Theory of Mind and Selective Attention, Response Inhibition, Cognitive Flexibility in Patients with Schizophrenia

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ABSTRACT

Introduction: The aims of the current study are to investigate the relationship between selective attention, response inhibition, and cognitive flexibility that are among executive functions and sociocognitive and socioperceptual theory of mind (ToM) functions and also to investigate whether selective attention, response inhibition, and cognitive flexibility are predictive factors for ToM functions in patients with schizophrenia.

Methods: Forty-seven patients diagnosed with schizophrenia and a control group consisting of 42 individuals were administered demographic information form, Wisconsin card sorting test (WCST), Stroop test, Eye test, Hinting test. Positive and negative syndrome scale was applied to the schizophrenia group.

Results: In comparison to the control group, the schizophrenia group

performed significantly worse on Eyes test and Hinting test. Eyes Test score and age, WCST perseverative error scores were significantly negatively correlated; education and WCST categories achieved scores were significantly positively correlated in patients with schizophrenia. Age and cognitive flexibility were found to predict the Eyes test score in patients with schizophrenia.

Conclusions: ToM functions that are important in maintaining socioperceptual functioning are closely related with cognitive flexibility, and impairment in cognitive flexibility may predict the ToM functions in patients with schizophrenia.

Keywords: Schizophrenia, executive functions, socio-cognitive theory of mind, socio-perceptual theory of mind

INTRODUCTION

Impairment in cognitive functions is a fundamental symptom of schizophrenia. The cognitive functions that are suggested to be affected the most are: executive functions, attention, perceptual/motor processing, sustained attention, verbal learning, verbal, and spatial working memory, and verbal fluency (1,2,3). Impairment in cognitive functions in patients with schizophrenia influences social and occupational abilities and quality of life negatively (4).

Theory of mind (ToM) is a concept that is used to express one of the most important sociocognitive abilities that has a role in social interactions of an individual (5). ToM is defined as the ability to explain other's apparent behaviors by attributions to their mental states. In other studies, ToM is discussed with respect to two subtypes. The definition provided by Premack and Woodruff corresponds to the type currently known as sociocognitive ToM (6). Sociocognitive ToM is the ability to attribute other's mental states based on their behaviors. As for socioperceptual ToM, it is the ability to infer other's mental states by attributing meaning to perceptual stimuli such as facial expression and tone of voice (5). Predominantly, false belief tests measure sociocognitive ToM function, whereas eye test measures socioperceptual ToM function (7,8). Meta-analytic studies conducted about ToM impairment in schizophrenia point out that ToM deficits in patients with schizophrenia have a very large impact size (9,10,11).

Some researchers suggest that in healthy individuals, there are some brain regions and special neural modules that are activated by ToM tests and that are related with ToM functions (12,13). In this context, impaired ToM function is argued to be related with ToM module except and above cognitive functions (14,15).

However, studies conducted with healthy controls indicate that cognitive functions such as executive functions, learning, and working memory are related with performance in ToM tests (5). In addition to this, the nature of the relationship between the impairment in cognitive functions seen in schizophrenia and ToM functions is discussed and the need for further studies is indicated (16).

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The purposes of this study are to investigate the relationship between selective attention, response inhibition, and cognitive flexibility which are among the executive functions in patients with schizophrenia and sociocognitive and socioperceptual ToM functions and to determine whether selective attention, response inhibition, and cognitive flexibility functions predict ToM functions. The hypothesis of the study is that in patients with schizophrenia, impairment in selective attention, response inhibition, and cognitive flexibility predicts sociocognitive and socioperceptual ToM functions.

METHODS

Sample

Forty-seven patients diagnosed with schizophrenia according to Diagnostic and Statistical Manual of Mental Disorders- Revised Edition (DSM-IV) prepared by American Psychiatric Association and a control group matched with respect to gender, age, and duration of education and which consists of 42 individuals who applied to health committee to obtain a health record for various reasons were included in the study (17). Inclusion criteria for the study were indicated as: being between the ages of 18 and 65 years, not being in an acute psychotic relapse according to the clinical assessment, not having been undergone an electroconvulsive treatment in the last 6 months, not having a alcohol or substance abuse or dependence, not having a history of head trauma, not having central nervous system disorders that may affect cognitive functions and mental retardation, not having a visual impairment and color blindness that may interfere with neuropsychological testing, and being literate. The study was approved by the ethical committee, and a written informed consent was obtained from the participants. Scales were administered by one of the psychiatrists of the study, and tests were administered by a psychologist. The following forms, scales, and tests were applied.

