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Pathogenesis of white matter lesions in Alzheimer's disease and depression

SIR: O'Brien *et al* (1996) highlight the associations between deep white matter lesions (DWML) and depression and between periventricular lucencies (PVL) and Alzheimer's disease. Although the contribution of vascular risk factors to these associations was closely examined, the influence of cerebrovascular disease in the pathogenesis of both white matter lesions remains unclear. Firstly, it is striking that vascular risk factors were significantly more common in depressed subjects than in those with Alzheimer's disease. However, notwithstanding the fact that the association between DWML and depression still existed after controlling for these risk factors, it is possible that other vascular risk factors may not have been taken into account. Those subjects with depression who had a past history of transient ischaemic attacks do not appear to have been excluded from the sample; it is possible that such episodes may have contributed to the development of DWML. The role of 'silent' infarcts may also be important, given their association with radiological changes and disruption of frontal connections (Meyer *et al*, 1995). A role for DWML as a risk factor for depression is put forward; again, a vascular contribution may be important in view of 'pre-stroke depression' found to be a possible risk factor for completed stroke (Colantonio *et al*, 1992).

The authors found no evidence of an association between PVL (which they suggest may involve other pathophysiological mechanisms) and vascular risk factors. Using both linear and volumetric measures, Schmidt (1992) found PVL to be significantly more common in vascular dementia than probable Alzheimer's disease. Furthermore, such lesions have also been shown to predict later development of clinically apparent cerebrovascular disease (Lopez *et al*, 1992). Thus, the role of cerebrovascular disease in the development of PVL remains open to speculation.

Before a more definitive statement about the role of vascular risk factors in the pathogenesis of white matter lesions can be made, prospective clinicopathological studies (including the use of *in vivo* neuroimaging) are needed to allow a better understanding of the relative contributions of vascular and non-vascular factors to such lesions in depression and Alzheimer's disease.

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Drug induced psychosis

SIR: We agree with the main conclusion of Poole & Brabbins (1996) that the use of the term "drug induced psychosis" may cause misunderstanding and should be discontinued. We would nevertheless like to draw the readers' attention to what seems to be a misunderstanding of our research on cannabis and schizophrenia (Andréasson *et al*, 1987, 1989; Allebeck *et al*, 1993).

The aim of our studies was not to elucidate the concept of "drug induced psychosis", but to assess the role of cannabis as one of several risk factors for schizophrenia. Poole & Brabbins are incorrect in saying that we did not take account of confounding factors that might be related to the exposure (cannabis use) as well as the outcome (schizophrenia). A number of potential confounders were analysed first by stratified analysis and then in a logistic model. The relative risk of schizophrenia among cannabis users decreased in these analyses, indicating that some of the association could be explained by these factors. Even in the logistic model, simultaneously controlling for a number of background factors, the relative risk for schizophrenia was significantly increased among high consumers of cannabis as compared to non-users. Additional analyses (Andréasson *et al*, 1989) showed that cannabis use indeed preceded the onset of schizophrenic symptoms and that other indicators of mental disturbances, which could act as precursors of both