Theory of mind impairment and its clinical correlates in patients with schizophrenia, major depressive disorder and bipolar disorder

Yan-yu Wang [a,b,c], Yi Wang [a,*], Ying-min Zou [a,c], Ke Ni [a,c,d], Xue Tian [b], Hong-wei Sun [b], Simon S.Y. Lui [a,e], Eric F.C. Cheung [e], John Suckling [f], Raymond C.K. Chan [a,c,*]

[a] Neuropsychology and Applied Cognitive Neuroscience Laboratory, CAS Key Laboratory of Mental Health, Institute of Psychology, Beijing 100101, China
[b] Department of Psychology, Weifang Medical University, Shandong 261053, China
[c] Department of Psychology, University of Chinese Academy of Sciences, Beijing 100048, China
[d] Mental Health Center of Qiqihar city, Heilongjiang 161006, China
[e] Castle Peak Hospital, Hong Kong Special Administrative Region, China
[f] Department of Psychiatry, University of Cambridge and Cambridgeshire and Peterborough NHS Trust, Cambridge CB2 0SZ, United Kingdom

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ABSTRACT

Background: Although Theory of Mind (ToM) impairment has been observed in patients with a wide range of mental disorders, the similarity and uniqueness of these deficits across diagnostic groups has not been thoroughly investigated.

Methods: We recruited 35 participants with schizophrenia (SCZ), 35 with bipolar disorder (BD), 35 with major depressive disorder (MDD), and 35 healthy controls in this study. All participants were matched in age, gender proportion and IQ estimates. The Yoni task, capturing both the cognitive and affective components of ToM at the first- and second-order level was administered. Repeated-measure ANOVA and MANOVA were conducted to compare the group differences in ToM performance. A network was then constructed with ToM performances, psychotic and depressive symptoms, and executive function as nodes exploring the clinical correlates of ToM.

Results: Overall, ToM impairments were observed in all patient groups compared with healthy controls, with patients with SCZ performing worse than those with BD. In second-order conditions, patients with SCZ and MDD showed deficits in both cognitive and affective conditions, while patients with BD performed significantly poorer in cognitive conditions. Network analysis showed that second-order affective ToM performance was associated with psychotic and depressive symptoms as well as executive dysfunction, while second-order affective ToM performance and negative symptoms showed relatively high centrality in the network.

Conclusions: Patients with SCZ, MDD and BD exhibited different types and severity of impairments in ToM subcomponents. Impairment in higher-order affective ToM appears to be closely related to clinical symptoms in both psychotic and affective disorders.

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1. Introduction

Theory of mind (ToM), one of the key aspects of social cognition, refers to the ability to infer others' aims, beliefs, intentions and emotional states (Premack and Woodruff, 1978; Schaafsma et al., 2015). ToM impairment has been reported in patients with mental disorders, such as schizophrenia (SCZ), bipolar disorder (BD) and major depressive disorder (MDD). In patients with SCZ, ToM impairments have been reported in both first-episode (Bora and Pantelis, 2013; Ho et al., 2015) and chronic phases (Bora et al., 2009a). Moreover, recent studies have also found these impairments in non-psychotic first-degree relatives of patients with SCZ and individuals with ultra-high risk for psychosis (Bora and Pantelis, 2013), suggesting that ToM impairments may be a trait marker of SCZ. Furthermore, meta-analytic studies have also found a large effect size for deficits in ToM performance in patients with BD, especially in acute episodes ($d = 1.23$) (Bora et al., 2016a) and a moderate ToM deficit in patients with MDD ($d = 0.51$–0.58) (Bora and Berk, 2016).

Although many previous studies on ToM have been carried out in each of the diagnostic groups mentioned above, it is still not clear whether patients with SCZ, BD and MDD share similar or distinct ToM impairments. Of the few studies directly comparing ToM performance across diagnostic groups, most were limited to a comparison between two groups. For example, Purcell et al. (2013) found comparable ToM impairments between remitted BD and MDD patients, while a number of other studies did not find significant ToM impairment in MDD

patients (Bazin et al., 2009; Berecz et al., 2016; Mellick and Sharp, 2016; Wilbertz et al., 2010). Some studies have even reported better ToM performance in depressed adolescent boys (Mellick and Sharp, 2016) and women with a maternal history of depression (Harkness et al., 2011). Similarly, previous studies comparing ToM performance in SCZ with BD patients suggested that SCZ patients might be more impaired in ToM than BD patients (Caletti et al., 2013; Guastella et al., 2013; Lahera et al., 2015), while some studies reported similar extent of ToM impairment in these two groups of patients (Donohoe et al., 2012; Thaler et al., 2013).

One possible explanation for the inconsistent findings may be the use of different tasks for ToM assessment. Recent studies have suggested that there are dissociable cognitive and affective components of ToM, with the cognitive component of ToM focusing on the inferences of others' beliefs, while the affective component of ToM refers to the inferences of others' feelings (Shamay-Tsoory and Aharon-Peretz, 2007; Shamay-Tsoory et al., 2007). Shamay-Tsoory et al. (2007) found that first-episode patients with SCZ performed significantly worse in affective ToM, but not cognitive ToM. Donohoe et al. (2012) found that BD patients presented comparable deficits with SCZ patients on the "Reading the Mind in the Eyes Task" (an affective ToM task), but only subtle deficits compared with SCZ patients on the "Hinting Task" (a cognitive ToM task). These findings suggest that patients with SCZ and BD may be similarly impaired in affective ToM while patients with BD may be less impaired in cognitive ToM.

