Functional hemispheric asymmetry and nicotine dependency as variables mediating neurobiological vulnerability to schizotypy in a non-clinical population of college students

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Abstract

In the present study, schizotypal personality traits and their neuropsychological correlates were examined among a non-clinical sample, so as to gain insight into the variables mediating neurobiological vulnerability to schizotypy. To that effect, 50 young adults completed the Oxford-Liverpool Inventory of Feelings and Experiences, the Fagerström Test of Nicotine Dependence, the Edinburgh Handedness Questionnaire, and a dichotic listening task. Analyses revealed a significant right-hemisphere dominance association to positive schizotypy, and a left-hemisphere dominance association to negative schizotypy. Nicotine dependence emerged as a significant correlate of positive and overall schizotypy, and left-hemisphere dominance. Gender-based interactions were significant for females on positive schizotypy, nicotine dependence and right-hemisphere dominance, and on negative schizotypy for males. The findings of this study can be used to advance our understanding of the factors of risk and resilience in the schizophrenia spectrum.

Keywords: brain laterality; schizotypy; psychosis proneness; psychotropic

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1. Introduction

Significant evidence suggests a relation between two apparently different phenomena arising from two diverse scientific fields: schizotypy from the field of psychopathology, and brain laterality from the field of neuropsychology (Weinstein & Graves, 2002). Schizotypy, particularly in a clinical context, is treated as a pathological condition (Mohr & Claridge, 2015). Meehl (Meehl & E., 1962) introduced schizotypy as a genetic diathesis-stress model, portraying the nature of the individual's latent proneness to schizophrenia (Lenzenweger & Korfine, 1992). Schizotypy is a condition characterised by mild psychotic-like symptoms. In non-clinical populations, schizotypal symptoms are quantitatively sub-clinical, yet qualitatively analogous, to those of schizophrenia (Barnett & Corballis, 2002; Premkumar et al., 2012). In other words, the construct represents a latent personality organization that harbours the liability for schizophrenia (Lenzenweger, 2006). Schizotypy prevalence is estimated at .6 to 1.1 percent of the general population (Lenzenweger, 2008).

Schizotypy is commonly assessed via self-report questionnaires, representing a dimensional approach to psychotic-like symptoms in dimensions known from the schizophrenia taxonomy; namely, positive [PS], negative [NS], and disorganized or cognitive disorganization [CogDis] schizotypy (Herzig et al., 2015). Popular measures include the Oxford Liverpool Inventory of Feelings and Experiences (O-LIFE; Oldfield, 1971), the Magical Ideation Scale (MI; Eckblad & Chapman, 1983) and the Schizotypy Personality Questionnaire (SPQ; Raine, 1991). Higher scores connote higher proneness to psychosis, displaying symptoms akin to those of schizophrenia patients, as well as similar cognitive (Buchy, Woodward, & Liotti, 2007), sensory-motor (Lenzenweger & Gold, 2000), neurophysiological (Mohanty et al., 2005; Shenton, Dickey, Frumin, & McCarley, 2001) and neurobiological (Murray, Lappin, & Di Forti, 2008) irregularities.

A partial, at least, aetiological overlap between schizotypy and schizophrenia presents a viable and congruent approach towards expanding our understanding of schizophrenia spectrum disorders. In lieu of established similarities and points of departure between the two constructs, it comes as no surprise that current scientific research is geared towards

deepening an understanding of their underlying mechanisms (Lenzenweger & Korfine, 1992). Additionally, research on schizotypy offers a structured model of research observation by eliminating confounding effects of medication in schizophrenia patients. Moreover, research in schizotypy is of importance in its own right, as elevated schizotypy has been associated with substance misuse (Skosnik, Spatz-Glenn, & Park, 2001; Williams, Wellman, & Rawlins, 1996) and disturbances across educational, professional, emotional and social facets of one's life (Cohen, Mohr, Ettinger, Chan, & Park, 2015). Increasing our understanding of the mechanisms underlying the aforementioned disturbances could facilitate the evolution of intervention strategies (Ettinger et al., 2015).

