Eur Arch Psychiatry Clin Neurosci (2007) 257:318–324 DOI 10.1007/s00406-007-0723-5

ORIGINAL PAPER

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Reduced planum temporale volume and delusional behaviour in patients with schizophrenia

Received: 6 July 2006 / Accepted: 16 January 2007 / Published online: 27 April 2007

Abstract The structural abnormality of planum temporale (PT), a part of the superior temporal heteromodal association cortex involved in auditory and language processing, has been implicated in the pathophysiology of schizophrenia. However, its relationship to clinical manifestations remains unclear. Magnetic resonance images were obtained from 17 right-handed Japanese men with schizophrenia and from 22 age-, handedness-, and parental socioeconomic-status-matched healthy Japanese men in order to manually evaluate grey matter volumes of Heschl's gyrus (HG) and PT. Psychiatric symptoms were assessed using positive and negative syndrome scale among the patients. Compared with healthy participants, patients with schizophrenia were associated with a statistically significant PT grey matter volume reduction without left or right lateralization, whereas HG volume was preserved. Smaller right PT volume was significantly correlated with more severe delusional behaviour in the patients. Previous investigations have focused on smaller-than-normal left PT in the pathophysiology of schizophrenia; however, the present results suggest a possible role of the right PT, which is involved in social cognition such as understanding the intentions of others, in the production of psychotic experiences in patients with schizophrenia.

Key words schizophrenia · MRI · planum temporale · superior temporal gyrus · delusion

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Introduction

In the past decade, accumulated evidence has suggested that schizophrenia is a brain disorder with frontal and temporal lobe abnormalities even at brain morphological level (reviewed in refs. [15, 21, 32]). Schizophrenia is also clinically characterized by psychotic experiences such as auditory hallucinations and delusions (reviewed in ref. [7]). Since these characteristic clinical manifestations might originate from brain pathology, the relationship between brain structural abnormality and psychotic experiences have been examined by numerous previous studies (e.g. [33]). However, previous literature is inconsis-

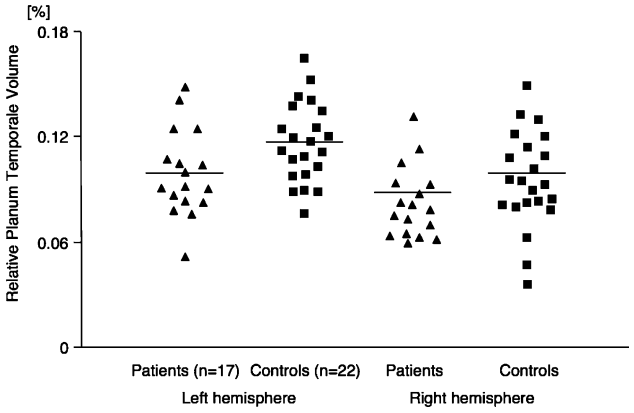

Fig. 1 Left and right volumes of the planum temporale for patients with schizophrenia (n = 17) and controls (n = 22). Horizontal lines indicate means

tent on the neuroanatomical correlates of psychotic experience.

The temporal lobe has long been a focus of interest with regard to the origins of positive symptoms (reviewed in ref. [26]. In previous studies, reduced grey matter volume of the superior temporal gyrus (STG) (e.g. [2, 12, 16, 27, 33, 40]) as well as that of Heschl's gyrus (HG) and planum temporale (PT) [4, 11, 17, 20, 27, 28, 34, 36, 42] have been consistently demonstrated in patients with schizophrenia. It has been also suggested that the volume reduction of these superior temporal structures was a specific feature of patients with schizophrenia, compared with patients with affective psychosis [11, 12, 16, 17].

The STG is further decomposed into the HG, which mainly contains primary auditory cortex, and the PT, which lies in the most posterior portion of STG and contains auditory association and Wernicke's language area in left hemisphere. Based on the prior knowledge of their contributions to auditory and language function in humans, HG and PT have been thought as candidates for the neural basis of language-related psychotic symptoms such as auditory hallucinations and thought disorder in patients with schizophrenia (Fig. 1).

Our previous study showed a significant association between left smaller PT volume and reduced phonetic mismatch strength in left hemisphere [40, 42]. Based on the finding, it was predicted that structural abnormalities of PT could underlie the functional abnormalities of fundamental language-related processing such as thought disorder in schizophrenia. In line with the hypothesis, Sumich et al. [35] employed "delusional behaviour", a composite score of delusions, grandiosity, suspiciousness and unusual thought disorder, to examine functional correlates of structural abnormality of PT in patients with first episode psychosis.

