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A comparison of conversion rates, clinical profiles and predictors of outcomes in two independent samples of individuals at clinical high risk for psychosis in China

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ABSTRACT

Objective: In a previous epidemiological study, we reported on the ascertainment and outcomes of "clinical high risk" (CHR) individuals at the Shanghai Mental Health Center (SMHC, "2011 cohort"). The current study compares demographic and clinical characteristics, including conversion rates, of this sample with a subsequently recruited, independent CHR sample and with published data from western samples.
Method: A new sample of 100 CHR subjects ("2013 cohort") was selected based on screening and semi-structured interviews. Both studies used the Structured Interview for Prodromal Syndromes (SIPS) for CHR assessment and conducted a naturalistic two-year follow-up. The two cohorts were compared on conversion rates, demographic and clinical characteristics, psychosis risk symptoms, and risk factors for psychotic conversion.
Results: Ninety one (91%) of the 2013 cohort subjects completed the clinical two-year follow-up and 25 (27.5% of the 91) converted to a psychotic disorder over the follow-up period. A comparison of conversions to full psychosis between the 2013 and the 2011 cohorts showed no significant difference in time to conversion (Pairwise comparison: $\chi^2 = 0.3$, $p = 0.562$). Both cohort studies showed that CHR subjects with more severe clinical symptoms at baseline and decline in functioning were more likely to convert to psychosis.
Conclusions: Conversion rates in this new, independent Chinese sample are similar to those reported in non-Chinese samples and to the 2011 cohort. Future research is needed to examine whether the implementation of early intervention for CHR/prodromal symptoms reduces the risk of psychosis and decreases the conversion rate.

1. Introduction

Numerous studies (Addington et al., 2011a; Cannon et al., 2008; Lemos-Giraldez et al., 2009; Nelson et al., 2013; Yung et al., 2008) and meta-analyses (Fusar-Poli et al., 2012; Fusar-Poli et al., 2016a; Giuliano et al., 2012) over the past two decades have described clinical syndromes (Fusar-Poli et al., 2016b; Lo Cascio et al., 2016) that are predictive of later psychotic illness. These are considered to represent a clinical high risk (CHR) or prodromal phase of psychosis (also called ultra high risk/UHR or At Risk Mental State/ARMS). One focus of this research has been to determine the degree of risk these syndromes convey. However, published conversion rates are quite variable across countries and over time and all studies show high false positive rates due to limited specificity of current CHR syndromes. In fact, recent follow-up studies of CHR samples have provided evidence suggestive of a declining conversion rate compared to earlier studies (Hartmann et al., 2016; Nelson et al., 2016; Yung et al., 2007), though reasons for this cohort effect are not clear. As argued by Yung et al. (2007), the decline is possibly due to either greater awareness, the implementation of more effective treatments in those identified as CHR, or dilution during identification (including greater numbers of subjects who are false positives to begin with). It would be helpful to clarify this question by

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comparing conversion rates in two sequential, matched cohort samples from the same research and clinical setting, which does not employ a specific treatment program.

Since 2010, a series of clinical investigations of early identification of psychosis were conducted at the Shanghai At Risk for Psychosis Program ("SHARP") of the Shanghai Mental Health Center (SMHC) (Zhang et al., 2015a; Zhang et al., 2015b; Zhang et al., 2015c; Zhang et al., 2014). The SMHC is the largest outpatient mental health clinic in China and provides medication management and psychotherapy. The Chinese research and clinical team at SHARP has been working closely with a U.S. team led by Dr. Larry Seidman (Beth Israel Deaconess Medical Center, Harvard Medical School). Together, they have implemented a systematic research program focused on the CHR phase of psychosis and its identification in Mainland China. Between 2010 and 2011, the team set up a standard procedure for clinical screening, assessment, diagnostic consensus conferences, and periodic site trainings. Then, from 2011 to 2012, an epidemiological study was carried out to determine the frequency of CHR syndromes in a hospital population of Chinese youths presenting for care (Zhang et al., 2014). We found a 2-year conversion rate of 29.1% (Zhang et al., 2016), comparable to that of specialized help-seeking samples world-wide (29%) (Fusar-Poli et al., 2012). The current study compares features of this 2011 cohort with a subsequent study (2013–2015) supported by an R21 MH093294 Fogarty/NIMH grant, "Broadening the Investigation of Psychosis Prodrome to Different Cultural Groups". While the SHARP clinicians and researchers have increasing awareness of CHR syndromes and the need for referral in the Shanghai clinical community, guidelines for treatment of CHR have not yet been fully developed or implemented.

What is unclear at present, however, is whether there is a change in conversion rate over time among the Chinese CHR population as reported in other settings around the world. This is a key issue for further investigating the concept of CHR in China. Since 2013, we have recruited and conducted two year follow-ups on 100 CHR subjects using the same raters and same procedures as in our epidemiological study (2011 cohort). We hypothesized that the "dilution" phenomena would not occur in the current Chinese setting given the lack of time and specific psychiatric treatments for this condition in Shanghai. To be specific, we hypothesized that the conversion rate of the new 2013 cohort would not show significant decline compared to the previous 2011 cohort. However, we anticipate clinicians would be more experienced in identifying CHR, thus reducing false positives. We also examined additional risk factors for future conversion in the two cohorts. We hypothesized that the risk factors for conversion would not significantly differ between the two cohorts.

