2. Methods

2.1. Subjects

Thirty-seven schizotypal disorder patients (24 males and 13 females; mean age=25.8 years, SD=5.4, range=18–37) who met the ICD-10 criteria for research (World Health Organization, 1993) were examined. They were recruited from patients who visited the clinics of the Department of Neuropsychiatry, Toyama Medical and Pharmaceutical University Hospital, with schizotypal features accompanied by distress or associated problems in their lives and who needed to receive consistent clinical follow-up. Candidates who had a previous history of overt psychotic episode or met the ICD-10 criteria for schizophrenia during the follow-up period were excluded. The mental condition of each subject was assessed by well-trained psychiatrists approximately every 2 weeks to check for the emergence of overt psychotic symptoms as part of an early intervention program for psychoses, and none of the 37 patients have developed overt schizophrenia to date (mean follow-up period after MRI scanning=2.0 years, SD=1.7). All available clinical information and data obtained from a detailed review of the clinical records and structured interviews using the Comprehensive Assessment of Symptoms and History (CASH) including the chapter on premorbid or intermorbid personality (Andreasen et al., 1992) were stored in a database. The subjects were diagnosed by consensus reached by at least two experienced psychiatrists based on these data. Twenty-nine patients were outpatients, and the other eight underwent closer clinical and medical examinations including MRI during short-term admission. At the time of MRI scanning, 32 of the 37 patients were treated with low-dose antipsychotics, of which 11 patients were treated with typical neuroleptics and 21 patients received atypical neuroleptics. The remaining five patients were neuroleptic-naïve. Clinical symptoms were rated within 1 month of scanning using the Scale for the Assessment of Negative Symptoms (SANS; Andreasen, 1984a) and the Scale for the Assessment of Positive Symptoms (SAPS; Andreasen, 1984b). Their mean scores for the SANS and SAPS were 42.4 (SD=23.0, range=5–84) and 16.0 (SD=8.9, range=0–31), respectively. Thirty-three of the 37 patients with schizotypal disorder were also assessed using the Brief Psychiatric Rating Scale (BPRS; Overall and Gorham, 1962). Their mean total BPRS score was 38.4 (SD=9.7, range=19–61).

The schizophrenic comparison group was composed of 62 patients with schizophrenia [32 males and 30 females, mean age=25.8±4.9 (SD) years, range=18–36], and this group contained 58 schizophrenia patients (31 males, 27 females) who were examined in our previous study of the whole insular cortex volume (Takahashi et al., 2004a). All patients fulfilled the ICD-10 diagnostic criteria for research on schizophrenia (World Health Organization, 1993). All but one of the schizophrenia patients were receiving neuroleptic medication; 30 patients were treated with typical neuroleptics and 31 patients with atypical neuroleptics. At the time of the MRI study, their mean scores on the SANS and SAPS were 46.8 (SD=23.4) and 25.2 (SD=20.4), respectively.

The control subjects consisted of 69 healthy volunteers [35 males and 34 females, mean age=24.0±6.5 (SD) years, range=18–38] recruited from among members of the community, hospital staff, and medical and pharmaceutical students, and included 61 subjects who participated in a previous study (Takahashi et al., 2004a). They were given 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. The control subjects were not screened with a standard measure such as the Structured Clinical Interview for DSM-IV Axis II Personality Disorders (SCID-II; First et al., 1997) and this may be a possible limitation of the study. However, all control candidates were interviewed and administered the Minnesota Multiphasic Personality Inventory (MMPI) by experienced clinical psychologists to obtain a rather homogenous control group without eccentric profiles on the MMPI. Although the MMPI has not proved very sensitive for the detection of schizotypy (Walters, 1983), approximately 17% of the candidates for normal controls were excluded for having an abnormal profile with a T-score for the validity scales or the clinical scales exceeding 70.

All subjects were physically healthy at the time of the study, and none had a lifetime history of serious head trauma, neurological illness or substance abuse. A handedness inventory developed by

Kameyama et al. (1981) consisting of 14 questions about hand preference was used to assess handedness; the subjects were right-handed except for one female patient with schizotypal disorder of unknown handedness.