Several previous studies have also reported a relationship between positive symptoms and STG structural abnormalities (e.g. [2, 20, 23, 33]).

However, a comparable number of studies have reported no significant results regarding the symptom–structure correlation (e.g. [11, 30, 31]). The present study was thus designed to examine the following issues. First, it was expected that volume reduction of left PT would be replicated in Japanese men with schizophrenia. Since previous studies have reported sex dimorphism [14, 19, 39] and ethnic differences [37, 43] in brain structures, the current study population was limited to Japanese males. Second, the relationship between the positive symptoms and the volume of HG and PT was investigated.

Method

Participants

Demographic data of participants are shown in Table 1. Seventeen male right-handed in- and out patients with schizophrenia were recruited from the Department of Neuropsychiatry, the University of Tokyo Hospital, Japan. Handedness were determined using the Edinburgh Inventory [25]; a laterality index of >0.8 was the cut-off for right-handedness. Diagnosis of schizophrenia was determined for each patient according to DSM-IV [1] criteria through the Structured Clinical Interview for DSM-IV Axis I Disorder (SCID-I) Clinical Version [5]. Psychiatric symptoms were evaluated using the Positive and Negative Syndrome Scale (PANSS; [18]. The

Table 1 Demographic characteristics of study participants

	Patients with schizophrenia (n = 17)		Controls (n = 22)		t-test	
Variables	Mean	SD	Mean	SD	t-value	p
Age (range)	29.5	5.5	29.1	2.8	0.29	n.s.
Education (years)	13.1	1.9	17.0	1.0	8.46	<0.01
SES[a]	4.2	0.9	1.6	0.5	11.6	<0.001
Parental SES[a]	2.5	0.6	2.4	0.6	0.62	n.s.
Neuroleptic dose[b] (mg/day)	429.8	337.2	–	–		
Onset of illness (years)	20.6	4.8	–	–		
Duration of illness (years)	8.8	4.9	–	–		
Positive symptoms	13.8	5.7	–	–		
Negative symptoms	17.8	2.9	–	–		
General psychopathology	33.8	6	–	–		

[a] Socioeconomic status, assessed using the Hollingshead. Higher scores indicate lower status
[b] Based on chlorpromazine equivalents

interview for symptom evaluation and diagnosis was done by a trained psychiatrist (H.Y.) within three days prior to MRI scanning. The schizophrenia subtypes present in the sample were: catatonic (n = 2), paranoid (n = 3), undifferentiated (n = 1), and residual (n = 11). Twelve patients received typical neuroleptics only; 2 received risperidone only; 3 received both.

Twenty-two right-handed age-, gender and parental socioeconomic status (SES)-matched healthy participants were employed as controls. SES was assessed using the Hollingshead scale [13]. There were no significant differences between the patients with schizophrenia and controls in age and parental SES, although the patients had significantly fewer years of education and lower socioeconomic status than controls (Table 1).

No participants in the present study were included in our previous study employing a different MRI acquisition sequence to measure the grey matter volumes of HG and PT [42]. To test the validity of intracranial volume measurement using optimized voxel-based morphometry (VBM) compared with the intensity based semi-automated method employed in our previous study [40], the MRI images were obtained from a completely different sample of 50 adult participants (see Sect. "MRI processing" for details).

The exclusion criteria for both groups were neurological illness, traumatic brain injury with any known cognitive consequences or loss of consciousness for more than 5 min, a history of electroconvulsive therapy, and substance abuse or addiction. An additional exclusion criterion for the control group was a history of psychiatric disease in themselves or a family history of axis I disorder in their first-degree relatives. The ethical committee of the University of Tokyo Hospital approved this study. After a complete explanation of the study to the participants, written informed consent was obtained.