Demographic Information Form

In this form prepared by the researchers, the participants were asked for age, gender, duration of education, and the participants of the schizophrenia group were asked about the duration of the disorder.

Positive and Negative Syndrome Scale (PANSS)

This scale is a 30-item, semi-structured interview for the assessment of symptom severity on a seven-point scale (18). The Turkish reliability and validity study of the scale was performed (19). In our study, positive, negative, and general psychopathology subscales and the total score were taken into consideration. The reliability Cronbach's alpha coefficient of PANSS was estimated to be 0.82 for the schizophrenia group.

Wisconsin Card Sorting Test (WCST)

WCST is a test that assesses abstraction/problem-solving and the response change in accordance with the obtained feedback in adults. It evaluates frontal lobe functions such as strategy formation and canceling and cognitive flexibility. The first version was developed in 1948 by Berg, and the latest revision was made by Heaton et al. (20). The Turkish reliability and validity study of WCST was performed (21). In this study, perseverative errors and categories achieved scores were used. The reliability Cronbach's alpha coefficient for these measurements was estimated as 0.84.

Stroop Test

This test measures perceptual configuration, ability to shift under the influence of changing demands, and "interfering effect," the response inhibition which is defined as the ability to suppress a usual behavioral pattern, the ability to perform an unusual act, and selective attention. The Turkish

reliability and validity of this test which is originally developed by Stroop was conducted (22,23). In our study, to evaluate response inhibition and selective attention, Stroop 5 seconds and Stroop 5 errors scores were used. The reliability Cronbach's alpha coefficient used in this study was estimated as 0.71.

Eyes Test

Reading the mind from the Eyes test was developed to assess the ability to infer emotions and was revised in 2001 (24,25). It consists of 36 pictures which depict only facial areas of the individuals. Turkish reliability and validity study was performed (26). Because of the exclusion of two items as a result low reliability coefficient in this study, the Turkish version consists of 32 items together with one practicing item. For each picture, there are four options, one of them being correct and the other three as distractors. At the administration, the participant was given the instruction as "Mark the item that best explains what the individual thinks or feels for each pair of eyes." In addition, at the time of administration, the participant is given a dictionary in which expressions that are used in the questions and words that have similar meanings with these expressions. Each question has only one correct answer. At the time of scoring, the number of correct answers is taken into consideration. Higher scores indicate better social cognition and ToM abilities. The reliability Cronbach's alpha coefficient for Eyes test is estimated as 0.93.

Hinting Test

In this test to evaluate the secondary ToM functions, one of the stories used in the study by Corcoran et al. was used (27). With this story, the ability of the participant to understand the real intention behind what is indirectly said is evaluated. The participant is read a paragraph such as "Elif's birthday is near." In this paragraph, Elif tells her father that she loves pets and especially dogs a lot. And then, the participants are asked "What does Elif actually mean while telling this?" In this point, the participant gets two points if the response is right. If the participant does not give the correct answer, then the story is continued as "Elif asks her dad if the pet shop would be open on her birthday" and the question asked is "What does Elif want her father to do?" If the answer is correct at this point, then a score of 1 is obtained and 0 points is given if the answer is false. This story has been used in another study in our country (28). The reliability Cronbach's alpha coefficient for the Hinting test is estimated as 0.66 in this study.

Statistical Analysis

To determine whether the quantitative variables had a normal distribution, Shapiro-Wilk test was applied. Groups were compared with t-test for normally distributed variables, Mann-Whitney U test for variables that are not normally distributed, and chi-square test for categorical variables. Because the data were not distributed normally in the patient group, Spearman correlation analysis was performed to determine the relationship between ToM tests and sociodemographic data, scales, and cognitive tests, whereas in the control group, Pearson correlation analysis was used, as the data was normally distributed. To determine the predictive factors for Eyes test and Hinting test separately, variables of age, gender, duration of education without consideration of significant between-group differences, and other variables that were found to have significant differences with the control group and variables with significant correlations (Stroop 5 seconds, Stroop 5 errors, WCST categories achieved, WCST perseverative errors for Eyes test and Stroop 5 seconds, Stroop 5 errors, WCST categories achieved, WCST perseverative errors for Hinting test) were taken as the independent variables and were entered into multiple (linear) regression (stepwise analysis). The statistical significance level was accepted as $p < 0.05$.

