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Clustering of Schizotypal Features in Unaffected First-Degree Relatives of Schizophrenia Patients

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Meehl conceptualized schizotypy as the phenotypic manifestations of a neural integrative defect resulting from a schizophrenia diathesis. The majority of schizotypy studies recruited subjects from the general population and revealed a multidimensional construct. This 2-phase investigation first examined the clustering of schizotypy in 194 unaffected relatives of schizophrenia patients using the Chapman Psychosis Proneness scales and then directly compared the cognitive profiles of negative schizotypal individuals and positive schizotypal individuals with schizophrenia patients and controls. In the first phase, cluster analysis categorized 194 unaffected relatives of schizophrenia patients into positive schizotypy (n = 33), negative schizotypy (n = 66), mixed schizotypy (n = 27), and low schizotypy (n = 64). Positive schizotypal participants showed more self-report pleasure experiences than negative schizotypal participants, replicating earlier cluster analytic findings. In the second phase, 27 negative schizotypal individuals, 18 positive schizotypal individuals, 19 schizophrenia patients, and 29 controls were recruited. Although the groups were matched in terms of age, gender, and IQ, they differed significantly in cognitive profiles. While schizophrenia patients exhibited the broadest cognitive impairments, negative schizotypal participants exhibited visual memory, working memory, and verbal fluency impairments, and positive schizotypal participants exhibited logical memory, visual memory, working memory, and theory-of-mind impairments. Among people with familial risk of schizophrenia, individuals exhibiting positive rather than negative schizotypal features resembled schizophrenia patients in cognitive profiles. Using the psychometric-familial method to identify schizotypy, our findings support the heterogeneity of schizotypy as well as the potential utility of the positive schizotypy dimension in genetically high-risk individuals to predict the risk of developing schizophrenia.

Key words: schizotypy/first-degree relatives/clustering analysis/cognitions

Introduction

Meehl[1] coined the term "schizotaxia" to describe the underlying neural integrative defect reflecting the genetic liability to schizophrenia, while the resultant personality organization was termed "schizotypy." According to this model, there are several possible outcomes of schizotaxia, ranging from the mildly compensated schizotypy to the most severe form of decompensaton, schizophrenia.[2] Schizotaxia is believed to be associated with cognitive and behavioral deficits, clinical and subclinical symptoms, and social impairment.[2,3]

Although Meehl's schizotypy is a taxonic construct,[3] different methods have been used to identify schizotypal individuals according to a dimensional construct.[4,5] Tsuang et al[6] distinguished the "psychometric high-risk method" (which was also termed "clinical method") from the "familial research method." The "psychometric high-risk method" typically recruits nonclinical samples such as college students with psychometrically defined schizotypy based on self-reported questionnaires. These subjects presumably have no family history of schizophrenia. On the other hand, the "familial research method" (also known as "genetic high-risk method") typically recruits unaffected relatives of schizophrenia patients. The

psychometric method and the familial method are 2 complementary means of detecting schizotypal individuals.

The heterogeneity of schizotypal features is well supported by empirical studies,[5,7,8] which consistently demonstrated the existence of multiple dimensions within the construct, echoing the positive and negative symptoms of schizophrenia. Whereas the positive dimension of schizotypy is characterized by perceptual aberrations and unusual ideations, the negative dimension of schizotypy is characterized by reduced emotion and social functioning.[9] Early studies[10] suggested that individuals elevated in the negative schizotypy dimension manifested marked social withdrawal, poor rapport, and decreased pleasure in social interactions. Similarly, previous studies[11–13] suggested that schizotypal individuals identified using the "familial research method" tended to exhibit more negative schizotypal features, while schizotypal individuals identified using the "psychometric high-risk method" tended to exhibit more positive schizotypal features. In addition, recent evidence also supported that existence of another subtype of schizotypy, exhibiting both positive and negative schizotypy dimensions, that is, mixed schizotypy.[14–16]

Notably, many previous studies[17–19] utilized different self-reported scales to measure schizotypal features. Whereas scales such as the Schizotypal Personality Questionnaire (SPQ)[20] or the Oxford-Liverpool Inventory of Feelings and Experiences (O-LIFE)[21] measure both different dimensions of schizotypy, the Chapman Psychosis Proneness Scales is generally believed to be one of the most comprehensive instruments to measure schizotypy dimensions.[22] Several previous studies[14–16] administered the Chapman scales to college students and classified the subjects based on the positive and negative dimensions of schizotypy.

