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Neurological soft signs and schizotypal dimensions in unaffected siblings of patients with schizophrenia

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ABSTRACT

The objectives were to determine the neurological soft signs (NSS) scores in unaffected siblings of patients with schizophrenia compared with healthy controls and to examine their relationships with schizotypal dimensions. Participants comprised 31 unaffected siblings of patients with schizophrenia and 60 healthy controls matched according to age, gender and school level who were assessed by the Schizotypal Personality Questionnaire (SPQ) and the Krebs et al. NSS Scale. Higher NSS total scores and sub-scores were found in the unaffected siblings compared with the controls. The SPQ total score was significantly higher in unaffected siblings compared with control subjects. The NSS total score was positively correlated with the SPQ total score and the SPQ disorganization sub-score in unaffected siblings of patients with schizophrenia. Additionally, in unaffected siblings, motor coordination and integration abnormalities were positively correlated with the SPQ total score and the cognitive-perceptual sub-score. Motor integration abnormalities were also correlated with the SPQ disorganization sub-score. These results reveal that NSS, especially motor signs, are associated with some schizotypal dimensions in siblings of patients with schizophrenia, suggesting the value of using both assessments to study high risk populations.

1. Introduction

Neurological soft signs (NSS) are minor or subtle neurological signs indicating non-specific cerebral dysfunction. NSS include different kinds of impairments in such functions as fine motor coordination, right–left orientation, laterality and sensory-perceptual performance. Many previous studies reported an increased number of NSS in first-degree relatives of patients with schizophrenia and in subjects at high risk for developing schizophrenia (Griffiths et al., 1998; Ismail et al., 1998; Chen et al., 2000; Lawrie et al., 2001; Yazici et al., 2002; Gourion et al., 2004), emphasizing the importance of these anomalies as schizophrenia vulnerability markers. However, the relationship between NSS and other clinical vulnerability markers, especially schizotypal features, has not been elucidated.

Schizotypal personality traits are found to be more frequent in first-degree relatives of schizophrenia patients than in normal controls (Kety et al., 1994; Kendler et al., 1995; Tsuang et al., 1999; Vollema et al., 2002). These findings suggest that higher rates of schizotypal traits in relatives reflect the biological-genetic vulnerability to schizophrenia. Many interviews and self-report questionnaires have been developed to assess schizotypal personality traits. The Chapman Psychosis-Proneness Scales have been used to assess both positive and negative schizotypy. The Perceptual Aberration Scale (PAS; Chapman et al., 1978a,b) and the Magical Ideation Scale (MIS; Eckblad and Chapman, 1983) assess positive schizotypy, whereas the Social Anhedonia Scale (SAS; Eckblad et al., 1982) and the Physical Anhedonia Scale (PhAS; Chapman et al., 1978a,b) assess negative schizotypy. The three-dimensional structure of schizotypy was demonstrated by the Schizotypal Personality Questionnaire (SPQ; Raine, 1991). Factor-analytical studies showed that questionnaire items of schizotypal traits can be reduced to three factors, i.e. the positive, negative and disorganization dimensions of schizotypy (Raine et al., 1994; Vollema and Hoijtink, 2000; Calkins et al., 2004).

Schizotypal personality features and some neurological abnormalities have been shown to aggregate in the relatives of schizophrenia patients, supporting the view that both are likely to reflect genetic contributions to liability to schizophrenia (Nuechterlein et al., 2002; Siever et al., 2002). However, limited studies have dealt with the relationship between NSS and schizotypal features. These studies have focused on samples of school or university students (Obiols et al., 1999; Barrantes-Vidal et al., 2003; Barkus et al., 2006). Only one recent study (Bollini et al., 2007) examined the first-degree relatives of schizophrenic patients. Results of these studies were divergent: some reported no

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Table 1
Demographic characteristics of unaffected siblings and healthy controls.

