Reduced Left Angular Gyrus Volume in First-Episode Schizophrenia

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Objective: Research suggests that the normal left-greater-than-right angular gyrus volume asymmetry is reversed in chronic schizophrenia. The authors examined whether angular gyrus volume and asymmetry were abnormal in patients with first-episode schizophrenia.

Method: Magnetic resonance imaging scans were obtained from 14 inpatients at their first hospitalization for psychosis and 14 normal comparison subjects. Manual editing was undertaken to delineate postcentral, supramarginal, and angular gyrus gray matter volumes.

Results: Group comparisons revealed that the left angular gyrus gray matter volume in patients was 14.8% less than that of the normal subjects. None of the other regions measured showed significant group volume or asymmetry differences.

Conclusions: Patients with new-onset schizophrenia showed smaller left angular gyrus volumes than normal subjects, consistent with other studies showing parietal lobe volume abnormalities in schizophrenia. Angular gyrus pathology in first-episode patients suggests that the angular gyrus may be a neuroanatomical substrate for the expression of schizophrenia.

Repeated-measures analysis of variance (ANOVA) was performed with one between-group variable (diagnosis) and two within-group variables (side and region). Comparisons of regions used relative gray matter volumes (absolute volumes/intracranial volumes), and measures were converted to z scores to eliminate the effect of absolute volume differences across regions of interest. Overall ANOVA revealed a significant group-by-hemisphere-by-region interaction ($F=3.36$, $df=2, 52$, $p=0.04$), suggesting regional laterality differences between groups. Follow-up ANOVA showed a significant group-by-side interaction for the angular gyrus ($F=7.80$, $df=1, 26$, $p=0.01$) but not for the supramarginal gyrus ($F=1.14$, $df=1, 26$, $p=0.30$) or postcentral gyrus ($F=0.04$, $df=1, 26$, $p=0.86$).

Paired t tests were used to assess volume asymmetries. Table 1 shows absolute and relative regional gray matter volumes. In the left angular gyrus, both absolute ($t=2.50$, $df=26$, $p=0.02$) (16.8% less) and relative ($t=2.25$, $df=26$, $p=0.03$) (14.8% less) volumes were smaller in patients with schizophrenia than in comparison subjects. Groups did not differ in gray matter volumes of the right angular gyrus, whether absolute ($t=0.09$, $df=26$, $p=0.93$) or relative ($t=0.44$, $df=26$, $p=0.67$) volumes were compared. Differences in asymmetric angular gyrus volume were present whether intracranial volume was used as a covariate or not. Comparison subjects showed a nonsignificant leftward asymmetry in angular gyrus (paired $t=1.05$, $df=13$, $p=0.31$), but patients with schizophrenia showed a larger right-greater-than-left volume asymmetry (paired $t=3.53$, $df=13$, $p=0.004$).

Regional asymmetry coefficients ($\frac{[\text{left minus right}]}{[\text{left plus right}]}$) multiplied by 100) were similarly analyzed. ANOVA for asymmetry coefficients showed marginal regional differences in asymmetry ($F=3.11$, $df=2, 52$, $p=0.05$) and a region-by-group interaction ($F=4.61$, $df=2, 52$, $p=0.01$). Only the angular gyrus showed significant group differences ($t=2.46$, $df=26$, $p=0.02$). To assess whether this difference was related to other regional asymmetries, we examined Pearson correlations between asymmetry coefficients for the angular gyrus and planum temporale for 21 of 28 subjects from previous analyses. This correlation was significant when the groups were pooled ($r=0.49$, $N=21$, $p=0.02$).

We found no relation between patients’ angular gyrus volumes or asymmetry coefficients and their BPRS thought disturbance factor (paranoia, hallucinations, or delusions).

### Discussion

Patients experiencing their first hospitalization for schizophrenia showed a large rightward asymmetry in the angular gyrus, due to significantly reduced left angular gyrus gray matter volume. Parietal lobe gray matter abnormalities were specific to the angular gyrus. This finding is consistent with other reports of parietal lobe abnormalities in chronic schizophrenia (5, 6), including reversal of left-greater-than-right inferior parietal lobule asymmetry (6, 7), localized to the angular gyrus (8). The present study extends earlier studies in chronic schizophrenia to patients experiencing their first episode of psychosis, where findings are not the result of chronic illness or factors related to long-term treatment.

It remains unclear when and why these inferior parietal lobule abnormalities develop. Crow (9) hypothesized that genetic determinants of cortical asymmetry represent the primary prenatal abnormality in schizophrenia. Altered angular gyrus asymmetry, as noted here, is consistent with this etiology. An alternative hypothesis is that polymodal...
association cortices, particularly left posterior perisylvian language areas, which include the angular gyrus, undergo a process of degeneration in late adolescence at or near the time of first hospitalization for schizophrenia (15).

We also found correlations between asymmetry measures for the angular gyrus and planum temporale, part of the superior temporal gyrus. Superior temporal and angular gyri are part of the left-hemisphere language network. Previous work from our laboratory revealed that the planum temporale had reversed asymmetry at first hospitalization (13, 15). Together, these data suggest that both chronic and first-episode schizophrenia are characterized by abnormal asymmetry present in brain regions involved with semantic processing (the angular gyrus and planum temporale). Such abnormalities in the neural substrates for language and thinking are likely germane to the pathophysiology of schizophrenia (9). The precise nature of this relationship and its etiological basis remain the subject of future research.

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