RESULTS

Between the patient and control groups, no differences with respect to gender, age, and duration of education were found ($\chi^2=0.122$ and $p=0.727$; $t=1.002$ and $p=0.319$; $z=-0.559$ and $p=0.549$, respectively) (Table 1). In the schizophrenia group, the age was between the 20 and 52 years and the duration of education was between 4 and 20 years, and in the control group, the age was between 22 and 61 years and the duration of education was between 1 and 17 years. The total PANSS score was determined as 59.64 ± 24.02 (between 30 and 112), PANSS positive score was 13.98 ± 6.48 (between 7 and 30), PANSS negative score 16.15 ± 7.62 (between 7 and 33), and PANSS general score was 29.81 ± 12.69 (between 16 and 68).

Table 1. Comparison of schizophrenia and control groups with respect to gender, age and duration of education

	Schizophrenia (n=47)	Control (n=42)	Statistical test
Female/Male (n)	24/23	23/19	$\chi^2=0.122$ $p=0.727$
Age years (mean $\pm$ sd)	39,28 $\pm$ 7,32	37,43 $\pm$ 10,00	$t=1.002$ $p=0.319$
Duration of education (median/%25-75)	11 (5-12)	11 (5-12)	$z=-0.559$ $p=0.549$
sd: standard deviation			

When the groups were compared with respect to cognitive tests, significant differences were determined between schizophrenia and control groups for Stroop 5 seconds, Stroop 5 errors, WCST categories achieved, and perseverative errors ($z=-4.130$ and $p<0.001$; $z=-2.503$ and $p<0.01$; $z=3.915$ and $p<0.001$; $z=-3.480$ and $p<0.001$, respectively). When the groups were compared with respect to ToM tests, the schizophrenia group was determined to have significantly lower scores than the control group in Eyes test and Hinting test ($t=-6.818$ and $p<0.001$; $z=5.144$ and $p<0.001$, respectively) (Table 2).

In the schizophrenia group, significantly negative relations between Eyes test score, age, and WCST perseverative errors score ($r=-0.383$ and $p<0.05$; $r=-0.377$ and $p<0.01$, respectively) and positive correlation between duration of education and WCST categories achieved score ($r=0.325$ and $p<0.05$; $r=0.415$ and $p<0.01$, respectively) (Table 3) were determined. No significant relationship was determined between Hinting test and other variables. In the control group, significantly negative correlations between Eyes test, age, and Stroop 5 seconds and Stroop 5 errors scores ($r=-0.407$ and $p<0.01$; $r=-0.414$ and $p<0.01$; $r=-0.353$ and $p<0.05$, respectively) and a significantly positive relationship with WCST categories achieved score ($r=0.331$ and $p<0.05$) were determined. In the control group, a significantly negative relationship between Hinting test and Stroop 5 seconds ($r=-0.424$ and $p<0.01$) and a significantly positive relationship with WCST categories achieved score ($r=0.308$ and $p<0.05$) were determined.

Table 2. The comparison of schizophrenia and control groups with respect to cognitive tests and ToM tests

	Schizophrenia mean $\pm$ sd/median (%25-75)	Control mean $\pm$ sd/median (%25-75)	Statistical test
Stroop 5 seconds	36.6 $\pm$ 13.27	25.31 $\pm$ 6.83	$z=-4.130$ $p<0.001$
Stroop 5 errors	4.09 $\pm$ 4.40	2.05 $\pm$ 2.37	$z=-2.503$ $p<0.01$
WCST categories achieved	2.38 $\pm$ 2.07	4.26 $\pm$ 2.05	$z=3.915$ $p<0.001$
WCST perseverative errors	42.98 $\pm$ 27.17	21.74 $\pm$ 11.12	$z=-3.480$ $p<0.001$
Eyes Test total score	15.21 $\pm$ 5.73	22.36 $\pm$ 4.10	$t=-6.818$ $p<0.001$
Hinting Test total score	0.85 $\pm$ 0.78	1.71 $\pm$ 0.51	$z=5.144$ $p<0.001$
ToM: theory of mind; sd: standard deviation; WCST: Wisconsin Card Sorting Test			

