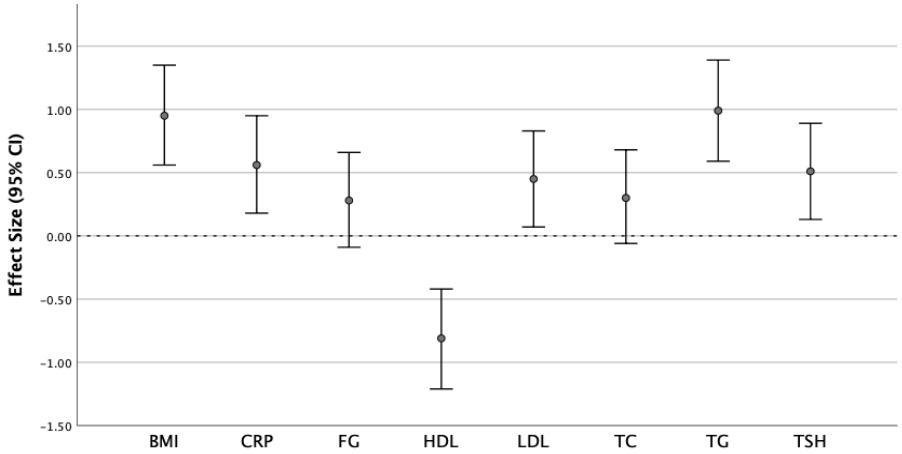

Figure 1. Differences in metabolic parameters between patient and control groups

BMI: Body Mass index, CRP: C-reactive protein, HDL: High Density Lipoprotein, LDL: Low Density Lipoprotein, TC: Total cholesterol, TG: Trigliseride, TSH: Thyroid stimulating hormone

Table 2. Correlation Coefficients among Sociodemographic and Clinical variables, Metabolic parameters, Bipolar Functionality Scale and RMET scores in the patients group

	RMET	BDFQ
Age	-.192	.079
Year of education	.365**	-.005
Duration of illness	-.160	-.033
Number of hospitalization	-.121	-.169
Number of depressive episodes	-.150	-.082
Number of manic episodes	-.264*	-.179
Triglyceride	-.291**	.075
Fasting glucose	-.230*	-.115
Waist circumference	-.300	.071
BMI	-.224*	.194
Total cholesterol	-.180	-.125
HDL	.243**	-.098
LDL	-.288**	.148
Height	,081	-.176
Weight	-.138	.039

*p<0.05 **p<0.01; RMET: reading the mind in the eyes test, BDFQ: Bipolar disorder functionality questionnaire, BD: Bipolar disorder, BMI: Body mass index, HDL:high density lipoprotein, LDL: low density lipoprotein

Table 3. Correlation Coefficients **among Bipolar Disorder Functioning Questionnaire Subscales and RMET scores in the patient group**

BDFQ Subtypes	RMET
Emotional functioning	0.162
Intellectual functioning	0.252*
Sexual functioning	0.279*
Feelings of stigmatization	0.145
Social withdrawal	0.035
Household relations	0.039
Relations with friends	0128
Participation to social activities	0.349**
Daily activities and hobbies	0.081
Taking initiative and self sufficiency	0.101
Occupation	0.279*
BDFQ – sum score	0.326**

*p<0,05 **p<0,01; RMET: reading the mind in the eyes test, BDFQ: Bipolar disorder functionality questionnaire,

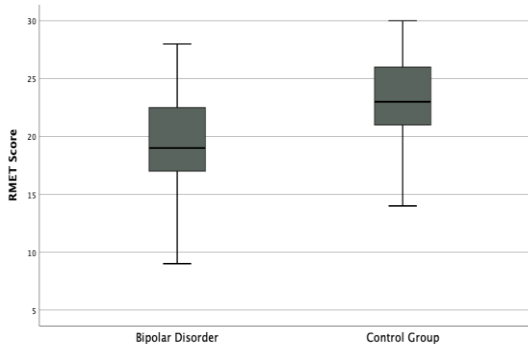

Figure 2. Comparison of RMET scores of patient and healthy control groups

DISCUSSION

The results of present study showed that patients with BD-I during the remission period have certain deficiencies in ToM compared to HC group. This result is consistent with previous studies indicating impairment in ToM is present in patients with BD even in remission periods. Although, deficits in ToM were more pronounced in manic or depressive episodes of BD, deficits in euthymic period have becoming increasingly noticeable[33]. Our results showed no correlation between RMET scores and measures for chronicity such as number of hospitalizations, depressive episodes. But there was a significant negative correlation between number of

manic episodes and RMET scores. These results are similar with results of the recent meta-analyses of Bora et al. which found significant relationship between severity of ToM deficit and YMRS scores, but no significant relation with HAM-D scores[12]. Mania related changes in the functional brain region such as ventral prefrontal cortex has a role in decision making and ToM. This also explains the effect of mania on ToM[34]. One of the main results of this meta-analyses is no significant effect of gender, age, education, illness duration was found on ToM scores in BD[12]. In our study, a positive correlation was found between education and RMET scores. But, higher RMET scores were found in HC group than BD group after adjusting for age, gender, and education level which may influence social cognition[14]. These results are very important to support the idea that even in remission period the nature of BD has an effect to impair the ability of ToM. Thus, these findings may be interpreted as ToM deficits can be a trait marker of BD. In addition to this, impaired ToM performance was also found in relatives of BD in previous studies and this finding supported the idea of ToM may be an endophenotypic marker of BD[35]. But further studies are needed to support this hypothesis.

