

Comparisons of schizotypal traits across 12 countries: Results from the International Consortium for Schizotypy Research

By: Eduardo Fonseca-Pedrero, Raymond C.K. Chan, Martin Debbané, David Cicero, Lisa C. Zhang, Colleen Brenner, Emma Barkus, Richard J. Linscott, [Thomas Kwapil](#), Neus Barrantes-Vidal, Alex Cohen, Adrian Raine, Michael T. Compton, Erin B. Tone, Julie Suhr, José Muñiz, Alicia Pérez de Albéniz, Axit Fumero, Stella Giakoumaki, Ioannis Tsaousis, Antonio Preti, Michael Chmielewski, Julien Laloyaux, Anwar Mechri, Mohamed Aymen Lahmar, Viviana Wuthrich, Frank Larøi, Johanna C. Badcock, Assen Jablensky, Javier Ortuño-Sierra

Fonseca-Pedrero, E., Chan, R.C.K., Debbané, M., Cicero, D., Zhang, L.C., Brenner, C., Barkus, E., Linscott, R.J., Kwapil, T., Barrantes-Vidal, N., Cohen, A., Raine, A., Compton, M.T., Tone, E.B., Suhr, J., Muñiz, J., Pérez de Albéniz, A., Fumero, A., Giakoumaki, S., Tsaousis, I., Preti, A., Chmielewski, M., Laloyaux, J., Mechri, A., Lahmar, M.A., Wuthrich, V., Larøi, F., Badcock, J.C., Jablensky, A., & Ortuño-Sierra, J. (2018). Comparisons of schizotypal traits across 12 countries: Results from the International Consortium for Schizotypy Research. *Schizophrenia Research*, 199, 128-134. <https://doi.org/10.1016/j.schres.2018.03.021>

***© 2018 Elsevier B.V. Reprinted with permission. This version of the document is not the version of record. ***



This work is licensed under a [Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License](#).

Abstract:

Background: Schizotypal traits are expressions of underlying vulnerability to psychotic disorders which have a potential impact on mental health status, neurocognition, quality of life, and daily functioning. To date, little research has examined epidemiologic landscape of schizotypal traits at the cross-national level. Our aim was to study the expression of schizotypal traits by sex, age, and country in a combined sample gathered from 12 countries. **Methods:** A total of 27,001 participants completed the Schizotypal Personality Questionnaire (SPQ). The mean age of participants was 22.12 ($SD = 6.28$); 37.5% ($n = 10,126$) were males. **Results:** Schizotypal traits varied according to sex, age, and country. Females scored higher than males in the positive dimension, whereas males scored higher in the disorganization dimension. By age, a significant decrease in the positive schizotypal traits was observed. Epidemiological expression of schizotypal traits varied by country. Moreover, several interactions by sex, age, and country were found. **Conclusions:** This pattern is similar to those found in patients with psychosis and psychotic-like experiences. These findings provide new insights and the opportunity to explore the phenotypic expression of schizotypal traits at cross-national level.

Keywords: Schizotypy | Schizotypal traits | Psychosis | Cross-cultural

Article:

1. Introduction

Schizotypal traits are often viewed as phenotypic indicators of liability for schizophrenia-spectrum disorders (Barrantes-Vidal et al., 2015; Fonseca Pedrero and Debbané, 2017; Lenzenweger, 2010; Meehl, 1962). They are seen as anomalies or deficits of cognitive (e.g., paranoid ideation, ideas of reference), social/emotional (e.g., anhedonia, lack of close friends), and behavioural systems (e.g., odd behaviour and language) (Cohen et al., 2015). In many respects, schizotypal traits resemble the clinical symptoms of schizophrenia, albeit without exceeding the clinical thresholds required for diagnosis with a mental disorder (Kwapil et al., 2017; Linscott and van Os, 2013). These set of traits cluster in a manner that is similar to the positive, negative, and disorganization symptom clusters observed in patients with schizophrenia (Liddle, 1987). Likewise, they are associated with the demographic, environmental, and genetic risk factors that predict psychotic disorder (Linscott and van Os, 2013; Morton et al., 2017). Schizotypal traits predict the onset of psychotic disorders (Debbané et al., 2015; Flückiger et al., 2016; Salokangas et al., 2013; Shah et al., 2012) as well as increased risk for non-psychotic psychopathology (e.g., depression, suicide) (Fisher et al., 2013; Kelleher et al., 2014; Schimanski et al., 2017) and impaired neurocognition, mental health status, quality of life, and daily functioning (e.g., Cohen et al., 2015; Ettinger et al., 2014; Siddi et al., 2017). These findings converge to suggest that schizotypy may be a useful phenotype for understanding the pathogenesis of psychosis.

Sex, age, country of origin, and ethnic or migrant status correlate with the expression of psychosis phenotypes at clinical and subclinical levels (i.e., psychosis symptoms, schizotypal traits) (Jongsma et al., 2018; Kelleher et al., 2012; Linscott and van Os, 2013; McGrath et al., 2008; McGrath et al., 2015; Nuevo et al., 2012; Spauwen et al., 2003; van Os et al., 2000). In general, females tend to have higher scores than males on the attributes comprising the positive dimension (e.g., ideas of reference, unusual perceptual experiences) whereas males have higher scores on those components comprising the negative (e.g., anhedonia) dimension (Bora and Arabaci, 2009; Fonseca-Pedrero et al., 2012; Kwapil et al., 2008; Mason and Claridge, 2006; Miettunen and Jääskeläinen, 2010; Raine, 1992). Some have observed minor departures from this general pattern, such as higher levels of social anxiety, which some view as a component of the negative dimension, among females (Bora and Arabaci, 2009).

Psychotic symptoms usually emerge during late adolescence or early adulthood, many years before clinical diagnosis (Fusar-Poli et al., 2014). Schizotypal traits are also more prevalent during childhood and adolescence than in adulthood (e.g., Fonseca-Pedrero et al., 2012). In non-clinical adult populations, age correlates positively with negative schizotypy and negatively with positive schizotypy (Mason and Claridge, 2006). On subscales of the Schizotypal Personality Questionnaire (SPQ) (Raine, 1991), Bora and Arabaci (2009) found that younger participants reported more self-reference ideas, odd beliefs, unusual perceptual experiences, odd behavior, and odd speech.