Evidence[9,23,24] suggested that schizotypy is associated with cognitive dysfunctions, consistent with Meehl's model[1] of schizotaxia. However, it is unclear whether the positive or the negative schizotypy dimension is more strongly associated with cognitive dysfunctions. A few previous studies[25,26] compared the cognitive performance of positive schizotypal individuals with that of negative schizotypal individuals and reported that negative schizotypy rather than positive schizotypy is associated with memory impairments. It is plausible that the heterogeneity of schizotypy indicated a varied degree of inherited genetic liability to schizophrenia.

This 2-phase investigation aimed to perform cluster analysis for schizotypal features using the Chapman Psychosis Proneness Scales in a sample of unaffected first-degree relatives of schizophrenia patients. Previous studies identified schizotypal individuals using the "psychometric high-risk method" and demonstrated that some subjects might be elevated in both the positive and negative schizotypy dimensions.[15,16] Based on empirical evidence[15,16] and the recent theoretical framework[5] to support the existence of different subtypes of schizotypy, we hypothesized that the clusters in our sample would consist of positive, negative, and mixed schizotypy groups (ie, exhibiting both positive and negative schizotypal features). Furthermore, we aimed to examine the relationship between the different schizotypy dimensions and cognitive functions. After 6 months, we specifically compared negative schizotypal individuals and positive schizotypal individuals with schizophrenia probands, in terms of their cognitive performance. Based on previous findings,[25,26] we expected that negative schizotypal individuals would resemble schizophrenia probands more closely than positive schizotypal individuals, in terms of cognitive performance.

Phase 1 Method

Recruitment and Procedure

The early psychosis invention clinic in Castle Peak Hospital is a research-oriented clinical center.[27] We first invited all outpatients with DSM-IV[28] schizophrenia in the clinic to volunteer the phone contacts of their unaffected relatives. A qualified psychiatrist contacted these unaffected relatives by phone and invited them to complete a set of self-reported questionnaires. The eligibility screening was conducted over the phone by the qualified psychiatrist using a structured interview. Inclusion criteria included (1) aged 16–65, (2) being a first-degree relative of schizophrenia patient, and (3) Chinese ethnicity. Exclusion criteria were as follows: (1) a lifetime history of DSM-IV psychiatric disorder, (2) known history of mental retardation, (3) self-reported substance misuse in the past 6 months, and (4) known history of neurological disorders. If the unaffected first-degree relatives of schizophrenia patients were eligible and willing to participate, they were asked to complete the following set of documents: the consent form, the eligibility checklist, and self-reported questionnaires on schizotypal features, anhedonia, and emotional expressivity. Out of 305 sets of questionnaires distributed to eligible participants, we were able to collect 205 sets. However, 11 of them could not be used (8 did not fall into our targeted age range, 1 self-reported a history of psychosis, 2 were missing too much data, ie, more than 10% of items on the self-reported questionnaires were incomplete). The final sample in the first phase of this study consisted of 194 unaffected first-degree relatives of schizophrenia patients. All participants provided informed written consent. This 2-phase investigation was approved by the local ethics committee.

Measures

To measure participants' schizotypal features, we administered 4 Chapman Psychosis Proneness Scales. The

positive dimension of schizotypy was measured using the Chinese version[16] of the Magical Ideation Scale (MIS),[29] which assesses beliefs about invalid causality, and the Chinese version[16] of the Perceptual Aberration Scale (PerAbS),[30] which measures transient body image and perceptual distortions. The negative dimension of schizotypy was measured using the Chinese version[31] of the Revised Physical Anhedonia Scale (RPAS),[32] which measured an individual's ability to experience sensory and aesthetic pleasure, and the Chinese version of the Revised Social Anhedonia Scale (RSAS),[31] which measured social withdrawal and deficits in the ability to experience pleasure from social and/or interpersonal relationships.

Two additional self-reported questionnaires were used for cross-validation. First, participants completed the Chinese version[33] of the Temporal Experience of Pleasure Scale (TEPS),[34] which measured the wanting-liking facets[35] of everyday life pleasure. Second, they completed the Chinese version[36] of the Emotional Expressivity Scale (EES),[37] which measured the extent of outwardly displayed emotions.