The demographic and clinical characteristics of the control subjects, patients with schizotypal disorder and patients with schizophrenia are summarized in Table 1. The three groups were matched on age, height or parental education. Although there were more male than female schizotypal patients, the difference in the gender ratios among the three diagnostic groups was not statistically significant (chi-square analysis, $\chi^2=2.20$, $P=0.333$). The control subjects had attained a higher mean level of education than had the patients with either disorder (control subjects, 15.7 ± 2.5 years; schizophrenia patients, 13.4 ± 1.9 years; schizotypal patients, 13.5 ± 1.9 years; ANOVA, $F=23.28$, $df=2,165$, $P<0.001$). The total SAPS score for the schizophrenia patients was significantly higher than that for the schizotypal patients (ANOVA, $F=6.60$, $df=1,96$, $P=0.012$), although there were no significant differences between patients with schizophrenia and schizotypal disorder for the total score for SANS. There were significant differences in medication dosage (ANOVA, $F=17.95$, $df=1,97$, $P<0.001$); the patients with schizotypal disorder took significantly smaller amounts of neuroleptics than did the patients with schizophrenia. This study was approved by the Committee on Medical Ethics of Toyama Medical and Pharmaceutical University. After a complete description of the study was given to the subjects, their written informed consent was obtained.

2.2. Magnetic resonance imaging procedures

Magnetic resonance images were obtained utilizing a 1.5-T Magnetom Vision (Siemens Medical System, Inc., Erlangen, Germany) with a three-dimensional gradient-echo sequence FLASH (fast low-angle shots) yielding 160–180 contiguous T1-weighted slices of 1.0-mm thickness in the sagittal plane. Imaging parameters were repetition time=24 ms, echo time=5 ms, flip angle=40°, field of view=256 mm, and matrix size=256×256 pixels. The voxel size was $1.0\times1.0\times1.0$ mm^3. Magnetic field inhomogeneities in our scanner were monitored with weekly phantom scanning and daily basic quality control, and had been stable over the MR acquisition time for this study.

Table 1
Clinical and demographic characteristics of normal control subjects, patients with schizotypal disorder, and patients with schizophrenia

Variable	Control subjects		Schizotypal patients		Schizophrenia patients	
	Male ($N=35$)	Female ($N=34$)	Male ($N=24$)	Female ($N=13$)	Male ($N=32$)	Female ($N=30$)
Age (years)	24.1 ± 5.1	23.8 ± 5.8	25.7 ± 5.8	25.9 ± 4.6	25.6 ± 4.8	26.0 ± 5.1
Height (cm)	171.9[a] ± 4.3	159.2 ± 4.5	170.8[a] ± 5.9	156.2 ± 4.6	170.7[a] ± 5.1	158.5 ± 4.0
Education (years)	16.6[b] ± 2.8	14.8 ± 1.6	13.4 ± 1.9	13.5 ± 2.0	13.5 ± 1.9	13.3 ± 1.9
Parental education (years)	13.0 ± 2.3	12.5 ± 2.3	12.1 ± 1.5	12.1 ± 2.3	12.2 ± 1.9	11.9 ± 2.4
Age at onset (years)	–	–	–	–	22.1 ± 4.5	21.9 ± 4.2
Duration of illness (years)	–	–	–	–	3.5 ± 3.9	4.4 ± 4.3
Duration of medication (years)	–	–	2.1 ± 3.8	0.9 ± 1.5	2.4 ± 2.9	3.3 ± 3.7
Drug (mg/day, haloperidol equiv.)[c]	–	–	5.1 ± 5.5	2.5 ± 1.6	11.7[d] ± 8.6	10.8[d] ± 10.4
Total SAPS score	–	–	15.8 ± 8.7	16.3 ± 10.1	23.0[e] ± 21.1	27.7[e] ± 19.8
Total SANS score	–	–	40.4 ± 23.4	46.5 ± 23.4	50.0 ± 22.4	43.4 ± 24.4

This values represent means ± SDs. SANS, Scale for the Assessment of Negative Symptoms; SAPS, Scale for the Assessment of Positive Symptoms.
ANOVA followed by Scheffé's test was used.
[a] $P<0.01$: compared with females.
[b] $P<0.01$: compared with female schizophrenia patients, male schizotypal patients, and female schizotypal patients; $P<0.05$: compared with female controls and male schizophrenia patients.
[c] The different typical and atypical neuroleptic dosages were converted into haloperidol equivalents according to Toru (2001).
[d] $P<0.01$: compared with schizotypal patients.
[e] $P<0.05$: compared with schizotypal patients.

