

A combined measure for detection of schizotaxia

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This study falls within research on schizotaxia, or neurocognitive risk markers of schizophrenia spectrum disorders, and its usefulness for early prevention strategies. Two samples of 60 adults and 65 children and adolescents, with some genetic or psychosocial high-risk individuals among them, were examined to compare the relationship between schizotypy dimensions and risk factors, and neurocognitive performance. One of the most practical aspects of this study was the proposal of a combined and straightforward measure of liability to schizophrenia spectrum disorders, in contrast to the current high availability of neurocognitive markers. For that purpose, several psychometric analyses were made exploring schizotypy dimensions, as well as 16 measures of cortical functions (executive, attentional, working memory and general cognitive functioning tasks) in adults and 20 measures in adolescents. In keeping with previous research, our results hypothetically indicate that the most accurate measure of schizotaxia combines negative traits of schizotypy, in the range of percentile 90 or higher in the Introverted Anhedonia subscale of the O-LIFE or percentile 85 or higher in the Negative Schizotypy subscale of the MSTQ and, on the other hand, a score of 5 or higher in a combined neurocognitive deficit scale in adults and 6 or higher in adolescents (the number of measures exceeding the threshold of deficit of the distribution scores). Moreover, some other independent measures of clinical and social function, and follow-up studies, are necessary to confirm the predictive validity of this measure of schizotaxia.

Medida combinada para la detección de la esquizotaxia. El trabajo se inserta en las investigaciones sobre esquizotaxia o los marcadores neurocognitivos de riesgo para los trastornos del espectro esquizofrénico y su utilidad para la prevención temprana. Se valoraron dos muestras de 60 adultos y 65 adolescentes, entre quienes se encuentran sujetos de alto riesgo genético y psicosocial, con el fin de comparar la relación existente entre las dimensiones de esquizotipia y los factores de riesgo, y el rendimiento neurocognitivo. Un aspecto práctico de este estudio es la propuesta de una medida sencilla y combinada de predisposición a los trastornos del espectro esquizofrénico, en vez de manejar el alto número de marcadores neurocognitivos de los que actualmente se dispone. Con este propósito, se llevaron a cabo diversos análisis psicométricos para explorar las dimensiones de esquizotipia, y se obtuvieron 16 medidas de funciones corticales (tareas ejecutivas, atencionales, de memoria operativa y de funcionamiento cognitivo general) en adultos y 20 medidas en adolescentes. En consonancia con investigaciones anteriores, nuestros resultados hipotéticamente indican que la medida más precisa de esquizotaxia puede incluir la combinación, por un lado, de rasgos negativos de esquizotipia, con una puntuación equivalente al percentil 90 o superior en la subescala de Anhedonia Introvertida del O-LIFE o al percentil 85 o superior en la subescala de Esquizotipia Negativa del MSTQ y, por el otro, una puntuación igual o superior a 5 en una escala combinada de déficit neurocognitivo en adultos, e igual o superior a 6 en adolescentes (es decir, el número de medidas que superan el umbral de déficit de la distribución de puntuaciones). No obstante, se considera necesario confirmar la validez predictiva de esta medida de esquizotaxia con otras medidas independientes y longitudinales del funcionamiento clínico y social.

The seminal work of Paul E. Meehl on schizotaxia, the genetic predisposition or the unexpressed liability to schizophrenia spectrum disorders (Meehl, 1962), opened the doors to a new view of these

disorders and to the determination of its core features. In subsequent reformulations of schizotaxia (Meehl, 1989, 1990, 1993), the notion was defined as a latent central nervous system integrative defect, derived from a genetic aberration in the neuron's synaptic signal selectivity (hypokrisia), and characterized by its influence on multiple psychophysiological and soft neurologic indicators, and by parametric aberrations in the acquisition and activation of diverse molar psychological functions (perceptual-cognitive, semantic, motivational, and affective). Allegedly, schizotaxia or the subtle neural integrative defect, inherited endophenotype, could result in

either a moderate outcome (the schizotypal personality structure) or a more severe outcome (the schizophrenia), depending on the protection and social reinforcement factors or risk environmental circumstances. Meehl conjectured that schizophrenia is not primarily a mental disorder but a neurologic disorder of genetic origin.

Accordingly, Meehl views schizotaxia as a neurophysiological basis for what Bleuler considered a core psychological trait (the associative loosening), that could result by social learning processes in schizotypal personality and that, once developed, is permanent but existing like other physical disorders (e.g., diabetes, gout, cardiac disease) in varying degrees of clinical compensation. The compensated schizotype, the decompensated, the disintegrated, and the deteriorated states are not disjunctive but successively inclusive categories, in Meehl's opinion; and schizophrenia, as a major psychological complication, is found in a minority (estimated in about 10 percent) of cases (Meehl, 2001). As Meehl points out, the absence of an only and necessary marker of the genetic predisposition to schizophrenia spectrum disorders makes sense to take into account a combination of deviant scores on several indicators (signs and symptoms, neuropsychological performance, and psychosocial functioning), and to apply taxometric statistical procedures in the study of the premorbid neurological substrate or latent liability (Meehl, 1995; Meehl, 1992).