Analysis

The Statistical Package for the Social Sciences (SPSS) 20.0 was used for data analysis. The Phase 1 sample was categorized into subgroups using *K*-mean clustering, based on participants' ratings on the 4 Chapman scales. We followed the same method as in the previous cluster analytic studies[15,16,38] on the Chapman scales. First, we combined the MIS and PerAbS scores to generate the positive schizotypy score and also combined the RPAS and RSAS scores to generate the negative schizotypy score. Second, we performed *K*-means iterative cluster analysis, based on the positive and negative schizotypy scores. In the iterative cluster analysis, a participant would be assigned to a cluster that fits closest, in terms of the positive and negative symptom dimensions. The value of the cluster center would then be recomputed, using the mean of all cases within the clusters, to form a new cluster center. The participants would then be reassigned to the new clusters using the same rule. These steps were repeated until no appreciable cluster center change could be found. The iterative cluster analysis allowed us to minimize the within-group differences (with maximum within-cluster homogeneity) and to maximize the between-group differences (with maximum between-cluster heterogeneity).

Using the *K*-mean clustering method as described above, we explored 10 different cluster solutions (ranged from 1 to 10 clusters) and estimated the total within-cluster sum of square in each respective cluster solutions. This strategy allowed us to determine the optimal number of clusters in our sample. Consistent with the previous cluster analytic findings,[14–16,39] the 4-cluster model appeared to be optimal, which consisted of 4 subgroups of schizotypy, ie, low schizotypy (LS), negative schizotypy (NS), mixed schizotypy (MS), and positive schizotypy (PS). Multivariate analysis of variance (MANOVA) was then carried out to test the discriminant validity of the cluster analysis. To cross-validate the resultant clusters of Phase 1 sample, we compared the TEPS and EES ratings between the 4 subgroups of participants, using ANOVAs.

Phase 1 Results

Our exploration of different cluster solutions showed that forcing an additional cluster into the 4-cluster solution did not improve much the total within-cluster sum of square. Supplementary figure 1 shows the results of the final 4-cluster solution of the *K*-mean iterative cluster analysis and the features of low schizotypy (n = 64), negative schizotypy (n = 66), mixed schizotypy (n = 27), and positive schizotypy (n = 33) subgroups in our sample. The subgroups did not differ in age (Kruskal-Wallis [3], P = .86) and gender ratio (χ^2 [3] = 2.18, P = .54).

As shown in table 1, MANOVA revealed that the 4 subgroups differed significantly in the overall schizotypal

Table 1. Age and Gender Distribution and Positive and Negative Schizotypy Scores for the 4 Schizotypy Clusters

Cluster	LS (n = 64)		NS (n = 66)		MS (n = 27)		PS (n = 33)		P	$F_{[3, 186]}/\chi^2$	Post Hoc Comparison
	Median/Ratio	IQR	Median/Ratio	IQR	Median/Ratio	IQR	Median/Ratio	IQR			
Age	45.50	30	43.50	27	47.00	26	28.00	29	.857	2.18	—
M:F	22:42	—	27:39	—	8:19	—	15:18	—	.537		
	Mean	SD	Mean	SD	Mean	SD	Mean	SD			
Pos. scores	0.122	0.513	0.141	0.515	0.272	0.803	0.275	0.696	<.001*	78.21	MS, PS > NS, LS
Neg. scores	0.306	0.342	0.415	0.402	0.482	0.372	0.344	0.353	<.001*	182.31	MS > NS > PS > LS

Note: LS, low schizotypy; NS, negative schizotypy; MS, mixed schizotypy; PS, positive schizotypy; M, male; F, female; Pos. scores, Positive Schizotypy Scores; Neg. scores, Negative Schizotypy Scores; IQR, interquartile range.
*$P \leq .05$.

features (F[6, 368] = 117.04, Wilks' lambda = 0.12. P < .001). Follow-up univariate ANOVAs found that the subgroups differed significantly in both the positive schizotypy dimension (F[3, 186] = 78.21, P < .001, partial eta squared = 0.56) and the negative schizotypy dimensions (F[3, 186] = 182.31, P < .001, partial eta squared = 0.75). Post hoc analysis showed that the positive schizotypy and mixed schizotypy groups had greater positive schizotypy scores than the negative schizotypy and low schizotypy groups (P's < .001). Post hoc analysis also revealed that the negative schizotypy scores were greatest for the mixed schizotypy group, followed by the negative, positive, and low schizotypy groups in respective order (ie, MS > NS > PS > LS, P's < .001).