ToM impairment has been widely observed in patients with first-episode and chronic schizophrenia, as well as individuals at ultra-high risk for psychosis and first-degree relatives of SCZ and BD patients (Bora, 2009; Bora and Pantelis, 2012, 2013; Bora et al., 2009a), and is thus considered to have trait properties. However, some other studies have found significant relationships between ToM impairment and clinical symptoms and cognitive functions (Bora et al., 2016a; Bora et al., 2009b). Mitchell and Young (2015) proposed that the relationship between ToM impairments and positive psychotic symptoms may not be disease-specific, but symptom-specific. Marjoram et al. (2005) examined ToM abilities in patients with SCZ and affective disorders and found that hallucinations and delusions were associated with ToM impairment, regardless of diagnosis. Bora et al. (2009b) reviewed ToM studies in SCZ spectrum disorders, affective psychosis and BD and suggested that ToM impairment may reflect executive dysfunction and residual symptom expression rather than a specific trait-marker.

It is well known that comorbid clinical symptoms exist in different mental disorders, and about 45% of people who meet diagnostic criteria of one mental disorder also receive another diagnosis (Kessler et al., 2005). It has also been reported that 18.6% of patients with MDD experience hallucinations and/or delusions (Ohayon and Schatzberg, 2002), while negative symptoms may also be stable trait-like features of illness that persist into periods where BD patients are free from mood episodes (Strauss et al., 2016). In addition, the association between positive and negative psychotic symptoms, affective symptoms and cognitive symptoms is complex. According to the framework of Research Domain Criteria (RDoC) (Insel et al., 2010), trans-diagnostic study designs may improve the identification of shared and unique biological mechanisms, thus promoting the development of improved prevention and treatment strategies. Although previous studies have partially investigated the relationship between clinical symptoms and cognitive functions and ToM impairments in different disorders using meta-analysis (Bora et al., 2016a; Bora and Berk, 2016; Bora et al., 2009b), traditional correlation analysis is unable to take into account all the symptom dimensions in examining the correlations between ToM performance and symptomatology. Recently, researchers have proposed a network perspective in understanding the psychopathology of mental disorders (Borsboom, 2017; Cramer et al., 2010). The network analysis approach, which considers the disorders in question as a system of casually connected symptoms rather than latent variables, has recently been applied in studies in psychiatry and psychology to examine the relationships between symptoms (Borsboom and Cramer, 2013). Using this approach, a network based on partial correlations between symptoms and/or clinical manifestations is constructed to assess the independent associations while controlling for other variables.

In this study, we used the Yoni Task, an instrument specifically designed to capture the cognitive and affective components of ToM, to compare the ToM performance of well-matched patients with SCZ, BD and MDD. We then adopted network analysis to examine the independent associations between clinical symptoms, ToM performance and executive function in these patients. We hypothesized that patients with SCZ, BD and MDD would exhibit significant ToM impairments compared with healthy controls; and among the three patient groups, patients with SCZ would show the greatest ToM impairment. We also hypothesized that ToM performance in these patients would be correlated with psychotic symptoms, depressive symptoms and executive function regardless of diagnosis.

2. Method

2.1. Participants

Based on the reported effect sizes (effect size = 0.60) from previous studies comparing ToM performance between patients with psychosis and healthy controls (Bora, 2009; Bora et al., 2016a; Bora and Berk, 2016), we calculated a sample size of 36 in each comparison group using G*power 3.1 software (Faul et al., 2007) at a statistical power of 0.8 and type I error rate of 0.05. Based on this estimation, 35 participants in each group who were well matched in age ($F = 1.860$, $p = 0.139$), gender proportion ($\chi^2 = 0.320$, $p = 0.956$) and IQ estimates ($F = 0.659$, $p = 0.578$) were recruited. The patient groups were recruited from either the Mental Health Center of Qiqihar City or the Mental Health Center of Weifang City. All of them fulfilled the DSM-IV (APA, 1994) diagnostic criteria for SCZ, MDD, and BD respectively. All patients were clinically stable with treatment. Their diagnoses were ascertained using the Mini-International Neuropsychiatric Interview (MINI) version 6.0.0 (Sheehan et al., 2009). Exclusion criteria of each diagnostic group were: a co-morbid DSM-IV Axis I disorder; a history of head injury or neurological disorder; a lifetime history of alcohol and substance abuse; severe hearing or visual impairment; and an IQ < 80 measured by the Chinese version of the Wechsler Adult Intelligence Scale-Revised (WAIS-R) (Gong, 1992). Healthy individuals were recruited from the community as controls. They were screened by a qualified psychiatrist using the MINI to ascertain the absence of lifetime or family history of mental disorders. Exclusion criteria for controls included a history of substance abuse in the past 12 months, a history of neurological disorders, a history of head injury with loss of consciousness for more than 30 min, and learning difficulties.

This study was approved by the Ethics Committees of the Institute of Psychology, Chinese Academy of Sciences, the Mental Health Center of Qiqihar City, and the Mental Health Center of Weifang City. All participants gave written informed consent.

2.2. Assessment

2.2.1. Assessment of ToM

The Chinese version of the computerized Yoni Task (Ho et al., 2015; Shamay-Tsoory et al., 2007) was used to assess affective and cognitive ToM. In total, there were 98 trials, including 32 for first-order ToM and 66 for second-order ToM assessment in the task. During each trial, a cartoon face of "Yoni" (Chinese name Xiaoming) was shown in the middle and four objects belonging to a single semantic category or faces were shown at the four corners. Participants were required to infer which one Xiaoming was referring to according to its eye gaze and facial expression. According to the content of inferences, there were three conditions: cognitive, affective and physical condition. In the first-order cognitive and affective conditions, participants were