Theory of Mind in Schizophrenia and Asperger’s Syndrome: Relationship with Negative Symptoms

Halide Devrimci Ozgun1, Ozugr Oner2, Bora Baskak3, Ferhunde Oktem4, Senay Olmez4, Kerim Munir5

ABSTRACT:
Theory of mind in schizophrenia and Asperger’s syndrome: relationship with negative symptoms

Objective: Although previous studies have shown that the theory of mind (ToM) ability is impaired in Asperger’s Syndrome (AS) and schizophrenia, few controlled studies compared the ToM performance between the two disorders. Besides, the relationship between the degree of ToM impairment and symptom dimensions is unclear, and presence of ToM impairment in remitted patients with schizophrenia is controversial. Here, we tested the hypothesis that schizophrenia patients with prominent negative symptoms were closer to AS patients and different than schizophrenia patients without prominent negative symptoms and healthy controls in terms of ToM functioning.

Method: Fourteen patients with AS, 20 with schizophrenia and 20 healthy controls, matched by age, educational level and IQ scores were enrolled. AS was diagnosed according to the DSM-IV criteria and independently confirmed by two psychiatrists. Schizophrenia patients were diagnosed by the Turkish version of Structured Clinical Interview for DSM-IV Diagnosis (SCID-II) and symptom severity was evaluated with the Scale for the Assessment of Negative and Positive Symptoms. Schizophrenia group consisted of clinically stable patients. The ToM battery included stories to assess first and second order false belief tasks (ToM1 and ToM2). The full-scale IQ, Verbal Comprehension, Freedom from Distractibility and Perceptual Organization subtests from the WAIS-R. Non-parametric tests were used to compare the neuropsychological performances of the three groups. In order to investigate whether schizophrenia patients with prominent negative symptoms were similar to AS patients, schizophrenia patients were divided into high (Sch-HN) and low (Sch-LN) negative-symptom subgroups by median split. For these four groups (AS, Sch-HN, Sch-LN, and controls) between group comparisons were performed. Correlations between the clinical measures and ToM performance were assessed by Spearman correlation test.

Results: AS and schizophrenia patients performed significantly worse than controls in the ToM2 task, while the AS group had worse ToM1 performance than both schizophrenia patients and healthy controls. The Sch-HN subgroup had significantly lower ToM2 scores than the Sch-LN patients, and worse ToM1 functioning than the controls.

Conclusions: These results suggest that clinically stable schizophrenia patients have ToM impairments. Sch-HN group performed comparably poorly as the AS group, while the Sch-LN group was relatively spared. The most profoundly impaired patients with schizophrenia in terms of ToM functioning were represented by those with high negative symptoms (Sch-HN). Similar to AS, a neuropsychological impairment in the Sch-LN group may not have developed ToM ability, or they may have lost their ToM capacity as a result of a neurodegenerative process during the illness. Supplementary studies using other methods (e.g., neuroimaging, neuropsychology) may highlight the brain regions that are affected differentially in AS and schizophrenia, the relationship of ToM impairments and negative symptoms, and the role of ToM impairments in the neurodevelopmental or neurodegenerative hypothesis of schizophrenia.

Key words: Theory of mind, schizophrenia, Asperger’s syndrome, Asperger’s disorder, negative symptoms, cognitive deficits

Bulletin of Clinical Psychopharmacology 2010;20:5-13
INTRODUCTION

Theory of mind (ToM) is the ability to attribute mental states including beliefs, intentions, desires and knowledge to oneself and others. As originally defined by Premack and Woodruff in 1978 (1), the ToM ability enables one to understand mental states of others in order to predict and explain their behavior. The ability of a person to understand that others may hold false beliefs that do not match his or her own knowledge is commonly referred as first order ToM; the ability to understand that someone else thinks what a third person believes is a second order ToM which is generally accepted as a more advanced ability. Several studies have investigated the ToM disturbances in various developmental disorders, most notably autism and related conditions. It has been shown that individuals with autism (2-4) or Asperger’s Syndrome (AS) (5-7) may fail to progress through certain cognitive developmental stages that may further lead to an impairment in the ToM ability.

