

Planum Temporale Asymmetry Reversal in Schizophrenia: Replication and Relationship to Gray Matter Abnormalities

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***Objective:** The planum temporale, the posterior superior surface of the superior temporal gyrus, is a highly lateralized brain structure involved with language. In schizophrenic patients the authors previously found consistent reversal of the normal left-larger-than-right asymmetry of planum temporale surface area. The original subjects plus new patients and comparison subjects participated in this effort to replicate and extend the prior study. **Method:** High-resolution magnetic resonance imaging of 28 schizophrenic patients and 32 group-matched normal subjects was performed. The authors measured planum temporale surface area, gray matter volume underlying the planum temporale, and gray matter thickness. Asymmetry indices for areas and volumes were calculated. **Results:** Overall gray matter and total brain volume were not significantly smaller in the patients than in the comparison subjects. As previously reported, there was striking reversal of the normal asymmetry for planum temporale surface area in the male and female schizophrenic subjects. Bilaterally, gray matter volume beneath the planum temporale was smaller in the schizophrenic patients, and the gray matter thickness of the right planum temporale was only 50% of the comparison value. Volume of planum temporale gray matter did not show significant asymmetry in either group. **Conclusions:** This study extends the finding of reversed planum temporale surface area asymmetry in schizophrenic patients and clarifies its relationship to underlying gray matter volume. Although right planum temporale surface area is larger than normal in schizophrenia, gray matter volume is less than the comparison value; thus, gray matter thickness is substantially less than normal. (Am J Psychiatry 1997; 154:661-667)*

Investigators studying the brains of schizophrenic patients have paid particular attention to limbic (mesial) temporal regions, following clinical observations of symptomatic schizophrenias (1). Neuropathologic examinations (2) and, later, magnetic resonance imaging (MRI) studies (3-5) showed temporal limbic abnormalities, including smaller than normal amygdala, hippocampus, entorhinal cortex, and parahippocampal gyrus.

More recently, investigators have also studied the lateral temporal neocortex, which to a large extent is ana-

tomically and functionally separate from mesial temporal structures. One neocortical region, the superior temporal gyrus, has been most often assessed, initially on the basis of physiologic observations (6). We (3) first noted low volume of the anterior superior temporal gyrus, associated with the severity of auditory hallucinations. Shenton et al. (4) reported low volume of the posterior superior temporal gyrus gray matter, associated with severity of thought disorder. Certain of these findings were later replicated (e.g., references 7 and 8), although not universally (9), and supported by related functional studies (10-12).

The planum temporale is a portion of the surface of the posterior superior temporal gyrus. It has interested schizophrenia researchers for several reasons. These include evidence of abnormalities of language (13), electrophysiology, and brain asymmetries (14-16) associated with schizophrenia. To our knowledge, there has been only one neuropathologic study of the planum temporale that compared schizophrenic patients and a normal comparison group (17). This assessed both surface areas and volumes, indicating reversed asymmetry

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TABLE 1. Descriptive and Demographic Data for 32 Normal Subjects and 28 Schizophrenic Patients^a

Characteristic	Normal Subjects		Schizophrenic Patients		Analysis		
	Mean	SD	Mean	SD	t	df	p
Age (years)	44.34	19.39	41.57	12.93	0.66	58	n.s.
Parental socioeconomic status ^b	2.18	0.91	2.83	0.83	2.48	58	<0.05
	N	%	N	%	χ^2	df	p
Female	9	28.1	7	25.0	0.08	1	n.s.
Black	9	28.1	14	50.0	3.02	1	n.s.
Right-handed	29	90.6	23	82.1	0.34	1	n.s.

^aCombined groups from previous study (19) and current study.

^bAccording to Hollingshead criteria (28).

of planum temporale *volume* in schizophrenia, mostly in men. A series of MRI studies of planum temporale *surface area* in schizophrenia provide conflicting results. As discussed previously (18, 19), these studies exhibit notable differences both in anatomical definitions for this complex structure and in the methods used to assess its surface area. Some investigators reported clear-cut reversals of asymmetry (19) or probable asymmetry disturbances (20–22), while others reported no differences between patients and normal comparison subjects (23, 24).

The current study had several purposes. First, we wished to extend our prior study of planum temporale surface area asymmetries (which involved a small number of closely matched subjects) and to replicate our prior finding in new subjects. Second, we wished to compare our finding regarding the *surface area* of the planum temporale to underlying abnormalities in *gray matter volume* and to relate these data to results of prior studies of thought disorder by Shenton et al. (4) and by us (7), as well as to results of other related investigations (17). Our conjecture was that we would replicate our previous finding regarding the relation between thought disorder and planum temporale asymmetry (19). We hypothesized that gray matter volume in patients would be especially low on the left side. Next, we wished to compare the asymmetry indices of the same area and gray matter volume measures to determine how these were related; here we had no prior hypothesis. Last, we wished to calculate gray matter *thicknesses* from surface area and volume to determine whether the asymmetry abnormalities in schizophrenia were related to thickness abnormalities.

METHOD

Subjects

We recruited 28 schizophrenic and 32 healthy comparison subjects, group matched for race and factors known to influence brain size or asymmetry—age, sex, handedness—but not for parental socioeconomic status. Fourteen of the schizophrenic patients and an equal

number of healthy comparison subjects had participated in our prior planum temporale study (19).

All of the schizophrenic patients were current inpatients or outpatients in the Johns Hopkins University Department of Psychiatry and met the DSM-III-R criteria for schizophrenia. Diagnostic reliability was maximized by using a consensus conference and contacting therapists regularly after study completion to detect possible diagnostic reclassification. Five patients were never treated; the remainder were taking standard neuroleptic drugs and in remission. We rated positive symptoms on the day of MRI scanning by using the Scale for the Assessment of Positive Symptoms (SAPS) (25); the raters exceeded an intraclass correlation of 0.90.

We recruited a healthy comparison group from hospital staff and the community by word of mouth or by advertisement. They had no personal or family psychiatric history as assessed by using DSM-III-R criteria. All of the subjects gave written informed consent after the study was described; the research was approved by the institutional review board. No subject had a history or MRI evidence of overt cerebral pathology, and none had a history of alcohol or substance abuse or of any medical illness known to affect the brain. No subject had a history or current evidence of dyslexia (which may be associated with variant planum temporale asymmetry) (26) or was selected for greater likelihood of aberrant asymmetry. Strong right-handedness as assessed by the Chapman scale (27) characterized 29 of the healthy comparison subjects and 23 of the schizophrenic subjects. Of the non-right-handers, all three normal comparison subjects were left-handed, while three of the five schizophrenic patients had mixed rather than left-hand dominance. Parental socioeconomic status was assessed by means of the Hollingshead criteria (28).

Mean group descriptive values are displayed in table 1. The two groups did not differ on age, sex, race, or handedness; the patients' parents had lower socioeconomic status.

Image Measures

We obtained MRI scans for all 60 subjects. High-resolution 1.5-mm thin coronal slices (N=124) were obtained by using spoiled-gradient recall acquisition in the steady state (GRASS) on a single 1.5-T General Electric Signa system (GE Medical Systems, Milwaukee, Wis.). The repetition time was 35 msec, the echo time was 5 msec with one repetition, the nutation angle was 45°, the field of view was 24 cm, and the matrix was 256 by 256. We acquired our images in the coronal plane, rather than the sagittal plane used by Steinmetz et al. in 1989 (29), because a coronal protocol yields more-distinct image slices through the planum temporale.

The locations of the anterior and posterior commissures and of several points within the interhemispheric fissure were recorded by using the software program MEASURE (30), developed in the Division of Psychiatric Neuro-Imaging at Johns Hopkins University School of Medicine. This program allows simultaneous viewing of a particular voxel in the coronal, sagittal, and axial planes. Precise boundaries and an account of the method's reliability are fully described elsewhere (18).

Surface measures. Briefly, surface areas of the planum temporale were calculated by forming a three-dimensional representation of the planum temporale's surface by tessellating the surface between serial slices with a series of triangles and summing the resulting triangle areas to obtain the planum temporale's area. It has been illustrated and described previously in detail (18, 19). The technique is highly reliable, with an interrater intraclass correlation of 0.98. An asymmetry index was calculated by using the formula (L–R)/0.5(L+R), where L and R are the planum temporale areas on the left and right sides, respectively. Similar indices were calculated for corresponding planum temporale volume measures.

Volume measures. Volume ratings of all regions (specified in the following) were made by a single rater (L.B.B.), blind to subject identity, from the same coronal spoiled-GRASS images. A three-dimensional volume-rendered reconstruction of the brain was made from these images by using MEASURE and a three-dimensional grid. Op-

timal grid sizes were determined as those yielding estimated coefficients of error of less than 5% for volume estimates from any plane. (The coefficients of error of these volume measurements were estimated by both Gundersen and Jensen's formula [31] and a refined version [32].)

The intraclass correlation coefficients for the intrarater reliability of all regions assessed varied between 0.99 and 0.92. The method is described in detail elsewhere (30).

The planum temporale has a variable gyral pattern that makes the delineation of its borders complex. The MEASURE software afforded the rater a view of the planum in three mutually orthogonal planes, which was helpful in identifying ambiguous areas, especially the anterior and posterior borders. This three-dimensional view was vital in establishing reliability. The transverse sulcus, recognized by its retroinsular origin, was used to define the planum temporale's anterior border. The posterior border was taken as the point of the upward angulation of the posterior ascending ramus of the sylvian fissure. The lateral border was defined as the lateral border of the supratemporal plane.

Heschl's gyrus was identified by its retroinsular origin, which was visualized best in reconstructed axial slices, especially in cases where secondary transverse sulci could be seen. The posterior border of the gyrus was defined by the transverse sulcus.

Cortical gray matter volume included the neocortical gray matter of the frontal, temporal, parietal, and occipital lobes.

Total brain volume included cortical (see the preceding) and subcortical gray matter plus white matter, cerebellum, ventricular CSF, and the brainstem superior to the foramen magnum.

Data Analysis

Gray matter thicknesses (in millimeters) were calculated by dividing volumes by corresponding surface areas. Analysis of variance (ANOVA), t tests, chi-square analysis with continuity correction, and Pearson correlations were used in the analyses. All tests of significance were carried out two-tailed.

RESULTS

Planum Temporale

Surface area. In all schizophrenic and normal comparison subjects we first examined planum temporale surface area asymmetry, as in our prior study (19). Using a factorial ANOVA, we analyzed the effect on the asymmetry index of diagnosis (normal versus schizophrenic), with sex, total brain volume, handedness, and study condition (prior versus new subjects) as covariates. We found a significant main effect of diagnosis ($F=54.43$, $df=1, 54$, $p<0.0001$); $\eta^2=0.53$, i.e., diagnosis accounted for more than 50% of the variance in planum temporale asymmetry. There was no effect of sex ($F=0.98$, $df=1, 54$, n.s.) and no interaction between sex and diagnosis ($F=0.30$, $df=1, 54$, n.s.). Handedness did not account for the asymmetry difference between diagnostic groups ($F=0.01$, $df=1, 54$, n.s.), and neither did brain volume ($F=0.62$, $df=1, 54$, n.s.). When study condition (prior versus new) was added to the model, the significance of the main effects was unchanged, and the effect of study membership was itself nonsignificant ($F=1.82$, $df=1, 52$, n.s.).

An analysis of the planum temporale surface areas was next carried out with just the new subjects (14 schizophrenic and 18 normal individuals). In the normal comparison subjects, the mean left and right

planum temporale surface area values were 901.47 mm^2 ($SD=379.47$) and 591.57 mm^2 ($SD=276.97$), respectively. For the schizophrenic subjects, the corresponding mean values were 770.87 mm^2 ($SD=177.54$) and 1000.82 mm^2 ($SD=310.86$). The schizophrenic patients had significantly larger planum temporale surface areas on the right ($t=3.93$, $df=30$, $p<0.0005$) and nonsignificantly smaller areas on the left ($t=1.19$, $df=30$, n.s.) than the normal subjects. The mean left-minus-right surface area values were 309.89 mm^2 ($SD=313.55$) for the normal comparison group and -229.95 mm^2 ($SD=319.50$) for the patients ($t=4.79$, $df=30$, $p<0.0001$). The mean planum temporale area asymmetry index was 0.44 mm^2 ($SD=0.39$) for the comparison group and -0.40 mm^2 ($SD=0.35$) for the patients ($t=5.03$, $df=30$, $p<0.0001$).

As shown in table 2 and figure 1, among the total group of subjects (28 patients, 32 normal subjects), the normal comparison group showed the expected finding of a larger planum temporale surface area on the left than on the right. As found previously, there was an opposite finding (right greater than left) for the schizophrenic subjects. Again, as seen in table 2, the planum temporale area asymmetry index for the schizophrenic group was reversed and its direction different from that for the normal subjects; the difference between groups was significant. The left planum temporale area of the schizophrenic subjects was significantly smaller than that of the comparison group, and the right area was significantly larger. ANOVAs covarying for either total brain volume or for same-side temporal lobe volume did not alter these findings. For the right planum temporale area, the F values ($df=1, 57$ in both cases) were 32.73 and 32.80, respectively ($p<0.0001$ in both cases). For the left planum temporale area, the F values ($df=1, 57$) were 4.34 and 5.54 ($p<0.05$).

There was no significant correlation between SAPS summary score for severity of formal thought disorder and area asymmetry measures ($r=0.14$, $df=26$).

Gray matter volume. We next considered planum temporale gray matter volume measures (see table 2 for these and subsequent measures). Although the patients had smaller values, particularly on the right side, these differences were not significant. ANOVAs covarying for either total brain volume or same-side temporal lobe volume did not alter the results. For right planum temporale gray matter volume, the F values ($df=1, 57$) were 1.34 and 1.10, respectively (n.s.). For left planum temporale gray matter volume, the F values ($df=1, 57$) were 0.01 and 0.19, respectively (n.s.). The correlations between planum temporale surface area and volume were 0.23 and 0.18 ($df=31$) for the left and right sides in the normal subjects, and the corresponding values for the patients were 0.27 and -0.19 ($df=27$); none was significant. Severity of thought disorder was related to left planum temporale gray matter volume ($r=-0.38$, $df=27$, $p<0.05$).

When gray matter volume asymmetry indices were calculated (table 2 and figure 2), the mean values for both diagnostic groups were close to zero, were positive

TABLE 2. Left and Right Surface Area and Gray Matter Measures for 32 Normal Subjects and 28 Schizophrenic Patients^a

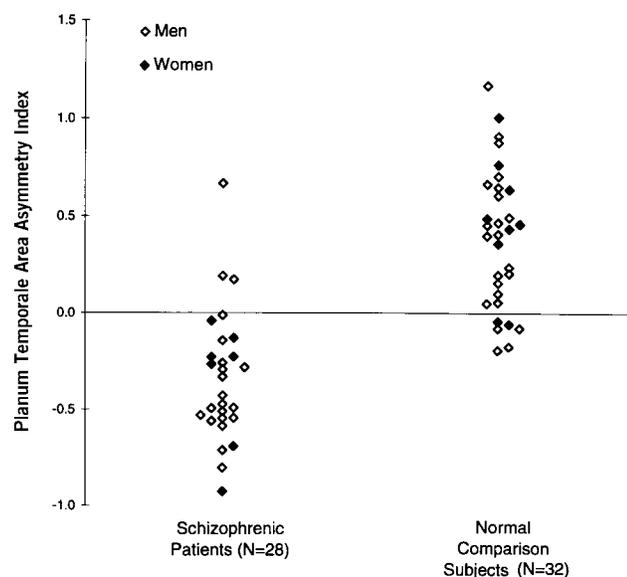
Measure	Normal Subjects		Schizophrenic Patients		Percent Difference	Analysis ^b		
	Mean	SD	Mean	SD		t (df=58)	p	
Planum temporale								
Area (mm ²)								
Left	870.81	302.71	713.40	210.63	-18.14	2.36	<0.05	
Right	602.32	247.96	1024.30	361.74	70.09	5.33	<0.0001	
Gray matter volume (cm ³)								
Left	2.97	1.54	2.82	1.52	-5.05	0.37	0.71	
Right	3.12	1.82	2.58	1.32	-17.31	1.34	0.19	
Gray matter thickness (mm)								
Left	1.78	0.85	2.10	1.09	18.0	1.26	0.21	
Right	2.92	0.97	1.46	0.94	-50.00	3.73	<0.001	
Asymmetry index ^c								
Area	0.39	0.36	-0.34	0.33	—	8.21	<0.0001	
Volume	0.03	0.71	0.06	0.59	—	0.17	0.86	
Heschl's gyrus								
Gray matter volume (cm ³)								
Left	4.16	1.62	3.98	1.89	-4.33	0.40	0.69	
Right	4.73	1.60	4.22	2.20	-10.78	1.01	0.32	
Volume asymmetry index ^c	-0.13	0.40	-0.05	0.60	—	0.59	0.56	
Total brain volume (cm ³)	1278.75	149.16	1227.67	186.64	-3.99	1.16	0.25	
Total gray matter volume (cm ³)	796.79	90.55	773.10	109.80	-2.97	0.90	0.37	

^aCombined groups from previous study (19) and current study.

^bSignificance values were calculated as two-tailed.

^cDefined as (L-R)/0.5(L+R), where L and R are the values on the left and right sides, respectively.

FIGURE 1. Laterality Indices for Left and Right Planum Temporale Surface Areas for Normal Subjects and Schizophrenic Patients^a



^aThe asymmetry index was defined as (L-R)/0.5(L+R), where L and R are the planum temporale surface areas on the left and right sides, respectively.

in both instances, and showed no significant between-group difference. They were also uncorrelated with the planum temporale surface area asymmetry indices ($r = -0.05$ and $r = 0.16$ for the patients [df=27] and normal comparison subjects [df=31], respectively).

Gray matter thickness. Values for planum temporale

gray matter thickness are shown in table 2. There was no difference between the patients and comparison subjects in left planum temporale gray matter thickness. The planum temporale gray matter thickness on the right side was 50% less in the schizophrenic patients than in the normal comparison subjects, a significant difference.

Heschl's Gyrus

Neither gray matter volumes nor their corresponding asymmetry indices differed significantly between the patients and the normal comparison group.

Total Brain

Total brain gray matter was 3% less in the patients than in the normal comparison group, a nonsignificant difference. Total brain volume was 4% less in the patients than in the normal comparison group; the difference was not significant.

DISCUSSION

The major result of the current study is replication of our original finding of reversal of planum temporale surface area asymmetry in schizophrenia (19) in an independent group of subjects, by means of our prior method. As previously, the asymmetry reversals were seen in schizophrenic patients of both sexes. Since ANOVA showed no effect of study condition, we collapsed the two groups (previous and new subjects) and were able to show reversed asymmetry in non-right-handed

patients and in a larger, group-matched (as opposed to individually matched) study group.

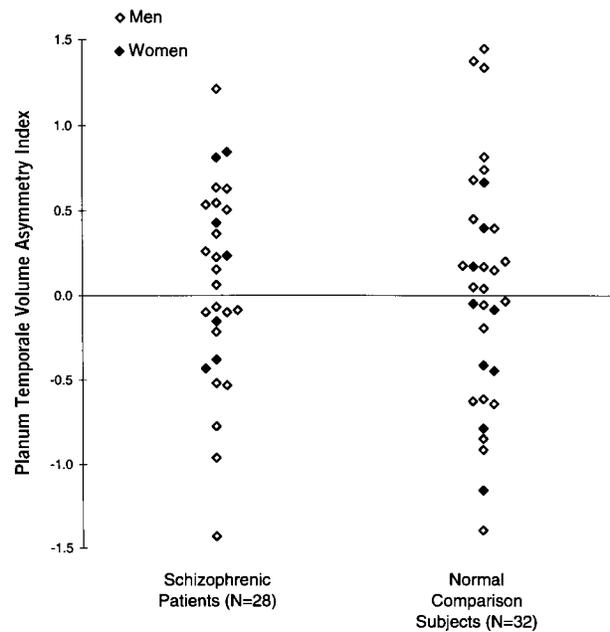
The planum temporale, part of the superior temporal gyrus, is a lateralized neocortical language region of possible relevance to two major symptoms of schizophrenia, auditory hallucinations (3, 8) and thought disorder (4, 7). Dipole modeling supports the location of a source generator for the normal P300 wave in the region of the planum temporale (33); this evoked potential is aberrant in schizophrenia. The planum temporale is normally an asymmetric structure (14), and Crow (15) and others (16) have emphasized the importance of disturbed asymmetries in schizophrenia. Finally, the planum temporale is one part of the heteromodal association neocortical network (34), which has been proposed to be especially affected in schizophrenia (35–37).

Our current result is consonant with other MRI findings suggesting differences in planum temporale surface area asymmetry between patients with schizophrenia and healthy comparison subjects (21, 22). However, two other groups found no such differences (23, 24) when using different MRI measurement methods. We have discussed what we believe may be difficulties with some aspects of these methods in another report (18).

The current study met the criteria for MRI investigations of the planum temporale suggested by Galaburda (38). We used a technique that in our hands demonstrates validity in showing the presence of the expected left-greater-than-right surface area asymmetry in dextral normal subjects (18). As we observed previously, the reversed asymmetry of planum temporale surface area in schizophrenia was characterized by a much larger planum temporale area on the right side and a somewhat smaller area on the left side in patients than in a matched healthy comparison group. The fact that gray matter volume is lower than normal, rather than higher, in the tissue underlying the larger surface area of the right planum temporale in schizophrenia implies a significant thinning of the cortex in this region. The left-side planum temporale thickness of the schizophrenic patients was slightly, but not significantly, greater than in the comparison subjects. Our estimate of cortical thickness of approximately 2 mm in the normal comparison group is consistent with previously published reports (39).

