Psychiatry Research: Neuroimaging 250 (2016) 29–32

Contents lists available at ScienceDirect

Psychiatry Research: Neuroimaging

journal homepage: www.elsevier.com/locate/psychresns

Decreased number of orbital sulci in schizophrenia spectrum disorders

Tsutomu Takahashi [a,*], Mihoko Nakamura [a], Yumiko Nishikawa [a], Yoichiro Takayanagi [a], Atsushi Furuichi [a], Mikio Kido [a], Daiki Sasabayashi [a], Kyo Noguchi [b], Michio Suzuki [a]

[a] Department of Neuropsychiatry, University of Toyama Graduate School of Medicine and Pharmaceutical Sciences, 2630 Sugitani, Toyama 930-0194, Japan
[b] Department of Radiology, University of Toyama Graduate School of Medicine and Pharmaceutical Sciences, 2630 Sugitani, Toyama 930-0194, Japan

ARTICLE INFO

Article history:
Received 26 January 2016
Received in revised form
5 March 2016
Accepted 15 March 2016
Available online 19 March 2016

Keywords:
Schizotypal disorder
Magnetic resonance imaging
Orbitofrontal cortex

ABSTRACT

An altered orbitofrontal sulcogyral pattern has been reported in the schizophrenia-spectrum, but it remains unknown whether they also have differences in the number of intermediate and posterior orbital sulci compared with healthy subjects. This magnetic resonance imaging study investigated the number of these sulci in 102 schizophrenia patients, 47 schizotypal disorder patients, and 84 controls. Both patient groups had a significantly lower number of both sulci bilaterally compared with controls, which was weakly associated with the severity of negative symptoms. Our results may reflect the neurodevelopmental pathology related to vulnerability to psychosis.

1. Introduction

Schizotypal (personality) disorder, which has attenuated forms of schizophrenic features without the manifestation of overt psychosis, is a prototypic disorder within the schizophrenia-spectrum. They are genetically related to schizophrenia and may share neurodevelopmental abnormalities with schizophrenia as a common neurobiological basis for vulnerability factors (Siever and Davis, 2004).

Altered surface morphology of the orbitofrontal cortex (OFC) has been reported in schizophrenia (Nakamura et al., 2007; Takayanagi et al., 2010; Cropley et al., 2015) and in genetic/clinical high-risk cohorts (Chakirova et al., 2010; Lavoie et al., 2014). These studies have mainly examined the sulcogyral pattern (i.e., variations in the 'H-shaped' sulcus defined by Chiavaras and Petrides (2000)), but recent studies have further demonstrated that the number of intermediate orbital sulci (IOS), which has considerable inter-individual variability, is decreased in first-episode (Bartholomeusz et al., 2013) or high-risk (Lavoie et al., 2014) subjects for psychosis. Lavoie et al. (2014) demonstrated that high-risk subjects were also characterized by a lower number of posterior orbital sulci (POS). Because the gross cortical folding patterns are largely established by birth (Chi et al., 1977), these findings may reflect neurodevelopmental anomalies related to a vulnerability to psychosis. Our recent study found no alteration of the H-shaped sulcogyral pattern in schizotypal patients (Nishikawa et al., 2016), but it remains unknown whether they exhibit the IOS/POS anomalies.

This magnetic resonance imaging (MRI) study investigated the number of IOS/POS in schizophrenia patients, schizotypal disorder patients, and healthy controls. Based on the concept of the schizophrenia-spectrum (Siever and Davis, 2004) as well as the findings of fewer IOS/POS in high-risk subjects regardless of future transition into psychosis (Lavoie et al., 2014), we predicted that schizotypal patients would share a lower number of IOS/POS with schizophrenia patients as a vulnerability marker.

2. Methods

2.1. Subjects

Forty-seven schizotypal disorder, 102 schizophrenia, and 84 healthy subjects were included (Table 1); their sample characteristics and the OFC H-shaped folding patterns have been described elsewhere (Nishikawa et al., 2016). All subjects were right-handed and physically healthy, and none had a lifetime history of serious head trauma, neurological illness, serious medical or surgical illness, or substance abuse.

