Neurological soft signs in psychometrically identified schizotypy

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Abstract:

Patients with schizophrenia often exhibit structural brain abnormalities, as well as neurological soft signs (NSS), consistent with its conceptualization as a neurodevelopmental disorder. NSS are mild, presumably nonlocalizing, neurological impairments that are inferred from performance deficits in domains such as sensory integration, motor coordination, and motor sequencing. The vulnerability for schizophrenia is presumed to be expressed across a broad continuum of impairment referred to as schizotypy. It is hypothesized that nondisordered people along the schizotypy continuum should exhibit elevated rates of NSS. The present study examined the relation of psychometrically identified positive and negative schizotypy with NSS using the Neurological Evaluation Scale in a nonclinically ascertained sample of young adults (n = 177). As hypothesized, negative, but not positive, schizotypy was related to increased NSS in tasks that assessed fine and gross motor coordination, motor sequencing, eye movement abnormalities, and memory recall. However, positive schizotypy was associated with increased NSS in tasks related to sensory integration dysfunction. In general, the positive × negative schizotypy interaction term was unrelated to individual NSS tasks. The findings support: a) the theory that the vulnerability for schizophrenia is expressed across a broad continuum of subclinical and clinical impairment referred to as schizotypy; b) the multidimensional structure of schizotypy; and c) the notion that schizotypy is an appropriate construct for understanding the etiology and development of schizophrenia-spectrum disorders.

Keywords: neurological soft signs | schizotypy | schizophrenia | neurodevelopment | psychology

Article:

1. Introduction

Current etiological models (e.g., [Andreasen, 1999] and [Weinberger, 1987]) posit that liability for schizophrenia arises from disruptions in neural development beginning in the prenatal period and culminating in late adolescence or early adulthood (Andreasen, 1999). Neural dysmaturation does not necessarily result in schizophrenia, but is expressed across a continuum of impairment referred to as schizotypy (Meehl, 1990). It is assumed that the majority of schizotypes will never develop schizophrenia, although they often exhibit mild/transient features of the disorder including cognitive, emotional, and biobehavioral impairment. Thus, schizotypy is expressed along a dynamic continuum – with schizophrenia and spectrum disorders being the most severe manifestations. Schizotypy (and by extension schizophrenia) is multidimensional in nature, with positive and negative schizotypy being the most consistently replicated factors ([Claridge et al., 1996], [Kwapil et al., 2008] and [Vollema and van den Bosch, 1995]). There is considerable cross-sectional and longitudinal evidence from premorbid (Walker et al., 1994), familial (Fish, 1987), and psychometric risk (Chapman et al., 1994) studies that supports schizotypy as an expression of neurodevelopmental vulnerability for schizophrenia.

Neurological abnormalities are present in the premorbid, acute, and residual phases of schizophrenia (e.g.,[Steen et al., 2006] and [Marenco and Weinberger, 2000]). Neurological abnormalities are traditionally divided into "hard" and "soft" signs. Hard signs are localizable neurological insults from illness, injury, or toxins. NSS are mild, nonlocalizable abnormalities indicating generalized disruption in neural circuitry between cortical and subcortical areas and are inferred from performance deficits in domains such as sensory integration, motor coordination, and motor sequencing (Buchanan and Heinrichs, 1989). Thus, NSS may reflect a phenotypic expression of neural dysmaturation and have been proposed as an endophenotype for schizophrenia (Chan and Gottesman, 2008).

The Neurological Evaluation Scale (NES; Buchanan and Heinrichs, 1989) is the most widely used instrument to assess NSS in schizophrenia. Approximately 50–65% of patients relative to 5% of nondisordered comparison participants exhibit NSS ([Bombin et al., 2005] and [Heinrichs and Buchanan, 1988]). Furthermore, NSS are more prevalent in patients with schizophrenia than other forms of psychopathology (Bombin et al., 2005), excluding cognitive disorders such as dementia. First-episode patients with schizophrenia exhibit more NSS compared to control groups ([Keshavan et al., 2003], [Sanders et al., 1994],[Scheffer, 2004] and [Venkatasubramanian et al., 2003]), suggesting that NSS do not simply reflect consequences of chronic illness. In addition, NSS appear to be present prior to the onset of schizophrenia (e.g., Walker et al., 1994). Studies generally have not found a relation between NSS and illness duration (e.g., Emsley et al., 2005) or with sex or medication status (e.g., Bombin et al., 2005).

Most studies support an association between negative symptoms and NSS, particularly sensory integration and motor sequencing ([Bombin et al., 2005] and [Yazici et al., 2002]). In contrast, multiple studies failed to find an association between NSS and positive symptoms ([Bombin et al., 2005] and [Yazici et al., 2002]).Bombin et al. (2005) indicated that most studies that supported this association also reported a relation between NSS and negative symptoms. Moreover, Scheffer (2004) reported a relation between NSS and positive and negative symptoms at baseline, but only with negative symptoms at follow-up.

