Schizotypy and pathological personality profile in siblings of patients with psychosis

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Schizotypy has been proposed to be the expression of the genetic vulnerability to schizophrenia. Schizotypal features have been associated with personality dimensions found in patients with psychosis. In this study, we compared the Dimensional Assessment of Personality Pathology - Basic Questionnaire (DAPP-BQ) scores of patients with psychosis, siblings scoring higher on schizotypy (SSHS), and siblings scoring lower (SSLS). The SSHSs displayed a DAPP-BQ profile characterized by high scores in the dimensions of affective lability, anxiousness, submissiveness, social avoidance, identity problems, oppositionality, narcissism, and restricted expression, distinguishing them from the SSLS. Due to these dimensions, SSHSs are more similar to the patients' DAPP-BQ profile. The results suggest that this pathological personality profile might contribute to increase the risk of developing psychosis in siblings who have more schizotypal features.

Esquizotipia y perfil de personalidad patológica en hermanos de pacientes psicóticos. Esquizotipia y perfil de personalidad patológica en hermanos de pacientes psicóticos. La esquizotipia ha sido propuesta como la expresión de la vulnerabilidad genética para la esquizofrenia. Las características esquizotípicas han sido asociadas con las dimensiones de personalidad encontradas en pacientes con psicosis. En este estudio comparamos las puntuaciones del Dimensional Assessment of Personality Pathology - Basic Questionnaire (DAPP-BQ) de pacientes con psicosis, hermanos con puntuaciones altas en esquizotipia (SSHS) y hermanos con puntuaciones bajas (SSLS). Los SSHS mostraron un perfil del DAPP-BQ caracterizado por puntuaciones elevadas en las dimensiones de labilidad afectiva, ansiedad, sumisión, evitación social, problemas de identidad, oposición, narcisismo y expresión restringida, distinguiéndolos de los SSLS. Estas dimensiones hacen a los SSHS más parecidos al perfil del DAPP-BQ de los pacientes. Los resultados sugieren que este perfil de personalidad patológica podría contribuir a incrementar riesgo de desarrollar psicosis en los hermanos que tienen más características esquizotípicas.

Family-genetic studies have shown the importance of genetics in the aetiology of psychosis (Tsuang, Gilbertson, & Faraone, 1991; van Os, Linscott, Myin-Germeys, Delespaul, & Krabbendam, 2009). Meehl proposed a model of the cause and pathogenesis of schizophrenia and related states, where polygenic potentiators play an important role in this developmental process, interacting with biopsychosocial factors (Meehl, 1990). Depending on the coexistence of these factors, the genetic vulnerability or schizotaxia could develop in clinical schizophrenia or nonpsychotic schizotypy (Meehl, 1990). In the genetic predisposition for schizophrenia, schizotypy was proposed to be a pure expression of schizotaxia (Braff & Freedman, 2002). Schizotypy have been related to schizophrenia and related states in a variety of domains: psychophysiology, neurocognitive performance, structures and functions of brain,

Fecha recepción: 20-4-10 • Fecha aceptación: 7-9-10 Correspondencia: Lorena Moreno Samaniego Hospital Psiquiàtric Universitari Institut Pere Mata, IISPV Universidad Rovira i Virgili 43206 Reus (Spain) e-mail: morenol@peremata.com personality, and psychosocial functioning (Barrantes-Vidal, Ros-Morente, & Kwapil, 2009; Cadenhead & Braff, 2002; Raine, 2006; Tsuang, Stone, Tarbox, & Faraone, 2002).

Some of the most widely used procedures to detect the risk for psychosis are the high-risk studies whose objective is to investigate the subjects who have traits and characteristics that make them vulnerable to develop the disorder. This population includes firstdegree relatives of patients with psychosis, who are in a greater genetic risk than general population, and who have personality characteristics that distinguish them from people without family history of psychotic disorders.

Elevated levels of schizotypal features have been reported in relatives of patients with psychosis, considering it as a risk factor for psychosis (Kendler & Walsh, 1995; Kremen, Faraone, Toomey, Seidman, & Tsuang, 1998; Vollema, Sitskoorn, Appels, & Kahn, 2002; Lien et al., 2010). In some studies it has been observed a defensive attitude of the relatives on the schizotypal assessment (Grove,Lebow,Clementz,Cerri,Medus,& Iacono, 1991; Gutiérrez, Caqueo, & Ferrer, 2006; Katsanis, Iacono, & Beiser, 1990; Albéniz, 2004). They participate in these studies because of their biological relation with the patient, and the schizotypal features are similar to the symptoms that can present their diagnosed relatives. Thus, we think it could be necessary to evaluate the defensive attitude of the relatives in schizotypal questionnaires to avoid any response bias.