According to our results, there was positive relation between RMET scores and BDFQ scores in patient group which means higher functionality is related with better ToM ability in BD. According to the literature, neurocognitive abilities are shown to be effective on everyday functioning of patients with BD[20]. ToM deficits are also related with problems in social interaction. This relationship has been shown in BD similar to that seen in schizophrenia[18,20]. 'Participation to social activities', 'sexual functioning', and 'intellectual functioning' subgroups of BDFQ are also found positively correlated with RMET scores in our study. Rosa et al. also reported that functionality deficits in BD mostly was observed in cognitive, sexual and interpersonal domains[36] which are similar with our results.

In our study, a significant difference was observed between patients and HC groups in terms of obesity and metabolic parameters as expected. Significantly higher BMI, WC, LDL, TG, CRP levels and reduced HDL levels were found in patient group compared to HC group. It has been known that obesity and metabolic abnormalities are more prevalent in patient with mental disorders[37]. Patients with metabolic abnormality have worse responses to treatment, lower social functionality, and show greater mortality. Recent studies showed that obesity and metabolic abnormalities might be related with cognitive deficits which mainly affects attention and memory[25]. Obesity, WC, and metabolic dysregulation were linked to problems with processing speed, attention, working memory. The link between metabolic dysregulation and neurocognition has been extensively studied. Several potential mechanisms, such as changes in the vascular, structural connections, and inflammation induced by metabolic disturbances may cause cognitive dysfunction. It has also been reported that obesity was linked with disruptions in white matter integrity, loss of brain-volume[38].

According to a recent meta-analysis, each metabolic parameter (ie., dyslipidemia, WC, obesity, insulin resistance) were found related with cognitive impairment in patients with schizophrenia[39]. Anjum et al., also investigated the relationship between cognition and metabolic dysregulation reported that HDL and TG were important predictors of cognition in patients with mental disorder and WC was one of the predictors of cognitive deficit and functioning[40]. Similarly, our results also showed that there is significant negative correlation between most of the metabolic parameters, BMI, WC, TG, FPG, LDL level, and ToM abilities and a positive correlation with HDL and ToM which means that obesity and metabolic dysregulation negatively affect social cognition. Recently, Cigliobianco et al. investigated the relationship between ToM and BMI in patients with schizophrenia and BD. According to the results of that study, BMI was found effective on ToM[41]. Recently, Tang et al. investigated the link between social cognition impairment and metabolic disturbances in patients with schizophrenia spectrum disorders and they reported a robust relationship between abnormal glucose metabolism and social cognition. Moreover, the correlation with social cognition and glucose abnormality was stronger than for non-social cognition[42]. Similarly, our results are important to support the idea of there is a relationship between metabolic dysregulation and impaired social cognition in patients with BD. Our study provided no information on the causality of these relationships. But several mechanistic pathways could explain the link between metabolic abnormalities and impaired social cognitive performance. First, BD is linked with increased inflammation and may cause metabolic abnormalities and decreased social cognition performance. Second,

metabolic dysfunction causes large vessel and microvascular changes that damage cerebral circulation and brain structure[42]. However, social cognition requires more complex integration of multiple cognitive systems than nonsocial cognition, making it more susceptible to disruptions in connectivity[43]. In accordance with these results, metabolic abnormalities may play a role in social cognition and treating metabolic abnormalities should be potential target to improve social cognition as well as functionality in patients with BD.

This study has certain strengths and limitations. We found higher RMET scores in HC group than BD group after adjusting for age, gender, and education level. It showed us the effect of the disease on social cognition. First of the limitation is this was a cross-sectional study and sample size was relatively small. Second, we obtained the blood samples from the hospital records respectively. Third, we could not assess IQ levels which can be effective on ToM. Fourth, we could not evaluate the effect of the psychotropic medication of the patient that may have potential impact on social cognition. Last and one of the important limitation of our study was we could not find causality for these relations. New researches should be focused on this causality to clear this relation.

In conclusion, this study is the first study to investigate the possible relationship between ToM abilities, metabolic parameters, and everyday functioning in patients with BD during remission period. Our findings showed that patients with BD have a lower performance on ToM than healthy controls during the remission period. RMET scores were found correlated with most of the metabolic parameters and functioning in patient group. As a result, metabolic dysregulation and ToM impairment should be potential treatment target for BD.

Yazar Katkıları: Çalışma konsepti/Tasarımı: GE, FK, HÜ, YEY; Veri toplama: DK, HÜ; Veri analizi ve yorumlama: GE, FK, HÜ, YEY; Yazı taslağı: FK, GE, YEY, HÜ; İçeriğin eleştirel incelenmesi: GE, FK; Son onay ve sorumluluk: FK, HÜ, YEY, GE; Teknik ve malzeme desteği: FK, HÜ, YEY; Süpervizyon: FK, GE, HÜ, YEY; Fon sağlama (mevcut ise): yok.
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Hakem Değerlendirmesi: Dış bağımsız.
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Author Contributions: Concept/Design : GE, FK, HÜ, YEY; Data acquisition: DK, HÜ; Data analysis and interpretation: GE, FK, HÜ, YEY; Drafting manuscript: FK, GE, YEY, HÜ; Critical revision of manuscript: GE, FK; Final approval and accountability: FK, HÜ, YEY, GE; Technical or material support: FK, HÜ, YEY; Supervision: FK, GE, HÜ, YEY; Securing funding (if available): n/a.
Ethical Approval: Ethical approval was obtained for this study from the Clinical Research Ethics Committee of Erenköy Research and Training Hospital for mental Health and Neurological Diseases with the decision dated 24.05.2021 and numbered 23.
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