MRI acquisition

The methods of MRI acquisition were described in detail elsewhere [40, 41]. Briefly, MRI data were obtained on a 1.5-Tesla scanner (General Electric Signa Horizon Lx version 8.2, GE Medical Systems, Milwaukee, WI, USA). For manual measurement of brain structures, a three-dimensional (3D) spoiled gradient recalled acquisition with steady state (SPGR) sequence was used. Of note, this sequence affords better contrast between the grey matter and white matter than the fast-SPGR sequence in our earlier study evaluating grey matter volumes of HG and PT [42]. The repetition time was 35 ms, the echo time 7 ms with one repetition, the nutation angle 30°, the field of view 24 cm, and the matrix 256 × 256 (192) × 124. A trained neuroradiologist (Ha.Ya. or O.A.) evaluated the MRI scans and found no gross abnormalities in any participants. Magnetic field inhomogeneity in our scanner was monitored with daily basic quality control, and has been stable over the MR acquisition time for this study.

MRI processing

The HG and PT grey matter regions of interest (ROIs) were outlined manually using a software package for medical image analysis (3D Slicer; software available at http://www.slicer.org) without knowledge of diagnosis. The landmarks to delineate HG and PT grey matter were similar to those described in elsewhere [11, 17] and the same as that employed in our previous fast-SPGR study [42]. Briefly, HG was first identified in the axial plane, a demarcation that helped pinpoint the location of HG on coronal images. In most cases, HG represented a single transverse convolution. In cases where more than one transverse convolution was present, we followed the literature definition; when multiple convolutions originated medially from a common stem, all were defined as HG (the sulcus (i) between these convolutions represents the sulcus intermedius of Beck); when they originated separately from the retroinsular regions, only the most anterior gyrus was labeled as HG, and more posterior gyri were identified as PT. The posterior border of HG (Heschl's sulcus) defined the anterior border of PT. Posteriorly, PT grey matter was traced on coronal images to the end of the Sylvian fissure, and the grey matter of the ascending ramus of the Sylvian fissure was also included. Thus, our definition of the PT included PT proper and its parietal extension. Once drawn, both HG and PT ROIs could be viewed in any plane and as a 3-dimensional object, for any further editing.

For measuring intracranial content (ICC), total grey matter, white matter, and cerebrospinal fluid, volumes were calculated from the optimized-VBM procedure [8]. Then ICC was calculated by summing up total grey matter, white matter, and cerebrospinal fluid volume. To validate this method, the ICCs of the pooled 50 participants were measured by both the optimized VBM and intensity-based semi-automated segmentation procedure using ANAYZE PC 3.0 [40]. The inter-method reliability was high (intraclass correlation coefficient = 0.96).

In most cases, HG represented a single transverse convolution (left: 88% of patients with schizophrenia, 91% of control participants; right: 88% of patients with schizophrenia, 77% of control participants). In the cases of more than one transverse convolution, we followed the definition used in the previous study [17]. The prevalence of double HG, multiple transverse gyri from a common stem arising separately, was not significantly different between groups (left HG: $[\chi^2] = 0.07$, $p = 0.78$; right HG: $[\chi^2] = 0.78$, $p = 0.38$).

For interrater reliability of the volumetric measurements, two raters (S.Y. and H.Y.), blind to group membership, independently traced ROIs. Ten cases were selected at random, and the raters traced ROIs on every slice. The intraclass correlation coefficient was 0. 97/0.91 for left/right HG grey matter, 0.91/0.92 for left/right PT grey matter, respectively. Intrarater reliability, computed using all of the slices from one randomly selected brain and measured by one rater (S.Y.) at two separate times (approximately 6 months apart), was >0.97 for all structures.

Statistical analysis

Group comparison

The relative volumes [(absolute ROI volume)/(ICC) × 100] were used as the dependent variable as is the standard method for MRI studies in schizophrenia (e.g. [3, 16, 17, 33]). We employed a repeated measure ANOVA with 1 between-subject factor (group: schizophrenia, controls) and 2 within-subject factors (hemisphere: left and right; region: HG and PT). Once a significant group-by-region or group-by-region-by-hemisphere interaction was found, follow-up analyses using repeated measures ANOVA separately for each region (HG or PT) were performed.

Correlational analysis

The association between the relative volume of ROI, which showed a significant group difference, and the severity of psychiatric symptoms was tested with Spearman's rank correlation in the patients group. In the correlation analysis, positive, negative and general psychopathology scores of PANSS were used. Delusional behaviour score was also used to investigate the relationship between unreality symptoms and the volumetric variables. Delusional behaviour was scored as the sum of P1 (delusions), P5 (grandiosity), P6 (suspiciousness) and G9 (unusual thought content), based on Sumich et al. [35]. Since our approach was hypothesis-driven, a statistically significant level was defined as $p < 0.05$ without Bonferroni correction.

