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Screening schizotypal personality disorder for detection of clinical high risk of psychosis in Chinese mental health services

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ABSTRACT

Schizotypal personality disorder (SPD) is viewed as a marker of prodromal psychosis. However, information regarding genetic risk (e.g. SPD) is often overlooked in the identification process. This study assessed whether SPD screening questionnaire help the prodromal psychosis (also widely applied "clinical high risk" (CHR) for clinical sample) detection in Chinese mental health service. This work also examined whether SPD had higher frequency in genetic risk population and CHR subjects. Two wave studies concerning the SPD identification was used for analysis. Wave 1 survey: 3075 subjects were assessed by Personality Diagnostic Questionnaire for SPD (PDQ-SPD) and Structured Clinical Interview for DSM-IV Axis II (SCID-II). Wave 2 survey: 2113 subjects screened with the prodromal questionnaire -brief version (PQ-B), PDQ-SPD, and interviewed by Structured Interview for Prodromal Symptoms (SIPS). Subjects with family history of mental disorders or with psychosis reported significantly higher scores in SPD. Receiver operating characteristic curves suggested that PDQ-SPD had moderate sensitivity and specificity for identifying CHR subjects. There was significant higher on SPD features in subjects with early stage (Course less than 1 year) of psychosis. Identifying SPD may be useful in early detection of psychosis especially in detecting the genetic risk syndromes and can be integrated with existing prodromal screen tools to improve its efficiency.

1. Introduction

Many advances have been made in understanding the relationship between schizotypal personality disorder (SPD) and schizophrenia (Erlenmeyer-Kimling et al., 1995; Fanous et al., 2007; Margetic et al., 2009; Tarbox and Pogue-Geile, 2011). Research has demonstrated that SPD is more prevalent in biological relatives of patients with schizophrenia (Appels et al., 2004; Fogelson et al., 1999; Joober et al., 2005). Twin studies have suggested moderate heritability (Kendler et al., 2007; Torgersen et al., 2000) and a genetic correlation has been found using gene linkage analysis (Ohi et al., 2012). The recent literature also suggests that individuals with SPD have similar impairments to those with schizophrenia in emotional expression (Cohen et al., 2012; Shi et al., 2012), interpersonal patterns (Kendler et al., 1995; Waldeck and Miller, 2000), and cognitive function (Cochrane et al., 2012; Noguchi et al., 2008). In addition, they demonstrate abnormalities with regard to phenomenological and neurobiological characteristics(McClure et al., 2013), but to a lesser degree. These finding suggest that at least some traits associated with SPD have a genetic or familial association with schizophrenia and belong to the spectrum of psychotic disorders (Tarbox and Pogue-Geile, 2011).

Evidence of the close relationship between SPD and psychosis suggests that SPD might be a marker of prodromal psychosis (e.g., genetic risk and deterioration syndrome, GRDS) (Miller et al., 2003). Prodromal psychosis is defined as a sub-threshold clinical presentation of psychosis with a high risk of developing a psychotic disorder in the next several years (Tandon et al., 2012). With the introduction of diagnostic interview tools for CHR in Chinese psychiatric practice, including the Structured Interview for Prodromal Symptoms (SIPS) and Scale of Prodromal Symptoms (SOPS) (Miller et al., 2002), Chinese clinicians have begun to identify CHR subjects. However, due to the limited clinical referral systems in China (Du et al., 2012), very few CHR subjects could be included in research programs by referral method. Therefore, a two-stage screening process combining the self-reported questionnaire and structured interview may result in a highly efficient recruitment method.

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Currently, there are several widely used screening tools (Ising et al., 2012; Kobayashi et al., 2008; Muller et al., 2010) in prodromal psychosis research and most are focused on attenuated positive symptoms (e.g., unusual thought content and abnormal perception). However, information regarding genetic risk (e.g. SPD) is often overlooked in the screening process. SPD has been identified for more than 10 years in China since CCMD-3 (Chinese Classification and Diagnostic Criteria of Mental Disorders, 3rd edition) was published in 2001. Although not widely found in practice, SPD is generally acceptable as a schizophrenic spectrum disorder with a genetic etiology by Chinese psychiatrists. Our previous survey (sample set 2006) (Zhang et al., 2012c) found a 2.8% (95% CI 2.2–3.4%) prevalence rate for DSM-IV SPD in outpatients of mental health service in China, but none of these patients had been diagnosed with CCMD-3 SPD. Consequently, integrating genetic risk inquiry questions to probe for psychotic family history and questions related to SPD into screening questionnaires for CHR detection is important and deserves attention.