1.1. Schizotypy risk factors: Psychoactive (or psychotropic) substances

Converging evidence supports the idea that psychotropic substance consumption, such as cannabis (Barkus, Stirling, Hopkins, & Lewis, 2006; Barnes, Mutsatsa, Hutton, Watt, & Joyce, 2006; Skosnik et al., 2001) and nicotine (de Leon, Diaz, Rogers, Browne, & Dinsmore, 2002; Esterberg, Goulding, McClure-Tone, & Compton, 2009) heavily influence the trajectories of both schizotypal and schizophrenic taxonomies. The relationship between dopamine-enhancing drugs (i.e. nicotine) and psychotic symptoms has been examined in both clinical and non-clinical populations, confirming the deterioration of positive psychotic symptoms in the former, and the instigation of psychosis in the latter (Moore et al., 2007; Sekine et al., 2001; Smith et al., 2009). Hence, enhanced dopaminergic activity has unsurprisingly been associated with schizophrenia spectrum disorders (Liouta, Smith, & Mohr, 2008). In construction of an exploratory model, we can assume nicotine acting as a possible mediating environmental factor, imitating the effects of typical neurobiological vulnerability to schizophrenia-related disorders.

1.2. Schizotypy and functional brain laterality

Brain laterality with left-hemisphere dominance (LHD) in language processing and selective attention tasks, and right-hemisphere dominance (RHD) in face recognition tasks, which have been reported in healthy populations seem to be diminished in both schizophrenia and schizotypy (Cohen & Davis, 2009; Suzuki & Usher, 2009). Inconsistencies regarding the relation of schizotypal dimensions and brain laterality exist in research, with some studies associating PS or CogDis with RHD (Herzig, Tracy, Munafò, & Mohr, 2010; Leonards & Mohr, 2009; Mohr & Claridge, 2015; Suzuki & Usher, 2009), others with LHD (Liouta et al., 2008; Mason & Claridge, 1999), whereas some studies report no laterality at all (Gooding & Braun, 2004; Herzig et al., 2010; Najt, Bayer, & Hausmann, 2012).

Several factors might account for the heterogeneity of the aforementioned findings. The scale employed to evaluate schizotypy seems to play a role (Liouta et al., 2008; Schofield & Mohr, 2014), since so far studies employing the MI scale have reported RHD (Mohr et al., 2005; Weinstein & Graves, 2002), whereas studies with the O-LIFE inventory have reported either RHD (Suzuki & Usher, 2009) or LHD (Liouta et al., 2008). Additionally, studies differ in terms of the laterality task utilised to assess brain laterality, with some using LHD tasks like dichotic listening tasks and lexical decision tasks, whereas others use RHD tasks like visual face processing tasks. It should be noted that so far only two studies have

employed both a RHD and a LHD laterality task and have found no significant relation between PS and brain laterality (Herzig et al., 2010; Schofield & Mohr, 2014).

Furthermore, findings are likely prone to gender differences: females have been found to score higher on PS, whereas males commonly score higher on NS (Miettunen & Jaaskelainen, 2010; Paíno-Piñeiro, Fonseca-Pedrero, Lemos-Giráldez, & Muñiz, 2008).

Another possible explanation of the inconsistent findings reported in the literature pertains to the elevated consumption of psychotropic substances (e.g. nicotine) commonly observed in schizophrenia populations. Herzig and associates (2010) recently examined the interaction between schizotypy, nicotine consumption and dependence on brain laterality, and demonstrated a RHD with elevated nicotine dependence, despite brain laterality having been found unrelated to nicotine consumption.

1.3. Aims and Hypotheses

The aim of the present study was to examine the association between self-reported schizotypy, nicotine dependence and brain laterality in a non-clinical population. Due to the high heterogeneity of past findings, the pursuit of forming a definitive hypothesis was challenging. Nonetheless, we expected to find a significant relation between RHD and both PS and CogDis. No association was expected between NS and brain laterality. Regarding nicotine dependence, it was expected that higher nicotine dependence would be associated with elevated PS and brain laterality with RHD.

2. Method

2.1. Ethics & Procedure

The project was reviewed by the Health and Human Sciences Ethics Committee with Delegated Authority and was allowed to proceed. The study was described in full to the participants, who were informed of the voluntary character of their participation and freely consented to participate.