In 1992, Frith proposed that ToM impairment might also lead to inaccurate attribution of mental states to others and paranoid delusions, as in schizophrenia (8). According to Frith, in contrast to individuals with autism, ToM skills in people with psychosis develop normally but are later ‘lost’ following the first psychotic episode. Since that time, several studies have investigated the specificity of ToM impairments in schizophrenia and the relationship between ToM impairment and various symptom domains. First of these studies suggested that ToM impairments in schizophrenia were observed in patients who are currently in a psychotic episode and particularly with paranoid symptoms (9,10). While some later studies replicated this finding (11-13), others have reported that ToM impairment is not specific to persecutory delusions (14-17). Several studies have reported that patients with negative symptoms (15,18-20) or disorganized patients performed worse on ToM tasks (21,22). It has subsequently been suggested that the ToM deficit in schizophrenia is more strongly linked to negative and behavioral symptoms than to positive symptoms such as delusions and hallucinations (23). In general, the precise relationship between impaired ToM and specific symptom domains in people with schizophrenia remains controversial.

Most of the studies mentioned above suggested that ToM impairment in schizophrenia was observed in psychotic episodes (9,11,12,14-17,22); and the deficit may disappear on remission of the episode (10,14). However, only Pickup and Frith (24) compared schizophrenia patients in a psychotic episode to remitted patients; and found that patients with behavioral symptoms performed significantly worse than both controls and remitted schizophrenics on a second-order ToM task. The researchers suggested that ToM impairment is a state rather than a trait characteristic in schizophrenia. On the other hand, regarding the trait hypotheses, several studies found ToM deficits in remitted schizophrenics (25-27); and also in relatives of schizophrenia patients (26,28).

It has been postulated that the progression of ToM impairment in schizophrenia might be different than that in autism or related disorders. In autism, ToM impairment invariably occurs earlier in the development. In fact, individuals with autism or related disorders may not be able to develop ToM ability at all. Typically, the symptoms of schizophrenia do not emerge until adolescence or early adulthood. Therefore, the ToM impairment observed in individuals with schizophrenia may not be evident or studied during early childhood years.

The severity of the ToM impairment in patients with schizophrenia is also controversial. Frith and Corcoran (10) found that schizophrenic patients performed poorly on both first- and second-order ToM tasks, similar to patients with autism and AS, whereas other researchers found intact performance on first order tasks and impairments only at the second order level (14,19,24).

A number of studies compared the severity of ToM performance in patients with autism, AS and schizophrenia (7,12,29). Craig et al. (12), showed that patients with schizophrenia and AS scored lower than controls in ToM tasks, while there were no significant differences between the patient groups. In a forensic sample, Murphy reported that both AS and schizophrenia patients had lower ToM performance than the patients with personality disorders while there was no significant difference between the former two groups (7). Pilowsky and colleagues (29) reported that while the patients with childhood-onset schizophrenia had better performances than those with autism in the deception task, one of the tasks that measure ToM ability, the two groups’
performances in the other ToM tasks were similar and worse compared to that among controls. These studies have controversy in terms of severity of the ToM impairment and suggest that the second order -but not the first order- ToM performance of patients with autism, AS and schizophrenia might in fact be quite similar.

In this study, we aimed to compare the ToM performance among adult male patients with AS, clinically stable schizophrenia patients, and age, gender and IQ matched healthy controls. We hypothesized that clinically stable schizophrenia patients have second order ToM impairment. However, ToM impairment in patients with AS would be more severe than those observed in clinically stable schizophrenia patients. We also hypothesized the severity of negative symptoms in schizophrenia would be correlated with the ToM impairment and the ToM performance of patients with schizophrenia, patients with prominent negative symptoms being closer to that observed among AS patients.