The images were transferred to a Unix workstation (Silicon Graphics, Inc, Mountain View, CA., USA), and the data were randomly coded and analyzed using the software package Dr View 5.3 (Asahi Kasei Joho System Co, Ltd, Tokyo, Japan) without knowledge of the subjects' gender and diagnosis. Details of the data analyses have been previously described (Takahashi et al., 2002a). Briefly, the scans were realigned in three dimensions to standardize for differences in head tilt during image acquisition and were then reconstructed into entire contiguous coronal images, with a 1-mm thickness, perpendicular to the anterior commissure–posterior commissure (AC-PC) line on the workstation. The signal-intensity histogram distributions from the T1-weighted images across the whole brain for each subject were used to segment the voxels semi-automatically into gray matter, white matter, and cerebrospinal fluid (CSF) according to the Alpert algorithm (Alpert et al., 1996). Although the images were not corrected for the magnetic field inhomogeneities, no visible effect on the quality of the segmentation was detected for any case. Before the volumetric analysis of the insular cortex, masks were semi-automatically created to demarcate the outer extent of the intracranial contents with the skull, scalp, and neck tissues removed, and therefore minimal manual editing of the masks was required.

2.3. Intracranial volume (ICV) measurements

Intracranial volume (ICV) was measured to correct for differences in head size. Before creation of the mask images, the 1-mm-thick coronal slices which had been corrected for head tilt were reformatted into consecutive 5-mm-thick sagittal slices with each voxel as $1 \times 1 \times 5$ mm^3. The intracranial cavity was manually traced for each slice using anatomical landmarks according to a study by Eritaia et al. (2000), and the ICV was calculated by summing the measured volumes of all slices.

2.4. Insular cortex measurements

First, based on the segmented gray matter images, the whole (short and long) insular cortex was traced on 1-mm consecutive coronal slices as described elsewhere (Takahashi et al., 2004a). Specifically, the most rostral coronal plane containing the insular cortex and the coronal plane containing the fusion of the superior and inferior circular insular sulci were chosen as anterior and posterior boundaries, respectively. On each coronal slice, the insular cortex was bounded superiorly by the superior circular insular sulcus and inferiorly by the inferior circular insular sulcus or the orbitoinsular sulcus.

Next, we followed the course of the central insular sulcus in three dimensions from the limen insulae and distinguished between the short and long insular cortex on coronal 1-mm slices (Fig. 1). The insular cortex rostral to the slice showing the limen insulae was regarded as the short insular cortex. On more caudal coronal slices, the short and long insular cortices were divided in a superior–inferior direction by the central insular sulcus, which was readily identified on the coronal slices in most cases. As previously noted by Naidich et al. (2004), the central insular sulcus provided a prominent landmark on conventional sagittal images, even when it was not clearly seen on coronal slices.

All volumetric data reported in this study were measured by one rater (TT) who was unaware of the subjects' identity, gender, and diagnosis. To determine the reliability of the measurements, five subjects were randomly selected for a total of approximately 275 slices (approximately 55 slices per brain). The short and long insular cortices in a subset of these five subjects were measured independently by two raters (TT and RT), and intraclass correlation coefficients (ICCs) were calculated. The inter-rater ICCs of the short and long insular cortex measurements were greater than 0.93. Each volume was then remeasured after at least 4 weeks by the first rater; the intra-rater ICCs of the short and long insular cortex measurements were greater than 0.98.

2.5. Statistical analysis

The absolute insular cortex volume was analyzed using repeated measures multivariate analysis of variance (MANCOVA) with age, ICV, and dosage of neuroleptic medication as covariates, diagnosis and gender as between-subject factors, and hemisphere (left, right) and subregion (short, long) as within-subject variables. Since a significant main effect for the subregion was observed ($F=2469.84$; $df=1,162$;