The neurodevelopmental model posits that nondisordered individuals along the schizotypy continuum should experience mild/transient forms of the impairment experienced by patients with schizophrenia, including NSS. Rates of NSS in putative schizotypes identified by consanguinity are generally intermediate between patients with schizophrenia and healthy controls ([Bombin et al., 2005], [Ismail et al., 1998] and [Yazici et al., 2002]), although see Appels et al. (2002) and Egan et al. (2001). This relation suggests that NSS may be a promising marker of schizotypy and vulnerability for developing spectrum disorders. Few studies have examined the relation between NSS and psychometrically identified schizotypy. Barrantes-Vidal et al. (2003)found that negative and combined positive–negative schizotypy clusters reported more NSS than the control or positive schizotypy clusters. Barkus et al. (2006) reported that high scorers on two scales assessing positive schizotypy scored significantly higher than control participants on NES "total" and "others" subscales. However, they did not examine the presence of negative schizotypy. Bollini et al. (2007) found that interviewer-assessed schizotypal features, but not self-reported schizotypy, were related to NSS.
Although the relation of NSS and schizophrenia is well-documented, the following points limit conclusions drawn from the literature: 1) the internal consistency of NES subdomains and information about distributions of NES scores are rarely reported; 2) most studies do not report interrater reliability values; 3) bilateral task scores are often collapsed by taking the average or higher of the ratings, without conceptual or empirical justification; 4) studies typically only differentiate between right/left hand performance, rather than dominant/nondominant hand performance; and 5) most studies either fail to consider symptom dimensions or fail to examine the unique contribution of each dimension to the prediction of NSS.

This study examined the relations of psychometrically identified positive and negative schizotypy with NSS in a nonclinical sample of young adults. Given the robust relation of negative symptom schizophrenia with NSS, it was hypothesized that negative schizotypy would be significantly associated with elevated NES scores. Although there is some mixed evidence of an association between NSS and positive schizotypy, based on the conceptual and empirical evidence for both schizophrenia and schizotypy, we did not hypothesize such an association in the present study. However, consistent with the findings of Barrantes-Vidal et al. (2003), it was predicted that the positive x negative schizotypy interaction would account for significant variance over and above the schizotypy main effects. The present study also examined whether the NES, which was developed for use with patients, would be useful for detecting NSS in nonclinical schizotypy. The traditional ordinal scoring system (Buchanan and Heinrichs, 1989) was also compared to a continuous scoring method that included error count and latency ([Sanders et al., 1998] and [Sanders et al., 2006]).

2. Methods

2.1. Participants

The initial sample included 201 undergraduates. Three subjects were dropped due to history of neurological insult, two due to substance abuse, 18 due to unusable schizotypy questionnaires,

and one due to noncompliance with the procedures, resulting in a final sample of 177 subjects. The sample was 75% female and 25% male, with mean age of 19.6 years (range = 15.1–32.8).

2.2. Materials

2.2.1. Schizotypy questionnaires

The schizotypy questionnaires included the Perceptual Aberration (Chapman et al., 1978), Magical Ideation (Eckblad and Chapman, 1983), Physical Anhedonia (Chapman et al., 1976) and Revised Social Anhedonia Scales (Eckblad et al., 1982), and a 13-item infrequency scale (Chapman and Chapman, 1983). Exploratory and confirmatory factor analyses of the four schizotypy scales reliably produce two factors, positive and negative schizotypy, which account for 80% of the variance (Kwapil et al., 2008). Please see Kwapil et al. (2008) for a summary of the construct validity of the schizotypy factors. Participants in the present study were assigned positive and negative schizotypy dimensional scores, based upon factor loadings derived from a sample of 6137 undergraduates assessed by Kwapil et al. (2008).

2.2.2. Neurological Evaluation Scale

The NES primarily assesses sensory integration, motor coordination, and motor sequencing. It also assesses memory recall, eye movement abnormalities, frontal release signs, and cerebral dominance. It includes 26 tasks, with 14 measures assessed and scored bilaterally. Table 1 provides a listing of these tasks with brief descriptions drawn from Buchanan and Heinrichs (1989). The original NES employed an ordinal scoring system in which tasks were scored: 0 = no abnormality; 1 = mild, but definite impairment; and 2 = marked impairment. Subsequently, [Sanders et al., 1998] and [Sanders et al., 2006] developed continuous scoring systems for error count and completion time (when applicable). We examined the utility of both the ordinal and the continuous scoring systems in a nonclinical sample in the present study. The original NES battery was supplemented with the go-no-go task ([Merriam et al., 1990] and [Sanders et al., 2006]) and the palmomental reflex ([Sanders et al., 1994] and [Keshavan et al., 2003]). A detailed administration and scoring manual was developed in consultation with one of the NES authors (R.W. Buchanan, personal communication, March 2007). Participants also completed a screening questionnaire regarding vision and hearing, history of medical conditions and head injury, and medication, drug, and alcohol use.