2.2. Participants

Fifty students were recruited randomly on the basis of their presence at the campus of the Independent Science and Technology (IST) College in Athens, Greece. Ages ranged from 18 to 31 years (22.82 ±2.82; 22.72 ±2.59 for females; 22.92 ±2.89 for males), with a female to male ratio of 1:1. Inclusion criteria consisted of (i) English fluency, (ii) right-hand dominance and (iii) normal auditory capacity. Left-handed and ambidextrous subjects were excluded to minimize the possibility of introducing reduced brain asymmetry -due to handedness- as a confounding variable. By large, RHD is known to reflect the typical structural pattern of cerebellar asymmetry (right > left cerebellar hemisphere), whereas other types of handedness have been reported to represent a reduced or ipsilateral brain asymmetry (Papaeiliou, Polemikou, & Michaelides, 2012). Auditory function was further screened using the online audiogram hearing test (Pigeon, 2007), to

exclude any possibility of including participants with undiagnosed hearing impairments. Only subjects whose auditory threshold was higher than the clinical range (>10 dB) were included in the present study. Any participants who self-disclosed a family history of psychiatric or neurological illness, recent head trauma or substance misuse were also excluded.

2.3. Instruments

The following assessment instruments were used in the following order of application: Audiogram hearing test, EHI, O-LIFE, FTND and a dichotic listening task.

2.3.1. Oxford-Liverpool Inventory of Feelings and Experiences (O-LIFE)

The O-LIFE questionnaire was used to evaluate schizotypal traits. The O-LIFE is a validated tool of 150 self-report items measuring psychosis-proneness (Mason & Claridge, 2006; Mason, Claridge, & Jackson, 1995). The instrument, which consists of four subscales, ranks high on internal consistency, ranging from r = 0.72 to r = 0.89 between the subscales (Mason et al., 1995) and test-retest reliability, ranging from r = 0.76 to r = 0.93 (Burch, Steel, & Hemsley, 1998). PS is measured by 30 questions associated with magical thinking, paranoid ideation and hallucinatory experiences. CogDis is measured by 24 questions assessing lack of concentration, social anxiety and decision-making. NS is measured by 27 questions assessing the absence of delight from social and physical interactions. The fourth subscale evaluates Impulsive Nonconformity [IN] comprises of 23 items assessing bizarre behaviour and self-control deficiency. The aforementioned traits are not typically associated with schizotypy per se (Liouta et al., 2008), thus the scores yielded from the IN subscale were deemed unrelated to the purposes of the present study and, as such, were extracted from further analysis. All questions require yes/no responses (scored as +1/0, respectively). According to the instrument's creators, responses 55, 58-59, 62, 66-69, 71, 74-78 and 80 are reverse-coded; they were, thus, scored accordingly (Mason & Claridge, 2006). Scores for the three first subscales were calculated by summing item responses on each subscale separately. Overall schizotypy scores were obtained by summing the scores of the three subscales. Higher scores connoted higher levels of schizotypy. The three subscales of the O-LIFE questionnaire demonstrated a robust internal structure (Cronbach's α = .71).

2.3.2. *Fagerström Test of Nicotine Dependence (FTND)*

FTND was used to assess nicotine dependence (Heatherton, Kozlowski, Frecker, & Fagerström, 1991). FTND self-reports of cigarette smoking behaviour are measured along 6 items designed to measure the quantity of cigarette consumption, compulsion to use and dependence. Yes/no items are scored 0 or 1, and multiple-choice items are scored from 0 to 3, on 4-point Likert scale. Summed items yield a total score of 0-10. The individual's intensity of physical dependence on nicotine is scored high or low, accordingly; (1-2 = low, 3-4 = low to moderate, 5-7 = moderate, 8 and above = high nicotine dependence). The 6 items of FTND yielded a high internal consistency (α = .86).