2. Method

2.1. Participants

The 2011 cohort study (Zhang et al., 2014) was approved for epidemiological investigation of CHR by the Research Ethics Committee at the SMHC in 2011. The 2013 cohort for broader investigation of CHR subjects was approved by the Research Ethics Committee at the SMHC and Institutional Review Boards of Florida A&M University and Beth Israel Deaconess Medical Center (BIDMC). These subjects either participated in the 2011–2012 (2011 cohort) or the 2013–2015 (2013 cohort) study. As detailed in previous papers, the 2011cohort was made up of 117 CHR subjects attending their initial outpatient assessment at SMHC during 2011–2012, identified from a consecutive series of outpatients presenting to SMHC. The 2013 cohort was made up of 100 CHR subjects ascertained from 2013 to 2014. The two cohorts followed the same inclusion and exclusion criteria: (i) age of 15–45 years; (ii) individuals younger than 18 years had to be accompanied by either a parent or legal guardian; (iii) capacity to provide informed consent or assent if under 18; and (iv) must have completed at least six years of primary school education; (v) excluded for severe somatic diseases, such as pneumonia, cancer or heart failure, mental retardation, or dementia. All CHR subjects were diagnosed in a face-to-face interview with the Structured Interview for Prodromal Symptoms (SIPS) and rated on the Scale of Prodromal Syndromes (SOPS), Chinese version (Zheng et al., 2012). The researchers followed up with the CHR subjects two years after the baseline assessment. Clinical information was also collected from subjects' medical records and community clinicians.

In addition, the two cohorts were recruited with the same procedure. For detailed recruitment information, please refer to Zhang et al. (2014). In short, the 117 CHR subjects included in 2011-cohort were recruited from both clinic-wide questionnaire screening ($n = 89$) and clinician referrals ($n = 28$). The 89 CHRs were identified by a screening method (The Prodromal Questionnaire -Brief version: PQ-B) (Loewy et al., 2011). Patients received same-day SIPS/SOPS interview if they met the following criteria: (i) A total score of 3 or higher on the PQ-B; (ii) A PQ-B distress score of 6 or higher, and/or (iii) one or more first-degree relatives with affective or non-affective psychosis. As to the 2013-cohort, the 100 CHR subjects were recruited with the same procedure as the 2011 cohort, from both clinic-wide PQ-B screening ($n = 55$) and clinician referrals ($n = 45$). It should be noted that more of the 2013 subjects were ascertained and recruited through clinician referral.

2.2. Measures

2.2.1. SIPS/SOPS

The SIPS/SOPS (Miller et al., 2003) includes four domains of symptoms: positive (P), negative (N), disorganized (D) and general (G). It is a well-validated semi-structured diagnostic interview that assesses and identifies CHR syndromes, specifically Brief Intermittent Psychotic Symptom syndrome (BIPS), Attenuated Positive Symptom Syndrome (APSS), and/or Genetic Risk and Deterioration Syndrome (GRDS). The APSS criteria require that subjects receive a rating level of "3 (moderate)," "4 (moderately severe)," or "5 (severe but not psychotic)" on the positive symptoms scale of the SOPS (symptoms were rated based on a 7-point severity scale, from 0 to 6) and that at least one symptom worsened over the past year. The BIPS criteria require that subjects receive a rating of "6," which suggests a diagnosis of "severe and psychotic". Also, specific criteria for sufficient frequency and duration of symptoms must be met. In addition, GRDS is defined as having a genetic risk (one or more first-degree relative with an affective or non-affective psychotic disorder or meeting the DSM-IV schizotypal personality disorder criteria) accompanied by a drop of 30% or greater in the Global Assessment of Functioning (GAF) score in the past 12 months. Our team translated the Chinese version of the SIPS/SOPS (led by the first author) and tested the validity and reliability, which showed good inter-rater reliability ($r = 0.96$, $p < 0.01$ on the SOPS score) (Zheng et al., 2012). 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).

2.2.2. Follow-up outcome measures

There were 10- and 24-month follow-up assessments for each cohort. Subjects were seen by the same clinicians who completed interviews at baseline. The major outcome measure of the two cohort studies was conversion to psychosis. Conversion was operationalized as the criteria of POPS (Presence of Psychotic Symptoms in SIPS/SOPS) (McGlashan et al., 2010). Subjects had to demonstrate at least one psychotic level symptom (rated a '6') on at least one of the five P(Positive) symptoms (P1, unusual thought content; P2, suspiciousness; P3, grandiosity; P4, perceptual abnormalities; and P5, disorganized communication), with either sufficient frequency and duration or at a level that was disorganizing or dangerous (Addington et al., 2015).

2.2.3. Procedures

After an intake evaluation and a short screening questionnaire, potential CHR subjects were invited by either study clinicians or nurses

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