Some other researches (Faraone, Green, Seidman & Tsuang, 2001; Tsuang, Stone & Faraone, 2000; Tsuang, Stone, Tarbox & Faraone, 2002) have recently retained the core notion of schizotaxia introduced by Meehl, as a neural integrative defect, but reformulated the condition with the following differences: (a) they consider its etiology to derive from both a genetic factor and from biological consequences of adverse environmental factors (such as pregnancy or delivery complications), whereas Meehl proposed that the etiology was solely genetic; (b) they believe that schizotaxia reflects a multifactorial polygenic etiology, while Meehl thought it reflected the effects of a single, major gene; (c) they view many outcomes of the stable condition of schizotaxia, beside the only and most likely disorders of schizotypy or schizophrenia viewed by Meehl; and (d) unlike Meehl, they have begun to identify the components of schizotaxia, and to operationalize the concept, based on psychiatric signs (mild negative symptoms) and neuropsychological attributes found in first-degree relatives of schizophrenia patients.

To summarize the authors' knowledge (Faraone et al., 2001; Faraone, Kremen et al., 1995; Faraone, Seidman et al., 1995), schizotaxia and negative schizotypy are similar, and may describe the same syndrome. The schizotaxic subjects show significantly high ratings on negative (e.g., social isolation, interpersonal dysfunction, impoverished affective experiences or restricted emotion, and anhedonia) but not positive symptoms (e.g., ideas of reference, magical thinking, illusions and psychotic-like phenomena), and deficits in multiple cognitive domains (e.g., long-term verbal memory, attention, working memory, and/or executive functions). Accordingly, such studies designate schizotaxia as the syndrome of negative symptoms and neurocognitive dysfunction observed among relatives of schizophrenia patients, while they view schizotypal personality disorder as the heterogeneous schizophrenia-like syndrome, derived from clinical and family research methods (Kendler, 1985), in which positive symptoms dominate the clinical picture. Schizotypy is considered the «entrance door» to schizophrenia, where positive symptoms are also the target of current cognitive-behavioural interventions (Cuevas-

Yust, Perona-Garcelán & Martínez-López, 2003; Perona Garcelán & Cuevas Yust, 2002; Turkington, Kingdon & Chadwick, 2003).

Consistent with several studies, the core features of schizotaxia (negative symptoms and neurocognitive impairments) can be observed in 20 percent to 50 percent of relatives of schizophrenia patients; however, schizotaxia does not always evolve into the schizotypy, considering that only about 10 percent of adult family members of schizophrenia patients will become psychotic, and less than 10 percent will develop schizotypal personality disorder (Faraone et al., 2001; Kendler, 1985; Kendler et al., 1991; Olin & Mednick, 1996; Siever, Bergman & Keefe, 1995; Siever et al., 2002; Torgensen, 1985). These figures suggest that schizotaxia does not lead inevitably to schizophrenia or schizotypal personality disorder.

According to Faraone et al. (2001), schizotaxia and schizotypal personality disorder sometimes co-occur, but the lack of complete overlap between the two categories illustrates the concept that schizotaxia is a broader construct than the subset of schizotypal persons who have predominantly negative symptoms. The possibility that the genes predisposing to schizotaxia and schizotypal personality disorder may be related to different forms of schizophrenia is also suggested.

Previous research on schizotaxia and schizotypal personality disorder gave rise to several prevention strategies that are currently being used for early identification and treatment of vulnerable subjects, describing signs of emerging disorders, such as high-risk mental state features, attenuated or low grade psychotic symptoms, or a strong family history of psychotic disorder, in conjunction with a marked decrease in functioning (Birchwood, McGorry & Jackson, 1997; Johannessen, Larsen, McGlashan & Vaglum, 2000; McGlashan, Miller & Woods, 2001; McGorry et al., 1996). Behavioural-cognitive and pharmacotherapy approaches are used aimed at helping schizotaxic individuals; which implies that clinical manifestations of schizotaxia may be amenable to treatment before they develop further into a psychotic disorder.

Assuming a dimensional view of liability to schizophrenia, as it was supported by multigenic models of heredity of this disorder, it is likely that the interaction of multiple genes and environmental factors are necessary to explain its etiology; which phenotypically could be expressed through a low, average, or high frequency of risk markers. Individuals showing high risk markers would be particularly prone to schizophrenia, whereas individuals having moderate levels of risk factors would be prone to some other less severe but related disorders, such as the schizotypy personality disorder or schizotaxia. The multidimensional nature of schizotaxia could also make possible the existence of «healthy schizotypes» with functional behaviour in spite of some anomalous characteristics or experiences (McCreey & Claridge, 2002).