Rates of subclinical psychosis vary across cultures, countries, and ethnic groups (Larøi et al., 2014; McGrath et al., 2008, McGrath et al., 2015; Myers, 2011; Nuevo et al., 2012). For example, the prevalence of experiencing at least one psychotic symptom varies from 0.8% to 31.4% across world regions (Nuevo et al., 2012). Among residents of defined geographic regions, country of origin can predict variation in rates of hallucination experiences (Johns et al.,

2002). Similar differences across countries and ethnic groups are evident for schizotypal traits. Scores on measures of schizotypal dimensions vary among European countries (Fonseca-Pedrero et al., 2015; Ortuño-Sierra et al., 2013), between American and Spanish samples (Fonseca-Pedrero et al., 2017a; Kwapil et al., 2012), and within multiethnic populations (Cicero, 2016; Chmielewski et al., 1995; Kwapil et al., 2008). These differences have been obtained using diverse measures of schizotypal traits including the SPQ, the Chapman scales (Chmielewski et al., 1995), and the Oxford-Liverpool Inventory of Feelings and Experiences (O-LIFE) short-form (Fonseca-Pedrero et al., 2015). Significant cross-national variation is also evident in the incidence of psychotic disorder (Jongsma et al., 2018).

To date, little research has examined epidemiologic landscape of schizotypal traits at the cross-national level. There have been many investigations of the associations of sex, age, nationality, and ethnicity with schizotypal traits, in most studies comparisons have been restricted to Western countries or small numbers of countries. Given these limitations, our aim was to compare a broad array of schizotypal traits assessed with the SPQ from participants recruited in 12 Western and non-Western countries. We sought to better understand international variation in the self-report of schizotypal traits. We hypothesized that: (a) males would report more interpersonal (negative) and disorganized traits than females and that females would report more positive schizotypal traits than males; (b) younger participants would have higher scores than older participants in positive schizotypal traits; and (c) expression of schizotypal traits would vary across countries.

2. Method

This is one of a series of studies by members of the International Consortium for Schizotypy Research (ICSR) (<https://srconsortium.org/>). Other findings from the sample described here are reported by Fonseca-Pedrero et al., 2017b, Fonseca-Pedrero et al., 2018.

Table 1. Demographic characteristics of the sample.

	Country		Sex		Age		
	<i>n</i>	%	Male	Female	<i>M</i>	<i>SD</i>	Range
US	10,477	38.8	3162	7212	21.9	6.7	17–55
Spain	1123	4.2	224	899	20.2	2.0	18–29
New Zealand	1698	6.3	515	1183	20.1	3.0	17–51
Italy	649	2.4	305	344	24.3	3.5	19–38
Australia	1931	7.2	634	1294	28.5	11.2	17–55
Belgium	893	3.3	245	648	24.9	9.1	17–55
UK	774	2.9	291	483	21.6	4.4	17–49
Tunisia	458	1.7	137	321	20.4	1.4	18–29
China	4907	18.2	2973	1533	19.7	1.0	17–24
Canada	1849	6.8	562	1287	20.8	2.9	18–53
Greece	1041	3.9	390	651	32.4	9.9	17–55
Mauritius	1201	4.4	688	513	23.4	1.2	21–27
Total	27,001	100	10,126	16,368	22.6	7.1	16–68

2.1. Participants

Participants were recruited at 21 sites across 12 countries (United States of America, United Kingdom, China, Belgium, Spain, Italy, Tunisia, Australia, New Zealand, Canada, Mauritius, and Greece). The overall sample consisted of 27,001 participants. The mean age was 22.12 years

($SD = 6.28$; range 16–55 years). Participants were divided among three age groups: 17–19 year-olds ($n = 9333$; 34.6%), 20–25 year-olds ($n = 10,395$; 38.5%), and 26–55 year-olds ($n = 3160$; 11.7%); 15.2% ($n = 4113$) of participants did not provide their ages. Participants included 10,126 males (38.2%) and 16,368 females (61.8%); sex was not reported by 507 participants ($n = 26,494$). In this study we examined data at the country level, aggregating across research sites within each country. Table 1 shows socio-demographic characteristics of the whole sample by country. Information about the age, sex, and other characteristics of the samples from each site can be found in the supplementary material.

2.2. Instrument

The Schizotypal Personality Questionnaire (SPQ) (Raine, 1991) was used across all sites as a common index of schizotypal traits. The SPQ is 74-item self-report measure of positive, negative, and disorganized schizotypal traits. The SPQ yields nine subscale scores: Magical Thinking (Odd Beliefs), Unusual Perceptual Experiences, Ideas of Reference, Paranoid Ideation (Suspiciousness), Excessive Social Anxiety, No Close Friends, Constricted Affect, Odd Behaviour, and Odd Speech. Respondents rate each item using a dichotomous response (*yes, no*) and each subscale contains seven to nine items. Affirmative answers (item endorsements) are summed to compute subscale scores and an SPQ total score can be obtained as the total number of items endorsed.

In the present work we used SPQ versions adapted, translated, and validated for each country or language represented: English (Raine, 1991), Spanish (Fonseca-Pedrero et al., 2014), Italian (Fossati et al., 2003), Chinese (Chen et al., 1997), Arabic (Lahmar et al., 2014), French (Dumas et al., 2000), Creole (Reynolds et al., 2000), and Greek (Tsaousis et al., 2015).

Raine (1991) based the SPQ on the nine traits contained in the *DSM-III-R* definition of schizotypal personality disorder (American Psychiatric Association, 1987). Confirmatory factor analyses have demonstrated that the positive-negative-disorganized factor model provides a good fit to SPQ data (Fonseca-Pedrero et al., 2018). The positive (cognitive-perceptual) dimension comprises the Odd Beliefs, Unusual Perceptual Experiences, Ideas of Reference, and Suspiciousness subscales. The interpersonal (negative) dimension comprises the Excessive Social Anxiety, No Close Friends, Suspiciousness, and Constricted Affect subscales. The disorganized dimension comprises the Odd Behaviour and Odd Speech subscales.

2.3. Procedure

Conventions for obtaining informed consent required by each investigator's research institution and IRB or ethical committees were followed. All participants provided written informed consent prior to participation. The study was conducted in accordance with the guidelines of the Declaration of Helsinki (World Medical Association, 2013).

2.4. Data analyses

Descriptive statistics for the nine SPQ subscales, the three schizotypal dimensions and SPQ total score were calculated, both overall and for the sample as broken down by sex, age, and country.

Subsequently, country differences in SPQ scores were tested using analyses of variance (ANOVA): univariate ANOVA of the SPQ total and multivariate ANOVA (MANOVA) of the three SPQ dimension scores. (MANOVA was also applied to the nine SPQ subscale scores, with results from these analyses reported in the supplementary online material.) ANOVA and MANOVA included sex, age, and country as fixed factors. Partial eta squared (η_p^2) was employed as an effect-size estimate.