2.3.3. *Edinburgh Handedness Inventory (EHI)*

Although participants disclosed their hand preference during the recruitment phase, the EHI (Oldfield, 1971) was also administered as an additional confirmatory measure. The EHI includes 12 items, covering an array of lateralized, uni-

manual daily activities (e.g. writing, drawing, throwing) and hand dominance is established based on participants' self-reported preference in completing them. Subjects place check marks under 'Left' or 'right' to denote their hand preference (right = +1, left = -1, both = 0), yielding a summed score of -12 to -12. Elevated scores indicated a stronger right-handedness. Forty three out of 50 subjects displayed complete right-hand preference. The remaining subjects (n = 7) lacked a clear preference for two out of 12 actions (both hands), though they reported performing the rest solely with their right hands. Therefore, for those participants, a strong (albeit not extreme) dextrality can be safely assumed. Internal consistency for the 12 items of the EHI was excellent (α = .88).

2.3.4. Dichotic Listening Task

Brain laterality was measured by means of the Dichotic Listening Task. A Shure SM7B microphone and a Focusrite Octopre MkII microphone preamplifier were used for the recordings. Six nonsense syllables were presented, articulated by a pre-recorded female voice. Of those, three consisted of voiced (b, d, g) and three of unvoiced (k, p, t) consonants, paired with the vowel "a". Thirty unique pair combinations emerged from the initial 6 syllables (See Supplementary table 4). Each combination was presented to participants three times. Therefore, each participant listened to 90 stimuli presentations through stereo handsets plugged into the computer audio jack. A different pair of syllables was presented acoustically every five seconds. To avoid the effect of voice onset time, the Cool Edit software was used to ensure that both stimuli were presented simultaneously. At the same time another consonant-vowel syllable was presented visually, against a grey background on a computer screen. Following each trial, participants were asked to indicate whether the syllable they had seen was identical to the syllable they listened by their right or left ear, and to circle the appropriate word ("left" or "right") in a table they were provided with. The total of correct left hits, correct right hits, and correct total hits was calculated for each participant.

2.4. Data Analysis

The R Project for Statistical Computing, version 3.3.2, was used to execute all analyses. To employ a sensitive measure to side-favoring in lateralized task paradigms, a laterality index score for the dichotic listening task was calculated by subtracting the left hits (LH) from the right hits (RH) and dividing the difference by the sum of total hits (RH-LF/ TH) (Liouta et al., 2008; Marshall, Caplan, & Holmes, 1975). Positive values in the laterality index indicated left-hemisphere dominance (LHD), whereas negative values indicated right-hemisphere dominance (RHD). This index was employed in all the subsequent analyses for brain laterality. Shapiro-Wilk tests of normality indicated that data from both behavioural and schizotypy dimension tests were normally distributed (w-values > .9 and p-values > .5). When we examined for skewness and kurtosis values ranged from -0.8 to 0.8 and -2.0 to 2.0 respectively.

2.5. Design

One-way ANOVAs with gender as a grouping factor for age, schizotypal dimensions, nicotine dependence and brain laterality were conducted. Pearson correlation analyses with laterality index, schizotypal dimensions and nicotine dependence scores were performed for the whole sample and for females and males separately. Finally, multiple linear

regression analyses were conducted to examine whether schizotypy and nicotine dependence are significant predictors of brain lateralisation. Schizotypy and brain laterality were also examined as predictors of nicotine dependence. All p-values were two-tailed and the threshold of significance was set at .05. All analyses were adjusted for gender and age. A power analysis revealed that with a sample size of 50, threshold of significance at 0.05 and threshold of statistical power at 0.8, the minimum detectable effect size was r = .38.

3. Results

Descriptive statistics for the Edinburgh Handedness inventory, the Fagerström Test of Nicotine Dependence, the Oxford-Liverpool Inventory of Feelings and Experiences and the dichotic listening task are presented in Table 1.

Table 1. Group means and SD of values on each instrument arranged collectively (total sample) and by gender.