The studies listed above provide abundant support for the validity of schizotaxia as a theoretical construct that represents both a clinical meaningful condition and a risk factor for subsequent psychosis, but they do not validate schizotaxia as a specific syndrome. For that purpose, Tsuang et al. (2000) recently developed some tentative research criteria for schizotaxia based on the combination of negative symptoms and neuropsychological deficits of at least moderate severity. It is their contention that negative symptoms could be defined as six scores of 3 or higher on items of the SANS (Andreasen, 1983); and neuropsychological impairment could be defined as two standard deviation below appropriate norms in one cognitive domain (including tests of

attention/working memory, long-term verbal declarative memory, and executive functions), and at least one standard deviation below normal in a second domain.

The foregoing discussion has served to introduce three issues to be examined in this paper. The first concerns the relationship between schizotypy and neurocognitive functions in two adult and adolescent samples. It is hypothesised that significant neuropsychological deficits should be detected in subjects with high negative schizotypy, as compared with those with low negative schizotypy. Evidence suggests that subjects with schizophrenia spectrum disorders have deficits in executive functions (Lenzenweger, 1994; Lenzenweger & Korfine, 1995; Lenzenweger, Loranger, Korfine & Neff, 1997; Rawlings & Goldberg, 2001). The second question is about the relationship between genetic and psychosocial risk factors and neurocognitive functions. The study aimed to test the hypothesis that subjects with genetic and psychosocial risk factors of schizophrenia spectrum disorders will also show significantly more deficits in executive functions. To summarise, the third hypothesis that emerged from these analyses was that negative schizotypy and neurocognitive deficits could be useful features for the identification of schizotaxic subjects. Analysing the relationship between negative symptoms and neurocognitive deficits, it is proposed a combined measure as tentative criterion for identification of schizotaxic individuals.

Method

Participants

A total of 125 participants entered the study, divided into two samples of 60 adults and 65 adolescents. Normal and genetic or psychosocial risk groups were identified in each sample. The adult sample was made of 34 first-degree relatives of patients with schizophrenia (29 of them were siblings, and 5 parents and descendants), drawn from psychiatric units and family associations, and 26 relatives of non-psychotic patients. Of the total subjects, 38.3% were males ($n=23$) and 61.7% were females ($n=37$), aged between 18 and 59 years (Mean= 29.7; SD= 9.8). There were no significant differences between the two groups in terms of either age ($F=0.38$, $p=.54$) or gender distribution ($\chi^2=0.48$, $p=0.49$).

The children and adolescents sample was made of 65 subjects, 56.9% were males ($n=37$) and 43.1% females ($n=28$) aged between 8 and 18 years (Mean= 12.71; SD= 1.78), selected at random from supposedly differentiated populations, thus allowing the formation of two subgroups: a normal group, made up of 38 primary and secondary school children, and a psychosocial risk group made up of 27 residents in foster homes, aged between 8 and 18 years (Mean= 12.8; SD= 2.0). Genetic information was not available in the adolescents' sample; however, from a theoretical point of view, it is assumed that the two subgroups of subjects might be different in terms of risk of developing psychological disorders, if we take into account the psychosociological background, particularly higher family psychosocial problems and a greater number of environmental stressors, of the so-called risk group. Nevertheless, the two subgroups are relatively similar in terms of educational level and type of school attended (all state schools). There were no significant differences between the two subgroups in terms of either age ($F=0.11$, $p=0.74$) or gender distribution ($\chi^2=1.20$, $p=0.55$).

Measures

1. As a measure of psychometric schizotypy we used for each sample the following scales: (a) Adult subjects were administered an Spanish version of the Oxford-Liverpool of Feelings and Experiences (O-LIFE) (Mason, Claridge & Jackson, 1995), comprising four subscales of *Unusual experiences*, *Cognitive disorganisation*, *Introvertive anhedonia*, and *Impulsive non-conformity*. (b) Adolescents were administered a Spanish version of the Multidimensional Schizotypal Traits Questionnaire (MSTQ) (Rawlings and MacFarlane, 1994). This research team carried out a factorial analysis of the items making up the scale, obtaining the following three subscales: *Positive schizotypy* (which refers to characteristics of reality distortion, such as magical ideation, unusual perceptions and reference ideas); *Negative schizotypy* (referring to patterns of social isolation, anhedonia and restricted affect); and *Impulsive non-conformity* (referring to characteristics of impulsive-type personality, social anxiety and maladjusted behaviours) (Martínez Suárez et al., 1997).
2. Neurocognitive measures were selected to assess cognitive functioning:
 - 2.1. Two neuropsychological tests for assessing frontal executive functions: concepts formation, mental flexibility and planning, in the versions included in the STIM software package (provided by NeuroScan Technical Center, Inc.): (a) *Stroop Test* (Stroop, 1935), with the successive random presentation of 100 verbal stimuli in the form of words denoting four colours. Presentation of stimuli was carried out with a duration for each stimulus of 100 ms and a 1 s interstimulus interval. Four measures were obtained: number of correct responses, number of time outs, reaction time for congruent stimuli and reaction time for incongruent stimuli. (b) *Wisconsin Card Sorting Test* (WCST) (Heaton, 1981). Measures recorded were number of correct responses, number of errors and number of categories completed.
 - 2.2. Two memory tasks developed by this research team (Lemos-Giráldez, Inda-Caro, López-Rodrigo, Paíno-Piñeiro & Besteiro-González, 2000): (a) *Word Recognition Test* (*Test de Reconocimiento de Palabras*, TRP), based on the concept of reality monitoring, an experimental paradigm related to self-awareness and described by Johnson and Raye (1981). The use of this paradigm, which refers to those processes the individual uses for discriminating between an internal stimulus source and an external source, is supported by the assumption that schizotypal people may also have a tendency to make attributional errors of this type (Frith, 1992). The task comprises two distinct phases: in the first, a series of 30 words is presented on the computer screen and the subject is asked to write, for each one, another word conceptually related to it, thus forming a pair (for example, family-father). The subject must write the word on the keyboard, but without visual feedback of it on the screen as s/he writes it. Carrying out this task without this visual feedback, demanding that the person simply stores the memory at a central,