Participants with missing data for more than two SPQ items were excluded from the analyses. Where data were missing for one or two items, those data were imputed with regression-based estimates, to which an error component was added, using the SPSS Missing Value Analysis module. Following exclusion for missing data, the analysis sample consisted of 22,864 participants ($n = 9132$ males; $n = 9319$ aged 16–19 years, $n = 10,387$ aged 20–25 years, and $n = 3158$ aged 26–55 years). By country, the sample distribution was: USA = 8145, Spain = 1123, New Zealand = 1698, Italy = 649, Australia = 778, Belgium = 893, UK = 774, Tunisia = 458, China = 4257, Canada = 1849, Greece = 1040, and Mauritius = 1200. SPSS 22.0 (IBM Corp Released, 2013) was used for data analyses.

3. Results

3.1. Sex-related manifestation of schizotypal traits

There was no effect of sex on the SPQ total ($F_{(1,22,796)} = 1.22, p = 0.27, \eta_p^2 < 0.001$). In contrast, sex affected schizotypal dimensions ($\lambda = 0.998, F_{(3,22,794)} = 15.31, p < 0.001, \eta_p^2 = 0.002$) with differences between males and females for the positive and disorganization schizotypal dimensions, but not the interpersonal dimension (Table 2). Table 3 gives means and standard errors for SPQ dimensions for males and females. Females scored higher than males on the positive schizotypal dimensions; males scored higher than females on the disorganization dimension.

Table 2. P values and effect sizes by country, sex, and age for each schizotypal dimension.

Effect	Positive		Negative		Disorganized	
	<i>p</i>	η_p^2	<i>p</i>	η_p^2	<i>p</i>	η_p^2
Country	<0.01	0.013	<0.01	0.041	<0.01	0.013
Sex	<0.01	0.001	0.35		0.01	
Age	<0.01		0.69		0.07	
Country × Sex	<0.01	0.002	0.01	0.001	0.01	0.001
Country × Age	<0.01	0.004	<0.01	0.004	<0.01	0.004
Age × Sex	0.12		0.05		0.20	
Country × Age × Sex	0.08	0.001	0.89	0.001	0.84	0.001

Table 3. Estimated means scores and standard errors for the SPQ total score and schizotypal dimensions according to sex and age.

Schizotypal	Sex				Age					
	Male		Female		16–19 years-old		20–25 years-old		26–55 years-old	
	<i>M</i>	<i>SE</i>	<i>M</i>	<i>SE</i>	<i>M</i>	<i>SE</i>	<i>M</i>	<i>SE</i>	<i>M</i>	<i>SE</i>
Positive	8.60	0.17	9.59	0.20	9.56	0.17	9.23	0.09	8.49	0.37
Interpersonal	9.60	0.19	9.88	0.22	9.63	0.18	9.80	0.09	9.78	0.39
Disorganization	5.27	0.11	4.84	0.13	5.31	0.10	5.04	0.05	4.82	0.23
Total score	21.07	0.35	21.69	0.42	22.00	0.34	21.52	0.17	20.62	0.75

Note. *M* = Mean; *SE* = Standard error.

3.2. Age-related variability in schizotypal traits

There was no evidence that age group affected the SPQ total score ($F_{(2,22,796)} = 2.90, p = 0.055, \eta_p^2 < 0.001$) whereas age differences were evident on the three schizotypal dimensions ($\lambda = 0.999, F_{(6,45,588)} = 2.35, p = 0.029, \eta_p^2 < 0.001$; Table 2 shows *p*-values and effect sizes for each dimension). The significant age effects reflected a tendency for adolescents to report more schizotypal traits than older participants (Table 3). However, this main effect was qualified by an interaction between age and dimension such that the youngest group scored significantly higher than the other age groups in the positive schizotypal dimension. In contrast, no statistically significant differences among age groups emerged for the interpersonal and disorganization dimensions.

3.3. Country-related variability in schizotypal traits

SPQ total scores differed significantly across countries ($F_{(11,22,796)} = 26.56, p < 0.001, \eta_p^2 = 0.013$). Fig. 1 gives estimated mean total SPQ scores for each country. Participants from Tunisia and the UK obtained the highest SPQ total scores; participants from Italy obtained lower scores than participants from other regions.

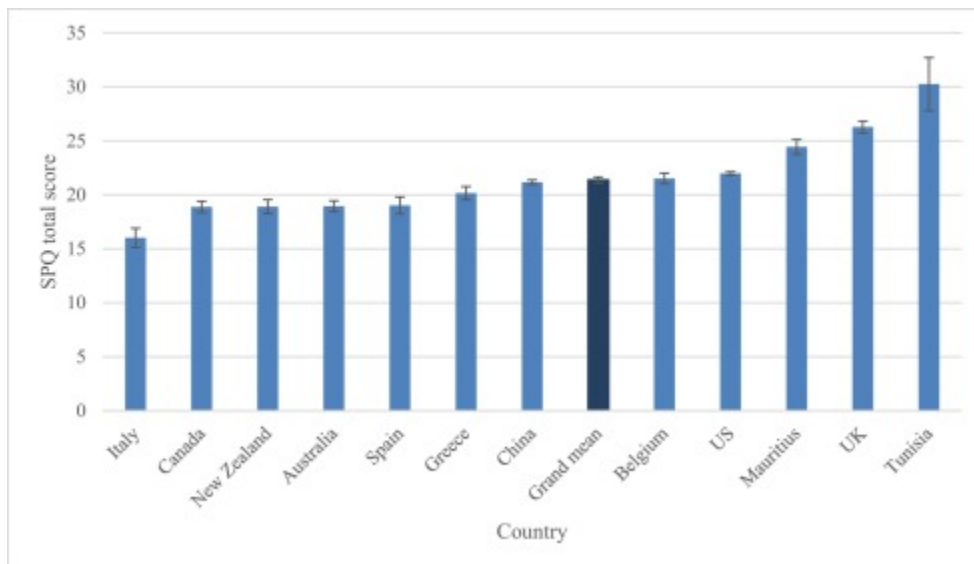


Fig. 1. Estimated means (standard errors) of SPQ total score across countries.

The MANOVA of schizotypal dimensions also showed differences across countries ($\lambda = 0.904, F_{(33,67,156)} = 70.57, p < 0.001, \eta_p^2 = 0.033$; Table 2 for *p* values and effect sizes). Mean scores on the positive schizotypal dimension, were highest for participants from Tunisia, and lowest for those from Canada and Italy (Table 4). Tunisian participants also scored highest on average on the interpersonal schizotypal dimension; mean scores were lowest for participants from China and Australia. On the disorganization schizotypal dimension, scores were highest for participants from the UK and lowest for those from Italy and Spain.