Measure	Total (n=50)		Females (n=25)		Males (n=25)		F-values	Effect size (Cohen's *d*)
Schizotypy*	34.78	±6.65	34.64	±7.42	34.92	±5.90	.02	-.04
*Positive schizotypy**	12.86	±4.09	15.24	±3.53	10.48	±3.10	25.42	1.43
*Negative schizotypy**	11.24	±4.30	8.92	±3.73	13.56	±3.56	20.25	-1.27
*Cognitive disorganization**	10.68	±2.48	10.48	±2.5	10.88	±2.49	.32	-.16
Nicotine dependence**	2.78	±1.95	3.76	±1.64	1.80	±1.76	16.64	1.15
Right hits†	13.68	±3.32	12.12	±3.02	15.24	±2.88	14.00	-1.06
Left hits†	14.90	±4.18	16.44	±4.51	13.36	±3.21	7.73	.79
Handedness‡	11.82	±.48	11.8	±.50	11.84	±.47	.085	-.08

Notes. ± = standard deviation; * = Oxford-Liverpool Inventory of Feelings and Experiences; ** Fagerström Test of Nicotine Dependence; † = Dichotic listening task; ‡ = Edinburgh Handedness inventory.

A one-way ANOVA with gender as a grouping factor on age indicated no significant age (always in years, ± SD) difference between female (22.72 ± 2.59) and male (22.92 ± 2.89) participants [F (2, 48) = .06, p = .80].

One-way ANOVAs with gender as a grouping factor on schizotypal dimensions, nicotine dependency and brain laterality yielded significant differences on PS, NS, nicotine dependency and brain laterality. Females scored higher on PS, nicotine

dependency and RHD, and males scored higher on NS. Differences in overall schizotypy, and CogDis did not yield statistically significant results.

Table2. Table displaying the ANOVASs with gender as a grouping factor on schizotypal dimensions, nicotine dependence and brain laterality.

	Schizotypy	*Positive schizotypy*	*Negative schizotypy*	*Cognitive disorganisation*	Nicotine dependence	Brain laterality
Gender	*F*(2,48) = .02 *p* = .88	***F*(2,48) = 25.42** ***p* ≤.001**	***F*(2,48) = 20.25** ***p* ≤.001**	*F*(2,48) = .32 *p* = .57	***F*(2,48) = 16.64** ***p* ≤.001**	***F*(2,48) = 17.67** ***p*≤.001**

Notes. Significant associations are presented in bold.

Correlation analyses were performed to examine the relation between schizotypal dimensions, nicotine dependency and laterality. Overall schizotypy was found to be highly associated with all three subscales (PS, NS, CogDis). Nicotine dependency was found to be positively correlated with overall schizotypy and PS and negatively associated with RHD. Additionally, PS was correlated with RHD, whereas NS was correlated with a LHD. The rest of the comparisons were not significantly correlated. The correlation analyses are presented on the subsequent table. Further analyses for females and males separately are presented in tables 4 and 5.

Table 3. Table displaying the correlation analyses between schizotypal dimensions, nicotine dependence and brain laterality.

	Schizotypy	*Positive schizotypy*	*Negative schizotypy*	*Cognitive disorganisation*	Nicotine dependence
Positive schizotypy	***r* = .61** ***p* ≤ .001**	-	-	-	-
Negative schizotypy	***r* = .64** ***p* ≤ .001**	*r* = -.09 *p* = .53	-	-	-
Cognitive disorganization	***r* = .55** ***p* ≤ .001**	***r* = .15** *p* = .28	*r* = .14 *p* = .37	-	-
Nicotine dependence	***r* = .47** ***p* ≤ .001**	***r* = .83** ***p* < .001**	*r* = -.13 *p* = .18	*r* = .11 *p* = .46	-
Laterality	*r* = -.19 *p* = .18	***r* = -.59** ***p* ≤ .001**	***r* = .29** ***p* = .04**	*r* = -.04 *p* = .75	***r* = -.49** ***p* ≤ .001**

Notes. Significant associations are presented in bold.

A multiple regression analysis was performed to examine whether scores in schizotypy and nicotine dependence could predict brain laterality. The enter method was employed and it was found that scores in schizotypy and nicotine dependence could explain a significant amount of variance in brain laterality. PS and NS were found to be significant predictors of brain laterality. Nicotine dependence and CogDis were not found to be significant predictors.

A second multiple regression analysis was performed to examine whether scores in schizotypy and brain laterality could predict nicotine dependence. The enter method was employed and it was found that scores in schizotypy and the laterality indices could explain a significant amount of variance in nicotine dependence. PS was found to be significant predictor of nicotine dependence. NS, CogDis and brain laterality were not found to be significant predictors. The following table displays the regression models.

