Correspondence

EDITED BY LOUISE HOWARD

Volume of parahippocampal gyrus and hippocampus in schizophrenia

Sir: Razi *et al* (1999) report a reduction in the volume of the parahippocampal gyrus and the hippocampus in patients with chronic schizophrenia. They also show an interaction with gender such that only females with chronic illness have smaller hippocampi. However, there are a number of problems with their study that should be addressed.

First, the authors have overlooked important literature in this area. There have been recent studies that are relevant to their findings, including a meta-analysis (Nelson *et al*, 1998) and a large-scale review (Lawrie & Abukmeil, 1998). Both of these articles conclude that schizophrenia is associated with a bilateral volumetric reduction of the hippocampus and amygdala. The patient populations reviewed in these papers were predominantly male and chronically ill, which contrasts with the data reported by Razi *et al* (1999). Further, two recent articles support the findings of these reviews. In the study by Hirayasu *et al* (1998), smaller volume of left posterior amygdala–hippocampal complex was identified in patients with first-episode schizophrenia/schizophreniform psychosis. In our study (Velakoulis *et al*, 1999), using a reliable method to trace the hippocampus only, smaller left hippocampal volumes were found in patients with first-episode psychosis, as well as in patients with chronic schizophrenia, in comparison with a large group of 140 normal controls. We have recently found that these changes were specific to males with schizophrenia; females did not differ from normal controls.

Second, in the study by Razi *et al* (1999) there may be inadequate power to detect volumetric differences in the first-episode psychosis patients (there were only seven males and six females in their first-episode sample). Our study (Velakoulis *et al*, 1999) suggested there were reduced hippocampal volumes in first-episode psychosis regardless of a diagnosis of affective psychosis or schizophrenia/schizophreniform psychosis.

Third, methodologies are available to reliably segment the hippocampus from amygdala using manual tracing (Cook *et al*, 1992). The definition of hippocampus and amygdala by Razi *et al* (1999) relies on external landmarks that may be subject to artefact such as the orientation of the brain (there is no indication that realignment of brains occurred prior to tracing). Tracing the hippocampus and amygdala as a single structure unnecessarily confounds statistical analysis. In addition, the mechanism of obtaining whole-brain volume is suboptimal, since a volume measurement was obtained only on slices containing the regions of interest. No rationale was offered for this procedure, nor an assurance of its validity. Also, only intra-rater reliability measures are reported, and then not specifically for each structure.

Finally, Razi *et al* (1999) suggest that the hippocampal volume reduction may be an artefact of ventricular enlargement. The implication is that there may be compression of the hippocampus by an enlarged ventricle, which would imply raised cerebrospinal fluid pressure. To our knowledge, there is no evidence of ventricular obstruction or hydrocephalus in schizophrenia. Interestingly, Razi *et al* (1999) note that they could not perform measurements on the temporal horn owing to its small size.

In summary, there are a number of methodological issues that may explain the difference between this study and a large body of literature that has identified reduced hippocampal volumes in schizophrenia.

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Hirayasu, Y., Shenton, M. E., Salisbury, D. F., *et al* (1998) Lower left temporal lobe MRI volumes in patients with first-episode schizophrenia compared with psychotic patients with first-episode affective disorder and normal subjects. *American Journal of Psychiatry*, **155**, 1384–1391.

Lawrie, S. M. & Abukmeil, S. S. (1998) Brain abnormality in schizophrenia. A systematic and quantitative review of volumetric magnetic resonance imaging studies. *British Journal of Psychiatry*, **172**, 110–120.

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Author's reply: Dr Wood *et al* suggest that the significance of our results is limited by several problems. In our report (Razi *et al*, 1999) we presented data from precise measurements of the hippocampus and parahippocampal gyrus on thinly sliced magnetic resonance imaging (MRI) scans. These show reduced volumes of both structures in individuals with schizophrenia, but only in patients with chronic schizophrenia and not in those with a recent onset of illness. We interpreted this finding to be consistent with the growing evidence that the brain continues to change after the onset of illness along with the development of chronicity (DeLisi, 1997; DeLisi *et al*, 1997; Woods, 1998; DeLisi, 1999). We also speculated that the reports in the literature of reduced volumes of the hippocampus on MRI may be due to the masking of hippocampal boundaries by subtle enlargement of the temporal horns of the lateral ventricles, rather than loss of hippocampal volume itself (i.e. an artefact of magnetic resonance images, not hydrocephalus as Wood *et al* thought we were implying). The latter was based on our review of the literature (Table 1 in Razi *et al*, 1999) and that of Dwork (1997) showing inconsistencies between findings of reduced hippocampus on MRI and a failure to replicate this finding in the majority of post-mortem studies in which the actual boundaries of hippocampus can