As shown in table 2, the resultant cluster grouping appeared to be valid, in view of the significant group differences in everyday life pleasure experiences and emotional expressivity, as measured by the TEPS and the EES. In particular, ANOVAs showed that the subgroups differed significantly in the TEPS anticipatory pleasure (F[3, 185] = 11.83, P < .001) and consummatory pleasure (F[3, 185] = 13.77, P < .001) subscales, and the EES emotion suppression subscale (F[3, 186] = 3.14, P = .03), but not the EES emotion expression subscale (F[3, 186] = 0.53, P = .66). Regarding the TEPS anticipatory pleasure subscale, post hoc comparisons showed that the low schizotypy and the positive schizotypy subgroups experienced more anticipatory pleasure in everyday life encounters than the negative schizotypy (P = .003) and mixed schizotypy groups (P < .001). Regarding the TEPS consummatory pleasure subscale, the low schizotypy and the positive schizotypy subgroups also experienced more "in-the-moment" (consummatory) pleasure than the negative schizotypy (P < .001 and P = .003, respectively) and the mixed schizotypy groups (P < .001 and P = .002, respectively). Regarding the EES emotion suppression subscale, post hoc comparisons revealed that the negative schizotypy subgroup tended to suppress their emotion more often than the low schizotypy subgroup (P = .03).

Phase 2 Method

Recruitment and Procedure

Six months after the completion of the first phase, we contacted all the participants in the positive schizotypy and negative schizotypy subgroups by phone and invited them to participate in the second phase of this investigation. We confirmed that none of the 33 positive schizotypy participants and 66 negative schizotypy participants had been admitted to any psychiatric unit and/or attended a psychiatric clinic. Over half (18 of 33) of the positive schizotypy group and 41% (27 of 66) of the negative schizotypy group consented to participate in the second phase. In addition, we recruited 31 DSM-IV[28] schizophrenia patients from our early psychosis intervention clinic[27] and 29 healthy controls from the neighboring community. The inclusion and exclusion criteria for the participants in the schizotypy groups were the same as in the Phase 1. Inclusion criteria for the schizophrenia patients and controls included age between 16 and 65, Chinese ethnicity, and ability to speak and understand Cantonese. Exclusion criteria for the schizophrenia patients were a known history of mental retardation, severe hearing or visual impairment, history of head injury or neurological disorders, history of substance abuse in the past 1 month, history of substance dependence in the past 6 months, history of receiving electroconvulsive therapy in the past 6 months, and having a score of 6 or above on items P1 (delusions), P2 (conceptual disorganization), and P3 (hallucinations) of the Positive and Negative Syndrome Scale (PANSS).[40] In addition to the same exclusion criteria as those for the schizophrenia

Table 2. ANOVA and Post Hoc Tests Comparing the Schizotypy Clusters

	LS (n = 64)		NS (n = 66)		MS (n = 27)		PS (n = 33)		$F_{[3, 186]}$	P	Post Hoc Comparison
	Mean	SD	Mean	SD	Mean	SD	Mean	SD			
TEPS[a]											
Anti_Pl	36.34	6.95	32.40	6.19	29.37	6.31	37.18	5.32	11.83	<.001*	LS, PS > NS, MS
Cons_Pl	43.70	6.75	37.51	7.16	36.19	6.85	42.67	5.85	13.77	<.001*	LS, PS > NS, MS
Total	80.05	12.70	70.03	11.87	65.56	11.29	79.85	9.78	15.33	<.001*	LS, PS > NS, MS
EES											
Supp	46.51	7.83	42.79	6.15	43.19	10.13	43.79	5.70	3.14	.027*	LS > NS
Exp	16.64	5.00	16.47	4.84	16.19	4.11	17.55	3.80	0.53	.660	
Total	63.16	9.59	59.26	7.42	59.37	11.34	61.33	6.13	2.55	.057	

Note: ANOVA, analysis of variance; LS, low schizotypy; NS, negative schizotypy; MS, mixed schizotypy; PS, positive schizotypy; TEPS, the Temporal Experience of Pleasure Scale; Anti_Pl, anticipatory pleasure; Cons_Pl, consummatory pleasure; EES, the Emotional Expressivity Scale; Supp, suppression factor; Exp, expression factor.
[a]One participant's data are missing.
*$P \leq .05$.

patients, all controls were interviewed by a qualified psychiatrist using structured interview to ensure the absence of a DSM-IV psychiatric disorder. All participants in the Phase 2 provided written informed consent.