Table 4 Table displaying the regression models.

Model 1*	F (4, 45) = 7.72, $p \leq .001$, R2= .64, R^2 adjusted = 0.35			
	Positive schizotypy	Negative schizotypy	Cognitive disorganization	Nicotine dependence
Laterality	***Beta* = -.62** **t(49) = -2.90** **$p \leq .01$**	***Beta* = .24** **t(49) = 2.06** **p = .0.4**	*Beta* = .11 t(49) = .09 p = .92	*Beta* = .03 t(49) = .25 p = .80
Model 2**	F (4, 45) = 27.02, $p \leq .001$, R2 = .84, R^2 adjusted = 0.68			
	Positive schizotypy	Negative schizotypy	Cognitive disorganization	Laterality
Nicotine dependence	***Beta* = .85** **t(49) = 8.36** **$p \leq .001$**	*Beta* = -.06 t(49) = -.68 p = .50	*Beta* = -.01 t(49) = -.18 p = .86	*Beta* = .03 t(49) = .25 p = .80

Notes. *Model 1: Predictors: Schizotypal dimensions and Nicotine Dependence. Outcome: Laterality; **Model 2: Predictors: Schizotypal dimensions and Laterality. Outcome: Nicotine Dependence. Significant associations are presented in bold.

3.*1. Gender-based Interactions*

Pearson's correlations were performed separately for male and female participants to examine the relationship between gender membership and (i) nicotine dependency, (ii) laterality, and (iii) different schizotypy subscale scores (namely: overall, PS, CogDis and NS).

3.2. Brain laterality and Nicotine dependency

Insofar as the relationship between brain laterality and nicotine dependency was concerned, results yielded an inverse moderate correlation amongst both female and male participants, indicating RHD.

3.3. Nicotine dependency correlations with schizotypal dimensions

For female participants, nicotine dependence produced moderate to strong positive correlations with all schizotypy dimensions. With regards to male participants, nicotine dependency produced positive correlations with schizotypy, ranging from moderate in the overall dimension, to strong, as evidenced in the PS dimension.

3.4. Brain laterality correlations with schizotypal dimensions

For female participants, inverse correlations, indicating LHD, emerged as a function of the association between brain laterality and two schizotypy dimensions. Specifically: overall schizotypy and PS. Statistically non-significant associations emerged for their male counterparts.

Table 5. Table displaying the correlation analyses between schizotypal dimensions, nicotine dependence and brain laterality only for females.

	Schizotypy	*Positive schizotypy*	*Negative schizotypy*	*Cognitive disorganisation*	Nicotine dependence
Positive schizotypy	***r* = .85** ***p* ≤ .001**	-	-	-	-
Negative schizotypy	***r* = .80** ***p* ≤ .001**	***r* = .53** ***p* ≤ .001**	-	-	-
Cognitive disorganization	***r* = .57** ***p* =.003**	*r* = .34, *p* = .10	*r* = .14 *p* = .51	-	-
Nicotine dependence	***r* = .54** ***p* = .01**	***r* = .69** ***p* ≤ .001**	***r* = .39** ***p* = .04**	*r* = .85 *p* = .03	-
Laterality	***r* = -.48** ***p* = .02**	***r* = -.48** ***p* = .02**	***r* = -.25** ***p* = .21**	*r* = -.25 *p* = .22	***r* = .40** ***p* = .04**

Notes. Significant associations are presented in bold.

Table 6. Table displaying the correlation analyses between schizotypal dimensions, nicotine dependence and brain laterality only for males.

	Schizotypy	*Positive schizotypy*	*Negative schizotypy*	*Cognitive disorganisation*	Nicotine dependence
Positive schizotypy	***r* = .66** ***p* ≤ .001**	-	-	-	-
Negative schizotypy	***r* = .70** ***p* ≤ .001**	*r* = .12 *p* = .58	-	-	-
Cognitive disorganization	***r* = .55**	***r* = .16**	*r* = .08	-	-

Nicotine dependence	***p* = .004** ***r* = .58** ***p* ≤ .001**	*p* = .45 ***r* = .86** ***p* ≤ .001**	*p* = .69 *r* = .01 *p* = .95	 *r* = .30 *p* = .15	-
Laterality	*r* = -.18 *p* = .38	*r* = -.07 *p* = .75	***r* = -.23** ***p* = .25**	*r* = -.01 *p* = .95	***r* = -.49** ***p* ≤ .001**

Notes. Significant associations are presented in bold.

