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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/

dependence diagnosis not in early or sustained full remission, (3) known mental retardation, and (4) history of neurological disease or clinically significant head injury. To maintain representativeness of the sample, the presence of Axis I illnesses, aside from psychotic and mood disorders, and Axis II disorders was not considered exclusionary. Controls were excluded if they endorsed any personal or family history (in first- or second-degree relatives) of psychotic or mood disorders.

2.2. Procedures and materials

The university's institutional review board approved the study. All participants provided written informed consent. Psychiatric diagnoses were ruled out using the psychotic disorders, mood disorders, and substance use disorders modules of the *Structured Clinical Interview for DSM-IV Axis I Disorders* (SCID) (First et al., 1998).

Axis II SPD symptoms were assessed using the *Structured Clinical Interview for DSM-IV Axis II Disorders* (SCID-II) (Spitzer et al., 1990). The assessor was blind to NSS and MPA scores when conducting the SCID-II interview. For this interview, nine DSM-IV SPD criteria are rated as: 1=not present, 2=present at a subthreshold level, or 3=present. In the current study, scores of 2 or 3 were considered meaningful because schizotypy is conceptualized as occurring on a continuum and both scores indicate the presence of atypical behaviors, beliefs, or interactions. The total number of items rated 2 or 3 (0–9) was used for analyses. The nine criteria also were used to derive subscale scores similar to dimensions frequently applied to schizophrenia symptoms, and analogous to the three dimensions measured by the self-report Schizotypal Personality Questionnaire (Raine, 1991), as described below. Thus, a cognitive–perceptual subscale, paralleling positive symptoms, was computed by summing the items for ideas of reference, odd beliefs, unusual perceptual experiences, and suspiciousness/paranoid ideation; an interpersonal subscale, reflecting negative symptoms, included suspiciousness/paranoid ideation, inappropriate/constricted affect, lack of close friends, and excessive social anxiety; and a disorganized subscale was derived using odd thinking/speech and odd/eccentric behavior/appearance.

The *Schizotypal Personality Questionnaire* (SPQ; Raine, 1991) is a self-report, easy-to-administer, 74-item questionnaire used to screen for schizotypy or SPD. Administration time is approximately 10 min. Each item presents a statement or question to the respondent, who circles "yes" or "no." All affirmatively-endorsed items count one point toward the total score (range: 0–74), with higher scores indicating higher levels of schizotypy. Examples of items include: "Have you ever had the sense that some person or force is around you, even though you cannot see anyone?" (cognitive–perceptual subscale) and "People sometimes find me aloof and distant." (interpersonal subscale). Internal consistency reliability, test–retest reliability, and criterion validity of the SPQ are acceptable (Raine, 1991). In a sample of 118 participants (relatives and controls) from this research group (many included in the current analysis), internal consistency of the SPQ subscales was found to be acceptable—.89, .89, and .84, respectively, for the cognitive–perceptual, interpersonal, and disorganized subscales.

The *Neurological Evaluation Scale* (NES) is a 26-item instrument designed to measure NSS in schizophrenia (Buchanan and Heinrichs, 1989), though it also has been used in studies of non-psychiatric participants (Obiols et al., 1999). Trained evaluators administer the scale, and items are scored 0=no abnormality, 1=mild but definite impairment, or 2=marked impairment. As indicated in the standardized instructions, two items—the suck and snout reflexes—are scored 0=absent or 2=present. Fourteen items are assessed bilaterally. Previous studies have either averaged bilateral items (Malla et al., 1997) or the higher of the two scores taken (Keshavan et al., 2003; Sanders et al., 2000, 2005). In this study, right and left scores were summed. Total administration time for the scale in this study was 29.4± 10.5 min (mode=30 min). All analyses were conducted with the total NES score (possible range: 0–76), and three previously-described subscale scores (Buchanan and Heinrichs, 1989): sequencing of complex motor tasks, sensory integration, and motor coordination (Table 1). A prior exploratory factor analysis including data from current study participants did not reveal latent factors more useful than these theoretically-derived