Therefore, two questions remain open: first, does SPD screening questionnaire help the CHR detection? Second, does SPD have higher frequency in genetic risk population and CHR subjects in clinical setting? In light of this, We had done the present paper utilizes two large-scale surveys of Chinese patients seeking mental health services to examine differences between family history, clinical diagnosis, and the course of psychosis in sub-groups of individuals with SPD. We also examine the value of using SPD questionnaires in clinical practice to assist in early identification of psychosis.

2. Methods

2.1. Informed consents

The Wave 1 study was approved for investigating the DSM-IV PD among Chinese population by the Research Ethics Committee at the Shanghai Mental Health Centre in 2006. Then, the same research ethics committee approved the Wave 2 study for identification of subjects with clinical high risk of psychosis in 2011. All participants in the two wave studies were given detailed explanation about the study, including a plain language statement written in their native language. Oral informed consents were obtained in the screening stage, and written informed consent was obtained before recruited for the interview. Only participants of the clinic who were judged to be fully competent to give informed consent for participation were included. When a potential participant is under 18 years old, we approached his/her family member to discuss the participation of the survey. In that case, written informed consent should be obtained from both the adolescent and family member. Participation could be withdrawn at any time, and non-participation in the research would no way affect the clinical care.

2.2. Procedure

Wave 1 survey (Fig. 1): the epidemiological survey of personality disorder (PD) was conducted at the Shanghai Mental Health Center in 2006. As detailed in previous papers (Zhang et al., 2012a, 2012b, 2012c, 2013) invitation letters were issued to outpatients using a systematic sampling method (i.e., select every 10th in psychotherapy and 20th in psychiatric clinics). The Personality Diagnostic Questionnaire Fourth Edition Plus (PDQ-4+) was used as screening tool for PD assessment, which included subscales of PDQ-SPD questionnaires. Those individuals whose PDQ-4+ test results were positive (total score higher than 28 or specific PD subscale scores higher than 4 or 5 according to DSM-IV specific PD criteria) entered the second stage of the Structured Clinical Interview for DSM-IV Axis II (SCID-II).

Wave 2 survey (Fig. 1): from March to September 2011, 2101 participants were consecutively screened for early identification of psychosis (Zhang et al., 2014). Several senior nurses with at least 10 years of experience in psychiatry administered the screening tests. Participants were fully informed that they were invited to join a clinical survey for identification of CHR. After participants and/or their guardians provided oral consent to join the survey, they were taken to a quiet room to complete PQ-B and PDQ-SPD (The 9 items of the PDQ-SPD are presented in the Appendix). Participants whose PQ-B total scores were greater than 3 and PQ-B distress scores were greater than 6, and/or had one or more first-degree relatives with affective or non-affective psychosis were referred for the SIPS/SOPS interviews.

2.3. Participants

Participants were recruited from the Shanghai Mental Health Center (SMHC), the largest mental health service setting in China. The Wave 1 survey included a representative sample of 3075 outpatients in 2006 and described in detail elsewhere (Zhang et al., 2012c), but are briefly reviewed here (In Fig. 1 below, we have included a sample flow chart showing enrollment of 850 outpatients with SZ). The sample of Wave 2 survey (Fig. 1) included 2113 participants enrolled in a CHR investigation conducted from March to September 2011. The 2113 participants recruited for the CHR identification study consisted of 2101 participants screened at their first clinic visit. An additional 12 outpatients, thought to be in the prodromal stage of psychosis, were referred by clinicians. After the interview of SIPS/SOPS, 91 subjects were identified as the clinical high risk for psychosis. Among them, 89 CHR subjects were from the screening method and only two were included by the referral method. Of the 91 CHR participants, 64 met criteria for APSS (attenuated positive symptom syndrome), 21 with GRDS, 2 with BIPS (brief intermittent psychotic syndrome), 3 met criteria for GRDS and APSS, and 1 met criteria for GRDS and BIPS.