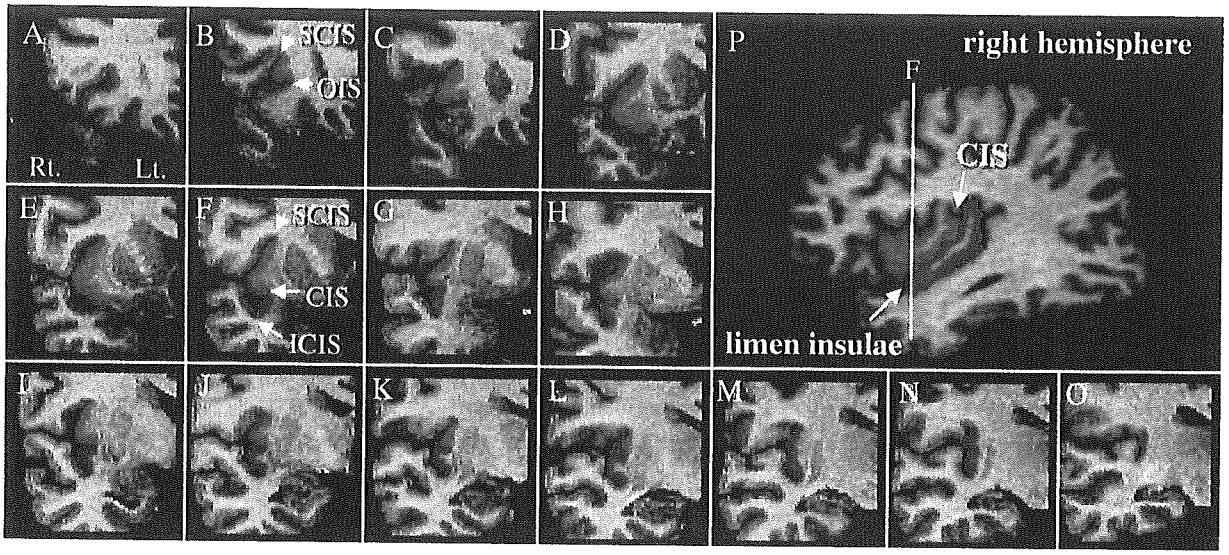

Fig. 1. Regions of interest manually traced in this study. The sample coronal slices (panels A-O) show delineations of the right short insular cortex (blue) and right long insular cortex (red), and panel P shows a sagittal view of the insular cortex in the right hemisphere. The coronal line F corresponds to panel F, a coronal slice showing the limen insulae. Abbreviations: CIS=central insular sulcus; ICIS=inferior circular insular sulcus; OIS=orbitoinsular sulcus; SCIS=superior circular insular sulcus.

$P<0.001$), the absolute volumes for the short and long insular cortex were then separately analyzed using the same model but with only hemisphere as a within-subject variable. As the schizotypal disorder patients took significantly smaller amounts of neuroleptics than the schizophrenia patients, the dosage of neuroleptic medication was used as the covariate for these analyses. For the comparison of the ICV, height was treated as covariate; groups did not significantly differ in ICV volume (Table 2). Post hoc Spjotvoll and Stoline tests, modified Tukey's tests for unequal sample size, were carried out to follow up the significant main effects or interactions yielded by these analyses (Fig. 2).

To analyze volume changes in relation to clinical symptoms, Spearman's rank correlation was calculated between the relative volumes for the long and short insular cortex and scores for the subscales of SAPS and SANS. The relative insular cortex volume, used to control for differences in head size, was obtained by dividing the absolute volume of the insular cortex by ICV and multiplying the result by 100. To examine the

Table 2
Intracranial volume (ICV) and absolute insular cortex volume in control subjects, patients with schizotypal disorder, and patients with schizophrenia

Brain region	Control subjects				Schizotypal patients				Schizophrenia patients				Analysis of covariance		
	Male (N=35)		Female (N=34)		Male (N=24)		Female (N=13)		Male (N=32)		Female (N=30)		Diagnosis effect[a]		
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	F	df	P
ICV (cm^3)	1579	99	1384	108	1584	108	1420	154	1567	136	1391	101	1.13	2, 161	0.325[b]
Short insular cortex (mm^3)													3.19	2, 159	0.044[c]
Left	5588	601	4808	686	5347	652	4981	542	5095	661	4689	695			
Right	5349	637	4695	588	5261	699	5112	807	4855	556	4458	639			
Long insular cortex (mm^3)													5.26	2, 159	0.006[c]
Left	2795	493	2649	449	2911	628	2899	481	2763	500	2357	550			
Right	2678	429	2627	336	2906	377	2650	405	2676	448	2372	474			

[a] For the other main effects and interactions, and the results of post hoc tests, see the text.
[b] Height was used as covariate.
[c] Age, ICV, and dosage of neuroleptic medication were used as covariates.

