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.

BALDWIN, R. C. & TOMENSON, B. (1995) Depression in later life. A comparison of symptoms and risk factors in early and late onset cases. *British Journal of Psychiatry*, **167**, 649–652.

FAZEKES, F., CLEIMERT, R., OFFENBACHER, H., *et al* (1993) Pathological correlates of incidental MRI white matter hyperintensities. *Neurology*, **43**, 1683–1689.

O'BRIEN, J. T., DESMOND, P., AMES, D., *et al* (1996) A magnetic resonance imaging study of white matter lesions in depression and Alzheimer's disease. *British Journal of Psychiatry*, **168**, 477–485.

RAO, R. (1996) Pathogenesis of white matter lesions in Alzheimer's disease and depression (letter). *British Journal of Psychiatry*, **169**, 114.

SALLOWAY, S., MALLOY, P., KOHN, R., *et al* (1996) MRI and neuropsychological differences in early- and late-life onset geriatric depression. *Neurology*, **46**, 1567–1574.

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.

BLOCH, Y., POLLACK, M. & MOR, I. (1996) Should the administration of ECT during clozapine therapy be contraindicated (letter)? *British Journal of Psychiatry*, **169**, 253–254.

BONATOR, R., SIROTA, P. & MEGGED, S. (1996) Neuroleptic-resistance schizophrenia treated with clozapine and ECT. *Convulsive Therapy*, **12**, 117–121.

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

https://doi.org/10.1192/bjp.169.5.671c Published online by Cambridge University Press

relatively small sample size they employed, I calculated the 95% confidence interval of their estimate of prevalence to see what happened if the similar studies were repeated in an independent setting (independent samples representing the population of the country) given the condition that the probability (prevalence) of developing the disease is assumed to be that obtained from the study of Honda *et al* and given the same sample size (9000). This turned out to be 11.6–30.6 per 10 000. Although this wide interval indicates some uncertainty in the estimate, the low limit still exceeds the level of 10 per 10 000.

The possibility may arise, however, that their prevalence result in an overestimate. The prevalence of childhood autism in Honda *et al*'s study could, in theory, be expected to be equivalent to their estimate of cumulative risk, if one assumed that children who moved out of that area with their parents over the five-year period were replaced by an influx of others at the same risk of developing the disorder. Instead, four children identified as having autism moved into the study area, whereas only one autistic girl moved out. The fact that there was attrition of 703 children in the 1988 birth cohort over the period studied, indicates a net outflow of that cohort from the area. As no information on the actual size of in- and outflow of the cohort is provided, it is impossible to estimate the risk, but it is probable that children at higher risk of autism were brought in by parents who might have understandably sought better care for their children afflicted with the condition. However, as the authors note, parents having an autistic child might have chosen to stay in the same area where it is easy to access special facilities and where well-organised education programmes are provided.

On the other hand, it is worth noting that all Japanese studies (six including that of Honda *et al*) but one, regardless of the size of denominators, have found a prevalence greater than 10 per 10 000. Some unique and societal factor may play a contributory role in better detection of the disorder. Despite the steady fall in the actual number of children in Japan, with a concomitant fall in the mean sibling number, the number of three-year-old children in nursery schools is increasing. This may reflect parents' anxiety about the development of communication skills in their children, particularly in urban areas. Even subtle problems in activities among peers could be readily brought to light in a society where children are compelled to start competitive racing at an increasingly earlier age and, furthermore, are culturally expected to assume a harmonious attitude as a member of group.

HONDA, H., SHIMIZU, Y., MISUMI, K., *et al* (1996) Cumulative incidence and prevalence of childhood autism in children in Japan. *British Journal of Psychiatry*, **169**, 228–235.

N. TAKEI

Institute of Psychiatry
London SE5 8AF, and
School of Health Sciences
University of Tokyo
Tokyo 113, Japan

Nefazodone-induced spontaneous ejaculation

SIR: The sexual side-effects of antidepressant drugs are frequent but under-recognised. They include decreased libido; impaired arousal/erection; delayed, absent, retrograde or painful ejaculation; and delayed or absent orgasm (Pollack *et al*, 1992). Nefazodone is considered to be superior to other antidepressant drugs by virtue of its relative lack of sexual side-effects (Feiger *et al*, 1996). We report a case of nefazodone-induced spontaneous ejaculation.

A 50-year-old man was referred with a first episode of major depression of six months' duration. He was sexually active, but the frequency of sexual intercourse and masturbation decreased from onset of the depression. He failed to respond to a series of antidepressants, including imipramine, sertroline, venlafaxine and lithium. He was then commenced on nefazodone 200 mg/day, and lithium was continued. At the next follow-up, three weeks later, he reported that he had stopped the nefazodone because of an embarrassing and distressing side-effect; he had spontaneous ejaculations on average seven times a day. These were preceded by an urge to pass urine and were not associated with sexual thoughts, erection or any pleasurable sensations. These ejaculations stopped within 24 hours of discontinuing nefazodone. He was not keen on a nefazodone challenge. He had no sexual side-effects with any other antidepressant drugs.

Since this patient did not have sexual side-effects on any other antidepressant, the unique pharmacological characteristics of nefazodone, i.e. serotonin reuptake inhibition and 5-HT_2 receptor blockade (Feiger *et al*, 1996), resulting in the facilitation of 5-HT_{1A} neurotransmission, were probably responsible for this side-effect. Selective 5-HT_{1A} receptor agonists markedly facilitate male rat sexual

https://doi.org/10.1192/bjp.169.5.671c Published online by Cambridge University Press