



Short communication

## Investigation of orbitofrontal sulcogyral pattern in chronic schizophrenia



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### ABSTRACT

Abnormalities of orbitofrontal cortex (OFC) pattern type distribution have been associated with schizophrenia-spectrum disorders. We investigated OFC pattern type in a large sample of chronic schizophrenia patients and healthy controls. We found an increased frequency of Type II but no difference in Type I or III folding pattern in the schizophrenia group in comparison to controls. Further large studies are required to investigate the diagnostic specificity of altered OFC pattern type and to confirm the distribution of pattern type in the normal population.

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## 1. Introduction

The human orbitofrontal cortex (OFC) shows large individual variability in sulcogyral pattern. Despite this variability, Chiavaras and Petrides (2000) identified three major OFC sulcogyral patterns in the general population (Type I, Type II and Type III) based on variations of the typical 'H-shaped' sulcal pattern. Of these, Type I is the most common, followed by Type II then Type III. As cortical gyrification is completed shortly after birth (Chi et al., 1977), and is a relatively stable characteristic (Magnotta et al., 1999), OFC sulcogyral pattern has been proposed to represent a marker of early neurodevelopment (Nakamura et al., 2007).

Altered OFC sulcogyral pattern has been reported in schizophrenia-spectrum disorders. The most consistent finding has been decreased Type I pattern in the right hemisphere (Nakamura et al., 2007; Nakamura et al., 2008; Takayanagi et al., 2010; Bartholomeusz et al., 2013; Lavoie et al., 2014). In addition, increased Type II (Bartholomeusz et al., 2013; Lavoie et al., 2014) and III

(Nakamura et al., 2007; Nakamura et al., 2008; Chakirova et al., 2010; Takayanagi et al., 2010) pattern in the right hemisphere has been reported in some but not all (Chakirova et al., 2010) cohorts. These findings suggest that Type I folding pattern may represent a resilience marker, whilst either Type II or Type III pattern may represent risk markers, for schizophrenia.

Given the discrepancies in the literature regarding the prevalence of Type II and III pattern types in the schizophrenia-spectrum disorders, the aim of this study was to investigate the distribution of OFC sulcogyral pattern in a large sample of individuals with chronic schizophrenia. We sought to determine whether Type I is reduced, and whether Type II or Type III pattern is increased, in schizophrenia patients compared to controls.

## 2. Methods

### 2.1. Participants

Data for the current study were taken from a previous study (Velakoulis et al., 2006). This consisted of 89 patients with chronic schizophrenia (duration of illness  $13.4 \pm 8.5$  years) and 87 healthy controls with no personal or family history of psychiatric disorder.

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Patients had a diagnosis of schizophrenia according to DSM-III-R diagnostic criteria and were recruited from the North Western Mental Health Program in Melbourne, Australia. Controls were recruited from similar sociodemographic areas as the patients. All patients had at least 2 years of neuroleptic exposure at the time of scanning. Exclusion criteria for all participants included a history of serious head injury, neurological disorder, seizures, impaired thyroid function, corticosteroid use or alcohol/substance abuse or dependence according to the DSM-III-R. Seventy-two of the controls were from our previous study (Bartholomeusz et al., 2013), with an additional 14 recruited. Seven participants (6 patients and 1 control) were excluded because of poor MRI quality, leaving a total sample of 83 patients and 86 controls. The Melbourne Health Human Research and Ethics Committee approved this study. Written informed consent was obtained from all participants.

2.2. MRI acquisition

Anatomical T1-weighted images were acquired on a 1.5-tesla Signa (GE Medical Systems, Milwaukee), resulting in 124 contiguous SPGR images (echo time=3.3 ms; repetition time=14.3 ms; flip angle=30 degrees; matrix size=256 × 256; field of view=24 × 24 cm matrix; voxel dimensions=0.938 × 0.938 × 1.5 mm).