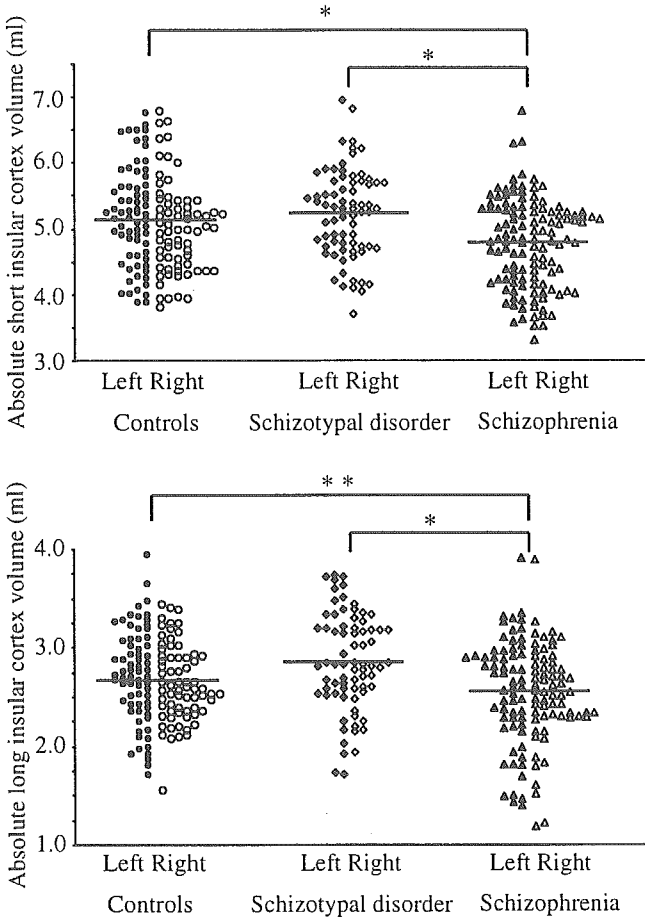

Fig. 2. Absolute volumes of the short and long insular cortex in control subjects (35 males, 34 females), schizotypal disorder patients (24 males, 13 females), and schizophrenia patients (32 males, 30 females). Horizontal lines indicate means. Post hoc Spjotvoll and Stoline tests: $*P<0.01$, $**P<0.05$.

effects of neuroleptic medication, correlations between the relative volumes for the long and short insular cortices and daily medication dosage and duration of neuroleptic medication were analyzed using Spearman's rank correlation coefficients. For the patients with schizophrenia, the correlation between the relative insular cortex volume and illness duration or age of onset was also analyzed. For these analyses, statistical significance was defined as $P<0.05$.

3. Results

3.1. Insular cortex measurements

Table 2 summarizes the short and long insular cortex measurements in schizophrenia patients, schizotypal disorder patients, and control subjects. Repeated measures MANCOVA revealed significant main effects for diagnosis ($F=6.06$; $df=2,159$; $P=0.003$), hemisphere ($F=23.55$; $df=1,162$; $P<0.001$), and subregion ($F=2469.84$; $df=1,162$; $P<0.001$). However, there was no significant diagnosis × subregion interaction ($F=1.80$; $df=2,162$; $P=0.169$). This indicates that the between-group difference in insular cortex volume was not specific for one subregion.

Lower order MANCOVA of the short insular cortex revealed significant main effects for diagnosis ($F=3.19$; $df=2,159$; $P=0.044$) and hemisphere ($F=8.91$; $df=1,162$; $P=0.003$), where patients with schizophrenia had a significantly smaller short insular cortex than schizotypal patients (post hoc test, $P=0.001$) and control subjects (post hoc test, $P=0.001$) bilaterally, and the short insular cortex volume was larger for the left than the right hemisphere for all diagnostic groups (post hoc test, $P=0.002$). There was no significant difference in short insular cortex volume between schizotypal disorder patients and control subjects (post hoc test, $P=0.827$), and no main effect for gender ($F=2.35$; $df=1,159$; $P=0.127$) or interaction among the factors was observed.

