

ORIGINAL PAPER

Yumiko Inoue · Kazuo Yamada · Masami Hirano · Manabu Shinohara ·
Toshio Tamaoki · Hironobu Iguchi · Yuji Tonooka · Shigenobu Kanba

Impairment of theory of mind in patients in remission following first episode of schizophrenia

Abstract The aim of this study was to investigate theory of mind (ToM) ability in patients in remission after the first episode of schizophrenia. A ToM task which contained four pictures was given to 30 patients with schizophrenia in remission and 30 matched healthy controls. Patients with schizophrenia in remission showed statistically significant impairment in the ToM tasks. ToM impairment was not correlated with psychiatric symptoms. Thus, ToM deficit in schizophrenia may be a trait marker.

Key words first episode of schizophrenia · schizophrenia · social brain · theory of mind (ToM) · state marker · trait marker

Introduction

Over the last decade, there has been increased interest in neurocognitive aspects of schizophrenia and their relationship with psychosocial outcome. “Theory of mind” (ToM) is one key aspect of social cognition. ToM is the ability to conceptualize other people’s mental states, such as their beliefs, knowledge and intentions, and hence explain and predict their behavior.

The brain regions involved in ToM are called the “so-

cial brain”, which mainly includes the orbitofrontal cortex, superior temporal gyrus, and amygdala (Brothers 1990; Dunbar 1998). Frith and Frith (1999) proposed that specific impairment of ToM abilities (ToM deficit disorders) may occur in psychiatric and neurological disorders with characteristic psychosocial impairment in a dedicated brain system. The hypothesis of ToM deficit disorders has been supported by some studies using brain imaging, and the prefrontal cortex was shown to be closely involved in ToM (Abu-Akel 2003; Vogeley et al. 2004; Abdi et al. 2004; Kitamura et al. 2005).

On the other hand, structural changes in the prefrontal cortex on brain imaging have been reported in patients with schizophrenia (Vogeley et al. 2003; Lee et al. 2004; Abdi et al. 2004; Falkai et al. 2004; Kawasaki et al. 2004).

The main conclusion of previous studies was that ToM deficit was a state marker rather than a trait marker, being closely related to clinical symptoms, although there was disagreement regarding which symptoms play the main role among paranoia (Frith et al. 1996), disorganization (Sarfati et al. 1999) and negative symptoms (Pickup et al. 2001).

The aim of this study was to investigate whether ToM deficit is present during remission after the first episode of schizophrenia, in order to further characterize the nature of ToM deficit in schizophrenia.

Methods

The subjects were 30 patients (5 male and 25 female; S-group) who met the DSM-IV criteria for schizophrenia during the first acute episode of paranoid type schizophrenia. Seventeen patients were in remission at the end of hospitalization and 13 went into remission during the clinical course some time after the first acute episode.

Patients with acute exacerbation were excluded. The severity of schizophrenia was assessed using the Brief Psychiatric Rating Scale (BPRS) (Overall and Gorham 1962). Patients with a history of neurological disorder, mental retardation, a history or presence of any serious physical disease, other serious psychiatric disorder, neurological disease, or substance abuse were excluded.

The controls were 30 healthy volunteers (C-group) matched for

Y. Inoue · K. Yamada · M. Hirano · M. Shinohara · T. Tamaoki ·
H. Iguchi · Y. Tonooka
Department of Neuropsychiatry
Graduate School of Medicine and Engineering
University of Yamanashi
1110 Shimokato, Tamaho-cho
Yamanashi 409-3898, Japan

Prof. S. Kanba (✉)
Department of Neuropsychiatry
Graduate School of Medical Sciences
Kyushu University, 3-1-1 Maidashi
Higashiku, Fukuoka 812-8582, Japan
Tel.: +81-92/642-5620
Fax: +81-92/642-5644
E-Mail: skanba@npsych.med.kyushu-u.ac.jp

sex, age, socio-economic and educational status, and who had no history or presence of psychiatric disorder or serious physical or neurological disease.

