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Original article

Structural alterations of the superior temporal gyrus in schizophrenia: Detailed subregional differences

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ABSTRACT

Background: Reduced gray matter volumes in the superior temporal gyrus (STG) have been reported in patients with schizophrenia. Such volumetric abnormalities might denote alterations in cortical thickness, surface area, local gyrification or all of these factors. The STG can be anatomically divided into five subregions using automatic parcellation in FreeSurfer: lateral aspect of the STG, anterior transverse temporal gyrus of Heschl gyrus (HG), planum polare (PP) of the STG, planum temporale (PT) of the STG and transverse temporal sulcus.
Methods: We acquired magnetic resonance imaging (MRI) 3T scans from 40 age- and sex-matched patients with schizophrenia and 40 healthy subjects, and the scans were automatically processed using FreeSurfer. General linear models were used to assess group differences in regional volumes and detailed thickness, surface area and local gyrification.
Results: As expected, patients with schizophrenia had significantly smaller bilateral STG volumes than healthy subjects. Of the five subregions in the STG, patients with schizophrenia showed significantly and marginally reduced volumes in the lateral aspect of the STG and PT of the STG bilaterally compared with healthy subjects. The volumetric alteration in bilateral lateral STG was derived from both the cortical thickness and surface area but not local gyrification. There was no significant laterality of the alteration in the lateral STG between patients and controls and no correlation among the structures and clinical characteristics.
Conclusions: These findings suggest that of five anatomical subregions in the STG, the lateral STG is one of the most meaningful regions for brain pathophysiology in schizophrenia.

1. Introduction

Schizophrenia is a common and complex psychiatric disease with cerebral alterations. Reduced brain volumes in multiple regions have been demonstrated by imaging studies using computed tomography (CT) and magnetic resonance imaging (MRI) in the last several decades [1,2]. Patients with schizophrenia show decreased whole brain volume, particularly gray matter (GM) volume, compared with healthy individuals. Although reduced regions in schizophrenia were inconsistent among imaging studies, meta-analyses have shown that patients with schizophrenia tend to exhibit a reduction in GM volume in the anterior cingulate, thalamus, frontal lobe, hippocampus, amygdale and superior and medial temporal gyri [3,4].

There has been an increasing body of literature supporting brain morphological alterations in the superior temporal gyrus (STG) in schizophrenia patients [4–10]. Patients with schizophrenia have smaller STG volumes compared with healthy subjects. Antipsychotic-naive individuals as well as individuals taking antipsychotics at ultra-high risk of psychosis also show significantly smaller STG volumes bilaterally compared with controls [11,12]. In addition, the volumetric reductions of the STG were more highly progressive in ultra-high risk individuals for psychosis as well as childhood onset and first-episode patients with schizophrenia compared with controls over time [9,10,13,14]. These previous studies have focused on brain volumes, but advances in neuroimaging data processing have made it possible to separate local gyrification (cortical folding patterns) as well as

Abbreviations: MRI, magnetic resonance imaging; ROI, region of interest; SE, standard error; STG, superior temporal gyrus; PT, planum temporale; HG, Heschl's gyrus; PP, planum polare.

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cortical thickness and surface area. To date, widespread reductions in cortical thickness, including in temporal regions, have been demonstrated in schizophrenia patients [15,16]. In addition, decreased cortical gyrification has been identified in schizophrenia patients compared with healthy individuals [17,18]. However, although a few studies have investigated the changes in the cortical area in schizophrenia patients [16,19], these findings were inconsistent among studies.

The STG is one of three gyri in the temporal lobe and is a long region located along the Sylvian fissure dorsally and superior temporal sulcus ventrally. The STG is divided into several regions both structurally and functionally [8]. The most anterior portion of the STG is the temporal polar cortex (Brodman's areas [BA] 38) [20]. The dorsal surface of the STG is located within the Sylvian fissure and is divided into Heschl's gyrus (HG), the planum polare (PP) and the planum temporale (PT) [21]. The STG contains several important structures of the brain, including the primary auditory cortex (BA 41/42) in the HG and the auditory association cortical areas (BA 22) in the anterior portion of the PT, which surrounds the HG [20,22]. Abnormalities in temporal lobe structures play a role in dysfunction of auditory and language processing, i.e., auditory hallucinations and thought disorders, in patients with schizophrenia [7,23,24]. Several researchers have tried to identify detailed regional differences of the STG in schizophrenia, and they found that patients with first-episode psychosis as well as schizophrenia and schizotypal patients had smaller volumes of the PT, HG or the posterior part of the STG compared to controls [5,9,13,25]. Kasai et al. found that patients with schizophrenia had a significant progressive decrease in STG, and this change was more prominent in the posterior portion of the STG compared with controls [6]. Furthermore, the long duration of untreated psychosis (DUP) was significantly associated with smaller GM volumes of the STG, particularly the PT, in schizophrenia patients [26,27].

