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Theory of mind impairments in patients with first-episode schizophrenia and their unaffected siblings

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ABSTRACT

Background: Theory of mind (ToM) impairment has been consistently demonstrated in patients with schizophrenia, but whether ToM impairments exist in unaffected siblings of patients with schizophrenia remains unclear. Few studies have examined the affective and cognitive components of ToM in schizophrenia. This study aimed to examine whether ToM impairments exist in patients with first-episode schizophrenia and their unaffected siblings, and whether there is any dissociation between the affective and cognitive components of ToM.
Method: We adopted a family-based case-control design. Participants were 41 patients with first-episode schizophrenia, 43 unaffected siblings, and 42 healthy controls. The Yoni Task which measures the participants' ability to understand first- and second-order affective versus cognitive ToM and the *Faux Pas* Task which taps into integration of the affective and cognitive components of ToM were administered. Multivariate and univariate ANCOVAs were used to examine the group differences in ToM, while controlling for other neurocognitive functions.
Results: Compared with controls, patients with schizophrenia and their unaffected siblings performed poorer on the *Faux Pas* Task ($p < 0.001$), with siblings having intermediate performance between patients and controls. Patients with schizophrenia performed worse than controls on second-order affective condition of the Yoni Task ($p = 0.004$), but their unaffected siblings did not ($p = 0.063$). We did not find any significant Group-by-Condition interaction in the Yoni Task ($p = 0.358$).
Conclusion: Patients with first-episode schizophrenia and their unaffected siblings exhibit ToM impairments, but no dissociation between affective and cognitive component of ToM was found. Our findings support the notion that ToM deficit may be a trait marker of schizophrenia.

1. Introduction

Theory of mind (ToM) refers to the ability to judge the mental states of self and others (Premack, 1978). ToM is an important domain of social cognition and has the strongest association with community functioning, compared with other cognitive functions (Fett et al., 2011). ToM impairments have been proposed as an explanatory model for some symptoms of schizophrenia; patients with schizophrenia having impaired ToM could misidentify their own inner thoughts as originating from the external world and eventually develop false beliefs or delusions (Frith, 1992).

There are controversies as to whether ToM impairment is a state or a trait phenomenon. Although recent meta-analyses (Sprong et al., 2007; Bora et al., 2009) supported the presence of severe ToM impairments (Cohen's $d = 0.90–1.26$) in patients with schizophrenia, the majority of previous studies were conducted in patients with chronic schizophrenia. Chronicity of illness is usually associated with long-term treatment interventions which might confound previous results. Relatively few studies have focused on ToM of first-episode schizophrenia; a recent meta-analysis (Bora and Pantelis, 2013) identified only eight studies in the literature which examined ToM in patients with first-episode psychosis. Several studies (Corcoran et al., 1995; Frith and Corcoran, 1996; Drury et al, 1998; Sarfati and Hardy-Bayle, 1999; Pickup and Frith, 2001) showed that patients with schizophrenia in complete symptom remission performed normally on ToM tasks, suggesting that ToM impairment may be state-dependent. However, other studies (Herold et al., 2002; Bertrand et al., 2007; Bora et al., 2008) demonstrated that clinically-stable patients with schizophrenia in remission still exhibited significant ToM impairments, thus suggesting that ToM impairments may be state-independent. It is unclear whether ToM impairment is attributable to other neurocognitive dysfunctions in schizophrenia. One previous study (Brune, 2003) reported that ToM

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impairment in schizophrenia disappear after controlling for IQ. However, another recent study (Bozikas et al., 2011) found that patients with schizophrenia exhibit ToM impairment, even when other neurocognitive functions are controlled for, suggesting that ToM impairment may be a trait marker. The notion that ToM impairment is a trait rather than a state phenomenon is further supported by family studies that examined ToM in unaffected first-degree relatives of patients with psychosis. A recent meta-analysis (Bora and Pantelis, 2013) found considerable ToM impairment (Cohen's $d = 0.37$) in unaffected relatives of patients with psychosis. Notably, the samples of first-degree relatives in many of these family studies comprised parents and siblings of patients with schizophrenia (Janssen et al., 2003; Kelemen et al., 2004; Versmissen et al., 2008; de Achaval et al., 2010). Although the meta-analysis found no effect of age on ToM deficit in relatives, it should be noted that parents of patients with schizophrenia have used up much of their lifetime risk for schizophrenia (Gottesman, 1991) and therefore compared with siblings and offspring, they may be subtly different and their inclusion in sampling might have confounded results in previous studies.