Lower order MANCOVA of the long insular cortex revealed significant main effects for diagnosis ($F=5.26$; $df=2,159$; $P=0.006$). Post hoc analyses showed the long insular cortex to be significantly reduced in the schizophrenia patients compared with the schizotypal disorder patients ($P<0.001$) and with the controls ($P=0.044$). No significant difference in the long insular cortex volume emerged between the schizotypal disorder patients and control subjects ($P=0.074$). There was no significant main effect for gender ($F=1.73$; $df=1,159$; $P=0.190$) or hemisphere ($F=3.79$; $df=1,162$; $P=0.053$), and no interaction among the factors was found.

3.2. Clinical correlations

For both patient groups, there were no significant correlations between the volumes for the short and long insular cortex and the scores for the subscales of the SAPS or SANS. For schizotypal disorder patients, the short and long insular cortex volumes were not correlated with the medication dosage or duration of

neuroleptic medication. For schizophrenia patients, insular cortex volume was negatively correlated with illness duration (right short insular cortex, Spearman's rho=0.39, $P=0.002$; left long insular cortex, Spearman's rho=0.47, $P<0.001$) and duration of neuroleptic medication (right short insular cortex, Spearman's rho=0.38, $P=0.002$) even after Bonferroni correction for multiple comparisons was made [i.e. $P<0.003$ (0.05/16)]. However, insular cortex volume was not correlated with age at onset of illness or dosage of neuroleptic medication.

4. Discussion

To our knowledge, this is the first volumetric MRI study to separately investigate sulcally defined short and long insular cortex volumes in schizophrenia spectrum disorders. The primary positive finding of this study was a significant volume reduction in the short and long insular cortices without a pattern of topographically specific localization for schizophrenia patients compared with schizotypal disorder patients and control subjects. In contrast, we found no volume differences in the short or long insular cortices between schizotypal disorder patients and normal controls.

The anterior and posterior portions of the insular cortex have been reported to have cytoarchitectural, connectional, and functional differences (Augustine, 1996; Duvernoy, 1999; Türe et al., 1999). The anterior portion, which is divided into three short insular gyri, has extensive connections with the frontal lobe. In contrast, the posterior portion of the insular cortex is formed by one or two long insular gyri and is seen to connect with both the parietal and temporal lobes. Functional neuroimaging studies have suggested that the short insular cortex is more involved in emotional and language-related functions, whereas the long insular cortex includes somatosensory and auditory processing areas [as reviewed by Augustine (1996), Nagai et al. (2001), Bamiou et al. (2003), and Naidich et al. (2004)]. Our findings are consistent with a recent MRI study by Kasai et al. (2003), who reported that both anterior and posterior insulae were significantly reduced in schizophrenia patients compared with control subjects and that group differences were not localized to a particular subregion. For the present study, we used the central insular sulcus as an anatomical boundary between the short and long insular cortex, whereas Kasai et al. (2003) used an alternative extrinsic landmark (mamillary body). Disruption of the paralimbic neural network including the insula has been proposed to contribute to the pathophysiology of schizophrenia by previous structural MRI studies (Goldstein et al., 1999; Shapleske et al., 2002). More specifically, functional neuroimaging studies have reported that various cognitive dysfunctions in schizophrenia such as emotional deficit (Crespo-Facorro et al., 2001a), recognition memory impairment (Crespo-Facorro et al., 2001b) or abnormal audiovisual speech perception (Surguladze et al., 2001) are mediated at least in part by the insular cortex. The insular cortex is engaged in a variety of cognitive functions, but its topographical localization has not been fully established. From the present and previous studies, it appears that the involvement of the insular cortex in schizophrenia is widespread and diffusely distributed rather than being specifically located in the anterior or posterior portion.

The sample characteristics of the clinic-based schizotypal disorder patients in our laboratory have been described in previous publications (Takahashi et al., 2002b, 2004b; Yoneyama et al., 2003; Kawasaki et al., 2004; Suzuki et al., 2004). The present study may not have been completely framed for direct comparisons with several previous studies in subjects with SPD since there are subtle but distinct differences between the diagnostic categories of schizotypal disorder (ICD-10) and SPD (DSM-IV). SPD is a stable personality, but schizotypal disorder in contrast requires a period of at least 2 years and the criteria include occasional transient quasi-psychotic episodes. Although all of the schizotypal subjects in this study also fulfilled DSM-IV criteria for SPD on Axis II, an additional diagnosis of brief psychotic disorder on Axis I was considered in eight subjects who experienced occasional transient quasi-psychotic episodes. In addition, schizotypal disorder "occasionally evolves into overt schizophrenia." Thus, schizotypal disorder in ICD-10 includes prodromal schizophrenia in addition to SPD as defined in DSM-IV. However, prior to the onset of psychosis, the clinical manifestations of two groups of patients who later develop schizophrenia or not are indistinguishable. The follow-up periods for the schizotypal patients in this