**METHOD**

**Subjects**

**AS patients:**

Patients were recruited from the outpatient psychiatry clinic of the Psychiatry Department, Ankara University School of Medicine and the Child Psychiatry Department, Hacettepe University School of Medicine, Ankara, Turkey. A diagnosis of AS was made according to the DSM-IV criteria. Two psychiatrists independently evaluated the subjects using a structured checklist. Parents of all subjects were also interviewed to obtain the subjects’ developmental history. None of the subjects had language delay. The diagnosis of AS was based on the full consensus by two clinicians. Clinical Global Impression (CGI) was used to evaluate clinical severity. Inclusion criteria were (1) DSM-IV AS diagnosis; (2) right-handedness; (3) being male; (4) aging between 18-45; (5) having an at least 8 years of education; (6) a CGI score lower than 5 (as a proxy for symptom stability). Exclusion criteria were (1) any neurological disorder; (2) a history of head trauma resulting in unconsciousness longer than 30 minutes; (3) substance dependence (except tobacco); and (4) WAIS-R Total IQ lower than 70.

**Schizophrenia Patients:**

All subjects were evaluated using the Turkish version of Structural Clinical Interview for DSM-IV Diagnosis (SCID-I). The final diagnosis of schizophrenia was made by two psychiatrists each independently endorsed the diagnose based on all available information. The Scale for the Assessment of Negative Symptoms (SANS), The Scale for the Assessment of Positive Symptoms (SAPS) and CGI were used to evaluate negative and positive symptoms and clinical severity respectively. SCID-I and other tools were administered by trained and certified researchers. Inclusion criteria for the schizophrenia probands were (1) a DSM-IV diagnosis of schizophrenia; (2) right handedness; (3) being male; (4) being aged between 18-45 years (to secure a comparable age frequency distribution); (5) having an at least 8 years of education; (6) a CGI score lower than 5 (as a proxy for symptom stability). Exclusion criteria were (1) any neurological disorder; (2) a history of head trauma resulting in unconsciousness longer than 30 minutes; (3) substance dependence (except tobacco); and (4) WAIS-R Total IQ lower than 70. In addition to the clinical scales; the information about the duration of illness, number of relapses and age of disorder onset were collected from schizophrenia patients.

**Healthy Control Subjects:**

Healthy controls were recruited locally and were administered SCID-I by a trained rater. Subjects who have any psychiatric disorder, history of any neurological disease, head trauma or substance dependence (except tobacco) and whose IQ scores lower than 70 were excluded.

Patients with AS, schizophrenia and healthy controls were matched for age, years of education and WAIS-R total IQ scores. All subjects or their parents/guardians gave their written informed consent. The study was approved by the ethics review committee of Ankara University.

**Clinical Assessment:**

**Structural Clinical Interview for DSM-IV Diagnosis (SCID-I).** SCID-I is a semi-structured interview for DSM-IV axis I diagnoses, which is administered by trained interviewers (30). It consists of 6 modules, and
usually administered within 25 to 50 minutes. It was translated into Turkish by Çorapçıoğlu et al. (31).

**Clinical Global Impression (CGI):** This scale is used to evaluate the severity and the improvement of symptoms in any disorder. Clinicians rate the severity and the improvement/deterioration of the disorder using their clinical experience and skills to score from 1 to 7 (32).

**The Scale for the Assessment of Negative Symptoms and the Scale for the Assessment of Positive Symptoms (SAPS, SANS).** These two scales have been developed by Andreasen (33,34) and have been extensively used to evaluate the positive and negative symptoms in schizophrenia. The SANS consists of 5 subscales and 25 items while the SAPS includes 4 subscales and 34 items. Clinicians score items from 0 to 5 using information obtained from the patient, the family and the hospital records, etc. Both scales were translated into Turkish by Erkoç and colleagues and reported to be valid and reliable (35,36).