The schizotypal patients were recruited from among the patients who visited our hospital with schizotypal features accompanied by distress or associated problems in their lives; their detailed sample characteristics have been described previously (Takahashi et al., 2006). Based on the data from the Comprehensive Assessment of Symptoms and History (Andreasen et al., 1992) and Structured Clinical Interview for DSM-IV axis II disorders (First et al., 1997), the subjects were diagnosed by the consensus of two experienced psychiatrists; all met the criteria for schizotypal

* Corresponding author.
E-mail address: tsutomu@med.u-toyama.ac.jp (T. Takahashi).

http://dx.doi.org/10.1016/j.pscychresns.2016.03.005
0925-4927/

Table 1
Demographic/clinical data and sulcus counts in the study participants.

	Controls	Schizotypal	Schizophrenia	Group comparisons
Male/female (*n*)	47/37	29/18	55/47	$\chi^2=0.80$, $p=0.672$
Age (years)	24.5 ± 5.7	25.0 ± 5.4	25.5 ± 5.5	$F(2, 230)=0.72$, $p=0.487$
Height (cm)	166.5 ± 7.7	165.9 ± 8.7	164.7 ± 8.0	$F(2, 230)=1.28$, $p=0.281$
Education (years)	16.0 ± 2.5	13.1 ± 2.0	13.4 ± 1.9	$F(2, 230)=42.67$, $p<0.001$; Con > Sz, SzTypal
Parental education (years)[a]	12.9 ± 2.3	12.3 ± 1.7	12.4 ± 2.1	$F(2, 221)=1.81$, $p=0.166$
Age at onset (years)	–	–	22.0 ± 4.5	–
Duration of illness (years)	–	–	3.6 ± 4.6	–
Duration of medication (years)	–	1.5 ± 3.0	2.6 ± 3.9	$F(1, 147)=2.61$, $p=0.108$
Drug (mg/day, haloperidol equivalent)	–	4.8 ± 5.7	10.3 ± 8.9	$F(1, 147)=15.30$, $p<0.001$; Sz > SzTypal
Total SAPS score[a]	–	16.0 ± 9.2	27.8 ± 21.3	$F(1, 139)=12.65$, $p<0.001$; Sz > SzTypal
Total SANS score[a]	–	41.9 ± 21.7	49.1 ± 23.4	$F(1, 139)=3.10$, $p=0.081$
Left IOS [*n* (%)]				$\chi^2=15.09$, $p=0.003$[b]
Single	30 (35.7)	26 (55.3)	48 (47.1)	
Double	42 (50.0)	20 (42.6)	52 (51.0)	
Triple	12 (14.3)	1 (2.1)	2 (2.0)	
Right IOS [*n* (%)]				$\chi^2=36.27$, $p<0.001$[b]
Single	20 (23.8)	26 (55.3)	56 (54.9)	
Double	52 (61.9)	21 (44.7)	46 (45.1)	
Triple	12 (14.3)	0 (0)	0 (0)	
Left POS [*n* (%)]				$\chi^2=25.92$, $p<0.001$[b]
Absent	26 (31.0)	27 (57.4)	58 (56.9)	
Single	41 (48.8)	20 (42.6)	39 (35.3)	
Double	17 (20.2)	0 (0)	5 (4.9)	
Right POS [*n* (%)]				$\chi^2=15.55$, $p=0.004$[b]
Absent	30 (35.7)	20 (42.6)	57 (55.9)	
Single	40 (47.6)	25 (53.2)	41 (40.2)	
Double	14 (16.7)	2 (4.3)	4 (3.9)	

Values represent mean ± SDs unless otherwise stated. Con, controls; IOS, intermediate orbital sulcus; POS, posterior orbital sulcus; SANS, Scale for the Assessment of Negative Symptoms; SAPS, Scale for the Assessment of Positive Symptoms; Sz, schizophrenia; SzTypal, schizotypal.