Personality traits that may be shared by everyone, such as neuroticism and extraversion, could be emphasized in schizotypy (Asai, Sugimori, Bando, & Tanno, 2010). Bora and Veznedaroglu (2007) hypothesized that only relatives with higher schizotypy would have a temperament and character profile similar to that of patients with schizophrenia. They administered the Temperament and Character Inventory (TCI; Cloninger, Pryzbeck, Svrakic, & Wetzel, 1994) in a two samples of relatives: with high and low schizotypy. High schizotypy group had higher scores on harm avoidance, and self-transcendence, compared with low schizotypy group, who had a more mature personality profile, with higher selfdirectedness and cooperativeness.

There are also other studies about the personality traits of these relatives, that found high scores on neuroticism, introversion, and rigidity, and low scores on frustration tolerance (Maier, Minges, Lichtermann, Heun, & Franke, 1994). Smith, Cloninger, Harms, and Csernansky (2008) found in siblings higher harm avoidance and self-trascendence of the TCI-R (Cloninger et al., 1994), compared with healthy subjects. They were more similar to patients on these dimensions, but differed from them by higher self-directedness and cooperativeness.

When these personality patterns of perceiving, relating and thinking about the environment and oneself, are inflexible and maladaptive, subjective distress or significant functional deficits can occur, developing into pathological personality. Livesley proposed a behavioural-genetic model of personality pathology and elaborated an empirical, dimensional measure, the Dimensional Assessment of Personality Pathology - Basic Questionnaire (DAPP-BQ; Livesley, Jang, & Vernon, 1998). Silberschmidt and Sponheim (2008) used the DAPP-BQ with relatives of patients with psychosis, and observed a pathological personality profile that distinguished them from healthy controls, showing lower stimulus seeking, and higher social avoidance, and a trend to higher scores on anxiousness, submissiveness, and restricted expression.

In this study we used the DAPP-BQ to evaluate the pathological personality traits in siblings of patients with psychosis, taking into account their schizotypal level. Our main objective is to test the hypothesis that siblings with more schizotypal features would have a similar personality profile to that of patients. To do this we aim first, to compare the DAPP-BQ pathological personality dimensions of the patients with those of the siblings, in order to test if the siblings would have lower scores than the patients. Second, to compare the pathological personality dimensions of the DAPP-BQ between patients, siblings with more schizotypal features, and siblings with less schizotypal features. In these comparisons we corrected the effects of gender and age. Third, we compared the sibling responses on the lie scale (L) of the EPQ-R to ensure that the division of the groups into higher and lower scores on schizotypy was not influenced by response bias. Finally, we explored the differences of the DAPP-BQ scores in siblings paired to replicate the results of previous analysis.

Methods

Participants

This is a cross-sectional, analytical study with different comparative groups. The study sample was made up of 72 subjects: 41 patients with psychosis, 31 siblings of patients with psychosis.

All subjects were recruited as part of a broader Psychosis Family Study investigating phenotypes and genotypes of functional psychosis. The patients were recruited from a short stay hospital unit at the Psychiatric University Hospital Institut Pere Mata (Reus, Spain), when they were clinically stable according to medical criteria. Patients were aged between 21 and 52 (M= 34.31, sd = 8.8). They presented psychotic disorders following DSM-IV criteria (American Psychiatric Association, 1994) after Schedule for Clinical Assessment in Neuropsychiatry (SCAN; Vázquez-Barquero, 1993) administration. These were: paranoid schizophrenia (34.1%), residual schizophrenia (24.4%), nonspecified psychotic disorder (14.6%), delirious disorder (12.2%), non-differentiated schizophrenia (9.8%), and schizoaffective disorder (4.9%). Patients were excluded from the study if they had cognitive failure, disabling psychosis, evidence of organic illness or drug-induced psychosis. The study also excluded those patients whose participation was not advisable according to medical criteria and those who had no siblings.