Demographic information was obtained via interview. Schizophrenia participants' clinical data such as age of onset, duration of illness, and medication dosage were gathered from medical records. We administered the PANSS and the Scale for the Assessment of Negative Symptoms (SANS)[41] to schizophrenia patients. Handedness was determined using the Annett Handedness scale.[42] IQ was estimated using a prorating method based on 3 subsets (arithmetic, similarities, and digit span) of the Wechsler Adult Intelligence Scale-Revised.[43]

Participants underwent a battery of cognitive assessments. Auditory and visuospatial memory was assessed using the Chinese version of the logical memory and visual memory reproduction subscales of the WAIS-R.[44] We utilized the Letter Number Span Test (LNT)[45] to measure working memory performance. To assess attention and inhibition, we used the computer-based Sustained Attention to Response Task (SART),[46] in which 225 digits (between 0 and 9) were presented serially and visually, each for 250 ms, followed by a 900-ms mask (ie, a cross at the center of the computer screen). Participants were asked to respond with a key press to each digit, but they had to withhold button pressing behavior when they encountered the digit "3," which only occurred in 25 out of 225 trials in the paradigm. We calculated the SART efficiency estimate,[47] which would take into account the number of correct responses per unit time, reaction time, and commission error (ie, incorrectly pressing a button at the occurrence of the digit "3"). Cognitive flexibility/set-shifting was measured by the modified Wisconsin Card Sorting Test (WCST).[48] We recorded the number of perseverative errors and total categories passed (maximum of 6). Initiation and generativity were measured by the animal name semantic verbal fluency test,[49] in which participants were required to state as many animal names as possible in a 60-second period. We recorded the total number of novel responses. To assess theory of mind (ToM), we administered the computerized cartoon-based Yoni Task.[50] Details of the Chinese version of this paradigm have been described elsewhere.[51,52] In short, participants were asked to look at the eye gaze and facial expression cues on the face of "Yoni," a cartoon character, in 6 different conditions, namely first-order cognitive (Cog1), first-order affective (Aff1), first-order physical (Phy1), second-order cognitive (Cog2), second-order affective (Aff2), and second-order physical (Phy2). Early studies[51,52] suggested that Aff2 and Cog2 are more sensitive in detecting ToM deficits in schizophrenia patients, and therefore, we only recorded the percentage of correct response in these 2 conditions.

Analysis

Group differences in demographics, estimated IQ, and cognitive performance were examined by chi-square tests for categorical variables and 1-way ANOVA with post hoc Hochberg GT comparisons for parametric data and Kruskal-Wallis test for nonparametric data.

Phase 2 Results

As shown in table 3, schizophrenia patients, unaffected relatives, and controls were matched in age, gender, and estimated IQ (P's > .05). The positive schizotypy group and the negative schizotypy group were having similar composition in terms of the ratio of siblings, parents, and offspring (χ^2 [2] = 0.135, P = .094). Among the schizophrenia group, 27 of them were receiving second-generation antipsychotics (SGA), 3 were receiving both conventional antipsychotics and SGA, and only one of them was receiving conventional antipsychotics alone. The mean chlorpromazine equivalence was 258.3 mg/d (SD = 187.7 mg/d).

As depicted in table 4 and supplementary figure 2, the 4 groups differed significantly across multiple cognitive tasks. After Bonferroni corrections, both schizophrenia patients (P = .026) and positive schizotypal participants (P = .001) performed significantly poorer than the healthy controls in terms of immediate recall of logical memory. Participants with positive schizotypy also performed poorer on the delayed recall of the logical memory task, relative to healthy controls (P = .001). Regarding the immediate recall of visual reproduction task, schizophrenia patients (P < .001), negative schizotypal participants (P = .008), and positive schizotypy participants (P = .020) all exhibited significant impairment, compared with controls. Similarly, on the delayed recall of visual reproduction task, schizophrenia patients (P = .001), negative schizotypal participants (P = .034), and positive schizotypal participants (P = .042) all performed worse than healthy controls.

