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Neurological soft signs in Chinese adolescents with schizophrenia and schizotypal personality traits

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ABSTRACT

Objective: Neurological soft signs (NSSs) may reflect neurodevelopmental anomalies in association with the spectrum of schizophrenia disorders. We examined NSSs in Chinese adolescents with schizophrenia and schizotypal personality traits.
Methods: Eighty-seven schizophrenic adolescents (SCH group), 85 adolescents with only schizotypal personality traits (SPT group), and 88 healthy controls (HC group) were enrolled. The NSS subscales of the Cambridge Neurological Inventory (CNI) were administered to all 260 participants.
Results: The NSS prevalence rates were higher in the SCH group than in the other two groups for both hands in the fist-edge-palm, Oseretsky, and graphesthesia tests. Relative to HCs, the SCH group also showed higher NSS prevalence rates in the right finger agnosia and right mirror movement of finger opposition tests. SCH > SPT > HC trends were observed for all NSS subscale scores and for the left, right, and total NSS scores.
Conclusions: To our knowledge, the present study is the first to examine NSSs in adolescents with schizophrenia and adolescents with schizotypal personality traits. These results provide preliminary findings suggesting that schizophrenia spectrum disorders may be characterized by developmental abnormalities in the central nervous system, and support the notion that NSSs may be schizophrenia spectrum disorder biomarkers.

1. Introduction

Schizophrenia is a serious mental disorder characterized by a variety of symptoms, including hallucinations, delusions, social withdrawal, and cognitive dysfunction (Evans et al., 2015). Generally, schizophrenia is considered to be neurodevelopmental in origin, with a pathogenesis that is influenced by the interaction of genes and the environment over the course of development. The neurodevelopmental model assumes that schizophrenia is the end state of an abnormal neurodevelopmental course that started years before symptom onset (Lewis and Levitt, 2002).

Schizophrenia is now considered one of a cluster of psychotic disorders (McClure et al., 2008), which includes schizotypal personality disorder (SPD). SPD is characterized by odd beliefs or magical thinking as well as unusual perceptual experiences and bodily illusions, inappropriate or constricted affect, and a lack of close relationships (Rosell et al., 2014). Individuals with SPD share a range of similarities with schizophrenic patients with respect to genetics, neurobiology, and phenomenology (Siever and Davis, 2004). These similarities may be indispensable for elucidating the pathogenesis of schizophrenia and determining what variables predict vulnerability to schizophrenia (Ettinger et al., 2014).

Neurological soft signs (NSSs) are subtle but observable impairments in motor and sensory functions (Bombin et al., 2005). NSSs have been associated with a range of neurocognitive and neuroanatomical abnormalities, and they may represent an underlying deficiency in neural integration (Chan et al., 2010a). In addition, NSSs may reflect cerebral dysfunction in neural networks, and they can provide information about the functional organization underlying a psychiatric disorder (Whitty et al., 2009; Zhang et al., 2015). NSSs have been described for a variety of psychiatric disorders, but are particularly prevalent in schizophrenia (Bachmann et al., 2014). A convergence of evidence points to there being highly preva-

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lent NSSs in adults with schizophrenia (Kolakowska et al., 1985; Heinrichs and Buchanan, 1988). A meta-analysis (Chan et al., 2010a) of 33 research studies in which large and reliable group differences (Cohen's d) were reported indicated that NSSs were present in a majority (73%) of the analyzed schizophrenic population.

Few studies have examined NSSs in SPD. Using the soft sign subscales of the Cambridge Neurological Inventory (CNI) and Schizotypal Personality Questionnaire, Chan et al. (2010b) found that the prevalence of NSSs was higher in individuals with SPD proneness (N = 64) than in those without it (N = 51). In another study, Cai et al. (2013a) found that adolescents with SPD proneness had higher prevalence rates of right diadocokinesia, left-fist-edge-palm, and left-right orientation sign positivity than non-prone controls (N = 116/group), and that they were more likely to exhibit at least one NSS than the controls. These results suggest that NSSs may reflect SPD-associated neural deficits.

Each of the aforementioned studies focused on NSSs in either schizophrenia or SPD. To our knowledge, no prior study has examined NSSs in both populations simultaneously. Understanding the intersection and overlap of NSSs in schizophrenia and SPD could enhance the utility of NSS assessments in studies of the mechanisms of schizophrenia spectrum disorders. Therefore, the aim of the current study was to explore NSS characteristics among schizophrenia patients and individuals with SPD. We hypothesized that individuals with SPD and schizophrenia would show higher prevalence rates of NSSs than normal controls, and that individuals with SPD would show less severe NSSs than schizophrenic patients.