Table 1. Description of NES subscales and subtests (adapted from Buchanan and Heinrichs, 1989).

Subscale	Subtest	Subtest description
Sensory integration	Audio-visual integration	Subject matches auditory tapping sounds with visually presented dots.
	Stereognosis a [and] b	Subject identifies an object in hand with eyes closed.

Subscale	Subtest	Subtest description
	Graphesthesia a [and] b	Subject identifies a number written on the tip of forefinger with eyes closed.
	Extinction	Subject identifies if touched on either right/left cheek, hand, or both.
	Right/left confusion	Subject points to right or left body parts of self or examiner.
Motor coordination	Tandem walk	Subject walks in a straight line for 12 ft, heel to toe.
	Rapid alternating movements a [and] b	Subject alternates slapping leg with palm and back of hand.
	Finger–thumb opposition a [and] b	Subject touches the tip of fingers (from forefinger to pinky) with the tip of thumb.
	Finger–nose test a [and] b	Subject touches tip of nose with tip of index finger with eyes closed.
Motor sequencing	Fist-ring a [and] b	Subject alternates hand position between fist and ring.
	Fist-edge-palm a [and] b	Subject alternates hand position between fist, edge of hand, and palm.
	Ozeretski	Subject simultaneously alternates both hands between fist and palm-down positions.
	Tap production	Subject produces a series of taps.
Other	Romberg test	Subject stands with arms held parallel to the floor with eyes closed for 1 min.
	Adventitious overflow [b]	Examiner assesses fluttering movement in subject's fingers, hands, and arms during Romberg.
	Tremor [b]	Examiner assesses subject's hand tremor during Romberg.
	Memory	Subject recalls four words at 5 and 10 min intervals.
	Tap reproduction	Subject reproduces a series of auditory taps.
	Mirror movements a [and] b	Examiner assesses parallel movements of fingers during finger–thumb opposition.
	Synkinesis [b]	Subject follows a pen cap with eyes only between right and left horizontal visual field.
	Convergence [b]	Subject follows a pen cap with eyes only as cap is moved toward nose.
	Gaze impersistence a [and] b	Subject fixes gaze on pen cap at a 45

Subscale	Subtest	Subtest description
		degree angle in right and left horizontal visual fields.
	Glabellar reflex	Examiner assesses subject's blinking when glabellar region is tapped.
	Snout reflex	Examiner places tongue depressor against philtrum and assesses puckering of lips.
	Grasp reflex a [and] b	Examiner assesses subject's flexion of fingers when palm is stroked.
	Suck reflex	Examiner places tongue depressor between subject's lips and assesses pursing or sucking.
	Go-no-go task (supplemental task)	Subject lifts hand when examiner raises two, but not one, finger.
	Palmomental task (supplemental task)	Examiner strokes subject's thenar eminence to assess contraction of mentalis muscles.

NOTE: measures of cerebral dominance (i.e., handedness, footedness, and eyedness) are also assessed, but not included in the NES subscales.

a Indicates right and left side assessed separately.
b Indicates right and left side scored separately.

2.3. Procedures

Participants completed the schizotypy questionnaires at group testings. The NES and screening questionnaire were administered at individual 1-h sessions by trained graduate and undergraduate researchers. NES performance for 89 of the participants was scored simultaneously by the administrator and an independent rater. The researchers were unaware of participants' schizotypy scores.

3. Results

Analyses were computed using MPlus5 and SPSS15. The schizotypy dimensional scores for the 177 participants in the present study (positive schizotypy: $M = -.01$, SD = 1.23, range = − 1.54–4.85; negative schizotypy: $M = .29$, SD = 1.20, range = − 1.79–3.30) had unimodal distributions and correlated, $r = .25$, $p < .001$.

3.1. Schizotypy and handedness

Based on NES criteria, 89% of participants were classified right-handed, 7% left-handed, and 4% mixed-handed. Given the small number of mixed-handed participants, handedness was reclassified as right and nonright. Binary logistic regressions indicated that handedness was unrelated to positive schizotypy (OR = .85, 95% CI = .54–1.33), negative schizotypy (OR = 1.11, 95% CI = .75–1.65) or the schizotypy interaction (OR = 1.27, 95% CI = .96–1.68).

Polychoric correlations (Drasgow, 1988) were computed to examine relations between dominant/nondominant hand performance[1] to determine whether to create a single variable across hands. There was little empirical support for combining ordinal or error count data for bilateral tasks, so these data were analyzed separately (Table 2). Pearson correlations were used to assess relations between dominant/nondominant hand performance for latency data given relatively normal distributions. Latency tasks with $r > .80$ were combined into a single variable by averaging across hands.

Table 2. Relation between dominant and nondominant hand for bilateral tasks.