Demographic characteristics	Unaffected siblings $n=31$	Healthy controls $n=60$	P
Mean age (years) ± S.D.	32.4 ± 6.2	30.8 ± 6.7	NS[a]
Min–Max	23–48	20–46	
Gender (M/F)	22/9	40/20	NS[b]
School level (years) ± S.D.	10.6 ± 4.3	9.8 ± 3.2	NS[a]
Handedness (R/L)	29/2	57/3	NS[b]

Note: [a]t-test [$df=89$]; [b]Chi-square test [$df=1$]; S.D.: Standard Deviation; NS: Non-significant.

association between NSS and schizotypal traits (Obiols et al., 1999), while others found an association of NSS with both negative and high schizotypy (Barrantes-Vidal et al., 2003) or with positive schizotypy (Barkus et al., 2006). Bollini et al. (2007) showed that NSS were associated with schizotypal features in a sample of healthy controls but not in first-degree relatives of patients with schizophrenia.

Furthermore, in patients with schizophrenia, the NSS scores were correlated with negative symptoms and disorganization symptoms (Bombin et al., 2005; Compton et al., 2007; Mechri et al., 2008). In the first-degree relatives of patients with schizophrenia, the relation between NSS and dimensions of schizotypy has not been elucidated. This approach holds the promise of elucidating continuities and discontinuities between schizotypy and schizophrenia (Fanous et al., 2001; Cannon et al., 2002). It can also permit the development of a composite phenotype, which increases the probability of identifying the genetic architecture of schizophrenia spectrum disorders (Cadenhead and Braff, 2002; Gourion et al., 2004; Siever and Davis, 2004).

The aims of this study were to determine the NSS scores in unaffected siblings of patients with schizophrenia compared with healthy controls and to examine the correlation between NSS scores and schizotypal dimensions.

2. Methods

2.1. Subjects

A case-controlled study was carried-out on 31 unaffected siblings of patients with schizophrenia (22 men and 9 women) and 60 healthy controls (40 men and 20 women). This study was conducted at a public mental health centre in the University Hospital of Monastir (Tunisia). Full siblings were recruited when visiting the patients with schizophrenia or upon invitation. Control subjects were recruited from the hospital staff. Both groups were matched according to age, gender and school level. All participants come from the same geographic area and were fluent French speakers.

Exclusion criteria were age superior to 50 years, presence of psychiatric disorder of axis I disorder of DSM-IV-TR (Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision), personal history of severe somatic or neurological disorder, and alcohol or psychoactive substance dependence. Psychiatric disorders were ruled out among siblings of patients with schizophrenia and control subjects by direct assessment, conducted by a senior psychiatrist according to the DSM-IV-TR check list (American Psychiatric Association, 2000). Control subjects had to be free of any axis I disorder and without any indication of psychotic disorders in their first degree relatives. All subjects gave informed consent and were assured of confidentiality of the data being collected. The demographic characteristics of the two groups are summarized in Table 1.

2.2. Procedure

All subjects were assessed with the French version of the Schizotypal Personality Questionnaire (SPQ) (Dumas et al., 2000) and the Krebs et al. (2000) Neurological Soft Signs Scale (NSS). The SPQ, developed by Raine (1991), is a 74-item self-report measure. It evaluates the nine features of schizotypal personality disorder, described by the DSM-IV-TR (American Psychiatric Association, 2000), regrouped in three dimensions: positive dimension or cognitive-perceptual dysfunction (referential thinking, magical ideation, unusual perceptive experiences and suspiciousness), negative dimension or interpersonal dysfunction (excessive social anxiety, constricted affect, and no close friends) and disorganization dimension (odd beliefs, odd or eccentric behavior). A dimensional approach to schizotypal personality by calculating the SPQ total score and sub-scores for each dimension was taken.

The NSS scale, validated by Krebs et al. (2000), is composed of 23 items rated from 0 to 3, regrouped in five consistent factors: Motor coordination (hand dysrhythmia, finger opposition, fist edge–palm, foot dysrhythmia, alternative movements: foot speed, alternative movements: hand speed, standing heel-to-toe), Motor integration (Romberg, apraxia, tandem walk, finger-to-nose, gait, tongue protrusion), Sensory integration (stereognosia, hand–face, constructive apraxia, graphesthesia, RL [right-left] recognition), Quality of lateralization (RL confusion, lateral preference, RL asymmetry), and Involuntary movements (abnormal movement and posture, mirror movements). The NSS total score and sub-scores for each of the factors were calculated.