study were relatively short and some of them may have been at risk for developing psychosis later; they could be diagnosed as being in the prodromal phase of schizophrenia but not as SPD according to the concept of DSM-IV. We therefore adopted the ICD-10 criteria for schizotypal disorder in the present study. With regard to the symptom severity, the total BPRS score of our schizotypal subjects (mean=38.4, SD=9.7) was comparable to those (mean=37.5, SD=6.2) of previous MRI studies on mostly neuroleptic-free clinic-based subjects with SPD (Hazlett et al., 1999; Byne et al., 2001). However, our cohort may have included subjects with more serious symptoms than the SPD subjects in previous studies since most of the schizotypal disorder patients in the present study were taking neuroleptic medications.

Our results suggest that the volumes for the short and long insular cortices were reduced in overt schizophrenia but were preserved in schizotypal disorder. This may explain the decreased magnitude in cognitive/social deficits and symptomatology for schizotypal disorder relative to schizophrenia. Interestingly, it has been suggested that the abnormalities associated with the insular cortex are relevant to hallucinations (Crespo-Facorro et al., 2000; Shergill et al., 2000; Shapleske et al., 2002), which are a cardinal feature of schizophrenia but not prominently seen in schizotypal subjects. In a recent review of neurobiological abnormalities found in SPD, Siever and Davis (2004) hypothesized that while temporal volume reductions appear to be common to both SPD and schizophrenia, there may be preservation of frontal lobe volume in SPD compared with schizophrenia. Despite the above-mentioned differences in the sample characteristics between laboratories, Kurachi (2003a,b) suggested a similar hypothesis based on studies concerning cognitive characteristics and brain morphologic changes in schizotypal disorder and schizophrenia patients, i.e., the temporal lobe changes may underlie a vulnerability to schizophrenia and latent dysfunction in these lesions may become clinically apparent due to additional frontal lobe changes in schizophrenia. Based on these hypotheses, it may be reasonable to suppose that the long insular cortex, connecting with the temporal regions, is reduced in schizotypal patients as well as schizophrenia patients, while the short insular cortex, which has close connections with frontal cortex, is preserved in schizotypal patients. Such parallel reductions in associated regions in SPD were found in the volume of the thalamus; Byne et al. (2001) reported that size of the pulvinar, which projects to temporal lobe structures, was reduced in SPD as well as schizophrenia patients, while the size of the dorsomedial nucleus of the thalamus, associated with the prefrontal regions, was decreased only in the schizophrenia patients. Contrary to predictions, however, the present findings suggest that the insular cortex in schizotypal disorder patients shows no topographically specific volume changes. Although not supported directly by the present findings, the validity of these hypotheses seems worthy of further testing. Additional comprehensive assessment of multiple brain regions in the same group would be essential for the understanding of the brain morphologic characteristics of the schizotypal patients.

Some limitations of the present study should be mentioned. First, our results were not in agreement with those of a previous voxel-based MRI study carried out by our group (Kawasaki et al., 2004), in which reduced gray matter of the left insular cortex was found in schizotypal disorder patients. Although the validity of VBM has been tested in comparison with conventional region-of-interest (ROI) measurements (Wright et al., 1999; Suzuki et al., 2002), as discussed by Kasai et al. (2003), the results of the voxel-based methods could remain at odds with manual ROI methods, which are the current gold standard. Although we cannot clearly explain the reason for the differences in the results between the VBM and manual ROI analyses, the morphologic changes of the adjacent structures such as the superior temporal gyrus or the inferior frontal gyrus might have influenced the results for the insular cortex. A second limitation is that most of the patients were receiving neuroleptic medication. A relationship between brain morphologic features and neuroleptic medication has been reported in schizophrenia (Keshavan et al., 1994, 1998; Chakos et al., 1995; Gur et al., 1998), and insular cortex volume in schizophrenia was negatively correlated with duration of neuroleptic medication in the present study. This correlation was not found for the schizotypal patients, and the dosage of neuroleptic medication taken at the time of the scan in this study was not related to insular cortex volume. However, the

effects of cumulative years of medication treatment on the schizophrenia patients cannot be ruled out. A third limitation is that the control subjects in the present study were not selected to be educationally equivalent to the patients with both disorders. However, we optimally matched the parental education among the three groups according to the notion that matching on the basis of the educational level of the parents may reduce confounding factors in selection of control groups when brain measures are studied (Andreasen et al., 1990). In addition to these limitations, the relatively small sample size of female schizotypal disorder patients also limited our ability to generalize the findings of the present study. The morphologic characteristics of this disorder should be extensively examined with a larger female sample in future studies to confirm and extend the present findings.