NES task	Ordinal[a]	Error[a]	Latency[b]
Stereognosis	−.01	.03	
Graphesthesia	.53 □	.49 □	
Rapid alternating movements	−.01	.11	.93 □
Finger–thumb opposition	.50 □□	.39 □	.90 □
Finger–nose test	.37 □		
Fist-ring	.79 □	.47 □	.91 □
Fist-edge-palm	.45 □	.45 □	.92 □
Adventitious overflow	.97 □		
Tremor	.96 □		
Mirror movements	.58 □		
Synkinesis	.55 □		
Convergence	.95 □		
Gaze impersistence	.51 □		.23 □□
Grasp reflex	.80 □		
Palmomental reflex		.39 □	

□□$p < .01$. p□≤□.001.
a Polychoric correlation.
b Pearson correlation.

3.2. Descriptive statistics and interrater reliability

Table 3 presents descriptive data, interrater reliability, and analysis plan for each NES subtest. Pairs of raters (selected from 6 judges) rated 50% of the sessions; therefore, a one-way random effects model was used to analyze interrater reliability (Shrout and Fleiss, 1979). The mean interrater reliability was .90 (SD = .11) for ordinal data; .93 (SD = .08) for error count data; and .99 (SD = .01) for latency data. Overall, 87% of the tasks had interrater reliability above .80. Given concerns regarding the applicability of the NES for nonclinical samples, nine subtests were dropped that exhibited poor interrater reliability (<.70) or minimal response variance ($\sigma \leq .32$). There were no differences in NSS rates across age, sex, or ethnicity.

Table 3. Descriptive statistics.

Task	Mean	SD	Skew	IRR	Analysis plan
Audivisual integration					
Error count	.42	.74	1.85	.97	Negative binomial regression
Ordinal	.39	.65	1.43	.96	Categorical regression
Stereognosis					
Dominant—error count	.04	.20	4.77	.85	Drop
Nondominant—error count	.27	.47	1.40	.92	Negative binomial regression
Dominant—ordinal	.05	.21	4.42	.85	Drop
Nondominant—ordinal	.26	.46	1.44	.92	Categorical regression
Graphesthesia					
Dominant—error count	.83	1.01	1.27	1.00	Negative binomial regression
Nondominant—error count	.63	.84	1.37	1.00	Negative binomial regression
Dominant—ordinal	.74	.79	.50	1.00	Categorical regression
Nondominant—ordinal	.57	.72	.86	1.00	Categorical regression
Face–hand test					
Error count	.04	.22	6.23	.66	Drop
Ordinal	.04	.22	6.23	.66	Drop
Right–left confusion					
Error count	.86	.97	.82	.98	Negative binomial regression
Ordinal	.79	.84	.41	.99	Categorical regression
Tandem walk					
Error count	.16	.45	2.94	.96	Negative binomial regression
Ordinal	.19	.52	2.75	.98	Categorical regression
Rapid alternating movements					
Dominant—error count	.06	.29	5.03	1.00	Drop
Nondominant—error count	.15	.45	3.41	1.00	Negative binomial regression
Dominant—latency	14.12	3.07	2.49	.99	Linear regression
Nondominant—latency	14.02	3.10	2.68	.97	Linear regression
Average latency	14.06	3.03	2.71	.99	Linear regression
Dominant—ordinal	.05	.22	4.12	.79	Drop

Task	Mean	SD	Skew	IRR	Analysis plan
Nondominant—ordinal	.12	.34	2.80	.95	Categorical regression
Finger–thumb opposition					
Dominant—error count	.31	.68	2.99	.79	Negative binomial regression
Nondominant—error count	.32	.67	2.29	.76	Negative binomial regression
Dominant—latency	12.40	2.85	1.04	.98	Linear regression
Nondominant—latency	12.37	2.77	1.09	.98	Linear regression
Average latency	12.39	2.74	1.07	.99	Linear regression
Dominant—ordinal	.07	.31	4.98	*	Drop
Nondominant—ordinal	.08	.30	3.63	.86	Drop
Finger–nose test					
Dominant—ordinal	.60	.68	.69	.87	Categorical regression
Nondominant—ordinal	.66	.70	.58	.84	Categorical regression
Fist-ring					
Dominant—error count	1.09	1.47	2.21	.94	Negative binomial regression
Nondominant—error count	.66	1.21	2.53	.95	Negative binomial regression
Dominant—latency	30.26	7.42	1.42	.96	Linear regression
Nondominant—latency	29.41	7.14	1.27	.99	Linear regression
Average latency	29.84	7.12	1.27	.99	Linear regression
Dominant—ordinal	.20	.50	2.48	.83	Categorical regression
Nondominant—ordinal	.15	.40	2.78	.89	Categorical regression
Fist-edge-palm					
Dominant—error count	1.85	1.79	1.77	.97	Negative binomial regression
Nondominant—error count	1.07	1.24	1.22	.92	Negative binomial regression
Dominant—latency	42.02	8.54	.57	.94	Linear regression
Nondominant—latency	41.02	9.14	1.33	.99	Linear regression
Average latency	41.52	8.67	.94	.98	Linear regression
Dominant—ordinal	.47	.64	1.02	.88	Categorical regression
Nondominant—ordinal	.21	.45	2.00	.71	Categorical regression
Ozeretski					
Error count	3.91	5.25	2.57	.98	Negative binomial regression
Latency	18.48	5.39	1.19	.96	Linear regression