Table 3. The correlation between scales, cognitive tests and ToM tests in schizophrenia and control groups

	Schizophrenia		Control	
	Eyes test	Hinting test	Eyes test	Hinting test
Age	-0.383**	-0.123	-0.407**	-0.067
Duration of education	0.325*	0.183	0.096	0.065
Duration of illness	-0.245	-0.243	---	---
PANSS Total	0.110	-0.034	---	---
PANSS Positive	0.001	-0.078	---	---
PANSS Negative	0.025	-0.032	---	---
PANSS General	0.135	-0.068	---	---
Stroop 5 seconds	-0.207	-0.185	-0.414**	-0.424**
Stroop 5 errors	-0.050	0.078	-0.353*	-0.272
WCST categories achieved	0.415**	0.260	0.331*	0.308*
WCST perseverative errors	-0.377**	-0.214	-0.241	-0.273
ToM: theory of mind; PANSS: positive and negative syndrome scale; WCST: Wisconsin Card Sorting Test; * $p<0.05$; ** $p<0.01$				

For the schizophrenia group, none of the dependent variables entered into multiple linear regressions with respect to the Hinting test remained until the last step in the model. In the schizophrenia group, as a result of analysis of variance in multiple linear regression model for Eyes test, the model was determined to fit the model ($F=12.596$ and $p<0.001$). The score that schizophrenia obtained from the Eyes test was determined to be predicted by dependent variables of age and WCST categories achieved ($\beta=-0.323$ and $p<0.01$; $\beta=1.225$ and $p<0.01$, respectively) (Table 4).

For the control group, the result of analysis of variance in the multiple linear regression model was determined to have a fit with respect to Eyes test and Hinting test ($F=7.960$ and $p<0.01$; $F=8.752$ and $p<0.01$, respectively). The score that the control group obtained from Eyes test was found to be predicted by dependent variables of age and Stroop 5 seconds ($\beta=-0.143$ and $p<0.05$; $\beta=-0.214$ and $p<0.05$, respectively), and Hinting test score was determined to be predicted by Stroop 5 seconds ($\beta=-0.031$ and $p<0.01$) (Table 5).

DISCUSSION

In our study, it was shown that patients with schizophrenia had worse performance than healthy controls in terms of executive functions that are evaluated by Stroop and WCST and ToM functions that are evaluated with Eyes test and Hinting test. These results are compatible with the results of many studies conducted up to now (1,2,3,9,10,11,29).

Our study showed that in both the schizophrenia and control groups, there was a negative relationship between age and Eyes test; and in patients with schizophrenia, there was a positive relationship between the duration of education and Eyes test and also that worse performance was predicted by increases in age for both of the groups. The finding that the increase in the duration of education was associated with increases in Eyes Test performance in healthy controls was previously demonstrated in other studies (26,30). In previous studies conducted up to date in patients with mood disorders, the age was determined to not affect the Eyes test performance and this finding was interpreted as Eyes test's being more related with the emotional domain than the cognitive functions. (31,32,33).

Table 4. Linear Regression Analysis for Eyes Test in the schizophrenia group

Independent variables	Dependent variable Eyes test			
	β	SH	St. β	p
Age	-0.323	0.094	-0.412	<0.01
WCST Categories achieved	1.225	0.333	0.443	<0.01
Constant	24.964	3.835	--	<0.001

WCST: Wisconsin Cart Sorting Test; β : Beta; St. β : standardized beta; SH: standardized error; For Eyes Test $R^2=0.6033$

The underlying reason for the prediction of worse performance in Eyes test by the increases in age in patients with schizophrenia may be indicating that different from mood disorders, socioperceptual ToM functions are influenced as the illness progresses. In this respect, studies that including both mood disorder and schizophrenia patients, are required.