The sibling group were divided into two groups with the cutoff point in the mean Schizotypal Personality Questionnaire (SPQ) total score (M=9.42, sd=7.95). Those who scored above the mean, were called «siblings scoring higher on schizotypy» (SSHS), and those who scored below, «siblings scoring lower on schizotypy» (SSLS). SSHS group were made up of 4 men (36.4%) and 7 women (63.6%) aged between 23 y 53 (M=39.41, sd=9.9). These were siblings of different types of patients with psychosis: 54.5% schizophrenia, 36.4% delusional disorder, 9.1% non-specified psychotic disorder. The SSLS group were made up of 11 men (55%) and 9 women (45%) aged between 26 and 58 (M=39.74, sd=10.6). These were also siblings of different types of patients: 75% schizophrenia, 20% non-specified psychotic disorder, and 5% schizoaffective disorder. Siblings were excluded if they were adopted or they had psychotic symptoms (SCAN - measured).

Figure 1 shows the sample selection process flowchart.

Instruments

The Schedule for Clinical Assessment in Neuropsychiatry questionnaire (SCAN; Vázquez-Barquero, 1993) was used to determine the patients and siblings diagnosis. This questionnaire contains a set of instruments integrated into a semi-structured psychiatric interview based on the PSE-10 (Present State Examination - Tenth Edition). The psychiatric diagnosis were obtained in accordance with DSM-IV criteria (American Psychiatric Association, 1994), generated by the CATEGO programme.

To assess the schizotypal features of the siblings, we used the Schizotypal Personality Questionnaire (SPQ) by Raine (1991), in its Spanish version translated and validated by Grasa, Morte, Benito, Gich, Torrubia, & Barbanoj (2004). The SPQ is a self-assessment scale containing 74 items with a yes/no answer format and a scoring range of 0 to 74. SPQ is based on the DSM-III-R criteria for Schizotypal Personality Disorder (Spitzer, Gibbon, Skodol, Williams, & First, 1990). Higher scores indicating higher levels of self-reported schizotypy. The Spanish version of the scale has shown a high internal reliability (α =.90), which is equal to Raine's original version. The criterion validity is high and correlates significantly with the SCID-II measurements (r=.694, p<.01), as well as the convergent validity on the O-LIFE scale (r=.696, p<.01) (Mason, Claridge, & Jackson, 1995). In general, the good psychometric properties of the original version of the SPQ are maintained. This



Figure 1. Sample selection process flowchart. SPQ: Schizotypal Personality Questionnaire; SSHS: siblings scoring higher on schizotypy; SSLS: siblings scoring lower on schizotypy. *There were two patients who had two siblings in the sample

questionnaire has been used previously in a Spanish sample of siblings of patients with psychosis (Albéniz, 2004).

We use the lie escale (L) of the Spanish version of the Eysenck Personality Questionnaire - Revised (EPQ-R; Eysenck & Eysenck, 1997), which is part of the test battery of the Psychosis Family Study, to compare the responses of the two sibling groups. This scale is suitable for measuring the positive distortion trend in these conditions under which concealment would seem appropriate because they were biological relatives of hospitalized patients. The L scale has 18 items with a yes/no answer format. In the Spanish version, this scale has a high internal reliability (α = .76 for men, and α = .77 for women), and high test-retest reliability (*r*= .86).

Pathological personality was evaluated using the Dimensional Assessment of Personality Pathology - Basic Questionnaire (DAPP-BQ; Livesley, Jackson, & Schroeder, 1992; Livesley et al., 1998) in its Spanish adaptation by Gutiérrez-Zotes et al., (2008). It is a self-administered questionnaire containing 290 items with five answer options for each item. The items include 18 dimensions or traits of pathological personality: submissiveness, affective lability, anxiousness, insecure attachment, cognitive dysregulation, identity problems, social avoidance, oppositionality, narcissism, stimulus seeking, callousness, rejectionality, conduct problems, restricted expression, intimacy problems, compulsivity, suspiciousness, and self-harm. These dimensions are grouped together forming four second-order factors or domains: emotional dysregulation, dissocial behaviour, inhibitedness and compulsivity. The Spanish version shows a high internal reliability (α = .75 to .93), correlation coefficients were on average .07. A review of the DAPP-BQ can be found in Hernández, Gutiérrez, Valero, Gárriz, Labad, and Gutiérrez-Zotes (2009). This questionnaire has

been used previously in relatives of patients with schizophrenia (Silberschmidt & Sponheim, 2008).