3.4. Interactions among country, sex, and age as predictors of schizotypal traits

For SPQ total score, the Country \times Sex interaction was not significant ($F_{(11,22,796)} = 2.07$, $p < 0.05$, $\eta_p^2 = 0.001$) but the Country \times Age interaction was ($F_{(20,22,796)} = 4.29$, $p < 0.001$, $\eta_p^2 = 0.004$). Results were not significant, however, for interactions between Sex \times Age ($F_{(2, 22,796)} = 2.66$, $p = 0.070$, $\eta_p^2 = 0.001$) and Country \times Sex \times Age ($F_{(20, 22,796)} = 0.76$, $p = 0.776$, $\eta_p^2 = 0.001$). Closer examination of the Country \times Sex interaction revealed that scores were higher for females than males in several countries, including Italy, Tunisia, and Australia (Table 5). Associations with age also varied by country such that in some countries, such as the US, members of the youngest group scored higher than those in the other age groups. In other countries, such as Tunisia, in contrast, the older age group scored higher than youngest group.

Table 4. Schizotypal dimension scores by country.

Country	Positive		Negative		Disorganized	
	<i>M</i>	<i>SE</i>	<i>M</i>	<i>SE</i>	<i>M</i>	<i>SE</i>
US	8.58	0.08	10.56	0.09	5.22	0.05
Spain	7.79	0.39	9.33	0.42	3.97	0.24
New Zealand	7.91	0.32	8.40	0.34	4.57	0.20
Italy	6.95	0.43	7.57	0.46	3.79	0.27
Australia	8.19	0.25	7.44	0.27	5.17	0.15
Belgium	8.39	0.25	10.30	0.26	5.34	0.15
UK	10.48	0.27	11.37	0.29	7.13	0.17
Tunisia	13.72	1.20	13.75	1.29	6.94	0.74
China	10.44	0.10	7.05	0.11	4.87	0.06
Canada	7.19	0.25	8.94	0.27	4.78	0.16
Greece	9.52	0.31	9.55	0.33	4.11	0.19
Mauritius	11.14	0.34	12.71	0.36	4.57	0.21
Grand mean	9.17	0.13	9.74	0.14	5.06	0.08

Note. *M* = Mean; *SE* = Standard error.

Table 5. Estimated means scores and standard errors for the total score of SPQ according to country, sex, and age.

Country	Sex				Age groups					
	Male		Female		16–19 years-old		20–25 years-old		26–55 years-old	
	<i>M</i>	<i>SE</i>	<i>M</i>	<i>SE</i>	<i>M</i>	<i>SE</i>	<i>M</i>	<i>SE</i>	<i>M</i>	<i>SE</i>
US	22.62	0.26	21.33	0.19	22.43	0.21	23.08	0.26	20.41	0.36
Spain	18.91	1.33	19.13	0.86	20.57	0.67	20.67	0.68	15.83	2.17
New Zealand	18.58	1.07	19.21	0.72	18.37	0.46	19.28	0.49	19.05	1.82
Italy	14.80	1.35	17.23	1.13	15.79	2.41	16.87	0.61	15.39	0.89
Australia	17.53	0.82	20.34	0.59	21.81	1.13	20.75	0.72	14.24	0.71
Belgium	21.70	0.86	21.31	0.50	25.44	1.03	20.07	0.70	18.99	0.84
UK	26.35	0.86	26.22	0.66	28.42	0.80	24.58	0.64	25.85	1.27
Tunisia	27.81	2.56	32.71	4.19	24.70	1.38	28.40	0.73	37.67	7.19
China	21.08	0.23	21.25	0.35	21.31	0.32	21.03	0.26	–	–
Canada	19.59	0.86	18.17	0.57	20.25	0.55	19.57	0.40	16.83	1.39
Greece	20.14	1.08	20.16	0.61	22.89	1.55	19.59	0.93	17.96	0.47
Mauritius	25.08	1.03	23.81	0.90	–	–	24.32	0.38	24.57	1.31

Note. *M* = Mean; *SE* = Standard error; In Mauritius and China there are two age-groups without participants.

MANOVA indicated interactions between Country \times Sex ($\lambda = 0.995$, $F_{(33,67,156)} = 3.54$, $p < 0.001$, $\eta_p^2 = 0.002$), Country \times Age ($\lambda = 0.990$, $F_{(60,68,005)} = 3.91$, $p < 0.001$, $\eta_p^2 = 0.003$)

significantly predicted SPQ scores for the three schizotypal dimensions (Table 2). Results were not significant for interactions between Sex and Age ($\lambda = 0.999$, $F_{(6, 45,588)} = 1.96$, $p = 0.067$, $\eta_p^2 = 0.000$) and for Country \times Sex \times Age ($\lambda = 0.997$, $F_{(60, 68,005)} = 1.22$, $p = 0.122$, $\eta_p^2 = 0.001$).

Decomposition of the significant interactions yielded evidence of a complex pattern of associations (see Supplementary materials for complete results). For instance, females from most countries scored higher than males on the positive schizotypal dimension; however, males from Mauritius scored higher than women and no significant sex differences were evident for participants from the US, Canada, and Greece. For the interpersonal schizotypal dimension, mean scores were similar across sex for most countries; however, female participants from Spain, Italy, and Tunisia, scored higher than males. Men from all countries except Australia obtained higher scores than women on the disorganized schizotypal dimension.

4. Discussion

To improve understanding of both the phenotypic expression of schizotypal traits and the various manifestations of psychosis liability (Cohen and Fonseca-Pedrero, 2017), we set out to examine differences according to sex, age, and nationality in the expression of schizotypal traits using a large sample of participants recruited from 12 countries ($n = 27,001$). To our knowledge, this is the largest comprehensive study of schizotypal traits in a non-clinical sample published to date. This collaborative effort, in which multiple research groups have shared data, has provided an unprecedented opportunity to explore the epidemiologic landscape of schizotypal traits with a single instrument—the SPQ.

The results have demonstrated that schizotypal traits varied according to sex, age, and country. Females scored higher than males in the positive dimension, whereas males scored higher in the disorganization dimension. By age, a significant decrease in the positive schizotypal traits was observed. Epidemiological expression of schizotypal traits varied by country. Moreover, several interactions by sex, age, and country were found. If schizotypal traits reflect liability for schizophrenia-spectrum disorders, schizotypy and psychosis should be associated with the same variables. In this study, sex, age, and country were differentially associated with schizotypal traits in ways that approximately mirror associations with diagnosed psychotic disorders and subclinical psychotic experiences (e.g., schizotypal traits and psychotic-like experiences) (Jongsma et al., 2018; Kelleher et al., 2012; Linscott and van Os, 2013; McGrath et al., 2008; McGrath et al., 2015; Nuevo et al., 2012; Spauwen et al., 2003; van Os et al., 2000).

