White matter lesions in depression and Alzheimer's disease

SIR: Rao (1996) comments that subjects who had transient ischaemic attacks "do not appear to have been excluded" from our magnetic resonance imaging (MRI) study (O'Brien *et al*, 1996), which showed an association between deep white matter lesions (DWML) and depression. There is nothing in our paper to suggest this. Indeed, subjects with a past history of stroke and transient ischaemic attacks were specifically excluded. We did find that subjects with depression had more vascular risk factors than controls or subjects with Alzheimer's disease. This is not surprising as an association between vascular disease and depression has long been recognised and has been confirmed by Baldwin & Tomenson (1995). However, we showed that even controlling for known vascular risk factors (either by excluding such subjects or by regression analysis), DWML were still significantly more common in depressed subjects, particularly those presenting with their first ever depression in late life. Interestingly, the latter finding has recently been replicated by Salloway *et al* (1996). However, as we state in our paper, this does not mean that these lesions do not represent vascular disease; it may be that depressed subjects are particularly liable to develop vascular changes in the brain, perhaps as a result of genetic susceptibility or some environmental factors.

Rao's suggestion that periventricular lesions (PVL) involve vascular mechanisms simply because they are found commonly in patients with vascular dementia is unduly simplistic. Such an association does not imply cause. Moreover, there has been some good work looking at the pathological basis of white matter lesions, which clearly demonstrates that mild-to-moderate PVL (at least in non-depressed subjects) have a pathogenesis that is quite distinct from that of DWML and is unlikely to be simply vascular in origin (e.g. Fazekes *et al*, 1993).

The recent demonstration that white matter lesions on MRI, hitherto felt to be fairly non-specific features, can be separated into different types, which show particular associations with specific psychiatric disorders, is an exciting development that may have importance in advancing our understanding of the pathophysiology of these illnesses. Attributing all such lesions to cerebrovascular disease is no longer tenable. We are pleased that Rao agrees with us that the way forward is for prospective clinico-pathological studies to further elucidate the clinical, structural and biochemical correlates of such lesions.

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J. T. O'BRIEN
D. AMES

Brighton Clinic
Newcastle General Hospital
Newcastle upon Tyne NE4 6BE

ECT with clozapine: efficacy and safety

SIR: Bloch *et al* (1996) question whether combined treatment with clozapine and ECT should be contraindicated, as a result of their experience with one patient who developed a prolonged seizure. A recent report (Bonator *et al*, 1996) describes four previously treatment-resistant patients who received clozapine and ECT in combination. Three of these patients responded well, and none suffered prolonged seizures, tachycardia or orthostatic hypotension. Although particular vigilance is clearly required with any unfamiliar treatment combination, it appears that clozapine and ECT can be safely given together, and can be effective where conventional treatment has failed.

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K. TREZISE

Kidderminster General Hospital
Bewdley Road
Kidderminster DY11 6RJ

Childhood autism in Japan

SIR: Honda *et al* (1996) reported, in a well-conducted study, the highest risk-estimate of childhood autism (in particular, prevalence of 21.1 per 10 000) of all studies that have hitherto been published. As the authors are concerned about the