Task	Mean	SD	Skew	IRR	Analysis plan
Ordinal	.79	.85	.42	.96	Categorical regression
Tap production					
Error count	.40	.82	2.82	.88	Negative binomial regression
Ordinal	.34	.61	1.59	.96	Categorical regression
Romberg					
Ordinal	.06	.26	4.87	*	Drop
Adventitious overflow					
Dominant—ordinal	.49	.65	1.00	.89	Categorical regression
Nondominant—ordinal	.46	.65	1.11	.92	Categorical regression
Tremor					
Dominant—ordinal	.14	.41	3.02	.74	Categorical regression
Nondominant—ordinal	.12	.38	3.32	.61	Categorical regression
Memory—5 min delay					
Error count	.33	.61	1.81	1.00	Negative binomial regression
Ordinal	.33	.59	1.63	1.00	Categorical regression
Memory—10 min delay					
Error count	.40	.63	1.49	1.00	Negative binomial regression
Ordinal	.39	.61	1.33	1.00	Categorical regression
Tap reproduction					
Error count	1.05	1.05	.99	.90	Negative binomial regression
Ordinal	.95	.85	.09	.94	Categorical regression
Mirror movements					
Dominant—ordinal	.82	.56	.05	.91	Categorical regression
Nondominant—ordinal	.67	.55	.03	.74	Categorical regression
Synkinesis					
Dominant—ordinal	.29	.55	1.76	.95	Categorical regression
Nondominant—ordinal	.28	.50	1.56	.93	Categorical regression
Convergence					
Dominant—ordinal	.40	.57	1.09	.88	Categorical regression
Nondominant—ordinal	.46	.64	1.06	.79	Categorical regression
Gase impersistence					
Dominant—latency	1.28	4.63	3.72	1.00	Censored regression
Nondominant—latency	1.31	4.64	3.91	1.00	Censored regression

Task	Mean	SD	Skew	IRR	Analysis plan
Dominant—ordinal	.11	.36	3.58	.96	Categorical regression
Nondominant—ordinal	.13	.41	3.34	1.00	Categorical regression
Glabellar reflex					
Error count	1.29	1.43	2.05	.76	Negative binomial regression
Ordinal	.08	.30	3.63	.65	Drop
Snout reflex					
Ordinal	.00	.00		**	Drop
Grasp reflex					
Dominant—ordinal	.16	.45	2.85	1.00	Categorical regression
Nondominant—ordinal	.10	.35	3.73	.89	Categorical regression
Suck reflex					
Ordinal	.02	.22	9.11	1.00	Drop
Palmomental reflex					
Dominant—error count	.31	.93	4.67	.38	Drop
Nondominant—error count	.32	1.42	7.71	.59	Drop
Go-no-go task					
Error count	.71	1.16	2.38	.97	Negative binomial regression

IRR = Interrater reliability.*Negative average covariance.**No variance.

3.3. NES subtest analyses

To examine the relations of positive and negative schizotypy with NSS, a series of regression analyses was conducted with NES scores as the dependent variables. Positive and negative schizotypy were entered at the first step, so the effects of each could be assessed with the other partialed out. The positive × negative schizotypy interaction was entered at the second step to examine its effect over and above the main effects. The ordinal and error count data for NES tasks were highly positively skewed. Therefore, traditional OLS linear regression was deemed inappropriate and nonparametric techniques were used. Categorical regressions (Cohen et al., 2003) were used for ordinal data, negative binomial regressions (Agresti, 2007) for error count data, and linear regressions for latency data.

Table 4 presents the regression analyses for NES subtests. In general, negative, but not positive, schizotypy was associated with NSS. Negative schizotypy was associated with increased NSS in tasks that assessed fine and gross motor coordination, motor sequencing, eye movement abnormalities, and memory recall. Positive schizotypy was associated with a few tasks that assessed sensory integration dysfunction. The schizotypy interaction term was generally unrelated to NES tasks. There was no evidence of a speed–accuracy tradeoff on the timed tasks.

Table 4. NES subtests.