Smaller than normal volumes of the entire brain, cortical gray matter, and multiple brain regions have been reported in schizophrenia (2, 5, 40). Our current finding of general slightly, nonsignificantly lower than normal total brain and gray matter volumes is in agreement with our prior finding of local rather than global gray matter abnormalities in schizophrenia (36). We doubt that the lack of significance for total brain and gray matter volume is due to a low number of subjects. Given the values of *t* we obtained, even a group of several hundred subjects would fail to yield significant group differences. Parental socioeconomic status, age, sex, and race are commonly examined in brain studies to help control for possible effects on overall brain volume. Because no such volume differences were seen in

FIGURE 2. Laterality Indices for Left and Right Planum Temporale Gray Matter Volumes for Normal Subjects and Schizophrenic Patients^a



^aThe asymmetry index was defined as $(L-R)/0.5(L+R)$, where L and R are the planum temporale gray matter volumes on the left and right sides, respectively.

the current study, we feel it unlikely that the difference between the patients and comparison group in parental socioeconomic status could have contributed to our present planum temporale finding.

We previously stated that “a surface area measurement for a structure such as the planum temporale stands in an unknown and probably complicated relationship to other measurements (such as volume) that could be obtained from the cortical gray matter beneath this surface” (19). Our *surface area* measurements (which have dimensions of square millimeters) are incommensurate with *volume* measurements of the superior temporal gyrus gray matter, such as those of Shenton et al. (4) or Menon et al. (7). The gray matter volumes of the planum temporale in the current study showed no tendency toward the asymmetry seen in normal subjects for planum temporale surface area (14, 18, 29). Surface area and volume measures were in fact uncorrelated on either side in either diagnostic group. This may conceivably be due to a restriction of range that obscured a true relationship. Alternatively, surface area, but not volume, may be related to convolutedness of the cortical surface. We were unable to explore this latter possibility in the current study.

The patients' gray matter volume of the left planum temporale showed the expected negative correlation with severity of thought disorder, in agreement with prior reports, including our own (4, 7). Measurements of planum temporale surface area asymmetry were unrelated to this variable, a finding that differs from that

in our previous study. The reason for this difference is unclear, but it may be related to the greater heterogeneity of the patients examined in the current study. In this study we did not compare any posterior superior temporal gyrus measure with clinical ratings of auditory hallucinations. Our prior investigations showed a relationship between severity of this symptom and anterior superior temporal gyrus volume (3), a brain measure not assessed in the present study.

A single prior postmortem study (17) showed left-greater-than-right asymmetry of planum temporale gray matter volume in a normal comparison group, which we did not find here. That study also showed reversed asymmetry of planum temporale gray matter volume in schizophrenia, which we did not demonstrate. This discrepancy may be due to inadvertent inclusion of part of the temporoparietal junction that ascends in the plane of the lateral sulcus, which is reported to minimize or obscure planum temporale area asymmetries (41).

There are two possible ways to account for the greater than normal right planum temporale area. In one case, a structure can be magnified by a linear factor α , without any accompanying shape change. The resulting magnified surface area would increase as α^2 and the volume would increase as α^3 . In the case of our own data, a simple shape change resulting from linear magnification of the right planum temporale could not be operating in schizophrenia, as the percentage-wise increment in gray matter volume is less than that seen for surface area. Rather, our findings are more consistent with greater than normal "rugosity," or surface folding, of the right planum temporale in schizophrenia.

Our study does not address the etiology of the disturbed asymmetry or cortical thinning. Given that the asymmetric pattern of the planum temporale is obvious by the 29th–31st week of gestation (42), our result is consistent with a disruption of normal fetal neurodevelopment, as also suggested by other evidence (2, 43, 44). Crow (15) and others (16) are proponents of the view that schizophrenia involves a marked developmental disturbance of normal brain asymmetries. We believe that the abnormalities that we have observed in schizophrenia may represent the end result of related processes: fetal neuronal migration and/or differentiation defects (2, 43) followed by abnormal neural pruning in adolescence (44). Their separate contributions could not be determined in the present investigation. Microscopy studies are one means of validating our data on gray matter volume. These and related functional investigations are discussed in another paper (45). Disruptions of pruning are also consistent with the view of Galaburda (26), who stated that "lack of elimination [of neurons] may be the common theme in symmetry and migration anomalies."

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