**Neuropsychological Assessment**

The tests were administered and evaluated by two experienced clinical psychologists, and their overall agreement was over 90%.

**Theory of Mind (ToM) Tests:**

The battery included stories to assess first and second order false belief tasks (ToM1 and ToM2). All stories were read aloud twice by the rater and repeated upon request. The subject was expected to repeat the story and answer some control questions in order to verify if the task was comprehended. Each task comprised a short scenario followed by some set of questions for which, when answered correctly a point was gained. The answers were prompted: Fail or pass. The first task (ToM1) was about ‘John, Mary and the ice-cream man’; and second task was about ‘Peter and Jane shopping’. After reading the scenarios, the subjects were asked a naming question, prompt questions, a reality question, a memory question, and a belief question. The naming and prompt questions were expected to control the effect of memory. The second order task scenarios were based upon those developed by Perner and Wimmer (37) and by Bowler (38). These tasks were adapted to the Turkish characters and cultural context.

**Wechsler Adult Intelligence Scale–Revised (WAIS-R):**

The battery has been used to evaluate the IQ of adult subjects; however, individual sub-tests have also been utilized extensively in research (39). We used the three factor solution of WAIS-R as well as the full-scale IQ score in order to have a more reliable estimate of attention and comprehension: Verbal Comprehension (Information, Reasoning, Similarities and Vocabulary), Freedom from Distractibility (Digit Span, Digit Symbol, and Arithmetic) and Perceptual Organization (Picture Completion, Object Assembly, Block Design) (40).

**Data Analysis:**

We used non-parametric Kruskal-Wallis H and follow-up Mann-Whitney U tests with Bonferroni correction to compare the neuropsychological performances of the three groups. Correlations between the clinical measures, neuropsychological measures and ToM performances were calculated by Spearman correlation test. In order to investigate whether schizophrenia patients with more prominent negative symptoms were similar to AS patients, we used median split to divide schizophrenia patients into high (Sch-HN, n=10) and low (Sch-LN, n=10) negative-symptom subgroups. With these four groups (AS, Sch-HN, Sch-LN, and controls) we repeated the analysis, and reported these later results when significant.

**RESULTS**

**Demographic and Clinical Variables:**

Fourteen AS, 20 schizophrenia patients and 20 control subjects were included in the study. Age, years of education and WAIS-R Total IQ scores were similar among the groups (Table 1). All AS and schizophrenia patients were out-patients and clinically stable. Six of the AS patients were on atypical antipsychotic and antidepressant medication, and the rest of them were drug-free. All schizophrenia patients were under antipsychotic medication: 15 patients were on atypical antipsychotics, 5 were on classical antipsychotics, and 3 were also on 3–6 mg/day biperiden in addition to the
antipsychotic drug. SAPS Total score was not significantly different between the Sch-HN and the Sch-LN subgroups ($z=-0.15$, $p=0.912$). Since these two subgroups were defined on the basis of their SANS scores, Sch-HN group obviously had a higher SANS score ($z=-3.8$, $p<0.001$). Other clinical details of schizophrenia patients are presented on Table 1.

### Analysis between the groups:

Minimum-maximum and median scores of the neuropsychological tests are presented in Table 2. Kruskal-Wallis H test revealed that ToM1 ($x^2=18.1$, df=2, $p<0.001$), and ToM2 ($x^2=24.0$, df=2, $p<0.001$) scores were significantly different among the groups. Mann-Whitney-U tests revealed that both AS and schizophrenia groups had significantly lower ToM2 scores than controls ($z=-4.1$, $p<0.001$ and $z=-3.7$, $p<0.001$, respectively). AS cases had worse ToM1 performance than both control and patients with schizophrenia ($z=-4.5$, $p<0.001$; $z=-2.4$, $p=0.03$, respectively). ToM1 performance was also lower in the schizophrenia group than controls ($z=-2.5$, $p=0.012$).