Table 1
NES subscales and items

NES subscale	NES items
Sequencing of complex motor tasks	Fist-ring test
	Fist-edge-palm test
	Ozeretski test
	Rhythm tapping
Sensory integration	Audio–visual integration
	Stereognosis
	Graphesthesia
	Extinction
	Right–left orientation
Motor coordination	Tandem walk
	Rapid alternating movements
	Finger-thumb opposition
	Finger-to-nose test

Table 2
MPA subscales and items

MPA subscale	MPA items
Eyes	Biocular diameter
	Direction and degree of eye fissure
	Presence of epicanthus and hypertelorism
Ears	Ear protrusion
	Abnormal anterior surface of the ear
	Enlarged lobe size
	Low set ears
	Adherent ear lobes
	Malformed ears
	Soft and pliable ears
	Asymmetrical ears
Hands	Abnormal nail morphology
	Curved fifth finger
	Presence of slight transverse palmar crease
Feet	Third toe equal in length/longer than second toe
	Merging of two middle toes
	Large gap between the first and second toes

subscales (Compton et al., 2006). To assess inter-rater reliability of NES items, the kappa statistic (Cohen, 1960) was calculated after the NES had been independently rated for six participants by five raters. Mean kappa values for items comprising the sequencing of complex motor tasks, sensory integration, and motor coordination subscales, respectively, were .80, .97, and .80.

MPAs were recorded using a structured scale adapted from two instruments (Lane et al., 1997; Waldrop and Halverson, 1971). Four subscales were used in this study: eye, ears, hands, and feet (Table 2). Assessments were conducted in a standardized manner using a caliper, protractor, ruler, and measuring tape. Most items were scored as 0 = absent or 1 = present. Administration time for the entire instrument was 16.6 ± 6.5 min (mode = 15 min). Regarding inter-rater reliability, for continuous facial measures such as biocular distance, intraclass correlation coefficients (ICCs) were calculated using a two-way mixed (judges fixed) effects analysis of variance model in which the five assessors were the fixed effect while the six target ratings were the random effect (Shrout and Fleiss, 1979). ICCs for the facial measures ranged from .75 to .90 (average = .81). For categorical MPA items, the mean kappa value derived from independent ratings of six participants by five raters was .76.

2.3. Data analysis

Pearson product-moment correlations and Spearman correlations were used for normal and non-normal distributions, respectively. Where covarying was indicated, partial correlation coefficients were computed, using *SPSS* for parametric (Pearson) partial correlations and *SAS* for nonparametric (Spearman) partial correlations. Independent samples Student's *t*-tests for normal distributions and Mann Whitney *U*-tests for non-normal distributions were used to examine group differences. All analyses were 2-tailed. Bonferroni corrections were applied within but not across hypotheses/research questions.

3. Results

3.1. Sociodemographic variables in relatives and controls

With respect to sociodemographic variables, there were several differences between the relatives and controls (Table 3). Controls were significantly older than relatives ($t = 2.65$, $p = .01$). There were more females than males in the relative group compared to an even distribution in the control group ($\chi^2 = 7.00$, $p = .01$). More controls were unemployed compared to the relative group ($\chi^2 = 6.39$, $p = .01$), though there were no differences between the two groups in terms of race, educational attainment, or marital status.

3.2. Interview-based SPD criteria scores and self-reported SPQ scores

In relatives of schizophrenia patients, clinician-assessed SPD SCID-II criteria scores (total, cognitive–perceptual, interpersonal, and disorganized) were: 1.39 ± 1.69, 0.67 ± 1.17, 0.75 ± 0.90, and 0.04 ± 0.20, respectively. Among controls, scores were: 1.72 ± 2.22, 0.64 ± 1.02, 0.81 ± 1.08, and 0.32 ± 0.63, respectively. Not surprisingly, 41% of participants did not exhibit SPD features based on the SCID-II. Also, no participants met full diagnostic criteria for SPD. Analyses involving these scores relied on nonparametric tests. In general, relatives