self-awareness level, has been shown to be an experimental condition that hinders its execution in schizophrenic patients. In the second phase, which takes place approximately 30 minutes after completion of the first without prior warning, all the words (those generated by the computer programme and those generated by the subject) are presented successively in random order, and the subject is asked to identify their origin (external or internal). Two different types of error are recorded, corresponding to the source to which the words are attributed: internal attribution errors (when a word generated by the subject is attributed to the computer, that is, a self-generated word is considered hetero-generated), and external attribution errors (when a word initially generated by the computer is identified as being produced by the subject). (b) *Visual Test of Working Memory (Prueba Visual de Memoria Operativa, PVMO)*, designed for assessing functional memory through the use of visual stimuli (a series of computer screens presented with green or blue circles distributed in different ways). The subject must count the number of green circles that appear in each screen presentation. At a given moment, s/he is asked to recall the number of green circles in each of the screens. The difficulty level of the task increases progressively as the number of screens the person has to remember rises. Number of errors were registered.

- 2.3. A *Continuous Performance Test*, which was also included in the STIM package (CONCPT), consisting of a visomotor task in which the response must be contingent on the appearance of two successive letters. In the version used, the subject is presented with 400 stimuli (4 blocks of 100 letters each) in random order, with a duration for each stimulus presentation of 50 ms and an interstimulus interval of 1 s. Measures processed for this study were means of correct responses (hit-rates), errors of commission (false alarms), and reaction times expressed in ms.
- 2.4. Finally, several verbal, motor, and general cognitive functioning tasks were also administered: *Trail Making Test*, parts A and B (Reitan, 1958). 1. In adults: *Digit Symbol* subtest from the WAIS. 2. In adolescents: (a) *Verbal Fluency Task*, that requires the subject to produce, in 90 seconds, as many words as possible beginning with a given letter. Target letters used were T, P, C and S; (b) Subtests of *Similarities*, *Vocabulary*, *Digit Symbol* and *Block Design* from the WISC.

All tests were administered individually. Tasks from 2.1 to 2.3 were presented on a computer screen and the whole testing procedure was fully computerized. All stimuli were central on the computer screen.

Procedure and data analysis

Participants were individually examined on two separate occasions, the first to complete the questionnaire of schizotypy, and some days after were scheduled for a second testing session that included the administration of neuropsychological tasks in a quiet, comfortable, and conventionally lighted laboratory room of

the Faculty of Psychology. The order of tests and stimulus presentation was identical for all the subjects.

Before each experimental block, the task was explained and commenced when the subject could explain the rules to the examiner. Participants were instructed to respond as quickly and accurately as possible, and started each block by pressing the space bar. No feedback about performance was given to any of the participants during the tasks.

Since our first and second hypotheses focus on group comparisons, multivariate analyses of variance (MANOVAs) were also conducted to determine whether there were overall schizotypy or risk group differences on the neurocognitive measures. If the overall Wilks' λ was significant, univariate F s were computed to determine group differences on individual neurocognitive measures. As an index of effect size we report eta square (η^2). When $\eta^2 > .15$ effects are 'large' in magnitude, and when $\eta^2 > .06$, effects are 'medium'.

Concerning the third hypothesis, starting from the descriptive statistics obtained from the neurocognitive variables, cut-off score points were selected to establish the threshold of deficit in the examined functions. Those points were located in the percentile 80 of each variable (or in the percentile 20, depending on the orientation of the measure). These percentiles were taken as cut-off scores points after finding out that they allow to clearly discriminate those extreme subjects of higher and lower schizotypy, as we have confirmed in previous studies (Lemos-Giráldez et al., 2000).

In order to obtain a combined scale of neurocognitive deficit, the number of variables in which each subject has shown a deficient performance has been added. This is to say the number of measures placed in the deficit range (above percentile 80 or below percentile 20). Taking into account that the total number of neurocognitive measures was 16 for the adults and 20 for the adolescents, the corresponding score for the combined deficit scale could be placed between 0 and 16, or between 0 and 20, respectively. Finally the relationship between the combined scale and the scores on the schizotypy scales were analysed.

Results

Schizotypy factors and neurocognitive functions

Correlations between the scales of schizotypy and neurocognitive measures in adults and adolescents are shown in Table 1.