As hypothesized, the manifestation of schizotypal traits varied across nations; however, means schizotypal scores were similar across countries. Compared to those from other countries, Tunisian participants had higher scores on almost all schizotypal dimensions. In particular, Tunisian and UK samples obtained the highest total scores on the SPQ and Italy the lowest. The Chinese sample had a distinct pattern of ratings, with magical ideation and lower indices of interpersonal schizotypal traits. In addition, the pattern of results found is clearly modulated not only by country but as by its interactions with sex and age. To date, most of the cross-national research of schizotypy involved comparison between two or four countries (Fonseca-Pedrero et al., 2015; Fonseca-Pedrero et al., 2017a; Sierro et al., 2016; Kwapil et al., 2012; Ortuño-Sierra et

al., 2013), thus it is quite difficult to compare these results with previous research. For instance, Fonseca-Pedrero et al. (2015) using the s-OLIFE across four European countries (UK, Switzerland, Italy, and Spain), found differences when the mean scores were compared. The Spanish sample, compared to other countries, showed the lowest score on unusual experiences, anhedonia, and impulsive nonconformity dimensions. In another study Fonseca-Pedrero et al. (2017a), found that the American group scored higher than the Spanish group in all schizotypal traits, except Ideas of Reference and Suspiciousness. These findings, therefore, are convergent with those from previous studies measuring psychotic symptoms and subclinical psychotic symptoms and experiences (Jongsma et al., 2018; Larøi et al., 2014; McGrath et al., 2008, McGrath et al., 2015; Myers, 2011; Nuevo et al., 2012).

In the present study, we did not have a priori hypotheses on how schizotypy would differ across participating countries. We assume that differences across countries would reflect a range of factors. These included methodological variability, such as the use of different strategies for ascertaining and recruiting participants. It must be added that the exclusive use of the SPQ to measure schizotypal traits, while advantageous in that it provided consistency across the compiled datasets with regard to the domains surveyed, may also have functioned in distinctive ways in different countries. The SPQ in particular was developed in North America and has been most widely used in that context. The instrument may thus reflect idiosyncrasies of that society that do not translate easily to other cultural contexts. One question that inevitably arises is whether the observed differences according to country, sex, and age are substantively informative about schizotypy or whether they simply reflect systematic measurement error embedded within the instrument used to collect the data. In this framework, the effect sizes found are relevant and should be considered carefully, particularly given that nationality contributes much more variance to SPQ scores than age or sex. It must be noted that the sex and age effects are mostly trivial, contributing to very little variance in ratings. Similarly, the country x sex and country x age effects are small contributors to observed variance.

Our data do not provide answers to this question, but we urge future researchers to consider it seriously. Cultures may also vary in the degree to which accept particular symptoms (e.g., hallucinations and magical thinking) as normative experiences. For instance, some experiences that members of individualistic cultures identify as anomalous or unusual may be more readily tolerated by members of communal cultures. Future studies would benefit from taking an “anthropological” or proper cross-cultural approach that would allow researchers to explore these possibilities in depth and to both generate and test specific hypotheses. By assessing schizotypal traits in individuals who represent different cultures, we have the potential to gain important knowledge about cultural differences in social and affective functioning (Cohen et al., 2015) and to clarify how these cognitive, emotional, and motivational traits relate to important variations in human behavior (Henrich et al., 2010).

With regard to sex, females in our study scored higher than males on subscales within the positive schizotypal dimension, whereas males scored higher on subscales within the disorganization dimension. Scores did not differ significantly between males and females on subscales within the interpersonal schizotypal dimension. The observed differences between males and females were partially concordant with the results of studies that used other schizotypal/schizotypy scales. For instance, previous research has similarly demonstrated that

males show more disorganized traits than females (Bora and Arabaci, 2009; Mason and Claridge, 2006), whereas females report more positive schizotypal (i.e., odd beliefs) traits than males (Bora and Arabaci, 2009; Fonseca-Pedrero et al., 2012; Kwapil et al., 2008; Raine, 1992). The literature is mixed with regard to sex differences on measures that tap the interpersonal schizotypal dimension; whereas some have found no significant sex differences (Bora and Arabaci, 2009), others found evidence that males and females differ on this dimension (Fonseca-Pedrero et al., 2012; Kwapil et al., 2008; Mason and Claridge, 2006; Miettunen and Jääskeläinen, 2010; Raine, 1992).

With strong consistency across countries, adolescents scored higher than participants from other age groups on subscales within the positive schizotypal dimension. This finding is in line with previous research, which has demonstrated that adolescents tend to score higher than adults (university students or general population) on measures of most schizotypal dimensions (Badcock and Dragovic, 2006; Bora and Arabaci, 2009; Chen et al., 1997; Fonseca-Pedrero et al., 2012; Fossati et al., 2003), particularly the positive dimension (Mason and Claridge, 2006). For instance, Bora and Arabaci (2009) found that younger participants scored significantly higher than older ones on subscales measuring ideas of reference, odd beliefs, unusual perceptual experiences, odd behavior and odd speech. Moreover, the results confirmed previous findings from meta-analyses and cross-national studies that other subclinical expressions of the psychosis phenotype (e.g., psychotic-like experiences) are negatively associated with age (Linscott and van Os, 2013; McGrath et al., 2015).

The current findings raise a potentially important clinical question regarding whether cultural differences in schizotypy are genuine differences that may stem from culture-specific environmental stressors, or whether they instead emerge as a function of a relative lack of cultural sensitivity in the application of DSM diagnostic criteria across cultures (Raine, 2006). This issue is particularly pertinent to the present study, as the SPQ was developed based on *DSM* criteria. Future research using this measure would benefit from careful consideration of the relevance of *DSM* criteria in the cultural context under study. Moreover, our cross-cultural findings could be of crucial relevance for research on psychosis and its early detection and prevention. For instance, they could be of value for determining cut-off points for detecting participants at risk for psychosis in the context of a given culture as well as age and gender. A practical implication is that studies comparing “high vs low schizotypy groups” need to use age and sex referenced norms that are also suitable to the specific culture from which participants are drawn. The results are also important clinically, in that they suggest that schizotypy must be considered as a valid construct around the world, and not just in Western culture. However, they also suggest that generalizations should be made only cautiously, given the interactions that we observed among sex, age, and country. These interactions, which raise the possibility of subtle individual variability in the manifestation of schizotypy, might be fruitfully explored in clinical settings using qualitative approaches or by examining associations between schizotypal phenotypes and genetic variants that are distributed unevenly across cultures. Finally, these data may allow us to further understand protective and risk factors for psychosis spectrum disorders at a cross-national level (Cohen et al., 2015).