Results

Volumes of ROIs

The absolute and relative volumes for HG and PT in the two groups were displayed in Table 2. The repeated-measures ANOVA of relative volumes did not

Table 2 Volumetric measures

Variables		Patient schizophrenia with (n = 17) Mean	Controls (n = 22) SD	Repeated measure ANOVA (follow-up analyses) Mean	SD	F	p
Absolute volume (ml)							
Intracranial contents		1680.4	142.2	1660.5	98.9		
HG	Left hemisphere	1.38	0.27	1.27	0.41		
	Right hemisphere	1.09	0.29	1.20	0.36		
PT	Left hemisphere	1.66	0.42	1.93	0.39		
	Right hemisphere	1.37	0.34	1.57	0.43		
Relative volume (%)							
HG	Left hemisphere	0.083	0.016	0.076	0.023	0.01	0.930
	Right hemisphere	0.064	0.016	0.072	0.019		
PT	Left hemisphere	0.099	0.025	0.116	0.023	6.50	0.015
	Right hemisphere	0.082	0.020	0.095	0.027		

HG: Heshl's gyrus, PT: Planum temporale

Table 3 Relationships between anatomical measures and psychotic symptoms

	Left PT		Right PT	
	Relative volume	Absolute volume	Relative volume	Absolute volume
Positive symptoms	0.19	0.30	−0.46**	−0.48**
Negative symptoms	0.14	0.12	0.20	0.17
General symptoms	−0.28	−0.34	−0.08	−0.21
Delusional behaviour	−0.02	0.08	−0.49*	−0.55*

* $p < 0.05$, ** $p < 10$
PT: Planum temporale

show a significant main effect of diagnosis (F [1, 37] = 3.11, p = 0.086); however, there was a significant group-by-region interaction (F [1, 37] = 4.56, p = 0.039). There was no group-by-hemisphere (F [1, 37] = 0.49, p = 0.49) or group-by-region-by-hemisphere interaction (F [1, 37] = 3.26, p = 0.079). Then we conducted follow-up analyses separately for HG and PT. For HG, there was no main effect of group (F [1, 37] = 0.01, p = 0.93). We found a group-by-hemisphere interaction for HG (F [1, 37] = 4.70, p = 0.037); however, this was not considered significant due to a lack of significant group-by-hemisphere or group-by-region-by-hemisphere interaction in the main analysis. For PT, there was a significant main effect of group (F [1, 37] = 6.50, p = 0.015), whereas there was no significant group-by-hemisphere interaction (F [1, 37] = 0.19, p = 0.67). These results suggest a total (left + right), that is, unlateralized, reduction of PT grey matter volume, and HG grey matter volume in patients with schizophrenia comparable with that of the control participants.

Correlational analyses

The results from the correlational analyses are summarized in Table 3. The relative volume of right PT showed a significant negative correlation with the score of delusional behaviour (R = −0.49, p = 0.047).

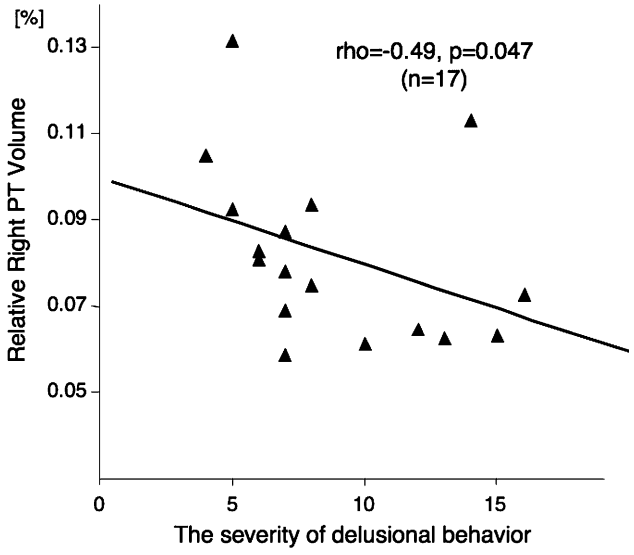

Fig. 2 Scatter plots depicting correlations between the right PT volume and the severity of delusional behaviour

Of note, the statistical conclusion remained the same when the absolute volume was used (R = −0.55, p = 0.023). The relative (R = −0.46, p = 0.061) and absolute (R = −0.48, p = 0.051) volumes of right PT were negatively correlated with the positive symptom severity, although the significance level of the correlations remained at the trend level. There were no significant correlations between the left PT volume and severity of psychiatric symptoms (Fig. 2).