There were no significant differences considering ToM1 and ToM2 scores between patients with AS and Sch-HN. AS group had lower ToM1 and ToM2 scores as well as WAIS Verbal Comprehension score than Sch-LN group ($z=-2.6$, $p=0.009$; $z=-2.7$, $p=0.007$; $z=-2.9$, $p=.004$, respectively). Sch-HN subjects had lower Tom1 and Tom2 scores when compared with controls ($z=-3.4$, $p<0.001$; $z=-4.2$, $p<0.001$, respectively). Sch-HN group also had lower Tom2 and Verbal Comprehension scores than Sch-LN group ($z=-2.7$, $p=0.007$; $z=-2.6$, $p=0.009$, respectively). Sch-LN and control ToM1 and ToM2 scores were not significantly different.

### Within group correlations among the WAIS-R, clinical variables and ToM tasks:

Table 3 summarizes the correlations of WAIS-R; Verbal Comprehension, Freedom from Distractibility, and Perceptual Organization scores and clinical scale scores.
with the ToM test scores in each group. In the AS group, WAIS-R Verbal Comprehension score was correlated with the ToM performance. In the schizophrenia group, verbal comprehension and negative symptom severity were closely related with the ToM2 performance and there were no significant correlations between other clinical variables and ToM performances. We did not find any significant correlation between WAIS-R and ToM scores in the control group.

**DISCUSSION**

Our results suggest that clinically stable schizophrenia patients have second order ToM impairments. On the other hand, patients with AS have lower first order ToM performance than those with schizophrenia patients as well as controls. These results are not surprising as ToM impairment has previously been noted both in AS (4-7) and schizophrenia (21,15,41,42).

In general, we found that patients with AS had worse ToM performance than patients with schizophrenia. Our results are in line with the previous studies indicating that the second order, but not the first order ToM ability is impaired in schizophrenia (14,19,24,43). Previous studies which compared the ToM ability in autism, AS and schizophrenia (7,12,29) showed that ToM performances were similar in the three disorders. However, there are some sampling differences between the present study and the former studies. The sample enrolled by Pilowsky et al. was restricted to patients with childhood-onset schizophrenia (29) which is generally regarded as a more severe form of the disorder. Therefore, schizophrenia patients in that study may be more impaired than the patients in the present study, which in turn may have led to more prominent deficits in ToM functioning. Similarly, in another study by Murphy et al. (7), forensic patients were enrolled and therefore the results of this study may not be valid for patients ascertained in outpatient clinics. Furthermore, the mean IQ among schizophrenia and AS groups was not comparable in that study.

Our results indicated that SANS Total score was negatively correlated with ToM functioning which is consistent with previous studies (15,18,21). When the schizophrenia patients were divided into high (Sch-HN) and low (Sch-LN) negative symptom sub-groups, it became evident that most of the ToM deficits in the schizophrenia patients might be particularly attributed to the Sch-HN patients. In fact, the patients with prominent negative symptoms had significantly lower ToM2 scores than the Sch-LN patients. Sch-HN group also had lower first order ToM functioning than the control group. While some studies reported lower performance in first order ToM tests (13,41), others did not (14,19,24,43). In details, Mazza et al. found that first order ToM performance was negatively correlated with psychomotor poverty scores, derived from the SANS (41). We showed that the Sch-HN group performed comparably poorly as the AS group, while the Sch-LN group was relatively spared. Our results may support Corcoran and Frith’s hypothesis that patients with prominent negative symptoms might have worse ToM performance and might not have developed ToM ability (44). Inspired by this hypothesis, we suggest that schizophrenia patients may somehow be similar to AS patients by means of ToM development; as a result of neurodevelopmental impairment in developing ToM ability.However, another explanation may involve that