Procedure

All of the participants consented to take part in the study voluntarily, without receiving any reward, and signed an Informed Consent form. The patients were asked for permission to seek the participation of their siblings, who were later contacted to explain to them the nature of the study and to obtain their signed Informed Consent form. Then they were explained how to fill in the selfadministered questionnaires. The patients completed the DAPP-BQ while they were hospitalized and clinically stabilized, and the siblings were given the SPQ and the DAPP-BQ to fill in at home.

Data analysis

We compared the sociodemographic characteristics of the three groups in the sample using contrast statistics such as chi squared (χ^2) for the categorical variables, difference mean (Student *t*-test) and ANOVA for the continuous variables.

A Kolmogorov-Smirnov test was done to evaluate the normality of the questionnaire scores. We used an ANCOVA with the Bonferroni correction to compare the DAPP-BQ scores of the groups, with gender and age as a covariates. We computed the effect size (omega squared, ω^2) of group from ANCOVA using the formula from Hays (1981) to adjust effect estimate from the eta squared (η^2), avoiding bias sample. We compared the scores of the two sibling groups on the L scale of the EPQ-R with a Student *t*-test. Finally, to compare the DAPP-BQ scores of the sibling paired, we analysed 23 pairs of patients with their respective siblings (Figure 1), using a Wilcoxon signed-rank test for two related samples.

The software used was the SPSS program, version 15.0.

Results

There were no significant differences between the three groups for sociodemographic characteristics, except for marital status, where patients were more single (82.9%) than SSHS (36.4%) and SSLS (40%) (Table 1).

The DAPP-BQ and SPQ scores were normally distributed. There were statistical significant differences (p < .05) in all the DAPP-BQ domains and dimensions between patient and sibling groups, except for intimacy problems (t=9.49, p=.346). When we compared the patient group with the SSLS group, these differences remained (Table 2). There were no statistical significant differences between patients and SSHS scores in the majority of domains and dimensions, except for cognitive dysregulation, suspiciousness, and dissocial behaviour, conduct problems, and callousness. Differences between the two sibling groups were mainly in the emotional dysregulation domain (except for insecure attachment, cognitive dysregulation, and suspiciousness), and in the inhibitedness domain (specifically on restricted expression) (Table 2). Figure 2 shows the pathological personality profiles of the three sample groups. The DAPP-BQ dimensions with a large effect size on the group differences following Cohen's benchmarks (Cohen, 1969) are in emotional dysregulation, affective lability, anxiousness, social avoidance, identity problems, oppositionaliy, cognitive dysregulation, narcissism, suspiciousness, dissocial behaviour, callousness, and restricted expression (Table 2).

Age had no covariance with any of the dimensions. Gender modified the effect of the dissocial behaviour domain scores (F= 4.514, df= 1, p= .037, η^2 = .065), and the conduct problems dimension (F= 8.421, df= 1, p=.005, η^2 = .115).

No statistical significant differences were found between the two sibling groups in the L scale of the EPQ-R (t= .315, p= .755). The mean scores of the two groups (SSLS: M= 9.85, sd= 4.308; SSHS: M= 10.27, sd= 3.069) in this scale were within the normative data of the Spanish sample (Eysenck & Eysenck, 1997). We have therefore considered that the division of the sibling groups into higher and lower scores on schizotypy was appropriate, and differences in pathological personality were valid.

In the evaluation of the scores of the subgroup of pairs of patients and siblings, all of the above findings that were statistically significant remained so. We also found a more similar pathological personality profile between patients and SSHS pairs, than between patients and SSLS pairs. Statistical significant differences also remained the same on paired comparisons of patients and SSHS, with three exceptions: patients scored significantly higher in compulsivity (z= -2.24, p= .025, Cohen's d= 1.259), whereas the differences disappeared in dissocial behaviour (z= -1.48, p= .139, Cohen's d= .60), and callousness (z= -1.54, p= .123, Cohen's d= .752). In paired comparisons of patients and SSLS, the only dimension without statistical significant difference between them was compulsivity (z= -1.76, p= .078, Cohen's d= .669). Patients continue having the highest scores in all dimensions, followed by