ToM is traditionally differentiated into first- and second-order, according to the level of complexity of the ToM tasks (Baron-Cohen, 1995). "First-order" ToM refers to the ability to distinguish between one's own belief and another person's belief. The more complex, "second-order" ToM refers to the ability to infer what a person is thinking about the belief of a third person. The relationship between first- and second-order ToM is intriguing. Recent research suggests that the ToM construct could be non-hierarchical, because a minority of schizophrenia patients who were impaired in first-order ToM could competently infer others' mind in a second-order ToM task (Stratta et al., 2011). Apart from the simple differentiation of ToM into first- and second-order, recent research (Kalbe et al., 2007) has proposed that ToM can be differentiated into affective ("hot") and cognitive ("cold") components. Cognitive ToM refers to the ability to make inferences about beliefs and motivations, while affective ToM refers to the ability to infer what a person is feeling (Brothers and Ring, 1992). The cognitive component of ToM, usually assessed by false belief tasks or hinting tasks, requires a cognitive understanding of the difference between the speaker's knowledge and that of the listener (knowledge about beliefs). On the other hand, the affective component of ToM, usually assessed by the *faux pas* and the irony tasks, is supposed to require an additional "empathic appreciation" of the listener's emotional state (knowledge about emotions). Many previous ToM studies did not attend to the "hot and cold" differentiation of ToM. A few previous studies (Herold et al., 2002; Mo et al., 2008) used two different paradigms to measure cognitive and affective ToM separately, and their results suggested that schizophrenia patients were specifically impaired in affective ToM. However, the use of two separate ToM tasks which differ in their demands on other cognitive abilities might have confounded the cognitive-affective dissociation of ToM. Recently, researchers (Shamay-Tsoory et al., 2007a) have devised a novel cartoon-based ToM paradigm based on eye gaze, i.e., the Yoni Task, as a refined tool to re-examine affective-cognitive ToM dissociation in schizophrenia. The Yoni paradigm has an advantage over the use of two separate ToM tasks, because it entails three highly comparable conditions (cognitive, affective and physical).

The present study aimed to (1) explore whether ToM impairments exist in patients with first-episode schizophrenia; (2) determine whether ToM impairment is a trait phenomenon or not, by studying unaffected siblings of schizophrenia patients; (3) examine whether there is an affective-cognitive as well as first- and second-order ToM dissociation in patients with schizophrenia and their unaffected siblings using the Yoni Task (Shamay-Tsoory et al., 2007a); and (4) examine the relationship between ToM and other neurocognitive functions. We hypothesised that patients with schizophrenia would have the worst ToM performance, and unaffected siblings would have a moderately impaired ToM performance compared with healthy controls. We also hypothesised that an affective-cognitive ToM dissociation would be found in patients with schizophrenia, with patients exhibiting more severe affective rather than cognitive ToM impairment.

2. Method

2.1. Participants

We recruited 41 clinically-stable out-patients with first-episode schizophrenia from an early psychosis intervention clinic in Hong Kong. The diagnosis was ascertained by the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I) (First et al., 1996). The exclusion criteria were: (1) co-morbid DSM-IV Axis I disorder; (2) life-time history of any DSM-IV disorder apart from schizophrenia; (2) mental retardation; (3) severe hearing or visual impairment; (4) history of head injury or neurological disorders; (5) history of receiving electroconvulsive therapy in the past six months; and (6) lifetime history of alcohol and substance abuse. We also recruited 43 first-degree siblings of the participating patients using the same exclusion criteria, except that siblings who had any lifetime history of psychotic disorder were also excluded. Forty-two healthy controls, biologically unrelated to the participating patients and siblings, were recruited from the neighbouring community, using the same exclusion criteria for the patients and the siblings, except that none of the controls had any lifetime or family history of psychiatric disorder. The siblings and the healthy participants were assessed by the SCID-I, administered by qualified psychiatrists, to ensure that they did not have any current or past history of psychiatric disorder. In the SCID-I interview, two siblings who did not meet the eligibility criteria because of depression and anxiety disorder were excluded. This study was approved by the local Ethics Committee.

Socio-demographic, clinical variables, and medication dosage in terms of chlorpromazine equivalent (Gardner et al., 2010) were gathered from medical records. Symptom severity was assessed using the Scale for the Assessment of Positive Symptoms (SAPS; Andreasen, 1984b) and the Scale for the Assessment of Negative Symptoms (SANS; Andreasen, 1984a). Intellectual functioning was estimated using a pro-rating method based on the arithmetic, similarities and digit span subscales of the Chinese version of the Wechsler Adult Intelligence Scale-Revised (Gong, 1992).

2.2. Assessments of theory of mind

The Chinese version of the computerised Yoni Task (Shamay-Tsoory et al., 2007a) was used to assess participants' ToM abilities. The Yoni Task assesses the participants' ability to judge others' mental states based on eye gaze and verbal cues. Fig. 1 shows the Yoni Task paradigm. It employs cartoon images and consists of first- and second-order mental state inferences. It comprises 64 trials, each showing the cartoon face of "Yoni" in the middle of the screen, and four coloured objects belonging to a single semantic category (e.g., fruits, chairs) or cartoon faces, one in each corner of the computer screen. Participants were asked to identify what "Yoni" was referring to, based on cues including verbal cues, eye gaze, and facial expression shown on the screen. The number of correct responses was recorded. The 64 trials were divided into three conditions: 24 trials of affective, 24 cognitive and 16 physical conditions. The cues in the affective conditions carried emotional salience, whereas the cues in the cognitive conditions were emotionally neutral. The cognitive and affective conditions involved mental inferences, while the physical condition only served as a control condition to measure the baseline performance for which no mentalising was involved. The accuracy of ToM performance in the Yoni task was calculated, with a score of 1 indicating complete accuracy.

The *Faux Pas* Task was derived from the '*Faux Pas* Recognition test' (Stone et al., 1998). *Faux pas* means "false step" and refers to a scenario in which a speaker said something he or she should not have said, while

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