Hippocampal and Superior Temporal Gyrus Volume in First-Episode Schizophrenia

The article by Velakoulis et al. reported the important finding of hippocampal volume reduction in first-episode schizophrenia and interpreted it as evidence in support of a neurodevelopmental model of this disorder. The authors stated that “no previous studies have examined the specificity of this finding to first-episode schizophrenia, compared with first-episode affective psychosis.” Probably because their article was in press (it was accepted for publication on October 2, 1998), Velakoulis and coworkers did not cite our report in the October 1998 issue of the American Journal of Psychiatry, which, to our knowledge, was the first published report of lack of specificity of hippocampal volume reduction in first-episode schizophrenia relative to first-episode affective psychosis. Our study used a spoiled gradient-recalled acquisition protocol, resulting in 124 contiguous 1.5-mm coronal slices, to evaluate the hippocampus in 17 patients with first-episode schizophrenic psychosis compared with 16 first-episode affective psychosis patients and 18 normal control subjects. The first-episode schizophrenic patients showed significant volume reduction in the left, but not right, hippocampus, compared with control subjects. Moreover, left hippocampal volume in first-episode affective patients did not differ statistically from first-episode schizophrenic patients or normal subjects. Additionally, in our study, both patients with first-episode schizophrenic and affective psychosis demonstrated left less than right asymmetry of hippocampal volume, while controls showed no such asymmetry. We think that the similarity between our findings and those reported by Velakoulis and colleagues reinforce each other in the conclusion that hippocampal volume abnormalities may not be specific to first-episode schizophrenia as compared with affective disorder.

Are there any brain regions that show volume reductions specific to schizophrenia, compared with first-episode affective disorder? Our study also evaluated gray matter volume of the superior temporal gyrus (STG), and found that the gray matter volume of the posterior portion of the left STG in first-episode schizophrenia was significantly less than in both first-episode affective disorder and in comparison subjects. Furthermore, patients with first-episode schizophrenia showed a reduced left rather than right asymmetry of this region compared with both first-episode affective psychosis patients and comparison subjects. This finding points to an apparent specificity of left STG volume reduction in first-episode schizophrenia. We think it would be both interesting and important for Velakoulis and colleagues to look at this region in their first-episode subject groups. We are in strong agreement with Velakoulis and coworkers about the importance of first-episode studies, and note that this group of subjects offers an ideal opportunity for longitudinal studies to clarify whether temporal lobe abnormalities are progressive over time.

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In reply

We thank Hirayasu and colleagues for their letter in response to our article on hippocampal volumes in patients with first-episode psychosis.1 We note that their first-episode study2 also examined patients with first-episode psychosis and included patients with schizophrenia/schizophreniform and affective psychosis. Few studies to date have examined the specificity of brain structural abnormalities to schizophrenia and no previous studies using high-resolution images have examined this issue.

The main findings from our study were that smaller left hippocampal volumes were found in both first-episode schizophrenia and first-episode affective psychosis, as well as in patients with chronic schizophrenia. Hirayasu and colleagues found significantly smaller volumes of the left posterior amygdala-hippocampal complex in the first-episode schizophrenia group but not in their patients with affective psychosis compared with their normal control subjects, but the 2 patient groups did not differ. The mean volume found for the affective psychosis patients was intermediate between the controls and those with first-episode psychosis. In contrast, they found clearer evidence that smaller left superior temporal gyrus was specific to schizophrenia.

There is an important methodological difference between the 2 studies that may account for the differing results. Our study differentiated the hippocampus from the...
amygdala by using the alveus as an internal landmark, allowing reliable differentiation of the head of the hippocampus from the amygdala. Hirayasu et al measured the amygdala-hippocampal complex as one structure and then divided it into an anterior and posterior component based on the mammillary bodies as an external landmark. According to this method, the anterior end of the posterior amygdalo-hippocampal complex includes a significant portion of the amygdala, in addition to the head of the hippocampus, which would add a significant volume to the posterior amygdala-hippocampal complex. Smaller amygdalae in patients with first-episode schizophrenia (or normal size amygdalae in patients with first-episode affective disorder) might account for the differences between the 2 studies. To our knowledge, amygdala volumes in first-episode schizophrenia compared with first-episode affective psychosis have not been reported.

In their study, Hirayasu and colleagues used a small group of 18 control subjects to compare with their patients, while in our study we used a large group of 140 normal controls. Using a large control group provided detailed information about the range of normal hippocampal volumes in a healthy population, while this may not be possible with a small comparison group as in the study by Hirayasu and colleagues. Comparison of the large normal range of hippocampal volumes to those of the patients shows that the percentage of patients who fell below the mean total hippocampal volume for normal controls vs greater than 1 SD below the normal control mean was: chronic schizophrenia, 93% vs 45%; first-episode schizophrenia, 78% vs 38%; and patients and first-episode affective psychosis, 70% vs 50%. The results cited in our article show that patients with affective psychosis differ significantly from normal control subjects, suggesting that smaller hippocampal volumes are not specific to schizophrenia.

The clearest results from the study by Hirayasu and colleagues suggest that smaller volume of the superior temporal gyrus is specific to schizophrenia while the results from our study indicate that smaller hippocampi are apparent in both schizophrenic and affective psychoses. Future studies need to recruit larger numbers of neuroleptic-naive patients and compare them with large and representative cohorts of normal subjects. We agree that the next phase of research needs to examine the progression of medial temporal changes. Our group has commenced longitudinal imaging in first-episode patients, as well as in a cohort of high-risk individuals scanned before illness and immediately after the onset of psychosis.

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