The details of assessment of IQ and the ToM tasks were described in our previous studies on ToM (Inoue et al. 2004).

Results

The baseline characteristics of the patients and controls are shown in Table 1. No statistically significant difference was found between the two groups.

In the results of ToM tasks, a significant difference was found in sequencing of the cartoon story (Fisher's exact test, $p = 0.030$). Eighty-seven percent of S-group and 97% of C-group passed the first order false belief task (Fisher's exact test, $p = 0.678$). In the second order false belief task, only 14 patients (47%) in S-group answered correctly, whereas 29 subjects (97%) in C-group passed the task, with a highly significant difference (Fisher's exact test, $p < 0.0001$). Twenty-seven patients (90%) in S-group performed well in the tactical deception task as compared to 30 (100%) in C-group (Fisher's exact test, $p = 0.23$). The sum score, which is the summed number of correct answers in sequencing, first order false belief task, second order false belief task and tactical deception, in S-group differed significantly from that in C-group ($z = -4.354$, $p < 0.0001$).

No significant correlation was observed between the ToM results and such parameters as age, sex, duration of education and IQ, in either the schizophrenia group or the control group (data not shown). No significant correlation was found between the ToM results in S-group and the duration of illness, scores of negative symptoms, positive symptoms or "suspiciousness" (data not shown).

Discussion

ToM impairment is present not only in the acute or chronic state (Herold et al. 2002; Brüne 2003) of schizophrenia, as reported previously, but also during remission after the first episode.

Most studies as summarized in the recent report by Keleman et al. (2004) suggested that ToM deficit was a state marker rather than a trait marker. On the contrary,

high risk studies on relatives of psychotic probands supported that ToM deficit is a trait marker (Pinkam et al. 2003; Janssen et al. 2003; Kee et al. 2004).

One of the reasons for this controversy could be differences in the ToM test batteries applied. Our test battery has no ceiling effect, which has been a problem with previous batteries. Another reason may be differences in the characteristics of subjects. No study has ever examined ToM ability in schizophrenic patients during recovery after the first episode.

The score of sequencing of the cartoon story in S-group was significantly lower than that in C-group in our study. No correlation was found between the sequencing task and the other ToM tasks in either the S- or C-group.

Although Brüne (2003) reported that the ability of sequencing depends on the ToM mechanism rather than executive function, Abu-Akel (2004) stated that ToM ability depends on working memory, executive function and other general cognitive abilities. Further studies combining the ToM test with other neuropsychological tests would provide more sensitive data for exploring the relationship between ToM and other cognitive abilities.

In conclusion, our results suggest that ToM deficit might be a trait marker in patients with schizophrenia. A prospective study of high risk subjects will give the final answer to this controversy.

References

1. Abdi Z, Sharma T (2004) Social cognition and its neural correlates in schizophrenia and autism. *CNS Spectrum* 9:335–343
2. Abu-Akel A (2003) A neurobiological mapping of theory. *Brain Res Rev* 43:29–40
3. Brothers L (1990) The social brain: a project for integrating primate behavior and neurophysiology in a new domain. *Concepts Neurosci* 1:27–51
4. Brüne M (2003) Theory of mind and the role of IQ in chronic disorganized schizophrenia. *Schizophr Res* 60:57–64
5. Dunbar RIM (1998) The social brain hypothesis. *Evolutionary Anthropol* 6:178–190
6. Falkai P, Tepest R, Honer WG, Dani I, Ahle G, Pfeiffer U, Vogeley K, Schulze TG, Rietschel M, Cordes J, Schonell H, Gaebel W, Kuhn KU, Maier W, Traber F, Block W, Schild HH, Schneider-Axmann T (2004) Shape changes in prefrontal, but not parieto-occipital regions: brains of schizophrenic patients come closer to a circle in coronal and sagittal view. *Psychiat Res* 132:261–271

Table 1 Baseline characteristics of patients and controls

	Schizophrenia group	Control group	Analysis
n	30	30	
Female : male	25 : 5	25 : 5	
Age (years), mean (S.D.)	27.03 (6.07)	27.93 (6.65)	$t = 0.568$, $p = 0.572$
Duration of education (years), mean (S.D.)	13.77 (1.94)	13.07 (2.08)	$t = -1.346$, $p = 0.183$
IQ, mean (S.D.)	103.07 (6.34)	102.03 (15.65)	$t = -2.54$, $p = 0.801$
Age at onset of illness (years), mean (S.D.)	23.9 (9.18)		
Duration of illness (years), mean (S.D.)	2.78 (1.57)		
Score of BPRS, mean (S.D.)	25.70 (4.63)		

7. Frith CD, Corcoran R (1996) Exploring 'theory of mind' in people with schizophrenia. *Psychol Med* 26:521–530
8. Frith CD, Frith U (1999) Interacting minds – a biological basis. *Science* 286:1692–1695
9. Herold R, Tenyi T, Lenard K, Trixler M (2002) Theory of mind deficit in people with schizophrenia during remission. *Psychol Med* 32:1125–1129
10. Inoue Y, Yamada K, Tonooka Y, Kanba S (2004) Deficiency of theory of mind in patients with remitted mood disorders. *J Affect Disord* 82:403–409
11. Janssen I, Krabbendam L, Jolles J, Os JV (2003) Alterations in theory of mind in patients with schizophrenia and non-psychotic relatives. *Acta Psychiatr Scand* 108:110–117
12. Kawasaki Y, Suzuki M, Nohara S, Hagino H, Takahashi T, Matsui Mie, Yamashita Ikiko, Chitnis XA, McGuire PK, Seto H, Kurachi M (2004) Structural brain differences in patients with schizophrenia and schizotypal disorder demonstrated by voxel-based morphometry. *Eur Arch Psychiatry Clin Neurosci* 254:406–414
13. Kee KS, Horan WP, Mintz J, Green MF (2004) Do the siblings of schizophrenia patients demonstrate affect perception deficits? *Schizophr Res* 67:87–94
14. Kelemen O, Kéri S, Must A, Benedek G, Janka Z (2004) No evidence for impaired 'theory of mind' in unaffected first-degree relatives of schizophrenia patients. *Acta Psychiatr Scand* 110:146–149
15. Kitamura H, Matuzawa H, Shioiri T, Someya T, Kwee IL, Nakada T (2005) Diffusion tensor analysis in chronic schizophrenia A preliminary study on a high-field (3.0T) system. *Eur Arch Psychiatry Clin Neurosci* (In press)
16. Lee KH, Farrow TFD, Spence SA, Woodruff PWR (2004) Social cognition brain networks and schizophrenia. *Psychol Med* 34:391–400
17. Overall JE, Gorham DR (1962) Brief Psychiatric Rating Scale. *Psychol Rep* 10:799–812
18. Pickup GJ, Frith CD (2001) Theory of mind impairments in schizophrenia: symptomatology, severity and specificity. *Psychol Med* 31:207–220
19. Pinkham AE, Penn DL, Perkins DO, Lieberman J (2003) Implications for the neural basis of social cognition for the study of schizophrenia. *Am J Psychiat* 160:815–822
20. Sarfati Y, Hardy-Baylè M-C (1999) How do people with schizophrenia explain the behaviour of others? A study of theory of mind and its relationship to thought and speech disorganization in schizophrenia. *Psychol Med* 29:613–620
21. Vogeley K, May M, Ritzl A, Falkai P, Zilles K, Fink GR (2004) Neural correlates of first-person perspective as one constituent of human self-consciousness. *J Cog Neurosci* 12:529–543
22. Vogeley K, Tepest R, Schneider-Axmann T, Hutte H, Zilles K, Honer WG, Falkai P (2003) Automated image analysis of disturbed cytoarchitecture in Brodmann area 10 in schizophrenia. *Schizophr Res* 62:133–140