<table>
<thead>
<tr>
<th>Table 3: The correlations of WAIS-R and clinical scores with the ToM performances in patients with AS, schizophrenia and controls (Spearman’s Rho)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>AS</strong></td>
</tr>
<tr>
<td>---------------------------------------------------------------</td>
</tr>
<tr>
<td>WAIS-R Verbal Comprehension</td>
</tr>
<tr>
<td>WAIS-R Freedom from Distractibility</td>
</tr>
<tr>
<td>WAIS-R Perceptual Organization</td>
</tr>
<tr>
<td>CGI</td>
</tr>
<tr>
<td>SANS Total</td>
</tr>
<tr>
<td>SAPS Total</td>
</tr>
</tbody>
</table>

WAIS-R: Wechsler Adult Intelligence Scale-Revised, CGI: Clinical Global Impression, SANS: Scale for the Assessment of Negative Symptoms, SAPS: Scale for the Assessment of Positive Symptoms, ToM1: first order theory of mind test, ToM2: second order theory of mind test, AS: Asperger’s Syndrome, Sch: schizophrenia, Cont: controls

*p<0.05, **p<0.01
they may have lost their ToM capacity as a result of a neurodegenerative process during the illness.

The prominent ToM deficit in patients with negative symptoms may be another reason for the discrepancy between our results and the other studies that compared patients with autism/AS and schizophrenia, since these studies did not investigate the effect of symptom dimensions on the ToM performance.

Brune have shown that the ToM performance might be associated with verbal abilities and attentional functioning measured by WAIS (45). In four sample groups, balanced for IQ, we found that the ToM1 and ToM2 performances were correlated with verbal comprehension scores in the AS and schizophrenia groups, respectively. Nevertheless ToM performance was correlated neither with general IQ nor attentional functioning. However, the Sch-HN patients had significantly lower verbal comprehension performance than the Sch-LN patients. On the other hand, schizophrenia with prominent negative symptoms generally correspond to a more ‘severe’ disorder with an earlier onset, more prominent cognitive dysfunction and a higher level of loss in social functioning. In this regard we think that severity of the ToM and verbal comprehension dysfunctions may attribute to the overall severity of the disorder.

Even the observed differences among groups were significant; the relatively small sample size is an obvious limitation of our study. The mean ToM2 score of the Sch-LN group was considerably lower than that of the control group, and with a larger sample this difference may have also reached significance. Due to the small sample size, we were also unable to investigate the effects of potentially important factors like duration of illness and treatment. Similarly, small sample size did not allow us to determine the effect of verbal comprehension and attentional functioning over ToM performance. Another limitation was the use of verbal ToM tests only. Finally, this study included male subjects and study results may not be valid for the female patients. However, AS is more prevalent among males and this was necessary for recruitment of AS patients and for a valid comparison.

In conclusion, our findings indicate that patients with AS have worse ToM performance than those with schizophrenia. However, both schizophrenia and AS patients have lower performances than healthy controls in second order ToM tasks. The most profoundly impaired patients with schizophrenia in terms of ToM functioning are represented by those with high negative symptoms (Sch-HN). Supplementary studies using other methods (i.e., neuroimaging/neurophysiology) may highlight the brain regions that are affected differentially in these groups and yield information about similarities and differences between AS and schizophrenia, the relationship of ToM impairments and negative symptoms, and the role of ToM impairments in the neurodevelopmental or neurodegenerative process of the illness. Significant differences between Sch-HN and Sch-LN patients may also have some practical implications. Since Sch-HN patients had worse ToM performance, our findings emphasize the need for more extensive psychosocial treatment and cognitive remediation programs that target schizophrenia patients particularly with predominantly negative symptoms and ToM impairments.

Acknowledgements:

The authors acknowledge the fellowship support by the Fogarty/NIH ICORTHA International Mental Health and Developmental Disabilities (MH/DD) Research Training Program at the Children’s Hospital Boston, Harvard Medical School (D43TW05807; Dr. K. Munir, PI), The Scientific and Technological Research Council of Turkey (Proje No: 105S141-HD-34) and Turkish Psychiatric Association.

References:


