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Planum Temporale and Heschl Gyrus Volume Reduction in Schizophrenia:

A Magnetic Resonance Imaging Study of First-Episode Patients

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Abstract

Background—Magnetic resonance imaging studies in schizophrenia have revealed abnormalities in temporal lobe structures, including the superior temporal gyrus. More specifically, abnormalities have been reported in the posterior superior temporal gyrus, which includes the Heschl gyrus and planum temporale, the latter being an important substrate for language. However, the specificity of the Heschl gyrus and planum temporale structural abnormalities to schizophrenia vs affective psychosis, and the possible confounding roles of chronic morbidity and neuroleptic treatment, remain unclear.

Methods—Magnetic resonance images were acquired using a 1.5-T magnet from 20 first-episode (at first hospitalization) patients with schizophrenia (mean age, 27.3 years), 24 first-episode patients with manic psychosis (mean age, 23.6 years), and 22 controls (mean age, 24.5 years). There was no significant difference in age for the 3 groups. All brain images were uniformly aligned and then reformatted and resampled to yield isotropic voxels.

Results—Gray matter volume of the left planum temporale differed among the 3 groups. The patients with schizophrenia had significantly smaller left planum temporale volume than controls (20.0%) and patients with mania (20.0%). Heschl gyrus gray matter volume (left and right) was also reduced in patients with schizophrenia compared with controls (13.1%) and patients with bipolar mania (16.8%).

Conclusions—Compared with controls and patients with bipolar manic psychosis, patients with first-episode schizophrenia showed left planum temporale gray matter volume reduction and bilateral Heschl gyrus gray matter volume reduction. These findings are similar to those reported in patients with chronic schizophrenia and suggest that such abnormalities are present at first episode and are specific to schizophrenia.

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Structural brain abnormalities in schizophrenia have been extensively investigated using magnetic resonance imaging (MRI). Several studies have reported abnormalities in portions of the superior temporal gyrus (STG) in patients diagnosed as having schizophrenia, including planum temporale (PT) and Heschl gyrus (HG) (primary auditory cortex). The impetus for much of this work is based on the role that the left (dominant) hemisphere PT plays in language processing and the role that the HG plays in the initial processing of auditory information.

DeLisi et al measured length of the sylvian fissure and reported asymmetry differences in patients with first-episode schizophrenia compared with controls. Reduced cortical PT volume was reported in a postmortem study in schizophrenia compared with controls, and we reported reduced left PT gray matter volume and a reversal of PT asymmetry in patients diagnosed as having chronic schizophrenia. Other investigators measuring PT area in schizophrenia also reported a reversal of the left larger than right PT asymmetry found in controls. However, several investigators have not reported abnormalities of PT asymmetry in schizophrenia. Of particular note, Kleinschmidt and colleagues reported no differences in PT area between first-episode patients with schizophrenia and controls. This lack of consistency in results is likely due to variations in the definition of PT, as discussed by Barta and coworkers.

Fewer studies of HG have been conducted, although asymmetrical length has been reported in HG (left greater than right) in healthy patients in a postmortem study by Musiek and Reeves. Only one group using MRI has reported a left HG volume greater than the right in controls and patients with paranoid schizophrenia. However, other investigators have reported no asymmetry between left and right HG and no difference in asymmetry between patients with schizophrenia and controls. To our knowledge, no studies have evaluated gray matter volume of HG and PT concurrently in patients with schizophrenia and those with affective psychosis at the time of first hospitalization.

It remains uncertain whether the psychosis associated with affective disorder and schizophrenia represents manifestations of different disorders or variants of a single disorder with somewhat different expressions. The MRI studies that evaluate both patient groups may assist in answering this question. We previously reported that first-episode patients with schizophrenia showed smaller gray matter volume in a posterior segment of STG than first-episode patients with affective disorder and controls. The MRI evidence also supporting pathophysiological differences comes from Pearlson and colleagues, who reported STG and medial temporal lobe abnormalities in patients with schizophrenia but not in patients with bipolar disorder.

The posterior STG segment, reported previously by us, included only a fraction of the whole PT, and HG was not evaluated. In the present study, gray matter volume of PT and HG was measured to determine whether PT and HG abnormalities are present at first episode and specific to schizophrenia as contrasted with first-episode manic psychosis.

RESULTS

There were no significant group differences in age. First-episode patients with schizophrenia showed significantly lower SES than comparison subjects, consistent with reduced functioning (Table 1). Parental SES was upper middle class or above for all groups, but parental SES of the schizophrenia group was lower than parental SES of the other 2 comparison groups. There were no significant differences between patients diagnosed as having schizophrenia and patients diagnosed as having mania on any of the clinical scale measures, age of first medication use, medication dose, or duration of illness. There were significant differences between the
patient groups in 4 items of the BPRS. Patients with schizophrenia showed higher scores (mean ±SD) in suspiciousness (schizophrenia, 4.26±1.88; mania, 2.96±2.14; \( t_{42}=2.07; P = .04 \)), hallucinatory behavior (schizophrenia, 3.05±1.81; mania, 2.00±1.01; \( t_{42}=2.06; P = .046 \)), and blunted affect (schizophrenia, 3.11±1.76; mania, 1.70±1.40; \( t_{42}=2.84; P = .007 \)) than patients with mania. In contrast, patients with mania showed higher scores for grandiosity (schizophrenia, 1.42±1.01; mania, 3.83±1.02; \( t_{42}=3.32; P = .002 \)). Total score on the BPRS, age of first medication use, and duration of medication use did not correlate with any ROI volumes. There was also no significant difference in ICC volume among the 3 groups.

**VOLUME OF THE PT AND HG**

The 3-factor ANCOVA revealed a significant group-by-side-by-region interaction (\( F_{2,61} = 4.41, P = .02 \)). Follow-up ANCOVA revealed a significant group-by-side interaction (\( F_{2,61}=7.62, P = .001 \)) in PT. One-way ANCOVA showed that left PT differed among groups (\( F_{2,61}=4.76, P = .01 \)), with the schizophrenia group significantly smaller than the control and mania groups (Tukey Honestly Significant Difference, \( P < .05 \)) (Table 2 and Figure 2). However, right PT was not different among groups.

For HG, there was a significant main effect for group (\( F_{2,61}=4.67, P = .01 \)), with no group-by-side interaction (\( F_{2,61}=0.21, P = .98 \)). Post hoc tests revealed that total (left and right) HG gray matter volume was significantly smaller in schizophrenic patients compared with patients with mania and healthy control subjects (Tukey Honestly Significant Difference, \( P < .05 \)) but that group differences for left and right HG did not reach significance by 1-way ANCOVA (\( F_{2,61}=2.11, P = .13 \); \( F_{2,61}=2.49, P = .09 \), respectively) (Table 2 and Figure 2). However, HG was significantly asymmetrical in all subjects (\( F_{1,61}=4.19, P = .04 \)).

Note that, compared with controls and patients with mania, patients with schizophrenia show gray matter volume reductions of 20.0% in left PT (effect size=0.91). In addition, compared with controls, patients with schizophrenia show gray matter volume reductions of 15.3% in left HG (effect size=0.71) and 10.6% in right HG (effect size=0.44). For HG (left+right), patients with schizophrenia, compared with controls and patients with mania, showed 13.1% (effect size=0.87) and 16.8% (effect size=1.16) volume reduction, respectively.

**CORRELATIONS BETWEEN ROI VOLUMES AND PSYCHOPATHOLOGY**

In an exploratory analysis, no factors or items of the BPRS significantly correlated (\( P < .05 \)) with absolute or relative volumes of PT or HG in first-episode schizophrenia or in first-episode mania. In addition, none of the cognitive tests were statistically significantly correlated with HG and PT volumes in this study.

**COMMENT**

Left PT gray matter volume was significantly reduced in first-episode patients with schizophrenia compared with controls (20.0%) and first-episode patients with manic psychosis (20.0%). Bilateral HG gray matter volume was also reduced in patients with schizophrenia compared with controls and patients with mania.

The present data are consistent with our earlier findings of left-lateralized volume reduction in posterior STG gray matter in both chronic and first-episode schizophrenia\(^{23,33}\) and enlarges the finding, since the region studied previously was only partially coextensive with PT. These data are also consistent with left PT gray matter volume reduction (28.2%) in patients with chronic schizophrenia.\(^6\) The present findings suggest that lateralized PT reductions are not due to confounds of long-term medication use or disorder chronicity and that abnormal left PT and
bilateral HG gray matter volumes are present at time of first hospitalization and are specific to schizophrenia.

Musiek and Reeves\textsuperscript{20} reported an asymmetrical length of HG (left greater than right) in healthy subjects. However, findings have been inconsistent in MRI studies of schizophrenia.\textsuperscript{7,12,14} Rojas and coworkers,\textsuperscript{21} for example, reported a left HG volume greater than the right in controls and patients diagnosed as having paranoid schizophrenia. The present results indicate an asymmetry of HG in all groups but also suggest bilateral HG reduction in the schizophrenia group. This raises the interesting question of primary auditory sensory deficits in schizophrenia, a question not yet completely investigated. For example, Holcomb and coworkers\textsuperscript{39} have documented that patients with schizophrenia have more difficulty than controls in differentiating high and low tones presented against a background of noise, and these patients often also show deficits in mismatch negativity, an electrophysiological index of echoic memory processes.\textsuperscript{40,41}

In the present study, clinical measures and ROIs were not significantly correlated. In patients with chronic disease, left anterior STG volume reduction has been reported to correlate with auditory hallucinations,\textsuperscript{42} and left posterior STG volume reduction has been reported to correlate with severity of thought disorder.\textsuperscript{4,33} Moreover, our laboratory found the suspiciousness/persecution sub-scale score of the Positive and Negative Syndrome Scale was associated with reduced left PT volume in patients diagnosed as having chronic schizophrenia.\textsuperscript{6} Correlations between clinical measures and reduced volumes in patients with chronic schizophrenia have been reported by several investigators.\textsuperscript{36,43,44} However, few MRI studies of first-episode schizophrenia have reported an association between structural abnormalities and symptoms. We suggest that at the time of first hospitalization symptom-MRI correlations might be less than in chronic schizophrenia because of either a lack of stability in psychiatric symptoms or an absence of more marked structural alterations.

The specificity of MRI abnormalities to schizophrenic vs affective psychosis is a long-standing conundrum, as is the more general question of whether these psychoses are manifestations of a single disorder. Our previous report indicated that volume reduction in left posterior STG gray matter was specific to schizophrenia, although volume reduction of the posterior amygdala-hippocampal complex was not different between patients diagnosed as having first-episode schizophrenia and patients diagnosed as having first-episode bipolar mania. A recent report by Velakoulis et al\textsuperscript{47} also showed left hippocampal volume reduction in first-episode schizophrenia and schizophreniform psychosis compared with healthy subjects, but, once again, no differences were reported between first-episode schizophrenia and first-episode affective psychosis. These findings suggest that abnormalities in left STG gray matter, including PT and HG, are specific to schizophrenic psychosis, in contrast to abnormalities in medial temporal structures. Furthermore, Schlaepfer et al\textsuperscript{43} reported that patients with bipolar disorder did not show heteromodal cerebral cortex volume reduction, whereas gray matter volume was reduced in patients with schizophrenia. More specifically, asymmetry reversal was reported for posterior STG in patients diagnosed as having schizophrenia but not in patients diagnosed as having bipolar disorder.\textsuperscript{24} Zipursky et al\textsuperscript{48} similarly found global volume reduction in gray matter in first-episode psychotic patients but not in first-episode affective psychotic patients. Harvey et al\textsuperscript{49} also reported a decrease in cortical volume in patients with schizophrenia but not in patients with bipolar disorder. Since we have not investigated frontal or parietal cortex, 2 other areas possibly implicated in schizophrenic and affective pathology,\textsuperscript{1,2} conclusions drawn herein about specificity apply only to the regions we have studied.

There are several caveats to this study. First, the sex distribution of our sample did not allow us to investigate this variable. We anticipate doing so in the future. Second, a previous study by our group failed to show a significant volume difference in HG between patients with
chronic schizophrenia and controls.有一种可能的原因可能是不同的方法被使用。在之前的研究所中，MRI的校正未被进行，而在现在的研究中我们使用了新的校正后程序和新的方法来采样体素。当我们评估两种方法，即校正前和校正后（N=10；5名具有精神分裂症的患者和5名对照组），我们没有发现显著的体积差异在PT或HG在与精神分裂症患者或对照组相关的2种方法。我们也发现了两种方法在内类相关系数的不同。更有可能的解释是我们在这项研究中发现的HG和PT的差异，但仅仅在我们的前一项研究中只在PT中发现。第三，将首次发病期视为首次住院的时间而不是为 Prodigal 症状的开始可能高估了发病期，但提供了不可否认的测量。首次住院在文献中与首次发病期是同义的。我们也提供了首次服药时间，这可能有助于澄清临床图景，对于具有显著症状的患者。

综上，我们发现PT和HG在第一次发病的疾病中体积减少，这可能表明与听觉处理和语言相关的结构异常。最后，我们建议研究早期的疾病提供一个主要优势，在慢性变量中没有诱因，并且，此外，为长期研究评估MRI变化提供基线。

SUBJECTS AND METHODS

SUBJECTS

患者在McLean医院，一家私人精神病医院在Belmont，Mass。35名精神分裂症患者在第一次住院后的2周内被测试，8名在4个月内被测试，1名在11个月内被测试。患者和对照组符合年龄（18–55岁）、智商高于75，右利手，无癫痫史，头部创伤伴意识丧失，神经学疾病，无物质使用障碍的历史。控制组没有轴I心理障碍，也没有患第一度相关精神障碍的一级亲属（自我报告）。

患者被诊断为使用DSM-III-R（SCID），26 医院病历。研究组由20名具有精神分裂症的患者（16名男性，4名女性）和24名具有 bipolar 症状的患者组成（18名男性，6名女性）。所有患者都被诊断为精神分裂症。更具体地说，6名患者具有精神分裂症的hallucinations，paranoia，ideas of reference，and delusions；1名患者有hallucinations，delusions，and ideas of reference；2名患者有hallucinations，paranoia，ideas of reference；2名患者有hallucinations and delusions；2名患者有delusions and paranoia；2名患者有hallucinations and paranoia；2名患者有hallucinations and delusions；3名患者有only delusions。两位患者有mania，hallucinations，paranoia，ideas of reference，and delusions；5名患者有hallucinations，delusions，and ideas of reference；2名患者有delusions，paranoia，and delusions；1名患者有hallucinations and delusions；1名患者有hallucinations and ideas of reference；2名患者有delusions and paranoia；5名患者有delusions and ideas of reference；5名患者有only delusions；1名患者有only paranoia。诊断在1年随访时被证实。在MRI之前使用抗精神病药物的中位数是短的（表1）。此外，服药时间和用药量与MRI体积没有显著相关性。在操作意义上，我们选择第一次住院日期为首次精神疾病。尽管症状的发作可能是一个更可靠的疾病开始的指标，在实践中这个回顾性的测量是很难验证的。为了比较目的，我们提供了第一次服药时间，我们认为更客观（大多是从医院的）
records) and nonequivocal than prodrome onset and thus possibly a better estimate of symptom onset. A group of 22 control subjects (SCID nonpatient edition\textsuperscript{27} and SCID-II\textsuperscript{28}; 20 men, 2 women), group matched for age, was recruited through newspaper advertisements. The present study reflects an increase in sample size (N=64) over our previous study (N=46)\textsuperscript{23} and presents new, more detailed measures of posterior STG anatomy, partially but not completely coextensive with our previous measures of posterior STG.

The Mini-Mental State Examination was used to rule out dementia or delirium. In addition, the information sub-scale of the Wechsler Adult Intelligence Scale–Revised\textsuperscript{29} was used to estimate general information, and the digits-forward and -backward subscales of the Wechsler Adult Intelligence Scale–Revised were used to evaluate immediate and short-term memory, attention, and concentration. Socioeconomic status (SES) and parental SES\textsuperscript{30} were also assessed. Psychosis was further evaluated using the Brief Psychiatric Rating Scale (BPRS).\textsuperscript{31} Social functioning was evaluated using the Global Assessment Scale\textsuperscript{32} (Table 1). After a complete description of the study, written informed consent was obtained from all subjects. Subjects were paid for participating.

MRI ACQUISITION PROTOCOL AND MRI POSTPROCESSING

The MRIs were obtained on a 1.5-T scanner (General Electric Scanner; GE Medical Systems, Milwaukee, Wis). Details concerning pulse sequences are provided elsewhere.\textsuperscript{33–35} Briefly, there were 2 MRI protocols. The first was a coronal series of contiguous images (repetition time=35 milliseconds, echo time=5 milliseconds, 1 repetition, 45° nutation angle, 24-cm field of view, number of excitations = 1.0, matrix=256×256[192 phase encoding steps]×124). Voxel (volume of pixel) dimensions were 0.9375×0.9375×1.5 mm. Data were reformatted in the coronal plane and analyzed as 124 coronal 1.5-mm-thick slices. This protocol was used to measure PT and HG. The second was an axial series of contiguous double echo (proton density and T2-weighted) images (repetition time=3000 milliseconds, echo time=30 and 80 milliseconds, 24-cm field of view, an interleaved acquisition with 3-mm slice thickness). Voxel dimensions were 0.9375×0.9375×3 mm. This latter protocol was used to evaluate total intracranial volume. To reduce flow-related artifacts and to obtain low arterial signal intensity, presaturation of a slab inferior to the head was performed in both the axial and coronal acquisitions. A semiautomated segmentation procedure\textsuperscript{33} was used on the axial slices to measure total intracranial content (ICC), including overall gray matter, white matter, and cerebrospinal fluid. An anisotropic diffusion filter was applied to reduce noise before processing each set of scans.\textsuperscript{35}

REALIGNMENT AND RESAMPLING PROCESS

Following acquisition, MRIs were aligned using the inter-hemispheric fissure in the anterior two thirds of the brain in the coronal and axial planes. After this alignment in 2 planes, the midsagittal plane was aligned to correct head tilt using the line between the anterior and posterior commissures. Images were also resampled using an algorithm to make them isotropic, with sides measuring 0.9375 mm. Comparisons in 5 patients with schizophrenia and 5 healthy subjects showed that this process did not alter either measured region of interest (ROI) volumes or segmentation values for gray matter, white matter, or cerebrospinal fluid.

DEFINITION OF HG AND PT

The ROI definitions for both PT and HG have been described in detail by us in a recent study.\textsuperscript{9} In the present study, we used criteria similar to both our previous work and to the work of Barta et al\textsuperscript{19} for delineating HG and PT. We defined HG as the first transverse gyrus commencing from a point at the posterior margin of the insula next to the end of an opercular branch of the postcentral gyrus, then traversing anterolaterally to the superior
aspect of the temporal lobe and terminating at the lateral border of STG. If there was an initial single gyral origin of HG, and then bifurcation into branches, both branches were defined as HG.

Briefly summarized, our ROI definition procedure involved first using axial MRIs for manually outlining HG. The marked voxels defining the axial HG outlines, once reformatted, helped to accurately pinpoint the location of HG on the coronal images, with HG tracing proceeding from the most posterior coronal image with a mark to the most anterior. In between these bounds, we manually outlined HG gray matter. As the Heschl sulcus reached the lateral border of STG, we included only the edge of gray matter of HG superior to the level of the white matter, i.e., the roof of the white matter of STG was the inferior boundary of HG gray matter, and the most lateral extension of white matter formed the lateral bound of HG. Finally, sagittal MRIs were used to check and confirm HG boundaries.

The anterior border of PT was defined by the posterior border of HG. The lateral border of PT was defined as the superolateral margin of STG, with the gray matter underneath being manually outlined. Posteriorly, PT gray matter was traced to the end of the sylvian fissure, as seen on coronal images, and then gray 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. Both PT and HG ROIs could then be viewed as 3-dimensional objects for any further editing (Figure 1).

Interrater reliability was computed for the ROIs by 3 independent raters (Y.H., S.T., and D.S.) who were blind to group membership. Ten cases were randomly selected for interrater reliability. An intraclass correlation coefficient was used to compute interrater reliability based on the 3 raters: 0.882 (left HG), 0.881 (right HG), 0.985 (left PT), and 0.950 (right PT).

STATISTICAL ANALYSES

One-way analysis of variance was used to test for group differences in age, SES, and parental SES. In addition, t tests were used to assess group differences in clinical measures, age of first medication use, and medication dose and duration of use. Tests for group differences in ICC were conducted with a 1-way analysis of covariance (ANCOVA), with age and parental SES as covariates.

For ROI analysis we used a mixed-model ANCOVA, using relative volumes with 1 between-subjects factor (group: schizophrenia, mania, or controls) and 2 within-subjects factors (side: left and right; region: HG and PT). Age and parental SES were used as covariates for all ANCOVAs. Follow-up analyses included a 2-factor (group and side) ANCOVA for each region (HG and PT), 1-way ANCOVA, and post hoc Tukey Honestly Significant Difference tests for individual regions, with left and right compared separately. For the analyses used herein, we used relative volumes of ROI computed as [(absolute ROI volume)/ICC] × 100. Adjusting for brain size by linear regression of absolute volumes on ICC and using the residuals for comparisons did not change the results reported herein (see Zipursky et al36 and Dickey et al37 for examples of this procedure).

Exploratory analyses of the relationship between absolute volumes of PT and HG and the 4 syndrome factors of the BPRS,38 as well as for each BPRS item, were evaluated using Spearman rho.

Acknowledgments

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References


Figure 1.
A, Coronal slice (1.5 mm) through the temporal lobe of a healthy control subject. The regions of interest for the structures are outlined: the gray matter of Heschl gyrus (HG) is red on subject left and green on subject right. The gray matter of planum temporale (PT) is labeled yellow on subject left and blue on subject right. B, Top-down view of the 3-dimensional reconstruction of HG and PT placed on top of an axial magnetic resonance imaging slice. Anterior is top. The HG is red on subject left and green on subject right, and PT is blue on subject left and yellow on subject right. C, Three-dimensional reconstruction of the left and right regions of interest, color coded as in section B but from a slightly different angle of rotation from that in section B. Note the tubular structure of the gray matter of the superior temporal gyrus, most clearly seen anteriorly, where gray codes non-HG, non-PT portions of superior temporal gyrus. D, Three-dimensional reconstructions viewed from a different angle from that in section C (D1 is subject right and D2 is subject left).
Figure 2.
Relative volume of the Heschl gyrus and planum temporale in patients with first-episode schizophrenia, patients with first-episode mania, and healthy control subjects. Horizontal lines represent means.
Table 1

Subjects’ Characteristics and Test Scores

<table>
<thead>
<tr>
<th>Variable</th>
<th>Patients With Schizophrenia (n = 20)</th>
<th>Patients With Mania (n = 24)</th>
<th>Healthy Subjects (n = 22)</th>
<th>df</th>
<th>F or t Values</th>
<th>p†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean ± SD (range), y</td>
<td>27.3 ± 7.0 (18–41)</td>
<td>23.6 ± 5.0 (19–41)</td>
<td>24.5 ± 4.7 (18–35)</td>
<td>2, 63</td>
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<td>.08</td>
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<td>Male/female</td>
<td>16/4</td>
<td>18/6</td>
<td>20/2</td>
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<td>...</td>
<td>...</td>
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<td>Handedness, mean ± SD</td>
<td>0.7 ± 0.1</td>
<td>0.7 ± 0.2</td>
<td>0.8 ± 0.2</td>
<td>2, 63</td>
<td>0.84</td>
<td>.44</td>
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<td>SES, mean ± SD‡</td>
<td>3.3 ± 1.2‡</td>
<td>2.5 ± 1.1</td>
<td>1.9 ± 0.6</td>
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<td>9.30</td>
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<td>Parental SES, mean ± SD‡</td>
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<td>1.4 ± 0.7</td>
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<td>2, 63</td>
<td>4.57</td>
<td>.01</td>
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<td>MMSE score, mean ± SD</td>
<td>28.5 ± 2.7</td>
<td>28.7 ± 1.6</td>
<td>29.0 ± 1.2</td>
<td>2, 63</td>
<td>0.82</td>
<td>.44</td>
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<td>WAIS-R score, mean ± SD</td>
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<td></td>
<td></td>
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<td>Information</td>
<td>20.5 ± 6.3</td>
<td>20.5 ± 4.8</td>
<td>21.2 ± 3.1</td>
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<td>2.56</td>
<td>.08</td>
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<td>Digits-forward</td>
<td>8.4 ± 2.2</td>
<td>8.1 ± 1.7</td>
<td>9.5 ± 2.6</td>
<td>2, 63</td>
<td>3.16</td>
<td>.05</td>
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<td>Digits-backward</td>
<td>6.7 ± 2.7</td>
<td>6.3 ± 2.2</td>
<td>8.1 ± 2.8</td>
<td>2, 63</td>
<td>2.84</td>
<td>.07</td>
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<td>GAS score, mean ± SD</td>
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<td>35.1 ± 10.4</td>
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</tr>
<tr>
<td>Age first medicated, mean ± SD, y</td>
<td>27.3 ± 7.1</td>
<td>23.7 ± 5.4</td>
<td>...</td>
<td>43</td>
<td>1.78</td>
<td>.08</td>
</tr>
<tr>
<td>Median duration (range) of medication use, mo</td>
<td>1.7 (0–18.8)</td>
<td>0 (0–18.8)</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>Medication dose (CPZ equiv), mean ± SD</td>
<td>249.4 ± 203.4</td>
<td>198.5 ± 171.0</td>
<td>...</td>
<td>43</td>
<td>0.84</td>
<td>.41</td>
</tr>
<tr>
<td>BPRS score, mean ± SD</td>
<td>36.8 ± 9.6</td>
<td>36.2 ± 11.7</td>
<td>...</td>
<td>43</td>
<td>0.20</td>
<td>.84</td>
</tr>
</tbody>
</table>

*SES indicates socioeconomic status; MMSE, Mini-Mental State Examination; WAIS-R, Wechsler Adult Intelligence Scale–Revised; GAS, Global Assessment Scale; CPZ equiv, chlorpromazine equivalent; BPRS, Brief Psychiatric Rating Scale; and ellipses, data not applicable. Handedness was assessed by a modified Oldfield Inventory (Oldfield, 1971), right-handed being above 0.

†Statistical significance was determined by a 1-factor analysis of variance.

‡Higher scores indicate lower SES.

§Post hoc Tukey Honestly Significant Difference test showed significant difference (P<.05) compared with patients with mania and comparison subjects.
Table 2

Absolute and Relative Volumes of Regions of Interest of Heschl Gyrus and Planum Temporale*

<table>
<thead>
<tr>
<th>Region</th>
<th>Patients With Schizophrenia (n = 20)</th>
<th>Patients With Mania (n = 24)</th>
<th>Healthy Subjects (n = 22)</th>
<th>df</th>
<th>F</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total ICC</td>
<td>1512 ± 97</td>
<td>1454 ± 140</td>
<td>1546 ± 161</td>
<td>2, 61</td>
<td>2.63</td>
<td>.08</td>
</tr>
<tr>
<td>Left planum temporale</td>
<td>1.88 ± 0.39†</td>
<td>2.23 ± 0.55</td>
<td>2.40 ± 0.63</td>
<td>2, 60</td>
<td>4.20</td>
<td>.02</td>
</tr>
<tr>
<td></td>
<td>(0.09 ± 0.02)</td>
<td>(0.16 ± 0.04)</td>
<td>(0.16 ± 0.03)</td>
<td>2, 61</td>
<td>4.76</td>
<td>.01</td>
</tr>
<tr>
<td>Right planum temporale</td>
<td>2.01 ± 0.48</td>
<td>1.80 ± 0.46</td>
<td>1.88 ± 0.48</td>
<td>2, 60</td>
<td>1.21</td>
<td>.30</td>
</tr>
<tr>
<td></td>
<td>(0.13 ± 0.03)</td>
<td>(0.13 ± 0.04)</td>
<td>(0.12 ± 0.03)</td>
<td>2, 61</td>
<td>0.98</td>
<td>.38</td>
</tr>
<tr>
<td>Left Heschl gyrus</td>
<td>1.42 ± 0.28</td>
<td>1.68 ± 0.38</td>
<td>1.73 ± 0.46</td>
<td>2, 60</td>
<td>1.96</td>
<td>.15</td>
</tr>
<tr>
<td></td>
<td>(0.09 ± 0.02)</td>
<td>(0.12 ± 0.02)</td>
<td>(0.11 ± 0.02)</td>
<td>2, 61</td>
<td>2.11</td>
<td>.13</td>
</tr>
<tr>
<td>Right Heschl gyrus</td>
<td>1.28 ± 0.32</td>
<td>1.43 ± 0.29</td>
<td>1.44 ± 0.46</td>
<td>2, 60</td>
<td>2.07</td>
<td>.14</td>
</tr>
<tr>
<td></td>
<td>(0.08 ± 0.02)</td>
<td>(0.10 ± 0.02)</td>
<td>(0.09 ± 0.03)</td>
<td>2, 61</td>
<td>2.49</td>
<td>.09</td>
</tr>
</tbody>
</table>

*Data are given as mean ± SD. Statistical significance levels are based on 1-factor analysis of covariance (ANCOVA). The df of ANCOVA varies because there are 2 covariates for intracranial contents (ICC) (age and parental socioeconomic status) and 3 covariates for absolute volumes (ICC, age, and parental socioeconomic status). The text uses relative volumes for statistical significance measures, but absolute volumes are also presented here for comparison purposes.

†Post hoc Tukey Honestly Significant Difference tests indicated that patients with schizophrenia were significantly different from patients with mania and comparison subjects.