<i>Table 1</i> Sociodemographic characteristics of the sample groups						
	Patients (n = 41)	SSHS (n = 11)	SSLS (n = 20)			
	Mean (sd)					
Age	34.31 (8.8)	39,41 (9.9)	39.74 (10.6)			
	n (%)					
Gender						
Male	29 (70.7)	4 (36.4)	11 (55.0)			
Female	12 (29.3)	7 (63.6)	9 (45.0)			
Marital status ^{a, b}						
Single	34 (82.9)	4 (36.4)	8 (40.0)			
Married / Separated	7 (17.1)	7 (63.6)	12 (60.0)			
Education						
Elementary / Primary	19 (46.3)	3 (27.3)	7 (35.0)			
Secondary / Universitary	22 (53.7)	8 (72.7)	13 (65.0)			
Occuppation						
Employee	33 (80.5)	9 (81.8)	17 (85.0)			
Student	3 (7.3)	1 (9.1)	0 (0.0)			
Retired	1 (2.4)	0 (0.0)	0 (0.0)			
Homemaker	1 (2.4)	1 (9.1)	3 (15.0)			
Pensioner	3 (7.3)	0 (0.0)	0 (0.0)			

Note: SSHS= siblings scoring higher on schizotypy; SSLS= siblings scoring lower on schizotypy.

p<0.05

^a Between patients and SSHS

b Between patients and SSLS

<i>Table 2</i> Analysis of covariance of the DAPP-BQ mean scores for each sample group								
Domains / dimensions DAPP-BQ	Patients (n= 41)	SSHS (<i>n</i> = 11)	SSLS (<i>n</i> = 20)					
		Mean (sd)		\mathbf{F}^*	ω^2			
Self-harm ^b	23.73 (11.6)	17.82 (8.6)	12.80 (1.9)	7.089	0.186			
Emotional dysregulation ^{b.e}	443.61 (98.1)	373.18 (69.9)	265.40 (51.3)	24.038	0.449			
Affective lability ^{b,c}	45.68 (14.1)	39.09 (9.9)	26.60 (6.8)	12.862	0.310			
Anxiousness ^{b,c}	47.27 (13.5)	40.00 (11.8)	25.20 (8.0)	17.958	0.377			
Submissiveness ^{b,c}	40.12 (8.7)	39.73 (12.0)	29.50 (5.2)	9.464	0.217			
Insecure attachment ^b	51.27 (14.6)	40.91 (13.5)	34.60 (9.0)	9.410	0.226			
Social avoidance ^{b,c}	47.00 (12.5)	40.91 (10.2)	26.40 (7.6)	20.795	0.384			
Identity problems ^{b,c}	42.95 (12.4)	35.45 (12.6)	24.80 (7.3)	16.046	0.314			
Oppositionality ^{b,c}	45.46 (10.5)	41.64 (14.2)	29.20 (7.5)	13.481	0.299			
Cognitive dysregulation ^{ab}	41.61 (13.9)	29.36 (5.9)	20.25 (4.6)	20.922	0.410			
Narcissism ^{b,c}	45.12 (12.7)	40.64 (9.8)	28.35 (8.1)	10.858	0.280			
Suspiciousness ^{a,b}	40.22 (12.9)	25.73 (6.0)	20.50 (4.6)	20.188	0.421			
Dissocial behaviour ^{a,b}	158.15 (41.5)	125.55 (15.8)	110.75 (17.6)	9.403	0.275			
Conduct problems ^{a,b}	34.46 (13.8)	22.00 (5.4)	22.55 (5.6)	5.604	0.208			
Rejectionality ^b	44.61 (11.5)	38.18 (8.0)	32.65 (7.5)	6.711	0.196			
Callousness ^{a,b}	37.56 (11.3)	28.18 (5.1)	25.50 (5.0)	8.526	0.251			
Stimulus seeking ^b	41.51 (12.1)	37.18 (9.5)	30.05 (7.2)	5.182	0.160			
Inhibitedness ^{b,c}	80.00 (18.7)	76.55 (10.1)	60.80 (12.7)	12.053	0.192			
Intimacy problems	34.32 (9.8)	36.18 (6.0)	30.05 (9.4)	4.182	0.027			
Restricted expression ^{b,c}	45.68 (11.1)	40.36 (7.6)	30.75 (5.5)	15.622	0.308			
Compulsivity ^b	57.32 (10.2)	49.00 (10.8)	45.85 (12.9)	7.290	0.162			
<i>Note</i> : SSHS= siblings scoring higher on schizotypy; SSLS= siblings scoring lower on schizotypy; <i>F</i> = statistic for the group effect; ω^2 = omega squared, represents the effect size of group from ANCOVA. * <i>df</i> = 2 <i>p</i> <0.05 (after Bonferroni correction) * Between patients and SSHS								

the SSHS, and finally by the SSLS. Therefore, the results from the ANCOVA remained.

