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Progressive decline of cognition during the conversion from prodrome to psychosis with a characteristic pattern of the theory of mind compensated by neurocognition

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ABSTRACT

The association between neurocognition and the theory of mind (ToM) abilities during the progression of psychosis is unclear. This study included 83 individuals with attenuated psychosis syndrome (APS), from which 26 converted to psychosis (converters) after a follow up period of 18 months. Comprehensive cognitive tests (including MATRICS Consensus Cognitive Battery, Faux-Pas Task, and Reading-Mind-in-Eyes Tasks) were administered at baseline. A structural equation modeling (SEM) analysis was conducted to estimate the effects of neurocognition on the ToM functioning in both APS and healthy controls (HC) datasets. At baseline, the converters and non-converters groups differed significantly on several domains of cognitive performance. The SEM analysis demonstrated that the path from neurocognition to ToM was statistically significant in the APS dataset ($p < 0.001$). However, in the HC dataset, the result of the same analysis was not significant ($p = 0.117$). Positive correlations between neurocognition and ToM were observed, and the most obvious correlations were found in the converters group compared with the non-converters group ($p = 0.064$) and compared with the HC group ($p = 0.002$). The correlation between ToM abilities and neurocognition may be increased during the progression of the condition, especially for individuals who convert to psychosis after a short period.

1. Introduction

Both the theory of mind (ToM, a subdomain of social cognition (Green et al., 2008)) and neurocognition impairments are the hallmarks of psychosis, and have been commonly observed in studies involving patients with schizophrenia. They have similar emphases in many domains related with psychosis. Extensive studies have linked cognitive deficits with patients' poor social functioning and psychological deficits (symptoms of negativity and passivity and behavioral signs, for example) (Lincoln et al., 2011; Mehta et al., 2014). Thus, it is not surprising that results of recent researches increased the interest in the interaction between the ToM and neurocognition, rather than only focus on a single domain of cognition. Consensus has been reached that social cognition is related to neurocognition, and the combination of both domains contributes to the outcome of post-onset psychosis. The pathways that link neurocognition, social cognition, and functional outcomes in psychotic disorders have become increasingly clear (Green et al., 2012; Schmidt et al., 2011). A large body of studies provides evidence for a mediation role of social cognition in psychosis and functional disabilities (Francesconi et al., 2016; Ventura et al., 2015).

However, it remains unclear whether there is a similar pathway between social cognition and neurocognition contributing to the onset of psychosis. Deficits of the ToM in the prodromal phase of psychosis have been extensively studied and the results are fairly consistent. Most of the research reported that the performances of ToM in at risk populations were intermediate between patients with full psychosis and healthy controls (Bora and Pantelis, 2013; Kim et al., 2011; Thompson et al., 2012). Some studies found significant differences in pairwise comparisons (Eack et al., 2010; Piskulic et al., 2016; Zhang et al., 2016b; Zhang et al., 2016c), whereas others did not (Pinkham et al., 2007; Stanford et al., 2011). The fact that the contribution of ToM

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to the onset of psychosis is a complex model rather than a one-way direction link. Our recent findings suggest that the combined index of neurocognition and ToM domains for attenuated psychosis syndrome (APS) individuals may be more effective in predicting the psychotic outcomes compared with a single cognitive domain (Zhang et al., 2016a). In other words, neurocognition and ToM should be considered together in order to understand the process of the psychotic onset, especially for their interactive patterns.

The aim of our current study was to explore the performances and relationships between the ToM and neurocognition in a cohort sample with APS at baseline. The baseline performances of a wide range of neurocognitive and ToM tasks were compared in patients who converted to psychosis within 18-month and non-converters. We predicted that the relationship between ToM and neurocognition will be increased in an APS sample compared with matched healthy controls, which would be more pronounced for converters who developed into psychosis.

2. Methods and materials

2.1. Subjects and procedures

The Research Ethics Committee of the Shanghai Mental Health Center approved this study in 2012. The study was conducted following the tenets of the Helsinki Declaration. The APS subjects were recruited from the Shanghai Psychotherapy and Psychological Counseling Center who were visiting the mental health service for the first time. The whole dataset analyzed in this study comprised 83 APS subjects and 90 healthy controls (HC) who completed both cognitive tests and at least 1 year of follow-up procedure. All participants gave written informed consent at the recruitment stage of the study. The subjects younger than 18 years of age had their consent forms signed by their parents. The APS subjects were identified by a structured face-to-face interview by the SIPS/SOPS (Structured Interview for Prodromal Symptoms/Scale of Prodromal Syndromes) (Miller et al., 2003). The exclusion criteria used were as follows: a history of severe somatic disease, substance abuse, dementia, or other cognitive deficits unrelated to psychosis. APS subjects were confirmed by using a face-to-face interview (also based on SIPS/SOPS), and followed up for 1 year. The APS group was divided into converters and non-converters groups according to the results of the follow-up. The HC group was recruited from the local school and community through an advertisement placed on the internet. The recruited subjects had negative neurological and psychiatric history. They were interviewed by the SIPS/SOPS to rule out any psychotic experiences. Their demographic background (e.g. age, gender, marital status, and years of education) were closely matched to the APS group.