In conclusion, the volume reduction of the insular cortex may be specific to overt schizophrenia, although there is no evidence for a topographically specific pattern of volume loss between the short and long insular cortices. The findings of the present study suggest that insular involvement may be implicated in the manifestation of overt psychosis.

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巻頭言

平成17年と日本の司法精神医学

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平成17年には日本の司法精神医学にとって、いくつかの重要な出来事があったと思われます。まず、平成15年に成立した「心神喪失者等医療観察法」が、2年後の平成17年7月から施行されました。東海・北陸地域の指定入院医療機関の一つとして、北陸病院に建設中の新病棟も平成18年2月に開設されるとのことです。第2に、日本司法精神医学会が設立され(理事長：松下正明先生)、平成17年5月21日（土）にさいたま市で第1回日本司法精神医学会（会長：山内俊雄先生）が約320名の出席のもとに開かれました。この会では秋元波留夫先生が「司法精神医学の存在理由は何か―心神喪失者等医療観察法の施行と関連して―」という題で特別講演をされました。

司法精神医学の充実には、それに携わる専門家の養成が必要です。これに関しては、平成17年度より厚生労働省の「こころの科学研究事業」として「司法精神医学の人材育成等に関する研究」の研究班（班長：林　拓二先生）がスタートしました。この研究班の活動の一つとして各地区での司法精神医学関係の研究会の開催を促進することが挙げられています。

この点では、北陸司法精神医学懇話会が平成4年に設立され、平成17年で14回を重ねているのは特筆するべきことと思います。このように長い年月にわたって懇話会を開催してきた地区は日本では大変まれであり、この懇話会を設立された会長の山口成良先生と事務局を担当してこられた松原三郎先生はじめ関係者の皆様の先見の明とそのご努力に敬服する次第です。これから北陸地域は日本の司法精神医学のモデル的地区として発展していく可能性があると思われます。

さて、ここで精神鑑定について一言述べたいと思います。秋元波留夫、山口成良編の「神経精神医学」(第2版、1998）の第25章「司法精神医学」(秋元波留夫）は、精神科医が熟読玩味するべき格調高い内容ですが、そこには「責任能力の判定にあたって司法から精神医学に求められる第一の命題は精神障害の存否、態様であり、第二は是非を弁別する能力、第三には弁別に従って行動する能力である」と述べられています。

このような精神鑑定について、精神医学的には近年どのように進歩があったでしょうか。精神鑑定の仕方は、事柄の性質上、短期間で変わるのは好ましくないでしょう。しかし、長年にわたって鑑定書に用いられる精神医学が同じだとすれば、それは精神医学の進歩の遅さを反映していることにもなります。また、鑑定人ごとに診断名が変わるようでは、精神医学に対する社会の信頼も損なわれます。診断面では、国際疾病分類第10版（ICD-10）やアメリカ精神医学会のDSM-Ⅳの導入により、診断の信頼性は向上していると思われます。今後、客観的補助診断法が開発されれば、さらに診断の確実性が増すと期待されます。弁別能力と行動制御能力の判定についてはどうでしょうか。これについては個々の事例について、診断、刑法に抵触する行為の弁別、日常社会生活能力などを総合して判定されていると思われます。弁別能力と行動制御能力は、人間の脳のはたらきであるという視点からは、認知神経心理学的にも検討されるべき事柄と思います。個々の事例を積み重ねる中で、将来的には認知神経心理学的研究の成果が精神鑑定にも活用されることが期待されます。このように司法精神医学の事例は、精神医学における重要な研究課題を提起しているように思われます。また、これに限らず、人間を対象にした臨床研究の意義が日本の医学界において高く評価されるようになることを願っています。

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司法精神医学の人材育成等に関する研究

平成17年度　総括・分担研究報告書

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