Compared with the healthy controls, all the other groups showed indications of less accurate executive functioning. The schizophrenia patients (P = .007), negative schizotypal participants (P = .021), and positive schizotypal participants (P = .001) were significantly less accurate on the LNT than the controls. Both the schizophrenia patients (P = .015) and the positive schizotypal participants (P = .005) achieved significantly fewer LNT categories than the controls. The schizophrenia patients (P = .002) and the negative schizotypal participants (P = .044) produced significantly fewer novel words on the verbal fluency task compared with the controls. The

Table 3. Phase 2 Results: Participants' Demographics and Clinical Characteristics

	Schizophrenia Patients (n = 31)		Negative Schizotypy (n = 27)		Positive Schizotypy (n = 18)		Healthy Controls (n = 29)			
	Mean	*SD*	Mean	*SD*	Mean	*SD*	Mean	*SD*	$F_{[3, 101]}/\chi^2$	*P*
Age (years)	32.48	11.27	32.89	11.44	34.61	13.34	28.38	9.83	1.37	.26
Handedness (right vs left)	28 vs 3		27 vs 0		18 vs 0		28 vs 1		4.71	.20
Gender (male vs female)	16 vs 15		11 vs 16		8 vs 10		11 vs 18		1.28	.73
Education (years)	12.55	3.21	12.15	2.97	11.89	3.77	14.86	2.23	5.44	**<.01**
Composition of unaffected relatives (parents vs siblings vs children)			5 vs 20 vs 2		4 vs 13 vs 1				0.14	.94
Estimated IQ	112.16	10.27	117.81	13.05	110.06	12.12	115.07	9.78	2.14	.10
Age of onset (years)	29.27	10.56								
Duration of untreated psychosis (months)	22.79	40.57								
Duration of illness (months)	35.27	40.39								
Chlorpromazine equivalence (mg/d)	258.29	187.66								
PANSS positive subscale	8.16	2.79								
PANSS negative subscale	9.52	2.47								
PANSS general subscale	18.77	2.10								
SANS affective flatting subscale	0.67	0.61								
SANS alogia subscale	0.35	0.49								
SANS avolition/ apathy subscale	0.41	0.55								
SANS anhedonia/ asociality subscale	0.79	0.83								
SANS attention subscale	0.42	0.65								

Note: IQ, intelligence, PANSS, the Positive and Negative Syndrome Scale, SANS, the Scale for the Assessment of Negative Symptoms.
$P < .05$ are in bold.

Table 4. Phase 2 Results: Cognitive Performances of Schizophrenia Patients, Unaffected Relatives, and Healthy Controls

	Schizophrenia Patients (n = 31)		Negative Schizotypy (n = 27)		Positive Schizotypy (n = 18)		Healthy Controls (n = 29)				Sch vs HC	NS vs HC	PS vs HC	Sch vs NS	Sch vs PS	PS vs NS
	Mean	*SD*	Mean	*SD*	Mean	*SD*	Mean	*SD*	$F_{[3,101]}$	*P*	Post Hoc Comparison (*P* values)					
Logical memory (immediate)	9.42	3.39	11.93	3.72	7.78	3.34	12.03	3.43	8.06	**<.01**	.26	1.00	**<.01**	**.04**	.51	**<.01**
Logical memory (delayed)	8.06	3.49	9.89	3.61	5.94	3.10	9.93	3.58	6.34	**<.01**	.22	1.00	**<.01**	.26	.23	**<.01**
Visual reproduction (immediate)	20.03	3.09	20.63	3.94	20.56	2.85	23.31	1.98	6.72	**<.01**	**<.01**	**.01**	**.02**	.97	.99	1.00
Visual reproduction (delayed)	19.23	3.40	20.22	4.30	20.00	2.77	22.72	2.31	6.07	**<.01**	**<.01**	**.03**	**.04**	.83	.97	1.00
LNT accuracy	15.45	3.09	15.67	3.41	14.22	4.68	18.34	2.53	6.73	**<.01**	**.01**	**.02**	**<.01**	1.00	.77	.64
LNT longest item pass	5.87	1.09	6.30	1.17	5.61	1.33	6.79	1.08	5.03	**<.01**	**.02**	.05	**.01**	.65	.97	.28
WCST correct response	35.03	3.95	36.50	0.91	34.39	5.44	36.14	1.51	1.67	.18						
WCST preservative error	1.55	1.39	1.11	1.34	1.83	4.72	0.90	0.94	0.84	.47						
Verbal fluency	18.45	4.11	19.67	5.86	19.50	7.91	23.66	4.44	5.07	**<.01**	**<.01**	**.04**	.07	.95	.99	1.00
SART efficiency	0.87	0.12	0.94	0.12	0.86	0.16	0.96	0.14	3.95	**.01**	**.04**	1.00	.09	.15	1.00	.25
Yoni Aff2	0.77	0.16	0.79	0.14	0.70	0.21	0.86	0.14	3.50	**.02**	.27	.63	**.01**	1.00	.57	.32
Yoni Cog2	0.70	0.19	0.81	0.16	0.65	0.24	0.87	0.15	7.24	**<.01**	**<.01**	.77	**<.01**	.15	.92	**.03**