Based on the scores from O-LIFE or MSTQ subscales, in the adult or adolescent samples, two groups were formed with those subjects in the bottom and top 20% of each factor of schizotypy, which make up the two levels for dependent variables.

Omnibus MANOVAs revealed no significant group effects when compared neurocognitive performance of adults in the low and high levels in each O-LIFE subscale; with Wilks' $\lambda = .085$, $p = .093$, in the Unusual Experiences factor ($n = 9/13$); Wilks' $\lambda = .227$, $p = .161$, in the Cognitive Disorganization factor ($n = 13/13$); Wilks' $\lambda = .278$, $p = .221$, in the Introverted Anhedonia factor ($n = 13/14$); and with Wilks' $\lambda = .235$, $p = .328$, in the Impulsive Non-conformity factor ($n = 13/11$). Neither significant overall MANOVA results were found when compared neurocognitive performance of adolescents in the low and high levels in the MSTQ subscales of Positive Schizotypy (Wilks' $\lambda = .248$, $p = .325$, $n = 15/15$) and of Impulsive Non-conformity (Wilks' $\lambda = .612$, $p =$

.730, $n = 25/20$). On the contrary, as expected, MANOVA results revealed significant when compared adolescents with low and high Negative Schizotypy (Wilks' $\lambda = .183$, $p = .026$ ($n = 18/16$).

We therefore examined each of the neurocognitive measures using univariate ANOVAs. These analyses revealed significant group differences with respect to the variables described in Table 2.

Table 1
Correlation between dimensions of schizotypy and neurocognitive measures

Variables	Adults (n= 60)				Adolescents (n= 65)		
	Unusual experiences	Cognitive disorganization	Introverted anhedonia	Impulsive non-conformity	Positive schizotypy	Negative schizotypy	Impulsive non-conformity
TMT-A Time in secs.	-.120	.140	.053	-.265*	.097	.046	-.047
TMT-B Time in secs.	.022	.137	.101	.047	.080	.267*	.102
Stroop:							
No. correct responses	.169	-.071	-.293*	.009	-.157	-.224	-.090
Time-outs	-.091	.057	-.013	-.218	-.055	.180	-.143
RT congruent stimuli	.115	.239	-.026	-.134	-.162	-.260*	-.003
RT incongruent stimuli	-.027	.019	-.010	-.233	-.106	-.226	-.111
CPT:							
Correct responses	-.003	-.043	-.025	-.117	-.043	-.217	.197
Errors of commission	-.006	-.064	.254*	.108	.083	.168	.011
Reaction time	-.044	.253	-.119	-.108	.056	.235	.083
WCST:							
Correct responses	-.293*	-.163	.075	-.031	-.043	-.299*	-.116
Errors	.115	.048	.149	-.084	-.087	.218	.050
Categories completed	-.326*	-.173	.053	-.037	-.042	-.284	-.106
TRP:							
Internal attribution errors	.042	-.220	.071	-.014	.087	.146	.052
External attribution errors	-.078	-.191	-.010	-.029	-.219	.185	.184
PVMO errors	-.149	.101	.243	-.101	-.035	.329*	-.001
WAIS: Digit Symbol	.394**	.084	-.069	.319*			
Verbal Fluency					-.035	-.200	-.120
WISC: Similarities					-.061	-.354**	-.123
Vocabulary					-.281*	-.417**	-.022
Block Design					-.137	-.182	-.265*
Digit Symbol					-.303*	-.452**	-.140

* ≤ 0.05 ; ** ≤ 0.01

Table 2
Results of ANOVAs comparing neurocognitive performance of the groups in the bottom and top 20% of the MSTQ negative schizotypy subscale

Variables	Low Negative Schizotypy (n= 18)	High Negative Schizotypy (n= 16)	F	p	η^2
TMT-B Time in secs.	83.72 (25.01)	117.75 (36.80)	10.142	.003	.241
Stroop: No. correct responses					
RT for congruent stimuli	74.96 (26.12)	57.52 (21.24)	4.080	.052	.113
RT for incongruent stimuli	807.34 (83.20)	622.85 (270.47)	7.594	.010	.192
RT for incongruent stimuli	849.35 (79.25)	689.75 (253.58)	6.445	.016	.168
WCST: Correct responses					
Categories completed	57.67 (4.45)	52.19 (10.85)	3.874	n.s. (.058)	.108
Categories completed	5.67 (.59)	5.00 (1.32)	3.765	n.s. (.061)	.105
TRP: External attribution errors	5.22 (2.80)	8.00 (4.77)	4.402	.044	.121
PVMO errors	11.94 (7.04)	21.13 (8.66)	11.604	.002	.266
WISC: Similarities					
Vocabulary	13.00 (3.22)	9.75 (4.23)	6.434	.016	.167
Vocabulary	10.56 (3.63)	5.81 (3.75)	14.022	.001	.305
Digit Symbol	12.78 (2.88)	9.00 (3.31)	12.679	.001	.284

Risk factors and neurocognitive functions

The comparison between first-degree relatives of non-psychotic patients and of patients with schizophrenia (low vs. high genetic risk), in the adult sample, revealed no significant differences in neurocognitive measures (Wilks' $\lambda = .642$, $p = .214$) or in the O-LIFE subscales (Wilks' $\lambda = .945$, $p = .545$); but as shown in Table 3, when compared adolescents with low and high psychosocial risk in the first MANOVA analytic step there were significant risk-group differences in either neurocognitive performance (Wilks' $\lambda = .448$, $p = .015$) or schizotypy subscales (Wilks' $\lambda = .826$, $p = .009$). Univariate F s revealed significant differences in neurocognitive measures and schizotypy scales in the expected directions.