4. Discussion

Insofar as the relationship between schizotypal dimensions and hemispheric lateralization is concerned, empirical findings in the existing literature have been far from unanimous. Previous studies have associate PS with RHD (Herzig et al., 2010; Leonards & Mohr, 2009; Mohr & Claridge, 2015; Suzuki & Usher, 2009), others with LHD (Liouta et al., 2008; O. Mason & Claridge, 1999) and yet others report no laterality at all (Gooding & Braun, 2004; Herzig et al., 2010; Najt et al., 2012). Moreover, an overconsumption of psychoaffective substances in individuals with psychosis has been repeatedly demonstrated (de Leon et al., 2002; Esterberg et al., 2009; Herzig et al., 2010), which may account for the heterogeneity of the reported schizotypy and brain laterality associations. The present study examined the association between schizotypy and brain laterality, while accounting for age and gender differences, handedness and nicotine dependence.

Nicotine dependence yielded associations with overall schizotypy, PS and RHD. Our findings agree with previously conducted research reporting relations of psychoaffective substances with higher schizotypy (Herzig et al., 2010; Najt et al., 2012) and RHD (Ernst et al., 2001; Rose et al., 2007). To our knowledge, the only study to have also investigated schizotypy, nicotine dependence and brain laterality is the study by Herzig and associates (2010) in which nicotine dependence was indeed significantly associated with RHD. Since RHD is inversely associated with higher nicotine dependence, it is possible it could also be linked with overconsumption of other drugs (Degenhardt, Hall, & Lynskey, 2001; Martínez-Ortega, Jurado, Martínez-González, & Gurpegui, 2006) and other types of impulsive behaviours, for instance binge eating episodes or gambling (Cilia et al., 2008; Uher & Treasure, 2005) assumed to contribute to reduction of asymmetry. For instance, along this line of thinking, Herzig et al. (2010) proposed that cannabis use may in fact balance rather than exacerbate uncommon hemispheric laterality patterns in schizophrenic patients. Similarly, Hahn, Neuhaus, Pogun et al. (2011) who examined altered laterality patterns in schizophrenia, reported a differential reduction of phonetic and emotional language asymmetries in a schizophrenic sample of men and women who smoked.

When gender differences were examined in our sample female participants scored significantly higher than males on nicotine dependence, which corroborates Berlin et al.'s (2003) findings of higher female FTND scores, possibly due to psychosocial factors, stimulation and tension alleviation. Nicotine dependence was significantly related to overall schizotypy, PS and NS in both genders. Nevertheless, we found associations between brain laterality, RHD, and FTND scores only on the female population. The phase of their menstrual cycle, which was unaccounted for, may partly explain these findings, as hemispheric dominance is known to transfer from left to right as the cycle progresses from the premenstrual to the menstrual phase (Heister, Landis, Regard, & Schroeder-Heister, 1989) reaching laterality pattern akin

to that of males during menstruation (Hausmann, Slabbekoorn, Van Goozen, Cohen-Kettenis, & Güntürkün, 2000). To substantiate our conclusion, we encourage further empirical research with heavy smokers where the effects of nicotine on behavior might prove to be more prevalent.

Furthermore, genetic studies point toward gender differentiations in the metabolism of nicotine, with women metabolising nicotine faster than men (Benowitz, Lessov-Schlaggar, Swan, & Jacob, 2006) a factor which could potentially influence nicotine dependence. Several other factors such as autonomy, motivational drive and sociocultural norms have also been reported as influential in nicotine dependence (West & Brown, 2013).