Note: NS, negative schizotypy; PS, positive schizotypy; Sch, schizophrenia patients; HC, healthy controls; PANSS, the Positive and Negative Syndrome Scale; LNT, the Letter Number Span Test; WCST, the Wisconsin Card Sorting Test; SART, the Sustained Attention Response Task; Yoni Aff2, the affective second-order Theory of Mind facet of the Yoni Task; Yoni Cog2, the cognitive second-order Theory of Mind facet of the Yoni Task.
$P < .05$ are in bold.

patient group also displayed less efficiency on the SART, $P = .036$.

Between-group comparisons in terms of ToM, as measured by the Yoni Task, also revealed significant group differences (P's < .05). Both the schizophrenia patients ($P = .004$) and the positive schizotypal participants ($P = .001$) performed poorly on the Cog2 of the Yoni Task. Furthermore, on the Aff2 of the Yoni Task, the positive schizotypal participants performed significantly worse than the controls, $P = .012$.

Discussion

This 2-phase study was one of the few studies to examine the clustering of schizotypal features in nonclinical populations at familial risk for developing schizophrenia. The 4 clusters found in the first phase of this study replicated prior studies[14–16] that were conducted in college samples. Differing from prior studies[15,16] that applied a forced 4-cluster solution to their college samples, our study using a "genetic high-risk" sample has adopted a more empirical approach to identify the apparently optimal 4-cluster solutions. Although recruitment of schizotypal participants in the second phase of this study was conducted in a dimensional approach rather than taxonic approach (thus differing from a recent study[19] that used the maximum covariance analysis to identify schizotypy), our resultant clusters showed significant differences in self-reported pleasure and emotional expressivity, suggesting the validity of our clusters. Importantly, our findings supported further research to identify schizotaxia using both the "genetic high-risk" and "psychometric high-risk" methods.[7] Moreover, our study is the one of the few attempts[53] to directly compare the cognitive performance of this kind of identified schizotypal sample with schizophrenia patients and healthy individuals. The second phase of this study further clarified the nature of positive and negative schizotypy, as our findings appeared to indicate that, compared to their negative schizotypal counterparts, unaffected relatives of schizophrenia patients exhibiting positive schizotypal features showed more severe "decompensation" in cognitive performance, to an extent similar to schizophrenia patients.

To our knowledge, this study is first of its kind to classify unaffected first-degree relatives of schizophrenia patients to different types of schizotypy, using the Chapman scales. After exploring alternative solutions, our cluster analysis in the first phase of this study yielded 4 schizotypy clusters, ie, low schizotypy, negative schizotypy, mixed schizotypy, and positive schizotypy. Comparing with previous studies[14–16] that recruited college populations and cross-validated the resultant 4 schizotypy clusters, based on interview[15] and questionnaire[15,16] measurements of psychopathology, our study only utilized self-reported questionnaires that tapped into anhedonia and emotional expressivity. On the other hand, our findings that mixed and negative schizotypal participants experienced less anticipatory and consummatory pleasure than positive and low schizotypal participants, and negative schizotypal participants suppressed emotion more severely than low schizotypal participants were consistent with prior findings.[16] However, we did not find any significant difference between the schizotypy clusters in the expression factor of the EES. Given that schizophrenia is a heterogeneous diagnostic entity with variable manifestations, our findings from cluster analysis revealed a similarly heterogeneous presentation of schizotypy. Findings as such appear to support the notion that schizotypy is a milder form of expression of the schizophrenia spectrum. In fact, the pattern of schizotypy clusters generated showed resemblance to those found in other cluster analytic studies conducted in schizophrenia samples.[54,55]