The results of the present work should be considered in the light of several limitations. First, there is an inherent problem in the use of self-report as an indicator of schizotypal traits.

However, despite their limitations, self-report instruments are brief, inexpensive, non-invasive, and user-friendly, and thus amenable to use in clinical research or community settings in which large samples may be screened. Also, the validity and clinical relevance of psychometric high-risk methodology has been documented and research has found this approach to yield concordant results with research on individuals with schizophrenic symptomatology (Cochrane et al., 2010) and with conventional interview-based high-risk approaches for studying psychosis (Barrantes-Vidal et al., 2013). Second, the nature of the sample, which was composed mostly of college students, may limit generalization of the results to other populations of interest. Samples from the general population may differ from college and adolescent samples in that age, sex, and other demographic variables may carry artificially increased weight. In fact, most of the subsamples used in this study are WEIRD (Western, Educated, Industrialized, Rich, and Democratic) individuals and are probably unrepresentative of the world's population (Henrich et al., 2010). Third, the fact that not all the samples used the SPQ infrequency response to detect those participants who displayed random or pseudo-random patterns of responses undermines the validity and generalizability of the results found in the present cross-national study. Finally, we do not have clinical information about any mental disorders present in the sample.

5. Conclusions

We have provided a comprehensive description of schizotypal traits using a large and multinational sample, with participants drawn from 12 countries. The present work aimed to improve understanding about the epidemiological distribution of schizotypal traits across nations at the population level. The findings indicate that schizotypal traits vary across country, sex, and age, and are associated with similar demographic factors to those found in patients with psychosis. In summary, these results provide more fine-grained analyses of phenotypic expressions of schizotypal traits to guide the field.

Future studies should focus on the manifestation of these traits across multiple levels of analyses, multiple indicators (e.g., genes, molecules, cells, circuits, physiology, behaviors, and self-report levels) and new procedures of assessment (e.g., experience sampling method). Furthermore, it is relevant to add new measurement models and theories (e.g., network analyses, chaos theory) to provide new insights in this arena (Borsboom, 2017; Fonseca-Pedrero, 2017; Nelson et al., 2017). The study of schizotypal traits is a field that is in clear expansion and several extremely interesting questions remain unresolved.

Contributors. E.F-P designed the study, coordinated the data collection, contributed to the data analyses, and was lead author of the manuscript. J. O-S. contributed to the data analyses and manuscript preparation. All the authors contributed to the study design and manuscript preparation. All authors have approved the final manuscript.

Role of funding source. E.F·P was supported by the Spanish Ministry of Science and Innovation (MICINN) (PSI2014-56114-P), by the Instituto Carlos III, Center for Biomedical Research in the Mental Health Network (CIBERSAM), and by 2015 edition of the BBVA Foundation Grants for Researchers and Cultural Creators. M.D was supported by the Swiss National Science Foundation (100019_159440). R.C. was supported by the Beijing Training Project for Leading Talents in S&T (Z151100000315020), the Beijing Municipal Science &

Technology Commission Grant (Z161100000216138), and the National Basic Research Program of China (Precision Psychiatry Program: 2016YFC0906402). JCB was partly funded by the Cooperative Research Centre-Mental Health, Carlton, Australia. S.G and I. T. were supported by the “ARISTEIA II” Action of the Operational Programme Education and Lifelong Learning and was co-funded by the European Social Fund (ESF) and National Resources [grant number KA 2990].

Conflict of interest. All the authors have declared that there are no conflicts of interest in relation to this study.

Acknowledgment. The authors do not have to declare any funding or administrative support for this manuscript.

References

American Psychiatric Association, 1987. Dignostic and Statistical Manual of Mental Disorders (3rd Ed. Revised) (DSM-III-R). The Association, Washington, DC.

Badcock, J.C., Dragovic, M., 2006. Schizotypal personality in mature adults. *Personal. Individ. Differ.* 40, 77–85.

Barrantes-Vidal, N., Gross, G., Sheinbaum, T., Mitjavila, M., Balleespí, S., Kwapil, T.R., 2013. Positive and negative schizotypy are associated with prodromal and schizophrenia-spectrum symptoms. *Schizophr. Res.* 145, 50–55.

Barrantes-Vidal, N., Grant, P., Kwapil, T., 2015. The role of schizotypy in the study of the etiology of schizophrenia spectrum disorders. *Schizophr. Bull.* 41, S408–416.

Bora, E., Arabaci, L.A., 2009. Effect of age and gender on schizotypal personality traits in the normal population. *Psychiatry Clin. Neurosci.* 63, 663–669.

Borsboom, D., 2017. A network theory of mental disorders. *World Psychiatry* 16, 5–13.

Chen, W.J., Hsiao, C.K., Lin, C.C.H., 1997. Schizotypy in community samples: the three-factor structure and correlation with sustained attention. *J. Abnorm. Psychol.* 106, 649–654.

Chmielewski, M., Fernandes, L.O., Yee, C.M., Miller, G.A., 1995. Ethnicity and gender in scales of psychosis proneness and mood disorders. *J. Abnorm. Psychol.* 104, 464–470.

Cicero, D.C., 2016. Measurement invariance of the schizotypal personality questionnaire in Asian, Pacific islander, white, and multiethnic populations. *Psychol. Assess.* 28, 351–361.

Cochrane, M., Petch, I., Pickering, A.D., 2010. Do measures of schizotypal personality provide non-clinical analogues of schizophrenic symptomatology? *Psychiatry Res.* 176, 150–154.

Cohen, A., Fonseca-Pedrero, E., 2017. Towards a schizotypy core: convergence and divergence of two empirically-derived self-report measures from a nonclinical sample. *J. Exp. Psychopathol.* 8, 265–287.

Cohen, A., Mohr, C., Ettinger, U., Chan, R.C.K., Park, S., 2015. Schizotypy as an organizing framework for social and affective sciences. *Schizophr. Bull.* 41, S427–435.

Debbané, M., Eliez, S., Badoud, D., Conus, P., Flückiger, R., Schultze-Lutter, F., 2015. Developing psychosis and its risk states through the lens of schizotypy. *Schizophr. Bull.* 41, S396–407.

Dumas, P., Bouafia, S., Gutknecht, C., Saoud, M., Dalery, J., d'Amato, T., 2000. Validation of the French version of the raine schizotypal personality disorder questionnaire—categorical and dimensional approach to schizotypal personality traits in a normal student population. *L'Encéphale* 26, 23–29.