Those participants from Wave 2 survey in the group with high-risk family history had at least one first-degree relative with psychosis, consistent with the genetic risk definition of CHR. Accordingly, low-risk family history was defined as having any family members with mental disorders or a first-degree relative with non-psychotic disorders. The control group included 366 participants who screened negatively on the Prodromal Questionnaire-Brief (PQ-B) and had no family history of mental illness. There were no differences among the 3 groups in age. However, the low-risk family history group had significantly more females and participants with non-psychotic disorders. To the grouping method for clinical feature in Wave 2 survey, we divided the sample into five subgroups based on diagnosis from the SIPS/SOPS interview and their clinical medical records.

2.4. Measures

2.4.1. Assessment of CHR

The PQ-B (Loewy et al., 2011) is a self-report questionnaire that identifies patients at high risk for psychosis. Compared to its prototype (the Prodromal Questionnaire (PQ) (Loewy et al., 2005)), the PQ-B only includes 21 items and focuses largely on positive symptoms. Participants are asked to rate prodromal or psychotic symptoms that have occurred in the past month by responding with "Yes/No." If participants respond "Yes," they are asked to rate the level of distress this symptom has caused on a scale from 1 to 5. The English version had been shown to have relatively high sensitivity (89%) and moderate specificity (58%) as a clinical screening tool. Our team developed the Chinese version of the PQ-B, using a rigorous translation process, and conducted a preliminary examination of its reliability and validity in a Chinese clinical population. In the current study, we employed the cut off score (a total score of 3 or more, a distress score of 6 or more) according to the paper by the authors of PQ-B. However, our results showed that the Chinese version of the PQ-B showed poor specificity in this sample, but that likely has something to do with the cut off point. We re-analyzed the data for more reasonable cut off score found that the higher cutoff point of PQ-B such as a total score of 6 or more or a distress score of 24 or more, the screening methods may be more effective and reasonable. (The PQ-B total score cutoff point of 6 for diagnosis of CHR yielded a sensitivity of 86.8% and a specificity of 47.6%. The PQ-B distress score cutoff point of 24 for diagnosis of CHR yielded a sensitivity of 83.8% and a specificity of 60.9%)

The SIPS and SOPS (Miller et al., 2003) are well-validated structured diagnostic interviews that assess CHR. The SOPS is organized into four domains: positive symptoms, negative symptoms, general symptoms, and disorganized symptoms. The CHR participants have one or more of the three psychosis-risk syndromes: BIPS, APSS, and GRDS. To meet APSS criteria, participants need to receive a rating of level "3", "4", or "5" on the positive symptoms scale of the SOPS. To meet BIPS criteria, participants need to receive a rating of "6", which suggests a diagnosis of psychosis. Additionally, criteria for sufficient frequency and duration of symptoms must be met. In addition, GRDS is defined as having one or more first-degree relatives with an affective or non-affective psychotic disorder and/or meeting the DSM-IV SPD criteria and having a 30% or greater drop in the Global Assessment of Functioning (GAF) score in the previous 12 months. The validity and reliability of the Chinese version of the SIPS/SOPS has been translated and examined by our team show good inter-rater reliability ($r=0.96$, $p<0.01$ on the SOPS score). The Cronbach's α for all SOPS items was 0.71, and the total SOPS score correlated significantly with the Chinese PANSS total score ($r=0.63$, $p<0.01$) (Zhang et al., 2014).

2.4.2. Assessment of personality disorders

The Chinese version of PDQ-4+ (Yang et al., 2002) and SCID-II (Dai et al., 2006) were used to assess for PD. Both instruments use DSM-IV PD criteria. The PDQ-4+ is a self-report questionnaire with relatively high sensitivity (89%) and moderate specificity (65%). It contents 12 subscales corresponding to the 12 Axis II DSM-IV PDs. Estimates of reliability and validity for the PDQ-4+ in the Chinese population were well within an acceptable level (the reliability of 12 subscales and total score are between 0.5 and 0.80, the Cronbach's α is between 0.55 and 0.78). In this paper,

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