	Ordinal			Error			Average latency[a]		
	Step 1		Step 2	Step 1		Step 2	Step 1		Step 2
	Positive schizotypy	Negative schizotypy	Interaction	Positive schizotypy	Negative schizotypy	Interaction	Positive schizotypy	Negative schizotypy	Interaction
NEScriterion	***β***	***β***	***β***	***B***	***B***	***B***	***β***	***β***	***β***
Audio-visual integration	.01	–.07	0	.03	.01	.03			
Stereognosis									
Nondominant	−.03	.13	−.10	−.01	**.17**[b]	−.01			
Graphesthesia									
Dominant	.02	.02	**−.16**[b]	.01	.08	**−.15**[c]			
Nondominant	**.17**[c]	−.03	−.09	**.12**[b]	−.03	−.05			
Right left confusion	**.16**[c]	.09	.06	**.14**[d]	.07	0			
Tandem walk	−.21	**.27**[c]	−.03	−.26	**.38**[c]	−.13			
Rapid movements							−.12	−.02	−.14
Nondominant	.11	.06	−.03	.02	.08	.01			
Finger–nose									
Dominant	.08	.03	−.06						
Nondominant	.13	.09	**−.15**[b]						
Fist-ring							.03	.07	**−.15**[b]
Dominant	−.13	.15	−.01	−.06	**.16**[b]	0			
Nondominant	−.04	.14	−.19	−.04	.10	**−.16**[b]			
Fist-edge-palm							−.01	.10	**−.17**[b]
Dominant	.11	**.22**[d]	−.01	.04	**.16**[d]	0			
Nondominant	.02	.08	−.05	.03	.04	−.06			
Ozeretski	.03	**.16**[c]	0	.02	**.16**[b]	−.03	−.02	.06	−.06
Tapping production	.02	0	−.11	−.05	.04	−.08			
Adventitious overflow									
Dominant	−.09	**.18**[c]	.12						
Nondominant	0	**.16**[c]	.06						
Tremor									
Dominant	.16	**.21**[b]	0						
Nondominant	.10	**.36**[e]	−.06						
Memory—5 min delay	−.05	**.24**[d]	−.11	−.04	**.26**[d]	−.11			
Memory—10 min delay	−.14	**.26**[e]	−.17	−.13	**.26**[e]	**−.15**[b]			

	Ordinal			Error			Average latency[a]		
	Step 1		Step 2	Step 1		Step 2	Step 1		Step 2
	Positive schizotypy	Negative schizotypy	Interaction	Positive schizotypy	Negative schizotypy	Interaction	Positive schizotypy	Negative schizotypy	Interaction
Tapping reproduction	−.04	.03	−.07	−.03	.01	−.05			
Finger–thumb opposition							−.10	.08	−.14
Dominant				−.06	.06	−.01			
Nondominant				−.22	.18	−.01			
Mirror movements									
Dominant	**.16**b	.06	−.07						
Nondominant	**.17**c	−.03	.01						
Synkinesis									
Dominant	.07	.13	**−.31**c						
Nondominant	**−.17**b	**.32**e	.07						
Convergence									
Dominant	−.09	.07	−.10						
Nondominant	−.03	**.17**c	.05						
Gaze impersistence									
Dominant	.01	.01	.03				.26	.73	.28
Nondominant	−.01	−.13	.15				−.37	− 2.39	2.18
Glabellar reflex				**−.11**b	.08	.02			
Grasp reflex									
Dominant	−.03	**.29**e	**−.34**c						
Nondominant	.12	.01	−.14						
Go-no-go task				**.20**c	.14	–.10			

a Latency data for Gaze impersistence was examined separately for dominant and nondominant hands.
b $p < .10$.
c $p < .05$.
d $p < .01$.
e $p < .001$.

3.4. NES composite analyses

Prior to examining the relation of schizotypy with the NES composite scores, the internal consistency of the composites was examined. Coefficient alpha is problematic with highly skewed data and it is difficult to disentangle whether a low alpha is due to the nature of the distribution or poor internal consistency. Therefore, a series of exploratory factor analyses (EFA)

was conducted. Consistent with NES subtest analyses, ordinal composites were specified as categorical distributions. EFA results for NES composites revealed that internal consistency was acceptable for motor sequencing and poor for motor coordination and sensory integration. As hypothesized, negative, but not positive, schizotypy was related to motor coordination, motor sequencing, "other," and "total" NES domains (Table 5). The positive × negative schizotypy interaction was significantly related to motor coordination and NES total. Simple slopes analyses indicated that participants with high scores on negative schizotypy and low scores on positive schizotypy performed worse in these domains, over and above the schizotypy main effects (Fig. 1 and Fig. 2). Contrary to our hypothesis, positive schizotypy was related to sensory integration dysfunction.

Table 5. NES composites excluding dropped tasks.

	Ordinal		
	Step 1		Step 2
	Positive schizotypy	Negative schizotypy	Interaction
NES criterion	*B*	*B*	*B*
Sensory integration dysfunction	.07[a]	.03	−.04[b]
Motor coordination	.05	.11[a]	−.07[a]
Motor sequencing	.01	.16[a]	−.03
Others	.01	.11[c]	−.05[b]
Total	.02	.11[d]	−.05[c]

a $p < .05$.
b $p < .10$.
c $p < .01$.
d $p < .001$.