Ettinger, U., Meyhöfer, I., Steffens, M., Wagner, M., Koutsouleris, N., 2014. Genetics, cognition, and neurobiology of schizotypal personality: a review of the overlap with schizophrenia. *Front. Psychiatry* 5, 18.

Fisher, H.L., Caspi, A., Poulton, R., Meier, M.H., Houts, R., Harrington, H., Arseneault, L., Moffitt, T.E., 2013. Specificity of childhood psychotic symptoms for predicting schizophrenia by 38 years of age: a birth cohort study. *Psychol. Med.* 43, 2077–2086.

Flückiger, R., Ruhrmann, S., Debbané, M., Michel, C., Hubl, D., Schimmelmann, B.G., Klosterkötter, J., Schultze-Lutter, F., 2016. Psychosis-predictive value of self-reported schizotypy in a clinical high-risk sample. *J. Abnorm. Psychol.* 125, 923–932.

Fonseca Pedrero, E., Debbané, M., 2017. Schizotypal traits and psychotic-like experiences during adolescence: an update. *Psicothema* 29, 5–17.

Fonseca-Pedrero, E., 2017. Network analysis: a new way of understanding psychopathology? *Rev. Psiquiatr. Salud. Ment.* 10, 206–215.

Fonseca-Pedrero, E., Lemos-Giráldez, S., Paino, M., Sierra-Baigrie, S., Muñiz, J., 2012. Phenotypic expression of schizotypal traits in an adolescent population. *J. Personal. Disord.* 26, 350–359.

Fonseca-Pedrero, E., Fumero, A., Paino, M., deMiguel, A., Ortuño-Sierra, J., Lemos Giraldez, S., Muñiz, J., 2014. Schizotypal personality questionnaire: new sources of validity evidence in college students. *Psychiatry Res.* 219, 214–220.

Fonseca-Pedrero, E., Ortuño-Sierra, J., Sierro, G., Daniel, C., Cella, M., Preti, A., Mohr, C., Mason, O.J., 2015. The measurement invariance of schizotypy in Europe. *Eur. Psychiatry* 30, 837–844.

Fonseca-Pedrero, E., Cohen, A., Ortuño-Sierra, J., Pérez de Albeniz, A., Muñiz, J., 2017a. Dimensional structure and measurement invariance of the Schizotypal Personality Questionnaire-Brief Revised (SPQ-BR) scores across American and Spanish samples. *J. Personal. Disord.* 31, 522–541.

Fonseca-Pedrero, E., Ortuño-Sierra, J., Lucas-Molina, B., Debbané, M., Chan, R.C.K., Cicero, D.C., Zhang, L.C., Brenner, C., Barkus, E., Linscott, R.J., Kwapil, T., Barrantes-Vidal, N., Cohen, A., Raine, A., Compton, M.T., Tone, E.B., Suhr, J., Bobes, J., Fumero, A., Giakoumaki, S., Tsaousis, I., Preti, A., Chmielewski, M., Laloyaux, J., Mechri, A., Lahmar, M.A., Wuthrich, V., Larøi, F., Badcock, J.C., Jablensky, A., Barron, D., Swami, V., Tran, U.S., Voracek, M., 2017b. Brief assessment of schizotypal traits: a multinational study. *Schizophr. Res.* 197, 182–191.

Fonseca-Pedrero, E., Debbané, M., Ortuño-Sierra, J., Chan, R.C.K., Cicero, D.C., Zhang, L.C., Brenner, C., Barkus, E., Linscott, R.J., Kwapil, T., Barrantes-Vidal, N., Cohen, A., Raine, A., Compton, M.T., Tone, E.B., Suhr, J., Muñiz, J., Fumero, A., Giakoumaki, S., Tsaousis, I., Preti, A., Chmielewski, M., Laloyaux, J., Mechri, A., Lahmar, M.A., Wuthrich, V., Larøi, F., Badcock, J.C., Jablensky, A., 2018. The structure of schizotypal personality traits: a cross-national study. *Psychol. Med.* 48, 451–462.

Fossati, A., Raine, A., Carretta, I., Leonardi, B., Maffei, C., 2003. The three-factor model of schizotypal personality: invariance across age and gender. *Personal. Individ. Difer.* 35, 1007–1019.

Fusar-Poli, P., Carpenter, W.T., Woods, S.W., McGlashan, T.H., 2014. Attenuated psychosis syndrome: ready for DSM-5.1? *Annu. Rev. Clin. Psychol.* 10, 155–192.

Henrich, J., Heine, S.J., Norenzayan, A., 2010. Most people are not WEIRD. *Nature* 466 (7302), 29.

IBM Corp Released, 2013. IBM SPSS Statistics for Windows, Version 22.0. IBM Corp, Armonk, NY.

Johns, L.C., Nazroo, J.Y., Bebbington, P., Kuipers, E., 2002. Occurrence of hallucinatory experiences in a community sample and ethnic variations. *Br. J. Psychiatry* 180, 174–178.

Jongsma, H.E., Gayer-Anderson, C., Lasalvia, A., et al., 2018. Treated incidence of psychotic disorders in the multinational EU-GEI study. *JAMA Psychiatry* 75, 36–46.

Kelleher, I., Connor, D., Clarke, M.C., Devlin, N., Harley, M., Cannon, M., 2012. Prevalence of psychotic symptoms in childhood and adolescence: a systematic review and meta-analysis of population-based studies. *Psychol. Med.* 9, 1–7.

Kelleher, I., Cederlöf, M., Lichtenstein, P., 2014. Psychotic experiences as a predictor of the natural course of suicidal ideation: a Swedish cohort study. *World Psychiatry* 13, 184–188.

Kwapil, T.R., Barrantes Vidal, N., Silvia, P.J., 2008. The dimensional structure of the Wisconsin schizotypy scales: factor identification and construct validity. *Schizophr. Bull.* 34, 444–457.

Kwapil, T.R., Ros-Morente, A., Silvia, P.J., Barrantes-Vidal, N., 2012. Factor invariance of psychometric schizotypy in Spanish and American samples. *J. Psychopathol. Behav. Assess.* 34, 145–152.

Kwapil, T.R., Gross, G.M., Silvia, P.J., Raulin, M.L., Barrantes-Vidal, N., 2017 Jul. Development and psychometric properties of the Multidimensional Schizotypy Scale: a new measure for assessing positive, negative, and disorganized schizotypy. *Schizophr. Res.* 20 (pii: S0920-9964(17)30402-4).

