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Associations between schizotypal features and indicators of neurological and morphological abnormalities

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Abstract

Objective: Limited research suggests that subtle neurological and morphological abnormalities that have been documented in patients with schizophrenia also may be associated with schizotypal traits in non-psychiatric samples. Based on the notion that neurological soft signs (NSS) may mark a genetic diathesis, this study hypothesized that NSS scores would be related to the level of schizotypy in relatives of schizophrenia patients and in controls. Additionally, associations between MPA scores and schizotypy were explored in these two groups.
Method: Twenty-six first-degree relatives of schizophrenia patients and 38 controls with no personal or family history of psychosis were assessed for schizotypy using the Structured Clinical Interview for DSM-IV Axis II Disorders schizotypal personality disorder module, as well as the self-administered Schizotypal Personality Questionnaire. The Neurological Evaluation Scale and a structured examination for MPAs also were administered.
Results: Mean schizotypy scores did not differ between relatives and controls. Both NSS and MPAs were associated with the level of interviewer-assessed schizotypal features in controls but not in relatives of patients with schizophrenia. NSS and MPAs were not associated with self-reported schizotypy in either group.
Conclusions: These findings demonstrate that both NSS and MPAs are associated with interview-based schizotypal traits, at least in non-psychiatric participants. Future research should seek to replicate these results in other samples of relatives and controls.

Keywords: Schizophrenia; Schizotypy; Neurological soft signs; Minor physical anomalies

1. Introduction

Research suggests a genetic link between schizophrenia and schizotypal personality features (Lenzenweger, 1999a,b; Siever et al., 1993). Individuals with schizotypal features exhibit cognitive and social deficits similar to, but less prominent than, those found in schizophrenia (Dickey et al., 2005; Gooding and Braun, 2004; Pickup, 2006). Subtle neurological abnormalities and minor morphological anomalies are found at higher rates among individuals with schizophrenia and presumably develop concurrently with neurodevelopmental abnormalities (Boks et al., 2000; Buckley et al., 2005). Neurological soft signs (NSS) and minor physical anomalies (MPAs) are considered risk markers

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for schizophrenia, and there is growing interest in the connection between these indicators and schizophrenia-spectrum disorders such as schizotypal personality disorder (SPD).

NSS are observable but subtle impairments in motor and sensory domains that are neither localized to a specific brain area nor pathognomic for any specific neurological disease (Obiols et al., 1999). Compared to healthy controls, individuals with schizophrenia have more NSS (Arango et al., 1999; Cox and Ludwig, 1979; Flyckt et al., 1999; Heinrichs and Buchanan, 1988). These findings are even observable in children prior to the onset of schizophrenia (Walker, 1994), first-episode patients (Dazzan and Murray, 2002), and antipsychotic-naive patients (Venkatasubramanian et al., 2003). NSS are related to more severe negative symptoms (Arango et al., 2000; Bombin et al., 2005; Chen et al., 2005; Malla et al., 1997; Prikryl et al., 2006; Yazici et al., 2002) and disorganized symptoms (Arango et al., 2000; Schroder et al., 1996); however, some studies have not found this correlation (Bartko et al., 1988; Braun et al., 1995).

Neurological abnormalities also are found in groups at high risk for schizophrenia, suggesting that NSS represent a genetic vulnerability marker (Tsuang, 2000). Some studies report elevated rates of NSS in healthy biological relatives of patients (Egan et al., 2001; Gourion et al., 2004a,b; Rossi et al., 1990; Yazici et al., 2002). Frequently, relatives' NSS scores are intermediate between those of patients and healthy controls (Kinney et al., 1986; Rossi et al., 1990; Yazici et al., 2002). Further, some studies reveal NSS elevations in healthy individuals with subtle signs of psychosis proneness (i.e., schizotypy) (Barkus et al., 2006; Barrantes-Vidal et al., 2003; Obiols et al., 1999). These findings suggest that neurological abnormalities may be related to the dimensional construct of schizotypy in addition to categorical disease classifications based on the presence of diagnostic criteria.

MPAs are subtle morphological abnormalities that may be markers of neurodevelopmental deviations (Buckley, 1998; Green et al., 1989; Lane et al., 1997; McGrath et al., 2002; Sivkov and Akabaliev, 2004). An insult during the prenatal period may interrupt fetal morphological and brain development (Green et al., 1989; Schiffman et al., 2002). MPAs include subtle abnormalities of the craniofacial region and limbs (Schiffman et al., 2002). Many studies have found that schizophrenia patients have more MPAs than healthy controls (Buckley, 1998; Buckley et al., 2005; Lane et al., 1997; McGrath et al., 2002; Schiffman et al., 2002; Sivkov and Akabaliev, 2004), and MPAs are observable in children prior to the onset of schizophrenia (Schiffman et al., 2002). Several studies have reported no association between MPAs and positive, negative, or disorganized symptoms (Lohr and Flynn, 1993; McGrath et al., 1995; Oosthuizen et al., 1998).

Findings from studies of MPAs in relatives of patients are mixed. Several studies report that relatives have no MPA elevations, showing frequencies similar to healthy controls (Gourion et al., 2003; Green et al., 1994; Hans et al., 2005), while others reveal that relatives have a similar number of MPAs to patients (Gourion et al., 2004a,b; Ismail et al., 1998, 2000). Interestingly, families with a single case of schizophrenia may manifest more MPAs than multiplex families (Griffiths et al., 1998), potentially suggesting that MPAs result from an insult during fetal development rather than from a genetic liability to schizophrenia.

Only one study has investigated MPAs in relation to schizotypal features. Weinstein and colleagues (Weinstein et al., 1999) reported that adolescents who met criteria for SPD using a structured interview had more MPAs than adolescents with other personality disorders and those with no psychiatric illnesses. No studies have examined MPAs and schizotypy in an adult non-psychiatric sample, especially one including biological relatives of schizophrenia patients.

The current study investigated relationships between schizotypy (assessed using a structured clinical interview and a self-report questionnaire) and NSS and MPAs in healthy relatives and non-psychiatric controls. Based on previous schizophrenia research, it was hypothesized that schizotypy would be positively correlated with NSS in biological relatives and in healthy controls (given the presumed dimensional nature of both risk markers). The relationship between schizotypy and MPAs in relatives and controls was considered an exploratory research question.

2. Methods

2.1. Setting and sample

This study was conducted at a large public-sector health system that primarily serves a low-income, African American population. Participants with schizophrenia invited at least one first-degree relative to enroll in the study, resulting in 26 relatives in this analysis. Thirty-eight controls were recruited from a medical clinic waiting room ($n=25$) and a methadone maintenance clinic adjacent to the community mental health center ($n=13$).

Exclusionary criteria for all participants included: (1) inability to speak English, (2) active substance abuse/