The primary outcome measure is the conversion to psychosis, as determined using the criteria of POPS (Presence of Psychotic Symptoms in SIPS/SOPS) (McGlashan et al., 2010). At least one psychotic level symptom (rated a “6” on at least one of the five positive symptoms) was required for fulfilling the POPS criteria, with either sufficient frequency and duration or at a level that was disorganizing or dangerous. The follow-up assessments took place 18 months after the baseline. Following confirmation of conversion in SIPS, the diagnostic category of transition was determined by applying DSM-IV (Diagnostic and statistical manual of mental disorder-IV) criteria for psychotic disorders and affective disorders with psychotic features.

2.2. Assessment

The APS subjects were assessed at entry and follow-up based on SIPS/SOPS. The SIPS criteria for APS emphasize onset or worsening in the past 1 year of at least one of the five positive symptoms (scales P1–P5: Unusual Thought Content, Suspiciousness, Grandiosity, Perceptual Abnormalities, and Disorganized Communication). A range of other potentially prodromal phenomena (negative, disorganized, and general symptoms) for description of APS clinical features was also included in the assessment. Symptoms were rated on a 0–6 scale, with scores of 3–5 in positive symptoms indicating attenuate psychotic symptoms. A senior psychiatrist who certified on SIPS at Yale University-sponsored SIPS/SOPS training was employed for conducting this assessment. The Chinese version of the SIPS/SOPS (Version 5) was translated by our team and tested for its reliability and validity on a Chinese clinical population (Zhang et al., 2014; Zheng et al., 2012).

The Chinese version of the MATRICS Consensus Cognitive Battery (MCCB) (Shi et al., 2013), based on the original version of the MCCB (Kern et al., 2008; Nuechterlein et al., 2008), was used for neurocognition assessment following the standardized guidelines of the manual. It covers seven domains: speed of processing (the Part A of Trail Making Test, the Symbol Coding of the Brief Assessment of Cognition in Schizophrenia and the Category Fluency Test), attention/vigilance (the Continuous Performance Test-Identical Pairs), working memory (The spatial span of the Wechsler Memory Scale-III), verbal learning (the Revised Hopkins Verbal Learning Test), visual learning (the Revised Brief Visuospatial Memory Test), reasoning and problem solving (the Neuropsychological Assessment Battery: Mazes), and social cognition (the Mayer–Salovey–Caruso Emotional Intelligence Test, MSCEIT). Due to the MCCB used here for assessing the neurocognition, the MSCEIT test, which was designed for social cognition, was not included. A composite T-score was generated using the MCCB computer program, which converts the raw scores to T-scores representing the overall neurocognitive performance. Age- and sex-corrected Chinese norms were used according to the guidelines outlined in the Chinese version of MCCB manual.

The ToM battery included two types of subtests: Reading the Mind in the Eyes Test (RMET) and Faux Pas (FP) test. A computer program based on E-prime 2.0 software integrating RMET and FP tests was developed to standardize the ToM assessments procedure. The RMET consists of 70 items, 36 items from the English version (Baron-Cohen et al., 2001) and 34 from the Chinese version (Wang et al., 2008). For each item, the subject sees a photograph of the eye region. Subjects are asked to select one of four words that most appropriately describes what the person in the photograph might be thinking or feeling, with one correct and three foils. The FP task (Baron-Cohen et al., 1999) consists of 20 verbal stories, including 10 with a social FP and 10 without. It requires subjects to identify whether someone in a variety of social situations had said something wrong or had upset others. We complemented these tests for covering the different aspects of ToM (Sabbagh, 2004), which are the ability of perception and reasoning of others' mind. The summation of percentage correct responses was automatically calculated by the program to obtain a composite ToM score.

2.3. Data analysis

SPSS version 16.0 (SPSS, Inc., Chicago, IL, USA) was used for data analysis. Explorations of all the variables by normality tests guided our choice of statistical tests. The sample was divided into three groups, namely the converter, non-converter, and HC group. Demographic details were analyzed to determine any significant group differences of baseline features between converters and non-converters. Parametric data were compared using independent sample *t*-tests, and discrete variables were compared using chi-squared test. Then, one-way ANOVA was performed to determine significant differences of cognitive performances among the three groups. We used SPSS and Analysis of Moment Structures (AMOS) version 20 to test our hypotheses. A Structural Equation Modeling (SEM) analysis was conducted to estimate the effects of neurocognition on ToM performance in 2 datasets (the APS and HC groups). The initial model parameters and coefficients generated the following: the chi-square (>0.5), the Goodness-of-Fit Index (GFI) (≥0.95), the Adjusted Goodness-of-Fit Index (AGFI) (≥0.90), and the Root Mean Square Error of Approximation (RMSEA) (≤0.8) (Al-Turkait and Ohaeri, 2010).

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