The STG can be anatomically divided into five regions:

- lateral aspect of the STG;
- anterior transverse temporal gyrus (of HG);
- PP of the STG;
- PT of the STG;
- transverse temporal sulcus [28].

However, which regions contribute to the volume reduction of the STG in schizophrenia patients remains unclear. In addition, it is unclear whether these volumetric alterations occur due to differences in cortical thickness, surface area, local gyrification (cortical folding patterns) or all of the above factors. To the best of our knowledge, there have been no studies that identified brain structural alterations in cortical thickness, cortical area or local gyrification or that examined volumes in the specific subregions of the STG in schizophrenia patients.

In the current study, to extract five anatomical subregions of the STG, we used a standardized method [28] to measure the GM volume and detailed cortical thickness, surface area and local gyrification index (LGI) in three-dimensional (3D) surface reconstructions. We investigated the morphological differences, lateralization of the alterations and effects of clinical characteristics in the five subregions of the STG between patients with schizophrenia and healthy subjects.

2. Methods

2.1. Subjects

Subjects for this study consisted of 40 age- and sex-matched patients with schizophrenia (45.0% males, 18 males/22 females, mean age ± SD: 36.3 ± 9.8 years) and 40 healthy subjects (45.0% males, 18 males/22 females, mean age ± SD: 36.1 ± 9.9 years). All subjects were of Japanese descent. Patients were recruited from both outpatients and inpatients at Kanazawa Medical University Hospital. Each patient with schizophrenia had been diagnosed by at least two trained psychiatrists based on an unstructured clinical interview and medical recodes; diagnosis was made based on the criteria of the fifth edition of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-5). Healthy subjects were recruited through local advertisements or from hospital staffs at Kanazawa Medical University. Psychiatrically healthy subjects were evaluated using an unstructured interview to exclude individuals who had current or past contact with psychiatric services or had received psychiatric medication. Subjects were excluded from this analysis if they had neurological or medical conditions that could potentially affect the central nervous system, such as atypical headache, head trauma with loss of consciousness, chronic lung disease, kidney disease, chronic hepatic disease, cancer with active stage, cerebrovascular disease, epilepsy, seizures, substance-related disorders or mental retardation. Demographic information is shown in Table 1. In the patients with schizophrenia, 38 patients received antipsychotic medication (2 typical, 28 atypical, and 8 a combination of typical and atypical), while two patients received no antipsychotics at the time of investigation. The mean age and gender ratio did not differ significantly between patients and controls ($P > 0.05$), while years of education, estimated premorbid intelligence quotient (IQ) and total GM volumes were significantly lower in patients than controls ($P < 0.05$). Written informed consent was obtained from all subjects after the procedures had been fully explained. This study was performed according to the World Medical Association's Declaration of Helsinki and approved by the Research Ethical Committee of Kanazawa Medical University.

2.2. MRI

All subjects underwent brain MRI scans using a Siemens 3T Magnetom Trio a Tim System (Siemens, Erlangen, Germany).

Table 1
Demographic information for patients with schizophrenia and healthy controls included in this study.

Variables	Schizophrenia ($N = 40$)	Control ($N = 40$)	P-values (z)
Age (years)	36.3 ± 9.8	36.1 ± 9.9	0.76 (0.31)
Gender (male/female)	18/22	18/22	> 0.99 (< 0.01)[a]
Education (years)	12.7 ± 1.6	17.0 ± 1.8	< **0.001 (−7.04)**
Estimated premorbid IQ	100.1 ± 10.9	110.0 ± 6.1	< **0.001 (−4.10)**
Handedness (rt./lt./bil.)	36/1/3	38/1/1	0.59 (1.05)[a]
Gray matter volume (ml)	616.8 ± 644.2	635.5 ± 110.2	**0.023 (−2.28)**
CPZeq (mg/day)			
Total antipsychotics	447.3 ± 390.8	–	–
Typical antipsychotics	50.9 ± 111.1	–	–
Atypical antipsychotics	396.4 ± 345.8	–	–
Age at onset (years)	25.9 ± 6.7	–	–
Duration of illness (months)			
Total patients ($N = 40$)	124.9 ± 118.4	–	–
First-episode patients ($N = 8$)	8.0 ± 4.4	–	–
Chronic patients ($N = 32$)	154.1 ± 115.0	–	–
PANSS positive symptoms	14.4 ± 5.6	–	–
PANSS negative symptoms	16.7 ± 6.6	–	–
PANSS general psychopathology	31.0 ± 8.5	–	–

CPZeq: chlorpromazine equivalents of total antipsychotics; PANSS: Positive and Negative Syndrome Scale. First-episode patients were defined as patients with a duration of illness less than 12 months, while chronic patients were defined as patients with a duration of illness more than 12 months. The current symptoms of schizophrenia were evaluated using the PANSS. Means ± SD are shown. Complete demographic information was not obtained for all subjects (estimated premorbid IQ in patients, $N = 37$; in controls, $N = 38$).

[a] χ^2 test. Significant P-values are shown in boldface and underlined.