Given that the resultant positive schizotypy cluster and negative schizotypy cluster were unlikely to exhibit a co-elevation of the positive and negative schizotypy dimensions,[14–16] these 2 cluster groups were specifically selected to examine the relationship of cognitive impairments with the positive and the negative schizotypy dimensions. Moreover, the inclusion of schizophrenia patients as a comparison group in the second phase of this study further allowed us to examine which schizotypy cluster group would have a higher resemblance to schizophrenia patients in terms of their cognitive profile. Consistent with previous findings,[56] the schizophrenia patients in our study exhibited a broad array of cognitive impairments compared with health controls, in auditory memory, visuospatial memory, executive function, attention, and ToM. The schizophrenia patients also exhibited the broadest cognitive impairments compared with the schizotypal relatives. Not surprisingly, given its status as a putative endophenotype of a schizophrenia diathesis,[57] working memory impairments were observed in schizophrenia patients, positive schizotypal relatives, and negative schizotypal relatives. Consistent with prior literature regarding unaffected first-degree relatives of schizophrenia patients,[58] both the positive schizotypal and negative schizotypal relatives exhibited several other cognitive impairments, compared with healthy controls.

Notably, our findings indicated that unaffected relatives of schizophrenia patients exhibiting positive schizotypal features were impaired in terms of auditory memory, visuospatial memory, working memory, and cognitive and affective facets of ToM. On the other hand, the relatives characterized by negative schizotypy were impaired in terms of visuospatial memory, working memory, and verbal fluency. These findings buttress support for earlier notion that negative schizotypy and positive schizotypy are distinct, separable constructs. Moreover, the pattern of cognitive impairments found in unaffected relatives exhibiting different schizotypal features appear to resemble the pattern found in clinical probands with schizophrenia. For instance, paranoid delusional symptoms

have been associated with ToM impairments in schizophrenia patients,[59] and logical memory impairments are believed to contribute to jumping-to-conclusions bias commonly found in schizophrenia patients with delusions.[60] On the other hand, evidence supported that schizophrenia patients with more prominent negative symptoms are associated with more impairments in verbal fluency.[61]

Taken together, these findings generally suggested that unaffected relatives of schizophrenia patients exhibiting positive schizotypal features showed more severe cognitive impairments than relatives characterized by negative schizotypy, and cognitively more resembled schizophrenia patients. It is possible that in people with a genetic diathesis for schizophrenia, the manifestation of positive symptoms would signify a higher risk of impending schizophrenia, similar to those defined as ultra high-risk/prodrome cases.[62] However, attenuated positive symptoms are found in 5% of the general population[4] and therefore might not signify prodromal schizophrenia. Moreover, it is likely that the positive schizotypes identified in prior college samples[14–16] may have inherited fewer schizophrenia susceptibility genes than either the negative or positive schizotypal individuals in our enriched familial schizotypal sample.

This study has several limitations. First, only 54.5% of the positive schizotypal relatives and 40.9% of the negative schizotypal relatives identified in the cluster analysis completed cognitive assessments. Thus, we had a smaller sample of unaffected first-degree relatives of schizophrenia patients than what would be optimal for subsequent analyses. Second, we cannot rule out the potential effects of selection bias. Third, we assumed that all participants classified by cluster analysis exhibited strong schizotypal features. Moreover, we did not measure the depressive symptoms in both positive schizotypal and negative schizotypal participants, which might exacerbate cognitive impairments. Last, we only recruited the positive schizotypy and negative schizotypy subgroups in the second phase of this study and did not examine the cognitive performance of the mixed schizotypy subgroup. It is noteworthy that those schizotypal individuals showing high levels of both positive and negative symptom dimensions might show the highest resemblance to schizophrenia patients and should be studied in further research using familial-psychometric schizotypy sample. Future studies should further explore the multidimensional construct of schizotypy, using both behavioral[5] and neurobiological approaches.[63]

To conclude, this 2-phase study demonstrated the heterogeneity of schizotypal features in unaffected relatives of schizophrenia patients. Our findings appeared to suggest that positive schizotypy in genetic high-risk individuals is associated with severe cognitive impairments, which might signify decompensated schizotaxia. Further studies on familial-psychometric schizotypy are recommended to refine the current conceptualization of "at-risk mental state" or prodrome. Longitudinal follow-up of these particular high-risk subgroups might identify cognitive predictors for conversion to schizophrenia.

Supplementary Material

Supplementary material is available at *Schizophrenia Bulletin* online.

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