A combined measure of schizotaxia

Table 4 shows all the variables used in the composition of the combined scale of the neurocognitive deficit, with the cut-off scores corresponding to percentiles 80 or 20, and the number of subjects which fall above or below those scores (criterion subjects). Considering the neurocognitive measures as a whole, the results reveal that 13,56% of the adults and 12% of the adolescents fall within the deficit range.

Bivariate Pearson's correlations between the combined scale of the neurocognitive deficit and the scores obtained in each of the scales of the schizotypy survey were carried out with all the subjects of each subgroup. In the sample of adults, a statistically significant correlation was found between the combined scale of neurocognitive deficit and the scale of Introverted Anhedonia of the O-LIFE ($r = .229$, $p = .048$). The correlations with the other three scales of this survey were much lower: Unusual Experiences ($r = .004$, $p = .978$), Cognitive Disorganisation ($r = .206$, $p = .120$) and Impulsive Non-conformity ($r = -.129$; $p = .335$).

In the sample of adolescents, the correlation between the combined scale of the neurocognitive deficit and the subscales of schizotypy reached higher statistical significance with Negative Schizotypy of the MSTQ ($r = .504$, $p = .000$), while the correlations

with the scales of Positive Schizotypy ($r = .144$, $p = .298$) and Impulsive Non-conformity ($r = -.117$, $p = .400$) were not significant.

Consequently, the results indicate the existence of a significant relationship exclusively between the neurocognitive deficit and the negative traits of schizotypy, both in adults and in adolescents.

In order to stress this relationship and at the same time finetune the cut-off scores which best discriminate the observed relationship between both variables, Contingency Analyses were carried out comparing different cut-off scores on the combined scale of neurocognitive deficit and on the scale of negative schizotypy. To this purpose, three cut-off scores on the scales of negative schizotypy and four cut-off scores on the scale of combined deficit were separately fixed for adults and adolescents, so to determine which are the levels that represent the best decision criterion on theoretical vulnerability. One point was given when the subject scored in the ranges below the cut-off score and two points were assigned when scored in the ranges above the cut-off score. Table 5 features the results of these analyses.

These results indicate that, in the sample of adults, the cut-off scores which best maximise the differences between the scale of Introverted Anhedonia and the combined scale of the neurocognitive deficit correspond to the ranges 1-89 and 90 or above in the percentiles of the O-LIFE, and of 0-5 and 6 or more points on the scale of the 16 measures of the neurocognitive deficit. This relationship shows a tendency towards the statistic significance ($p = .064$). Consequently, from a theoretical point of view, one can hypothesise that the subjects presenting a score on the subscale of Introverted anhedonia equivalent to percentile 90 or above, while the score on the combined scale of neurocognitive deficit is equal to 5 or above, would run a high risk of developing some kind of psychotic disorder. Of the total of 65 participants of the adult group, 14 subjects which meet both criteria were identified, which, consequently, could be considered schizotaxic. Of these 14 hypothetically schizotaxic subjects, 9 were relatives of patients with schizophrenia (genetic risk), and 5 belonged to the normal group.

In the sample of adolescents, the Contingency analyses reveal that the cut-off scores that best maximise the difference between

Table 3
Results of ANOVAs comparing neurocognitive performance of adolescents with low or high psychosocial risk

Variables	Low risk (n= 38)	High risk (n= 27)	F	p	η^2
TMT-B Time in secs.	90.74 (27.59)	130.30 (54.32)	12.699	.001	.054
Stroop: RT for incongruent stimuli	708.25 (210.57)	554.40 (241.44)	3.361	n.s. (.072)	.057
CPT: Correct responses	14.13 (1.89)	13.06 (1.85)	4.648	.035	.077
WCST: Correct responses	56.61 (6.66)	51.85 (10.19)	4.547	.037	.075
Errors of commission	46.32 (19.83)	58.44 (20.49)	5.227	.026	.085
Categories completed	5.52 (.89)	4.93 (1.24)	4.427	.040	.073
TRP: Internal attribution errors	6.39 (4.31)	10.52 (7.09)	7.392	.009	.117
PVMO errors	13.97 (7.94)	20.93 (10.96)	7.796	.007	.112
WISC: Similarities	12.61 (3.58)	9.00 (3.69)	14.267	.000	.203
Vocabulary	10.65 (3.95)	5.15 (3.56)	30.582	.000	.353
Digit Symbol	12.29 (3.17)	8.70 (3.02)	19.251	.000	.256
MSTQ: Negative schizotypy	2.05 (1.86)	3.67 (1.75)	12.343	.001	.166