2.3. OFC sulcogyral pattern classification

Classification of OFC pattern type was based on continuity among medial (MOS), lateral (LOS) and transverse (TOS) orbital sulci following the method of Chiavaras and Petrides (2000) and modified by Bartholomeusz et al. (2013), as previously described. Orbital sulci were traced in coronal and transverse planes in each hemisphere using Analyze 10.0 (Mayo Clinic), and visually inspected for classification into one of three types (Type I, II or III). Classification was performed by a single rater (PW) blinded to diagnosis and sex. Inter-rater reliability (PW and CB) was performed on 40 hemispheres blind to group. The intraclass correlation coefficients (Cronbach's α) were 0.946 for the right hemisphere and 0.922 for the left hemisphere.

2.4. Statistical analysis

All statistical analyses were performed using the Statistical Package for Social Sciences (SPSS) v19.0. Group differences in pattern type distribution, asymmetry, handedness and sex were assessed with Pearson's χ<sup>2</sup> statistics. Independent t-tests were performed to assess group differences in age. To account for potential sex effects, analyses were also conducted separately for males and females.

3. Results

Schizophrenia patients were significantly older (35 vs 27 years, *p* < 0.0001) and had a greater proportion of males (87% vs 64%, *p* < 0.001) than control participants. Univariate analyses of variance showed no significant effect of age on OFC type (hemispheres analyzed separately) or interaction between group and age.

There were no overall significant differences in the distribution of OFC type in each hemisphere between patients and controls (Table 1), although a trend existed for both hemispheres (right: *p* = 0.089; left: *p* = 0.078). Given this trend, we conducted post-hoc analyses for each type in each hemisphere separately. For the right hemisphere, Type II pattern was increased (χ<sup>2</sup>(1) = 4.7, *p* = 0.04) in patients compared to controls. For the left hemisphere, there were no significant group differences in each pattern type expression.

Table 1  
Distribution of OFC sulcogyral pattern type in psychosis.

	Current study		χ <sup>2</sup>	<i>p</i> <sup>a</sup>	Chiavaras and Petrides (2000)		Nakamura et al. (2007)		Chakirova et al. (2010)		Takayanagi et al. (2010)		Bartholomeusz et al. (2013)		Lavoie et al. (2014)	
	Chronic % (n)	HC % (n)			Chronic % (n)	HC % (n)	FEP % (n)	HC % (n)	FEP % (n)	HC % (n)	FEP % (n)	HC % (n)	FEP % (n)	UHR-P % (n)	UHR-NP % (n)	HC % (n)
Right hemisphere			4.87	0.089												
Type I	48 (40)	55 (47)			64 (32)	62 (31)	44 (15)	61 (22)	31 (13)	57 (20)	45 (43)	22 (11)	48 (37)	67 (39)		
Type II	29 (24)	15 (13)*			26 (13)	28 (14)	18 (6)	22 (8)	38 (16)	34 (12)	28 (27)	35 (17)	23 (18)	8.6 (5)		
Type III	23 (19)	30 (26)			10 (5)	10 (5)	32 (11)	11 (4)	31 (13)	9 (3)	27 (26)	43 (21)	29 (22)	24 (14)		
Left Hemisphere			5.12	0.078												
Type I	58 (48)	58 (50)			48 (24)	46 (23)	41 (14)	53 (19)	48 (20)	51 (18)	48 (46)	43 (21)	52 (40)	43 (33)		
Type II	14 (12)	26 (22)			34 (17)	36 (18)	27 (9)	25 (9)	31 (13)	31 (11)	25 (24)	33 (16)	16 (12)	27 (9)		
Type III	28 (23)	16 (14)			18 (9)	18 (9)	29 (10)	19 (7)	21 (9)	17 (6)	27 (26)	25 (12)	33 (25)	30 (16)		

Note: Chronic, chronic schizophrenia; HC, healthy controls; FEP, first-episode psychosis; UHR-P, ultra high risk individuals who later transitioned to psychosis; UHR-NP, ultra high risk individuals who did not transition to psychosis.

<sup>a</sup> Analyses of the group comparison between the current chronic schizophrenia and healthy control sample.

\* significance at *p* < 0.05.

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