Table 3
Sociodemographic characteristics of first-degree relatives and controls

Variable	Relatives ($n = 26$)	Controls ($n = 38$)
Age in years*	43.58 ± 14.30	51.68 ± 10.40
Female gender *	23 (88%)	20 (53%)
Race		
African American	23 (88%)	34 (89%)
Caucasian	3 (12%)	4 (11%)
Educational level in years	12.87 ± 2.54	12.47 ± 2.35
Marital status		
Never married	10 (38%)	12 (32%)
Married/living together	9 (35%)	10 (26%)
Separated/divorced/widowed	7 (27%)	16 (42%)
Employed *	15 (58%)	10 (26%)

* indicates a significant difference between relatives and controls, $p < .05$.

and controls did not differ in the number of SPD features. Specifically, Mann–Whitney *U*-tests revealed that the two groups manifested a similar number of total, cognitive–perceptual, and interpersonal SPD features. Surprisingly, on the disorganized subscale, controls appeared to have significantly more SPD features than relatives ($z=2.14$, $p=.03$). SPD criteria scores were not related to sociodemographic variables in either group.

Total, cognitive–perceptual, interpersonal, and disorganized SPQ scores for relatives were: 15.29±12.61, 6.04±6.04, 7.75±5.83, and 3.50±3.99, respectively, and for controls were 17.88±11.58, 7.56±5.37, 9.24±6.26, and 3.54±3.55, respectively. SPQ scores did not differ between relatives and controls. SPQ scores were not related to age and did not differ by sex or race for either group. However, among the relatives, educational level was negatively related to the SPQ interpersonal subscale ($r=-.51$, $p=.01$). Subsequent analyses including SPQ scores in relatives were covaried for education.

Table 4
Associations between interview-based SPD criteria scores and NES scores

	NES total score	Sequencing of complex motor tasks	Sensory integration	Motor coordination
Relatives				
Spearman correlations				
Total SPD criteria score	.20	−.20	−.16	.01
Cognitive–perceptual	.27	−.07	.07	.01
Interpersonal	−.06	−.25	−.35	−.01
Disorganized	–	–	–	–
Partial correlations (controlling for age and educational level)				
Total SPD criteria score	.06	−.26	−.19	.21
Cognitive–perceptual	.35	.04	.21	−.01
Interpersonal	−.32	−.36	−.49	.18
Disorganized	–	–	–	–
Controls				
Spearman correlations				
Total SPD criteria score	.42*	.41*	.32	.18
Cognitive–Perceptual	.16	.26	.35*	.09
Interpersonal	.51**	.45**	.27	.23
Disorganized	.41*	.44**	.26	.26
Partial correlations (controlling for age and educational level)				
Total SPD criteria score	.58*	.37	.54*	.26
Cognitive–perceptual	.26	.17	.57*	.10
Interpersonal	.72**	.47*	.43*	.37
Disorganized	.62*	.54*	.43*	.30

– indicates restricted range precluding statistical analysis.
* $p<.05$.
** $p<.003$ (Bonferroni-corrected for multiple correlations).

3.3. Neurological soft signs

NES total and subscale scores were significantly intercorrelated ($r=.48$–$.78$), though the NES motor coordination and sensory integration subscales were not significantly correlated ($r=.23$, $p=.07$). Thus, in general, there is a relatively high degree of relatedness between NES subscale scores. Nonetheless, previous research has found some support through factor analysis for these subscales (Emsley et al., 2005; Keshavan et al., 2003; Malla et al., 1997; Sanders et al., 2000), so total and subscale scores were used. Total NES scores averaged 16.53±8.85 and were normally distributed. NES scores for relatives were: total, 18.17±10.26; sequencing of complex motor tasks, 4.75±3.29; sensory integration, 4.46±3.15; and motor coordination, 1.91±2.13. NES scores for controls were: total, 15.54±8.02; sequencing of complex motor tasks, 5.35±3.57; sensory integration, 3.54±2.12; and motor coordination, 2.69±2.56.