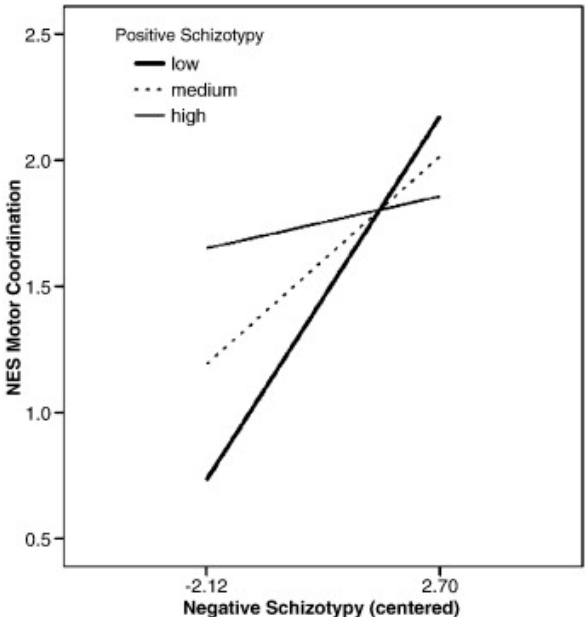

Fig. 1. Simple slopes analysis exhibiting the interaction between the predictions of positive and negative schizotypy and NES motor coordination (excluding dropped tasks).

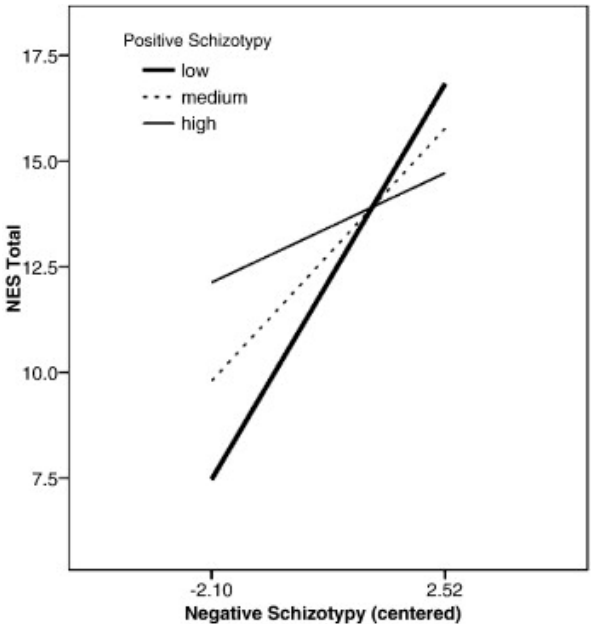

Fig. 2. Simple slopes analysis exhibiting the interaction between the predictions of positive and negative schizotypy and NES total (excluding dropped tasks).

4. Discussion

Current neurodevelopmental models posit that vulnerability for schizophrenia is expressed across a dynamic continuum of clinical and subclinical impairment referred to as schizotypy. A multidimensional model of schizotypy provides a promising framework to investigate etiological

factors relatively untainted by the catastrophic consequences of schizophrenia and to examine factors that either increase the likelihood of or protect against transition into schizophrenia-spectrum disorders. The present study extended the construct validation of schizotypy by examining relations between NSS and psychometrically identified positive and negative schizotypy.

As hypothesized, negative, but not positive, schizotypy was related to impairment in tasks that assessed fine and gross motor coordination, motor sequencing, eye movement, and memory recall. Positive schizotypy was associated with a few tasks that assessed sensory integration dysfunction (however, these unhypothesized findings require further confirmation). In general, the positive × negative schizotypy interaction term was unrelated to NSS tasks. These results are consistent with the schizophrenia literature and support the multidimensional framework of schizotypy. The schizotypy questionnaires did not inquire about neurological deficits – so the results are not simply due to overlapping content in the predictors and criteria. Furthermore, schizotypy was associated with NSS in participants who were drawn from a nonclinical sample and were functioning well enough to attend college (providing a conservative test of hypotheses). The present findings are consistent with the notion that positive and negative schizotypy differ in terms of expression and etiology. Conceptualizing and measuring positive and negative schizotypy (and by extension schizophrenia) in this manner may help to clarify inconsistencies in the literature that often treats schizophrenia-spectrum disorders as discrete and homogenous entities.