Two raters (AM and HS) were trained to perform the neurological assessment. The entire examination for NSS and SPQ scales took approximately 30 min per subject. The interrater reliability of the assessment of NSS was established by two raters who jointly examined 20 independent subjects. The intra-class correlation coefficient (SPSS: two-way Mixed Effect Model, confidence interval = 95%) was 0.90 [0.77–0.95], which was comparable to that found in the validation study (Krebs et al., 2000). The internal consistency of the SPQ, based on Cronbach's alpha coefficient, was 0.87 for total the SPQ and, respectively, 0.81, 0.73 and 0.64 for the positive, negative and disorganization sub-scales. These coefficients were similar to those reported by Dumas et al. (2000).

2.3. Data analysis

Statistical analysis was carried out with SPSS 10.0 software. Results were expressed as mean ± S.D.. Independent samples Student's t-tests and Chi-square tests were used to compute group differences for continuous and categorical variables, respectively. The correlation between NSS and SPQ scores was calculated using Pearson correlation coefficients, with a threshold of significance of $P \leq 0.05$.

3. Results

3.1. Neurological Soft Signs scores

Unaffected siblings had total score and sub-scores of NSS that were significantly higher than those of healthy controls (total mean score = 10.7 ± 3.4 *vs.* 4.2 ± 2.0, $t=9.84$, $df=89$, $P<0.001$) (Table 2). NSS total score and sub-scores were not related to age or school level, and did not differ by gender for either group.

3.2. Schizotypal Personality Questionnaire scores

The SPQ total score was significantly higher in unaffected siblings than in healthy controls (total mean score = 27.0 ± 8.8 *vs.* 22.1 ± 10.6, $t=2.19$, $df=89$, $P=0.03$). The cognitive-perceptual sub-score was 12.0 ± 4.9 for siblings *vs.* 10.1 ± 4.8 for controls ($t=1.77$, $df=89$, $P=0.08$), the interpersonal dysfunction sub-score was 10.3 ± 3.7 for siblings *vs.* 8.2 ± 5.9 for controls ($t=1.82$, $df=89$, $P=0.07$) and the disorganized sub-score was 4.8 ± 3.6 for siblings *vs.* 3.8 ± 1.9 for controls ($t=1.63$, $df=89$, $P=0.10$). SPQ scores were not related to age or school level, and did not differ by gender in either group.

3.3. Correlations between Neurological Soft Signs and Schizotypal Personality Questionnaire scores

A positive correlation was found between NSS and SPQ total scores in both sibling ($r=0.46$, $P=0.009$) and control groups ($r=0.28$, $P=0.03$). There was no significant difference between the two correlation coefficients ($P=0.36$). In unaffected siblings of

Table 2
NSS total score and sub-scores in unaffected siblings and healthy controls.

NSS scores	Unaffected siblings $n=31$	Healthy controls $n=60$
Motor coordination sub-score: mean ± S.D.	5.0 ± 1.8***	2.0 ± 1.5
Min–Max	2–9	0–6
Motor integration sub-score: mean ± S.D.	1.7 ± 1.0***	0.6 ± 0.8
Min–Max	0–4	0–4
Sensory integration sub-score: mean ± S.D.	2.7 ± 1.1***	1.0 ± 1.0
Min–Max	0–5	0–4
Quality of lateralization sub-score: mean ± S.D.	1.1 ± 1.0**	0.4 ± 0.7
Min–Max	0–4	0–3
Involuntary movement sub-score: mean ± S.D.	0.3 ± 0.4*	0.06 ± 0.3
Min–Max	0–2	0–2
NSS total score: mean ± S.D.	10.7 ± 3.4***	4.2 ± 2.0
Min–Max	5–17	2–10

Note: S.D.: Standard Deviation; NSS: Neurological Soft Signs.
Unaffected siblings *vs.* healthy controls t-test [$df=89$]: *$P<0.05$; **$P<0.01$; ***$P<0.001$.