FTND is commonly recognized as a well validated and reliable instrument. It has been used across several countries, age groups (Prokhorov et al., 2000) and types of clinical and/or non-clinical populations (Buckley et al., 2005; Weinberger et al., 2007). Nevertheless, its sensitivity in detecting factors potentially influencing nicotine dependence has been questioned (Colby, Tiffany, Shiffman, & Niaura, 2000; Steinberg, Williams, Steinberg, Krejci, & Ziedonis, 2005)

With regards to schizotypal dimensions, previous research has provided inconsistent findings regarding the relation between PS and brain laterality (Herzig et al., 2010; Liouta et al., 2008; Najt et al., 2012; Schofield & Mohr, 2014; Suzuki & Usher, 2009). Nevertheless, the majority of studies agree that NS is not linked to brain laterality (Mason & Claridge, 1999; Mohr et al., 2005; Schofield & Mohr, 2014; Suzuki & Usher, 2009; Weinstein & Graves, 2002; Gooding & Braun, 2004) whereas the study by Schofield and associates (2014) reports a significant relation with a left-hemisphere dominance. Regarding CogDis, once again, the existing literature is inconsistent with some studies reporting (i) an association with RHD (Herzig et al., 2010; Suzuki & Usher, 2009), (ii) some LHD (Liouta et al., 2008; Schofield & Mohr, 2014) or (iii) no association (Najt et al., 2012; Mason & Claridge, 1999). In the current study the O-LIFE questionnaire was employed to assess PS, and preceding studies that have used O-LIFE have reported either RHD (Suzuki & Usher, 2009) or LHD (Liouta et al., 2008). However, other studies with the MI scale seem to report only RHD (Mohr et al., 2005; Weinstein & Graves, 2002). One of the major differences between the two scales is that O-LIFE includes more items assessing experiences, whereas the MI scales focuses more on beliefs (Schofield & Mohr, 2014).

We found a significant relation between PS and RHD, and NS and LHD. Notwithstanding that dichotic listening is a right ear advantage (REA) task favouring LHD, which is associated with verbal processing (Hugdahl & Wester, 1992), our findings further endorse the importance of addressing the implications of brain laterality in the scientific study of schizophrenia spectrum disorders. Any methodological concerns regarding the laterality task selected also apply to most past research conducted in the field which is, as reviewed above, sparse on this topic. Only two studies were identified: that of Herzig et al. (2010) and that of Schofield and Mohr (2014), neither of whom reported associations between schizotypal dimensions and brain laterality.

In our sample females scored higher in PS, whereas males scored higher in NS, which agrees with previous studies (Miettunen & Jaaskelainen, 2010; Paíno-Piñeiro et al., 2008). When correlation analyses were run separately for males

and females, significant associations of overall schizotypy and PS with brain laterality, with RHD, were found only in females.

Given that the present study comprised of right-handed participants, and in view of the fact that the prevalence of right-handedness tends to be lower amongst individuals diagnosed with schizophrenia spectrum disorders (Somers, Sommer, Boks, & Kahn, 2009), it would make sense to question whether the population under investigation may have been susceptible to psychosis from the onset. From that perspective, a pre-selection bias might seem plausible. Nonetheless, in an attempt to counteract any confounding variables related to brain laterality due to handedness, in most studies investigating schizotypy and brain laterality, right-handed subjects are commonly recruited (Herzig et al., 2010). Future studies could include right and left-handed participants so as to compare differences based on group membership (Herzig et al., 2010; Somers et al., 2009).

5. Concluding remarks

We have examined whether functional brain laterality, a behavioural marker of the psychosis spectrum, is reduced in individuals with high nicotine dependence and higher PS scores. Our findings confirm that individuals highly dependent on nicotine and with elevated PS scores exhibit RHD patterns. Further exploration of this relationship could potentially lead to the early detection of risk and/or resilience factors associated with psychosis proneness, and ultimately intensify the effectiveness of health education programmes, interventions, outcomes and lead to more favourable prognoses. Investigation of brain laterality could also expand our knowledge regarding developmental and/or behavioural markers that may increase one's liability for developing psychosis prior to its onset.

Declaration of interest

The authors declare that they have no competing interest.

Contribution

All authors have made significant contributions to this manuscript in the following areas: design of the study, data collection, data analysis and interpretation, drafting and revising the manuscript. All authors have given final approval of this manuscript.

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