the scale of Negative Schizotypy of MSTQ and the combined scale of the neurocognitive deficit correspond to the ranges 1-84 and 85 or more in the percentiles of this subscale, and from 0-5 and 6 or more in the combined scale of 20 measures of the neurocognitive deficit. The relation between both cut-off scores was highly significant ($p = .005$). Therefore we could, from a theoretical point of view, hypothesise that a subject is schizotaxic when s/he presents a score equivalent to a percentile of 85 or above on the Negative schizotypy scale, and at the same time a score that is equal to or above 6 in the combined scale of neurocognitive deficit. In the adolescents' group, 14 out of the 60 participants meet both criteria, 11 of which belong to the subgroup of psychosocial risk (living in foster homes).

Discussion

In the present study, we compared neurocognitive measures and dimensions of schizotypy in an attempt to confirm *a priori* hypotheses about the relationship between cognitive deficits and negative schizotypy. As expected, our results confirm, in bivariate correlation analyses, that a specific and significant relationship exists between cognitive deficit and negative schizotypy. However, this relationship was stronger in the adolescent sample than in adults. When compared subjects scoring in the bottom with those scoring in the top 20% of the schizotypy scales, more significant relationship

emerged in the adolescent sample but not in adult subgroups, which could be due to a low sensitivity of the O-LIFE subscales.

We had also hypothesised that subjects with genetic and psychosocial risk factors of schizophrenia spectrum disorders will also show significantly more deficits in executive functions. The data reported here confirmed that it was true in the adolescents sample but, again, this hypothesis was not supported in adults. These unexpected finding, again, raise questions about the translation of the given MSTQ factorial structure to our culture.

The purpose of the third part of this study coincide with those of other authors in identifying those persons with schizotaxic characteristics. Schizotaxia is still an evolving concept, not a disorder with set criteria, although operationalized research criteria for schizotaxia were proposed on the basis of a combination of negative symptoms and neurocognitive deficits, two areas that have been the focus of the most robust findings in first-degree relatives of patients with schizophrenia (Tsuang et al., 2000; Tsuang et al., 2002).

In previous studies, carried out with clinical and normal populations, a clear relationship between schizotypic symptoms and cognitive dysfunctions (Lenzenweger, 1994; Lenzenweger & Korfine, 1995; Lenzenweger et al., 1997; Rawlings & Goldberg, 2001) has been found; therefore one of the most useful aspects for the clinical assessment and the early detection of risk subjects is to have at our disposal a measure that simplifies the process of

Table 4
Variables in the combined scale, cut-off scores, and subjects scoring in the top 80 percent and bottom 20 percent of the distribution of scores

Variables	Adults (n= 60)			Adolescents (n= 65)	
	Top and bottom percent	Cut-off score	No. of criterion subjects	Cut-off score	No. of criterion subjects
TMT-A Time in secs.	80	49.4	12	65.0	14
TMT-B Time in secs.	80	87.4	12	146.0	11
Stroop:					
No. correct responses	20	85.8	12	47.6	11
Time-outs	80	16.8	12	29.2	11
RT for congruent stimuli	80	833.39	13	856.35	11
RT for incongruent stimuli	80	863.26	12	906.36	11
CPT:					
Correct responses	20	14.75	24	12.95	11
Errors of commission	80	0.50	20	7.8	11
Reaction time	80	436.87	12	392.97	11
WCST:					
Correct responses	20	59.0	8	47.0	12
Errors	80	52.0	12	73.0	12
Categories completed	20	5.0	8	4.0	14
TRP:					
Internal attribution errors	80	8.0	13	13.2	11
External attribution errors	80	7.0	13	10.0	16
PVMO errors	80	12.0	12	26.2	11
WAIS: Digit Symbol	20	12.0	22		
Verbal Fluency	20			8.0	12
WISC: Similarities	20			7.2	11
Vocabulary	20			3.2	11
Block Design	20			7.0	14
Digit Symbol	20			8.0	14

determining the vulnerability to psychotic disorders, given the high quantity of existing neurocognitive measures. The development of a combined measure is considered reasonable, since the research concerning the neurocognitive deficit in schizotypy is in a sufficiently advanced stage as to select, from all the available tests and markers, those that best identify the psychometrically schizotypic subjects.

Another advantage added to the identification of high-risk subjects, by means of a combined measure, is that it reinforces the idea that psychotic signs start before the beginning of the disorder and psychotic versus nonpsychotic are polar extremes of a continuum that has intervening shades or gradations. Furthermore, those subjects with more than one behavioural or neurocognitive sign or marker of risk could be selected for the study of early processes of the illness, for the development and the validation of new vulnerability markers, and for early intervention programs.

