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Correspondence

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Epilepsy in adults with Down's syndrome

SIR: McVicker *et al* (*BJP*, April 1994, **164**, 528–532) have shown that late-onset seizures in people with down's syndrome are associated with dementia. The reported overall prevalence of 9.4% of seizure disorders in Down's syndrome is similar to that observed (10.2%) in the Leicester Down's syndrome cohort (Collacott, 1994) of 344 adults. The incidence of seizure disorders was 0.28 per 100 people per year in those aged less than 20 years. The incidence fell to a nadir of 0.09 in those aged 30–39 years, and then rose to maximum of 0.71 in those aged 50–59. Late-onset seizures were associated with clinical dementia. However, the use of the Adaptive Behaviour Scale demonstrated that seizures occurred when the dementing process was well advanced.

The similarity of the findings from two total population studies from different geographical areas of the UK is of considerable interest. Late-onset seizures in people with Down's syndrome indicate dementia unless proven otherwise.

COLLACOTT, R. A. (1994) Epilepsy, dementia and adaptive behaviour in Down's syndrome. *Journal of Intellectual Disability Research*, **37**, 153–160.

R. A. COLLACOTT
S-A. COOPER
Department of Psychiatry, University of Leicester

Pseudoautosomal linkage in schizophrenia

SIR: Crow *et al*'s account of the investigation of linkage between schizophrenia and sex chromosome pseudoautosomal markers (*BJP*, February 1994, **164**, 159–165) suffers from a flaw that the authors fail to mention: namely that the positive results can be attributed to the fact that their sample is biased towards an excess of same-sex male schizophrenic sibling pairs. Such a sample will produce spuriously positive lod and sibling pair linkage scores with markers near the pseudoautosomal boundary. Furthermore there are insufficient details about the analyses given in the paper to permit independent replication on further data sets.

The weakly positive lod scores reported are derived from a sample which has been used previously for the study of same-sex concordance (Crow *et al*, 1989) as well as linkage analysis (Collinge *et al*, 1991). We (Curtis & Gurling, 1990) drew attention to the excess of affected males in this sample of sibships. In reply, Crow *et al* (1990) conceded the correctness of our argument and in a reanalysis found that the evidence for increased sex concordance in affected schizophrenic pairs was much weaker than they had claimed. In the recent study, markers linked to sex are used and these will produce artefactual evidence in favour of linkage when there is an excess of affected sibling pairs who are concordant for sex. The fact that MIC2 is unlinked to schizophrenia in female meioses further supports the notion that the positive results reported with this marker are simply an artefact of the increased sex concordance.

The paper is also deficient because it gives no account of the penetrance functions or gene frequencies used for the linkage analyses. Nor do the authors clarify what they mean by "other major psychiatric disorders". The authors also fail to discuss the statistical interpretation of their findings. We are concerned that readers might gain the impression that the cited lod score of 2.44 provides noteworthy evidence of linkage: one would not normally regard a lod score of less than 3.00 as providing any worthwhile evidence for localisation of a disease locus. Multiple testing is carried out with three different markers and two transmission models. In addition, recombination fractions are allowed to vary independently for male and female meioses.

This means that it is likely for lod scores as high as 2.44 to occur entirely by chance, even without the effects of the sex-concordance bias. Lastly, we must