Discussion

The present study identified a statistically significant PT grey matter volume reduction without left or right lateralization in male patients with schizophrenia compared with healthy controls. In contrast, HG volume did not differ significantly between the patient

group and the control group. Furthermore, the smaller right PT volume was associated with more severe delusional behaviour in the patients.

The observed pattern of reduced PT and preserved HG in our study is generally in line with those of previous studies examining chronic [20, 42] and first episode patients with schizophrenia [34], although two studies examining samples of first-episode schizophrenia [11, 17] have found reduced HG volume as well as the PT volume reduction. However, our findings of non-lateralized reduction of PT were in contrast to previous studies reporting left-lateralized PT volume reduction [11, 20, 42], which deserves further discussion. Although the etiology of brain lateralization remains unclear, gender [19], culture and/or ethnicity [22] have been implicated in the normal hemispheric lateralization. The normal sexual dimorphism of superior temporal cortices has been reported by previous studies [10, 14, 19]. Given that all participants in the present study were males, in contrast to our previous study [42], a possible interaction between gender and diagnosis might account for the discrepancy in findings related to laterality. In addition, the posited role of the STG in the right hemisphere in functions such as discourse comprehension, discourse production, understanding metaphors, and humour [24] may be related to differences in culture and language. Therefore, cultural and/or ethnic differences might affect the pathophysiology of right STG in patients with schizophrenia. However, the pure ethnicity as well as pure gender of the current study sample might contribute to the clarity of the current findings. In line with this notion, a recent study [36] reported bilateral PT volume reduction in Japanese patients with schizophrenia compared with healthy Japanese individuals, although they reported that volume reduction was greater in left PT than in right PT. Furthermore, the patients with schizophrenia in the present study consisted mainly of chronically treated patients. Although the volumes of STG structures did not show any significant correlation with duration of illness or neuroleptic dose, the findings in the present study cannot totally rule out the possibility of subtle morphological change associated with chronic illness [16, 17] and medication [9]. Taken together, ethnicity, gender, chronic illness course and their possible interactions might contribute to the discrepancy of findings related to laterality between previous studies and the present investigation.

In the present study, the smaller grey matter volume of right PT showed significant correlation with the more severe delusional behaviours within the patient group. Although previous findings have emphasized the importance of left, but not right PT in the pathophysiology of schizophrenia (e.g. [2, 20, 23]), the present results indicate that right hemisphere PT may play a role in the production of psychotic experiences in patients with schizophrenia. Recently, a possible role of the right STG in human social cognition has received attention, whereas the left STG is a well-known center for language function. In order to compete and survive in our highly organized society, it is important to have the ability to recognize and relate to other members of the community [29]. In other words, human survival has depended to a large extent on accurate social judgment. Winston et al. [38] found that right superior temporal cortex showed enhanced signal change during explicit trustworthiness judgments in a recent functional MRI study. Although speculative, impaired social cognition such as intention reading in schizophrenia is at least in part mediated through right STG abnormalities, which may underlie the basis for production of delusional symptoms.

Supporting this speculation, Mitchell and Crow [24] suggest an important role of the right STG in discourse comprehension, discourse production, and understanding metaphors, indirect requests, humour and emotional prosody and its abnormality in schizophrenia. In addition, there is further supportive evidence of a right hemisphere link with delusional misidentification syndromes [6].

Conclusion

In conclusion, the present study demonstrated a significant PT grey matter volume reduction without hemispheric lateralization in male patients with schizophrenia compared with matched healthy controls. The smaller right PT volume further showed a significant association with more severe delusional behaviour in the patient group. These results suggest an important role of right hemisphere PT, which is involved in social cognition such as intention reading, in the generation of delusional behaviours in patients with schizophrenia.

Acknowledgements This study was supported by grants-in-aid for scientific research (No. 18019009 and 18390319 to KK, No. 17-5234 to MAR) from the JSPS and the MEXT, and by grants-in-aid (H17-Kokoro-Ippan 009, H18-Shi 7, H17-Koh 2 to KK) from the Ministry of Health, Labor and Welfare, Japan.

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