There were several differences in the relations between sociodemographic characteristics and NES scores for relatives and controls. Specifically, for relatives, age was positively related to total NES score ($r=.56$, $p=.01$), as well as to each subscale score (sequencing of complex motor tasks, $r=.59$, $p<.01$; motor coordination, $r=.41$, $p=.04$; sensory integration, $r=.44$, $p=.03$), but education level was not related to NES scores. For controls, age was positively correlated with sensory integration ($r=.34$, $p=.04$) and education level was negatively associated with total score ($r=-.48$, $p=.01$). Subsequent NES analyses with relatives were covaried for age and with controls were covaried for age and educational level. Group differences in NSS were not the focus of the present report and are described elsewhere (Compton et al., submitted for publication).

3.4. Minor physical anomalies

MPA scores in relatives were as follows: eyes, 4.13±2.36; ears, 2.67±2.20; hands, 1.44±2.12; and feet, .36±.76. Scores in controls were: eyes, 4.22±2.60; ears, 2.06±2.41; hands, 1.89±2.26; and feet, .29±.80. MPA subscale scores were not significantly associated with any demographic variables. Again, group differences in MPAs were not the focus of the current paper (Compton et al., submitted for publication).

3.5. Associations between schizotypy and neurological soft signs

Interview-based SPD criteria scores and NES scores were not associated in relatives but were correlated in controls (Table 4). That is, in psychiatrically-healthy individuals with no family history of schizophrenia, higher rates of schizotypal features were related to more NSS. When age and educational attainment were controlled, there were still no significant correlations between SPD criteria scores and NES scores in relatives, but there were additional consistent and remarkably strong correlations in controls (Table 4).

To be conservative, a Bonferroni correction was applied. All correlations in this matrix were evaluated against $p=.003$ (.05/16). About half of the correlations remained significant; the interpersonal and disorganized SPD dimensions were related to NES sequencing of complex motor tasks and the interpersonal dimension was related to NES total score. Thus, even when stringent statistical criteria were applied, there was a relationship between NSS and some SPD dimensions in controls.

The 13 controls recruited from a methadone maintenance clinic were removed and correlations were re-run with the remaining 24 controls. Resultant correlation coefficients were almost identical to coefficients computed with data from all of the controls combined. However, these correlations were no longer significant. The similar magnitude of the correlations but smaller sample size and lack of significance suggests there was a lack of power to detect the significant relationships in the restricted sample.

In each group, Pearson correlation coefficients were calculated to test for associations between NES scores and schizotypy scores (SPQ). Interestingly, however, there were no significant correlations, even when education was covaried (data not shown).

3.6. Associations between schizotypy and minor physical anomalies

Spearman correlation coefficients computed for interview-based SPD criteria scores and MPA measures yielded multiple significant relationships in controls but not in relatives (Table 5). To be conservative, a Bonferroni correction was applied. Two of eight correlations remained statistically significant—SPD cognitive–perceptual scores were correlated with MPAs of the feet, and SPD disorganized scores were correlated with MPAs of hands.

When the 13 participants from the methadone maintenance clinic were removed, correlation coefficients in the restricted group ($n=24$) were almost identical to coefficients computed with all of the controls combined. However, these correlations were no longer significant, again likely due to insufficient power.

Table 5
Associations between interview-based SPD criteria scores and MPA scores

	MPA—eyes	MPA—ears	MPA—hands	MPA—feet
Relatives				
Spearman correlations				
Total SPD criteria score	−.31	.15	.09	.23
Cognitive–perceptual	−.21	−.01	.32	−.02
Interpersonal	−.22	−.27	−.15	.34
Disorganized	–	–	–	–
Controls				
Spearman correlations				
Total SPD criteria score	.12	.38 *	.33 *	.34 *
Cognitive–perceptual	.20	.36 *	.25	.46 **
Interpersonal	−.03	.35 *	.35 *	.24
Disorganized	.11	.22	.45 **	.20

– indicates restricted range precluding statistical analysis.
* $p<.05$.
** $p<.003$ (Bonferroni-corrected for multiple correlations).