Lahmar, M.L., Gassab, L., Beltaief, F., Mechri, A., 2014. Psychometric properties of the Arabic version of the schizotypal personality questionnaire in Tunisian university students. *Tunis. Med.* 92, 318–322.

Larøi, F., Luhrmann, T.M., Bell, V., Christian, W.A.J., Deshpande, S., Fernyhough, C., Jenkins, J., Woods, A., 2014. Culture and hallucinations: overview and future directions. *Schizophr. Bull.* 40, S213–220.

Lenzenweger, M.F., 2010. *Schizotypy and Schizophrenia: The View from Experimental Psychopathology*. Guilford Press, New York.

Liddle, P., 1987. The symptoms of chronic schizophrenia: A re-examination of the positive-negative dichotomy. *Br. J. Psychiatry* 151, 145–151.

Linscott, R.J., van Os, J., 2013. An updated and conservative systematic review and meta-analysis of epidemiological evidence on psychotic experiences in children and adults: on the pathway from proneness to persistence to dimensional expression across mental disorders. *Psychol. Med.* 43, 1133–1149.

Mason, O., Claridge, G., 2006. The Oxford-Liverpool Inventory of Feelings and Experiences (O-LIFE): further description and extended norms. *Schizophr. Res.* 82, 203–211.

McGrath, J., Saha, S., Chant, D., Welham, J., 2008. Schizophrenia: a concise overview of incidence, prevalence, and mortality. *Epidemiol. Rev.* 30, 67–76.

McGrath, J.J., Saha, S., Al-Hamzawi, A., Alonso, J., Bromet, E.J., Bruffaerts, R., Caldas-de-Almeida, J.M., Chiu, W.T., de Jonge, P., Fayyad, J., Florescu, S., Gureje, O., Haro, J.M., Hu, C., Kovess-Masfety, V., Lepine, J.P., Lim, C.C., Mora, M.E., Navarro-Mateu, F., Ochoa, S., Sampson, N., Scott, K., Viana, M.C., Kessler, R.C., 2015. Psychotic experiences in the general population: a cross-national analysis based on 31,261 respondents from 18 countries. *JAMA Psychiatry* 72, 697–705.

Meehl, P.E., 1962. Schizotaxia, schizotypy, schizophrenia. *Am Psychol.* 17, 827–838.

Miettunen, J., Jääskeläinen, E., 2010. Sex differences in Wisconsin Schizotypy scales: a meta-analysis. *Schizophr. Bull.* 36, 347–458.

Morton, S.E., O'Hare, K.J.M., Maha, J.L.K., Nicolson, M.P., Machado, L., Topless, R., Merriman, T.R., Linscott, R.J., 2017. Testing the validity of taxonic schizotypy using genetic and environmental risk variables. *Schizophr. Bull.* 43, 633–643.

Myers, N.L., 2011. Update: schizophrenia across cultures. *Curr. Psychiatry Rep.* 13, 305–311.

Nelson, B., McGorry, P.D., Wichers, M., Wigman, J.T.W., Hartmann, J.A., 2017. Moving from static to dynamic models of the onset of mental disorder. *JAMA Psychiatry* 74, 528–534.

Nuevo, R., Chatterji, S., Verdes, E., Naidoo, N., Arango, C., Ayuso-Mateos, J.L., 2012. The continuum of psychotic symptoms in the general population: a cross-national study. *Schizophr. Bull.* 38, 475–485.

Ortuño-Sierra, J., Badoud, D., Knecht, F., Paino, M., Eliez, S., Fonseca-Pedrero, E., Debbané, M., 2013. Testing measurement invariance of the schizotypal personality questionnaire-brief scores across Spanish and Swiss adolescents. *PLoS One* 8.

Raine, A., 1991. The SPQ: a scale for the assessment of schizotypal personality based on DSM-III-R criteria. *Schizophr. Bull.* 17, 555–564.

Raine, A., 1992. Sex differences in schizotypal personality in a non clinical population. *J. Abnorm. Psychol.* 101, 361–364.

Raine, A., 2006. Schizotypal personality: neurodevelopmental and psychosocial trajectories. *Annu. Rev. Clin. Psychol.* 2, 291–326.

Reynolds, C.A., Raine, A., Mellingen, K., Venables, P.H., Mednick, S.A., 2000. Three-factor model of schizotypal personality: invariance across culture, gender, religious affiliation, family adversity, and psychopathology. *Schizophr. Bull.* 26, 603–618.

Salokangas, R.K., Dingemans, P., Heinimaa, M., Svirskis, T., Luutonen, S., Hietala, J., Ruhrmann, S., Juckel, G., Graf von Reventlow, H., Linszen, D., Birchwood, M., Patterson, P., Schultze-Lutter, F., Klosterkötter, J., 2013. Prediction of psychosis in clinical high-risk patients by the Schizotypal Personality Questionnaire. Results of the EPOS project. *Eur. Psychiatry* 28, 457–469.

Schimanski, I.D., Mouat, K.L., Billingham, B.L., Linscott, R.J., 2017. Preliminary evidence that schizophrenia liability at age 15 predicts suicidal ideation two years later. *Schizophr. Res.* 181, 60–62.

Shah, J., Eack, S.M., Montrose, D.M., Tandon, N., Miewald, J.M., Prasad, K.M., Keshavan, M.S., 2012. Multivariate prediction of emerging psychosis in adolescents at high risk for schizophrenia. *Schizophr. Res.* 141, 189–196.

Siddi, S., Petretto, D.R., Preti, A., 2017. Neuropsychological correlates of schizotypy: a systematic review and meta-analysis of cross-sectional studies. *Cogn. Neuropsychiatry* 22, 186–212.

Sierro, G., Rossier, J., Mason, O., Mohr, C., 2016. French validation of the O-LIFE Short Questionnaire. *Eur. Psychol. Assess.* 32, 195–203.

Spauwen, J., Krabbendam, L., Lieb, R., Wittchen, H.-U., van Os, J., 2003. Sex differences in psychosis: normal or pathological? *Schizophr. Res.* 62, 45–49.

Tsaousis, I., Zouraraki, C., Karamaouna, P., Karagiannopoulou, L., Giakoumaki, S.G., 2015. The validity of the schizotypal personality questionnaire in a Greek sample: tests of measurement invariance and latent mean differences. *Compr. Psychiatry* 62, 51–62.

Van Os, J., Hanssen, M., Bijl, R.V., Ravelli, A., 2000. Strauss (1969) revisited: a psychosis continuum in the general population? *Schizophr. Res.* 45, 11–20.

World Medical Association, 2013. World medical association declaration of Helsinki: ethical principles for medical research involving human subjects. *J. Am. Med. Assoc.* 310, 2191–2194.