The significant correlation exclusively found between negative schizotypy and neurocognitive functions is consistent with Meehl's contention about their common biological relatedness. Flat affect and particularly hypohedonia are the result of a heritable component of pleasure impairment, poligenically determined, and probably derived from a deviation in the microanatomy or neurochemistry of the limbic system (Meehl, 2001). The relationship between negative symptoms of schizotypy and neurocognitive deficit has been observed in non-clinical samples

(Dinn, Harris, Aycicegi, Greene & Andover, 2002; Kwapil, 1998), which seems to confirm our findings and the concept of schizotaxia used by other authors, apart from the presence of other neuropsychological abnormalities such as the deviation of the oculomotor tracking impairment and structural brain abnormalities (Faraone et al., 2001; Tsuang et al., 2002). On the other hand, family studies show that negative (in particular flat affect and abulia) but not positive symptoms of schizotypy are significantly more frequent in the relatives of schizophrenic patients and allow to differentiate them from the control population (Faraone et al., 1999; Kendler, Neale & Walsh, 1995; Tsuang et al., 2002).

This study aims at operatively establishing criteria in order to define schizotaxia combining the negative symptoms with the neurocognitive deficit, following the recommendations of other researchers (Cornblatt, Lencz & Obuchowski, 2002; Lencz, Raine, Benishay, Mills & Bird, 1995; Tsuang et al., 2002), and our results indicate that it is possible to trace consistent relationships. However, it is clear that the definition of the criteria of schizotaxia cannot be constrained exclusively to those of the components studied here, but it also has to integrate other independent clinical and of social functioning measures. Supposedly, the schizotaxic subjects should show poorer clinical or social function (in terms of signs and symptoms, quality of life, and social adjustment), as compared to normal population, and these differences must not be attributable to age, education, IQ, family genetic loading, gender,

Table 5

Results of the Contingency Analyses comparing several ranges below and over cut-off percentiles in negative schizotypy scales and scores in the combined scale of neurocognitive deficit

	Cut-off percentiles in Introverted anhedonia (O-LIFE)	Cut-off scores in the combined deficit scale	Contingency Coefficient	p
Adults	1-79/80+	0-7/8+	.00	1.00
		0-6/7+	.00	1.00
		0-5/6+	1.18	.28
		0-4/5+	.49	.22
	1-84/85+	0-7/8+	.00	1.00
		0-6/7+	.00	1.00
		0-5/6+	1.18	.28
		0-4/5+	.49	.22
	1-89/90+	0-7/8+	2.42	.12
		0-6/7+	2.42	.12
		0-5/6+	1.57	.21
		0-4/5+	3.42	.064
	Cut-off percentiles in Negative schizotypy (MSTQ-N)	Cut-off scores in the combined deficit scale	Contingency Coefficient	p
Adolescents	1-79/80+	0-7/8+	5.134	.023
		0-6/7+	5.134	.023
		0-5/6+	5.196	.023
		0-4/5+	3.243	.072
	1-84/85+	0-7/8+	5.845	.016
		0-6/7+	5.845	.016
		0-5/6+	7.912	.005
		0-4/5+	5.750	.016
	1-89/90+	0-7/8+	2.101	.147
		0-6/7+	2.101	.147
		0-5/6+	2.427	.119
		0-4/5+	1.601	.206

or co-morbidity psychiatric disorders. Accordingly, to validate the proposed criteria for schizotaxia and support the syndrome, converging evidence from multiple domains is necessary.

Nevertheless it must be pointed out that with the two characteristics here studied, a 21,54% of the potentially schizotaxic subjects has been identified, in the sample of adults, 64,29% of them belonging to relatives of schizophrenic patients. In the sample of adolescents, of whose family morbidity there is no information available, 23,33% of the sample are identified as schizotaxic, out of which 78,57% belong to the group living in foster homes. These data do not differ from those obtained by Faraone et al., as they observed neuropsychological deficits or negative symptoms in 20-50% of non-psychotic relatives in family studies (Faraone, Kremen et al., 1995; Faraone, Seidman et al., 1995).

In keeping with Tsuang et al. (2002), the results of our study indicate that a good procedure to determine that a subject shows some risk of developing psychotic disorders could be the combination, on one hand, of negative symptoms of schizotypy and, on the other hand, of the neurocognitive deficit in the prefrontal cognitive functions (in our study measured by means Stroop and

WCST tasks), memory (measured with TRP and PVMO tests), attention (measured with CPT), and executive functions (assessed with TMT, verbal fluency and subtests of WAIS or WISC). Consequently, the methods employed in this study show that it is possible to obtain a more precise measure of identifying adolescent and adult subjects which are more vulnerable to psychotic disorders. Furthermore, our results reveal that a broad number of subjects theoretically defined as «risk groups» due to the presence of genetic or environmental factors, display high scores in the measure derived from schizotaxia, which means that the theoretical value of that measure correlates to the presence of family morbidity and/or psychosocial risk factors.

Finally, although there is preliminary evidence that lends credibility to our proposal, a caution is needed regarding the predictive value of the combined measure of schizotaxia presented in this study. We would like to stress that it will be necessary to obtain converging follow-up evidence from multiple domains, by comparing subjects who met our criteria for schizotaxia with those who did not do so in independent measures of social functioning and clinical outcome.

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