The findings that negative schizotypy was associated with impaired motor coordination and motor sequencing are consistent with current neurodevelopmental models of schizophrenia. For example,Andreasen's (1999) theory of ‘cognitive dysmetria’ suggests that disruptions in the cortico-cerebellar-thalamic-cortical circuit (CCTCC), which is used to coordinate and sequence motor and cognitive activity, leads to abnormal output that characterizes the expression of schizotypy (and thus, schizophrenia). Moreover, Andreasen (1999) suggested that three “nodes” in the CCTCC may be particularly important in schizophrenia – the cerebellum, the prefrontal cortex, and the thalamus. The cerebellum is involved in motor movement and increasing evidence corroborates its role in the etiology of schizophrenia **(**Andreasen and Peirson, 2008). Imaging studies have shown that volumetric decreases in the cerebellum are related to deficits in tasks associated with motor coordination (Bottmer et al., 2005) and motor sequencing (Keshavan et al., 2003) in patients with first-episode schizophrenia. Moreover, abnormal motor movements in early childhood helped to discriminate siblings who developed schizophrenia from siblings who did not (Walker and Lewine, 1990), and predicted adult-onset schizophrenia (Walker et al., 1994) and enlarged ventricles in adult patients (Walker et al., 1996).

Deficits in memory recall were associated with negative schizotypy. Imaging studies (e.g., Crespo et al., 1999) link memory recall deficits to decreases in cerebral blood flow in patients with schizophrenia, supporting a generalized neurological deficit. The finding that verbal memory dysfunction has been observed at illness onset and in putative schizotypes (Eastvold et al., 2007) supports its use as a risk marker for schizophrenia.

This study also found that negative schizotypy identified elevated levels of eye movement abnormalities, consistent with the literature on smooth pursuit and saccadic movement

abnormalities in patients with schizophrenia (Levy and Holzman, 1997) and putative schizotypes ([Holzman et al., 1984] and [Gooding et al., 2000]). Eye movement abnormalities reflect impaired motion processing in the middle temporal lobe, rather than a deficit in vision, *per se* (Holzman, 2000). This suggests that neural dysmaturation may affect motion processing and result in abnormal eye movements across the negative schizotypy continuum.

Despite the fact that the NES was developed for patients, the study's nonclinical sample did not simply perform at ceiling on most tasks (and the performance variance was systematically related to schizotypy). However, several tasks were dropped because of little response variance or poor interrater reliability. The question remains whether this indicates that the neurological processes tapped by these tasks are not exhibited by nondisordered schizotypes, or the tasks were too simple to capture subtle deviancy characteristic of schizotypy. Ultimately, this needs to be examined empirically. As expected, performance on the NES tasks was positively skewed; thus, nonparametric techniques should be considered with data from nonclinical samples. This study also compared ordinal (Buchanan and Heinrichs, 1989) with continuous scoring ([Sanders et al., 1998] and [Sanders et al., 2006]). Both methods produced good interrater reliability; however, the continuous system captured more variance and had higher interrater reliability values compared to the ordinal system. Therefore, continuous scoring appears to be preferred with nonclinical samples that are expected to display a milder expression of NSS.

The internal consistency of the NES composites is rarely reported in the literature. In this study, only the motor sequencing composite exhibited acceptable internal consistency. This raises concerns about whether these composites are appropriate for nonclinical samples. However, since the consensus in the literature holds that negative, but not positive symptoms are related to NSS, it may be that the effect of negative schizotypy on the expression of NSS is so large that it is seen even with relatively unreliable indicators.

The study demonstrated that there was little support to combine or collapse bilateral task scores for ordinal or error count tasks (although there was support for latency tasks). Future research should examine these associations empirically before collapsing bilateral tasks and may consider coding handedness as dominant/nondominant to examine the relation between NSS and cerebral lateralization – two phenomena proposed to underlie schizophrenia etiology.

The results from this study support schizotypy as an expression of neurodevelopmental vulnerability for schizophrenia and corroborate the notions that neural dysmaturation predates the appearance of schizophrenia and can be detected across the schizotypy continuum. In addition, the differential relation of NSS with positive and negative schizotypy supports the multidimensional construct of schizotypy. Note that there is still controversy about whether schizotypy best reflects a proneness to psychosis or a normal personality trait (see [Meehl, 1990] and [Claridge, 1997]); however, the reliable identification of these underlying dimensions should facilitate the resolution of this larger issue. These findings also provide further support for using psychometric screening inventories to detect meaningful variation related to schizotypy and NSS. Future studies should employ the psychometric method to assess the relation between schizotypy and multiple domains of risk including biobehavioral, cognitive, and affective features to reliably indentify people along the schizotypy continuum. This will provide a

platform for longitudinal study, which will aid in our understanding of the development and expression of schizotypy.

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Contributors

This study was completed as fulfillment of Jessica Kaczorowski's Masters thesis. Jessica Kaczorowski and Thomas Kwapil designed the study, managed the literature searches, performed the statistical analyses, and wrote the manuscript. Jessica Kaczorowski was responsible for the subject recruitment and data collection. Neus Barrantes-Vidal provided consultation and contributed to the preparation of the manuscript. All authors contributed to and have approved the final manuscript.

Conflict of interest

None of the authors had conflicts of interest regarding the research described in the manuscript.

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1 For mixed-handed participants, dominant handedness was assigned to the writing hand.