Between patients and SSLS

Between SSHS and SSLS

Discussion and conclusion

In this study we tested that the DAPP-BQ dimensions were higher in patients with psychosis than in siblings of this type of patients, as we expected. Furthermore we showed that SSHS had similar DAPP-BQ profile to patients. These results are consistent with those of Bora and Veznedaroglu (2007), who emphasize the importance of schizotypy in vulnerability to schizophrenia, finding different personality profiles based on this characteristic.

The dimensions that describe the pathological personality profile of SSHS, and that make them more similar to patients with psychosis, belong to emotional dysregulation, and inhibitedness domains. On one hand, emotional dysregulation has been associated with the trait of neuroticism (Jang & Livesley, 1999;

Maruta, Yamate, Iimori, Kato, & Livesley, 2006; van Kampen, 2002), and when this trait is elevated, it has been related with the risk for developing psychosis (Olin & Mednick, 1996; Van Os & Jones, 2001). Furthermore, high scores on emotional dysregulation has been associated with schizotypal personality disorder (Pukrop, Gentil, Steinbring, & Steinmeyer, 2001). On the other hand, inhibitedness domain has been negatively associated with the trait of extraversion (Jang & Livesley, 1999; Maruta et al., 2006). And high scores on this trait contributed negatively to the risk of psychosis (Van Os & Jones, 2001). These findings suggest us that both being a SSHS and having high scores on emotional dysregulation and inhibitedness may contribute to increase the risk of developing psychosis. It could also be, as pointed out by Berenbaum, Taylor, and Cloninger (1994), that these pathological elevated dimensions, shared by relatives and patients, reflect illness variation rather than personality variation. SSLS, however, had a more adaptive personality, reflected by their low scores on DAPP-BQ. This profile, that distances them from patients, and from SSHS, could be a protective factor to them for psychosis.

Rrestricted expression and social avoidance dimensions, that characterize SSHS, were proposed by Livesley (2007) to describe schizotypal personality disorder. Social avoidance also appeared as a significant predictor for this personality disorder in the study of Bagge and Trull (2003). These dimensions have also been found with higher scores in relatives of patients with schizophrenia than in healthy controls (Silberschmidt & Sponheim, 2008). From these findings we think that these dimensions could be related to the expression of the schizotaxia in SSHS.

We don't think that all SSHS should develop clinical psychosis during the life course because of their personality profile. To know it we should do a longitudinal study. But, as pointed out by Barrantes-Vidal et al., (2009), although they will never descompensate, they may demonstrate this personality adjustment, similar to that of patients with psychosis.

In this study we found that a DAPP-BQ pathological personality profile characterized by high scores on the dimensions of affective lability, anxiousness, submissiveness, social avoidance, identity problems, oppositionality, narcissism, and restricted expression, can distinguish between siblings who had more schizotypal features and those who had less. This profile makes SSHS more similar to patients. These findings make us think that this DAPP-BQ profile may possible be related to increased vulnerability to psychosis in the SSHS.

A limitation of this study is that we didn't make a probabilistic sampling, restricting selection biases. People who accepted to take part in the study were motivated to collaborate, and in the case of patients were also chosen if they had a more appropriate symptoms for evaluation. Furthermore, the fact that patients were hospitalized generated a special condition to evaluation and results should be analyzed in this context. We think it could be interesting to replicate these findings with siblings of non-hospitalized psychotic patients.

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Figure 2. Curves of pathological personality profiles of the three sample groups. We emphasize the DAPP-BQ dimensions in which patients and siblings scoring higher on schizotypy (SSHS) differed from siblings scoring lower on schizotypy (SSLS). Data are expressed as mean of each group on DAPP-BQ dimensions. * p<0.05 differences between patients and SSLS and between SSHS and SSLS. Points on curves represent these significant differences

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