Similar to analyses involving NSS, self-report SPQ scores were not correlated with any MPA measure (data not shown) in either group.

4. Discussion

Some studies have found a higher rate of schizotypy in relatives of schizophrenia patients, especially in first-degree relatives, compared to non-psychiatric controls (Asarnow et al., 2001; Kendler et al., 1993; Maggini and Raballo, 2003). This study, however, did not reveal higher levels of schizotypy in relatives than controls. SPQ scores of relatives in this sample were similar to or lower than scores reported in several other studies (Vollema et al., 2002; Yaralian et al., 2000). Patients referred relatives willing to participate, and this may have resulted in a biased group of relatives with fewer schizotypal traits—relatives with suspiciousness, subtle thought disorganization, or interpersonal deficits may have been less likely to participate. Alternatively, some researchers explain the lack of difference between groups as resulting from defensive reporting in relatives (Calkins et al., 2004; Chang and Lenzenweger, 2005). Relatives have a heightened awareness of schizophrenia symptoms and associated sociocultural stigma, and as a result may present themselves as psychologically healthy.

The first study hypothesis was that schizotypy and NSS would be associated in both relatives and controls. Several studies have examined this association and report more NSS in individuals with schizotypal features (Barrantes-Vidal et al., 2003; Obiols et al., 1999). One study found that degree of neurological impairment predicted schizotypy in healthy college students (Barkus et al., 2006). The present hypothesis was partially supported—in the control sample, more neurological abnormalities were associated with more SPD features as determined by the SCID-II interview. Thus, it appears that the severity of neurological impairment may provide information about the degree of schizophrenia liability present.

The second objective of this study was to explore the relationship between schizotypy and MPAs. The present study is the first to date to examine this relationship in a sample including first-degree relatives and controls. There was a significant relationship between MPAs and schizotypal features in controls but not in relatives. The differential relationship for relatives and controls may reflect an especially healthy or overly-guarded relative group. MPAs appear to reflect the degree of psychosis proneness, at least in a sample of healthy individuals.

Several methodological limitations should be considered when interpreting these results. First, study participants were recruited from an urban, public-sector setting that serves a predominantly African American population; therefore, the sample may not be representative of broader populations. Also, about one-third of the control group was drawn from an outpatient methadone maintenance clinic, which also may limit the representativeness of the controls. However, analyses excluding these participants suggested similar study results. Nonetheless, future studies should include community controls, rather than clinic controls as a comparison, and they should rely on larger sample sizes. Second, as suggested previously, the relatives may have been an overly healthy group. Future studies may consider selecting a larger and more heterogeneous group of relatives. Third, based on previous factor analyses suggesting dimensionality, schizotypy was treated as a dimensional construct; however, merely measuring it as dimensional is not evidence of a dimensional latent structure. Future research is recommended on the latent structure of schizotypy. Fourth, assessors could not feasibly be blinded to participant group status for NSS and MPA measures. However, standardized instruments were used for both indices and all evaluators were trained to a high level of reliability. Furthermore, NSS/MPA assessors were blind to interview-based and self-report schizotypy scores, and the SCID-II interviewer was blind to NSS/MPA and SPQ scores.

This study reveals that NSS and MPAs are associated with schizotypal features in a sample of healthy controls but not in relatives of schizophrenia patients. These findings suggest that the presence of NSS and MPAs are associated with vulnerability for a schizophrenia-spectrum disorder and may even reflect the level of schizophrenia liability. No other study to date has examined the relationship between schizotypy and these indices in this type of sample. Additional studies are needed to clarify the nature of the relationships between schizotypy, NSS, and MPAs in samples that vary in schizophrenia liability. Further research is needed to explain why the correlations were apparent in controls but not in relatives, and why correlations were evident when schizotypy was interviewer-assessed but not when measured by self-report.

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