The main goal of our study was to investigate the relationship between selective attention, response inhibition, cognitive flexibility functions, and sociocognitive and socioperceptual ToM functions in patients with schizophrenia and to determine whether selective attention, response inhibition, and cognitive flexibility functions were a predictive factor in terms of ToM functions in patients with schizophrenia. In our study, it was determined that Eyes test score had a significant negative relationship with WCST perseverative error score, a significantly positive correlation with WCST categories achieved score and that cognitive flexibility level predicted better performance at the Eyes test in patients with schizophrenia. Since studies demonstrating that ToM and executive functions are impaired independent of each other (34), it is also indicated that impairment of ToM abilities cannot be explained just by lower intelligence levels and may be related with impairment of cognitive functions (14,15,35). In some of the studies that report impairment in ToM functions independent of cognitive functions in patients with schizophrenia, it is put forward that ToM functions are executed by special modules specific to this function (14,15). In one study, impairment in ToM functions predicted being in the schizophrenia patient group even when the cognitive functions under study were controlled (36). However, when these findings are taken together, our study may be supporting the notion that socioperceptual ToM functions and cognitive flexibility functions in patients with schizophrenia that are thought to be dorsolateral cortex functions cannot be thought separately and accordingly that ToM functions cannot be explained with a modular nature. Prefrontal and medial temporal cortex are important brain regions for ToM functions and executive functions (37). It may be possible that neural structures that have a role in executive functions and especially cognitive flexibility may also have a role in sociocognitive and socioperceptual ToM functions. Besides, in our study, the lack of correlation between ToM functions and cognitive flexibility instead of PANSS that assesses symptom severity may have a contribution to arguments that ToM functions and cognitive flexibility are among the core symptoms of schizophrenia. As for the control group, the finding that response inhibition as measured by Stroop Test predicted both sociocognitive and socioperceptual ToM functions may be indicating that the relationship between cognitive flexibility and sociocognitive ToM functions is more valid for schizophrenia.

In our study, the finding that the cognitive flexibility impairment was correlated with the Eyes test but not the Hinting test score seems to be interesting. WCST is a test that measures cognitive flexibility in general, and it would be more plausible for it to be correlated with the Hinting test performance that measures sociocognitive ToM functions. This finding of

Table 5. Linear regression analysis for Eyst Test and Hinting Test in the control group

Independent variables	Dependent variable							
	Eyes Test				Hinting Test			
	B	SH	St. β	p	B	SH	St. β	p
Age	-0.143	0.056	-0.349	<0.05	---	---	---	---
Stroop 5 seconds	-0.214	0.082	-0.357	<0.05	-0.031	0.011	-0.424	<0.01
Constant	33.139	2.757	--	<0.001	2.511	0.279	---	<0.001

β : beta; St. β : standardized beta; SH: standardized error; for Eyes Test $R^2=0.290$, for hinting test $R^2=0.180$

our study together with the results of regression analysis point out the idea that sociocognitive ToM functions are related more with cognitive flexibility than the socioperceptual ToM functions in patients with schizophrenia. However, the findings of our study may have been influenced by the Hinting test's being a relatively easier test that measures secondary level ToM functions and having a narrower scoring range.

Among the limitations of our study, we may indicate initially that all of the patients with schizophrenia being on medication which may be a confounding factor, the lack of assessment of cognitive and executive functions that may be related with ToM functions other than selective attention, and response inhibition and cognitive flexibility and not administering Clinical Global Impression Scale for schizophrenia group. Besides, choosing "being literate" as the lower limit of the inclusion criteria which may have affected the performance in executive functions is another limitation of our study.

Consequently, ToM functions that may have an important role in social functioning in patients with schizophrenia are closely related with executive functions, and impairment of dorsolateral cortex functions including cognitive flexibility has the power to predict ToM functions. For this reason, it must be kept in mind that cognitive impairment that is caused because of the illness itself or because of the medication may also affect ToM functions.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of local ethical committee.

Informed Consent: Written informed consent was obtained from patients who participated in this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - A.E.; Design - A.E., F.K., F.Ö.A.; Materials - F.Ö.A.; Data Collection and/or Processing - A.E., F.K., F.Ö.A., Ö.Ö., G.G.; Analysis and/or Interpretation - A.E., Ö.Ö.; Literature Search - A.E., F.K., G.G.; Writing - A.E., F.K., G.G.; Critical Reviews - F.Ö.A., Ö.Ö.

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