We chose to focus on an adolescent study population for several reasons. First, most schizophrenia NSS studies reported thus far have focused on adult patients and family members, while schizophrenia NSSs in adolescents have remained unexplored. Second, neuropsychological and neuromotor disturbances that emerge in childhood and adolescence could lead to subsequent interpersonal problems, such as withdrawal, and contribute to the consequent development of paranoid ideation, magical beliefs, and other schizoid behaviors (Cornblatt and Keilp, 1994). Third, a substantial portion (25 ~ 40%) of adolescents with SPD may develop schizophrenia eventually (Shapiro et al., 2011). Indeed, adolescents with SPD have a much higher probability of developing schizophrenia than adults with SPD (Diforio et al., 2000). Hence, it is important to gather knowledge about NSSs in adolescents with schizophrenia and SPD.

2. Materials and methods

2.1. Subjects

The study cohort included three groups: a healthy control (HC) group (N = 88, 41 boys and 47 girls; a schizotypal personality trait-positive (SPT) group (N = 85, 42 boys and 43 girls; and a schizophrenia diagnosed (SCH) group (N = 87, 38 boys and 49 girls).

The HC and SPT participants were recruited from five cities in China (Beijing, Changsha, Suzhou, Chengdu, and Yinchuan). We used a brief questionnaire to exclude adolescents with a history of psychotic illness, and we also excluded adolescents if they reported their family members suffering from psychosis. A total of 2861 adolescents (1395 boys and 1466 girls) completed questionnaires. From this sample, 85 adolescents with SPT only were detected according to a cut-off score for the SPD subscale of the Personality Diagnostic Questionnaire version 4+ (PDQ–4 +). An additional 88 adolescents without any pathological personality traits we detected were recruited by random selection from the same population. None of the SPT or HC participants reported having a history of using cannabis or any other drugs (Dervaux et al., 2010).

Schizophrenic adolescents were recruited from the Second Xiangya Hospital of Central South University in Changsha and the Sixth Hospital of Peking University in Beijing. All enrolled patients met the DSM-IV criteria, had no history of neurological illness or major head trauma, and were taking medication. The present study was approved by the Medical Ethics Committee of Central South University, and all participants provided written informed consent.

2.2. PDQ-4+

We administered the SPD subscale of the Chinese version of the PDQ-4+ to screen for schizotypal personality traits in recruited adolescents. The Chinese version of the PDQ-4+ has satisfactory test reliability and validity (Yang et al., 2002). We adopted the personality disorder criteria recommended for Chinese adolescents by Wang et al. (2013). In this study, the cut-off score for SPD designation was a score of $\geq$6 on the SPD subscale of the PDQ-4+.

2.3. CNI

We used the soft sign tests of the CNI to assess NSS severity (Chen et al., 1995). The instrument included tests of motor coordination, sensory integration, and disinhibition. The CNI has good construct, external validity, and interrater reliability (Zhang et al., 2015). We conducted the CNI in a standardized manner and fixed order. In the original scale, the test reactions were scored as follows: "normal", 0; "equivocal normal", 0.5, "abnormal", 1; "grossly abnormal", 2; and "missing", 9. In this study, scores were dichotomized to "0" (normal or equivocal) or "1" (abnormal or grossly abnormal) as described previously (Cai et al., 2013b).

2.4. Data processing and analysis

The data were analyzed in SPSS version 20. First, chi-square tests were applied to assess NSS prevalence rates (percentage with score of "1") across the three groups. The chi-square test results were partitioned according to the items with significant group differences. Second, the non-parametric Jonckheere-Terpstra test (Jonckheere, 1954), which was designed to detect alternatives of ordered class differences, was used to evaluate presumed trends in the data (i.e., SCH > SPT > HC). Statistical significance was defined as $\alpha = 0.05$, except for partitioning from the chi-squared test, for which significance was defined as $\alpha' = 0.0125$.

3. Results

3.1. Demographics

The demographic characteristics of each group are summarized in Table 1. There were no statistically significant differences among three groups in terms of age, gender, or dominant hand ratio.

3.2. Groups comparisons of NSSs

The prevalence rates of NSS positivity (dichotomous score of 1) for the three groups are reported in Table 2. Chi-square tests identified 12 items as differing between the groups ($\alpha = 0.05$), of which 8 remained statistically significant following further partitioning of the chi-squared test results ($\alpha' = 0.0125$).

The NSS summary scores and subscale scores for the groups are compared in Table 3. The predicted SCH > SPT > HC trend was observed for all NSS subscale scores, the left NSS score, the right NSS score, and the total NSS score.