[a] Data missing for some participants.

[b] There were no group differences between the schizophrenia and schizotypal patients (all $p>0.293$). When they were grouped together as the patient group, the triple-IOS (left, $\chi^2=13.43$, $p<0.001$; right, $\chi^2=22.44$, $p<0.001$) and double-POS (left, $\chi^2=17.91$, $p<0.001$; right, $\chi^2=10.94$, $p<0.001$) patterns were more common in the controls than in the patient group. The controls had 'two or more IOS' more often (left, $\chi^2=4.23$, $p=0.040$; right, $\chi^2=21.28$, $p<0.001$) and had absent-POS pattern less often (left, $\chi^2=14.66$, $p<0.001$; right, $\chi^2=5.51$, $p=0.019$) than the patient group. There were no differences between first-episode ($n=65$, defined as illness duration ≤1year or undergo first psychiatric hospitalization) and chronic ($n=37$) subgroups of current schizophrenia cohort (all $p>0.320$).

disorder (ICD-10) as well as for schizotypal personality disorder (DSM-IV). None of them have developed overt schizophrenia during at least the 2-year follow-up. At the time of scanning, 14 were treated with typical neuroleptics and 26 with atypical neuroleptics. The remaining seven were neuroleptic-naïve.

The schizophrenia patients fulfilled the ICD-10 criteria. All but two of the patients were on neuroleptic medication; 42 were treated with typical neuroleptics, 57 were receiving atypical neuroleptics, and one was receiving both typical and atypical. The clinical symptoms of the schizotypal and schizophrenia patients were rated at the time of scanning using the Scale for the Assessment of Negative and Positive Symptoms (SANS/SAPS; Andreasen, 1984).

The healthy controls were recruited from members of the community, hospital staff, and university students. They completed a questionnaire consisting of 15 items concerning their family and past histories, as well as present illness. They did not have any personal or family history of psychiatric illness in their first-degree relatives. This study was approved by the regional ethics committee. Written informed consent was obtained from all subjects.

2.2. Magnetic resonance imaging procedures

MR scans were acquired with a 1.5−T Magnetom Vision (Siemens, Erlangen, Germany) with a 3D gradient-echo sequence FLASH yielding 160–180 contiguous 1-mm slices in the sagittal plane (TR=24 ms, TE=5 ms, Flip=40°, FOV=256 mm, Matrix=256 × 256, and Voxel size=1.0 mm^3). Using Dr. View software (Infocom, Tokyo, Japan), brain images were realigned in three dimensions and then reconstructed into entire contiguous coronal images, with a 1-mm thickness, perpendicular to the anterior commissure-posterior commissure line.

According to the classification by Chiavaras and Petrides (2000), the IOS and POS were highlighted on consecutive 1-mm coronal slices and then assessed by viewing both coronal and axial 1-mm slices without gap (eFig. 1); a fissure clearly visible in at least 4 coronal and 4 axial slices was defined as a sulcus (Lavoie et al., 2014). One rater (TT) counted the number of each sulcus (IOS, single, double, or triple; POS, absent, single, or double) without any knowledge of the subjects' identity. Intra- and inter-rater (TT and MN) reliabilities (Cronbach's α) of sulcus counts in a subset of randomly selected 30 hemispheres were over 0.83 and over 0.89 for the IOS and POS, respectively.

2.3. Statistical analysis

Group differences in the number of IOS/POS were evaluated using χ^2 test. The relationships between the sulcus counts and the clinical/demographic variables were analyzed for each hemisphere using analysis of variance (ANOVA) with the sulcus count as a between-subject factor. The hemispheres with triple-IOS and/or double-POS in the patients were excluded from the ANOVAs due to small sample size ($n\leq 5$). Statistical significance was defined as $p<0.05$.

3. Results

The schizophrenia and schizotypal patients had a significantly lower number of both IOS and POS bilaterally compared with controls, but there was no difference between both patient groups