Child abuse and the clinical course of drug misuse

Charnaud & Griffiths (2000) in response to the finding of increased psychiatric symptoms in female drug users by Marsden *et al* (2000) postulate that this finding may be a sequela of earlier child abuse. It is interesting to note the high incidence of childhood sexual abuse found in their study population based in Cornwall. In a Dublin sample, the level of sexual abuse for both males and females was considerably lower (21%). However, the effects of abuse appeared to have a significant influence in subsequent clinical progression of substance misuse. Those patients with a history of sexual abuse in the past had a significantly younger mean age of first opiate use (16.7 years *v.* 19.1 years for those without a history of sexual abuse) (Browne *et al*, 1998). The duration of drug misuse was also considerably longer (mean 10.8 *v.* 8.4 years).

We would support the suggestion of Charnaud & Griffiths (2000) that the evaluation of previous history of sexual abuse can predict the best plan of treatment for these patients. We would suggest that the long-term clinical progression of sexually abused drug misusers is that of more rapid progression to intravenous drug misuse with all the prognostic features that this implies.

Charnaud, B. & Griffiths, V. (2000) Drug dependence and child abuse (letter). *British Journal of Psychiatry*, **177**, 84.

Marsden, J., Gossop, M., Stewart, D., *et al* (2000) Psychiatric symptoms among clients seeking treatment for drug dependence. Intake data from the National Treatment Outcome Research Study. *British Journal of Psychiatry*, **176**, 285–289.

Browne, R., Keating, S. & O'Connor, J. (1998) Sexual abuse in childhood and subsequent illicit drug abuse in adolescence and early adulthood. *Irish Journal of Psychological Medicine*, **15**, 123–126.

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Apolipoprotein E, Alzheimer's disease and Down's syndrome

We read with interest the article by Deb *et al* (2000) apparently demonstrating findings contrary to our own (Prasher *et al*, 1997). Overall, we agree with the findings by Deb *et al*, although clarification on several important points is required.

The principle reason why we did not find a statistically significant association (at the 5% significance level) between apolipoprotein E (ApoE) ε4 and Alzheimer's disease in adults with Down's syndrome was because at that time there was a much smaller sample size of adults with Down's syndrome and dementia available for meta-analysis (102 subjects previously included compared to 158 in Deb *et al*'s report). The three additional reports included in Deb *et al*'s meta-analysis are of significantly larger samples. However, even with this greater number of subjects available for meta-analysis the power remains at 76%. Given the proportions of ε4 in the groups with and without dementia in the Deb *et al* paper, for a power of 90%, a minimum of 224 adults with Down's syndrome and dementia are required to demonstrate statistical significance at the 5% level. Furthermore, the ε4 allele frequency in the different studies varies from 5.9% to 33.4% in subjects with dementia (Deb *et al*, 2000) and therefore future studies are still required if an association between ApoE ε4 genotype and Alzheimer's disease in adults with Down's syndrome is to be established.

Deb *et al* are incorrect to exclude the study by Wisniewski *et al* (1995) because "they diagnosed Alzheimer's disease on the basis of neuropathological findings alone". Wisniewski *et al* (1995) made a diagnosis of dementia (not Alzheimer's disease) by a clinical assessment alone "as judged by the physician following the patient". However, the inclusion of this study in the present meta-analysis makes little difference to the findings by Deb *et al* (2000) as only one person with an ε4 allele was present.

The increase in risk of developing dementia in adults with Down's syndrome (odds ratio 2.02) appears to be less than that in populations with no learning disability where it can be increased by as much as 30 times for people with two copies of the ε4 allele (Swartz *et al*, 1999). From the allele frequency given by Deb *et al* (2000) the diagnostic accuracy of ApoE ε4 for adults with Down's syndrome and dementia is of some clinical value. The sensitivity is 18% (95% CI 13.5–22%) and specificity 90% (95% CI 88–92%). The absence of an ε4 allele strongly suggests the absence of Alzheimer's disease. ApoE genotyping in the Down's syndrome population may possibly be used to screen for dementia.

We conclude, as previously (Prasher *et al*, 1997), that the presence of an ε4 allele is neither sufficient nor necessary to cause Alzheimer's disease but ApoE ε4 genotype does have a role to play in the presentation of Alzheimer's disease in adults with Down's syndrome. The effect is, however, 'overwhelmed' by the excessive amyloidosis due to the triplication of the amyloid precursor gene.

Deb, S., Braganza, J., Norton, N., *et al* (2000) *APOE* ε4 influences the manifestation of Alzheimer's disease in adults with Down's syndrome. *British Journal of Psychiatry*, **177**, 468–472.

Prasher, V. P., Chowdhury, T. A., Rowe, B. R., *et al* (1997) ApoE genotype and Alzheimer's disease in adults with Down's syndrome: meta-analysis. *American Journal on Mental Retardation*, **102**, 103–110.

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Authors' reply: We thank Drs Prasher & Haque for their interest in our paper and are pleased that they agree with our conclusions. It is quite obvious that the difference in findings in the meta-analysis between our study and Prasher *et al*'s study was due to the inclusion of data in our study that were not available at the time of Prasher *et al*'s study. According to our calculation, our meta-analysis has 92% power (95% CI 88–96%) at the 5% level. However, traditional power calculation is not applicable in this case because instead of simply adding allele frequencies among all studies, we have used the computerised version of the Woolf (1995) method of meta-analysis that takes account of each study individually. Also, because of the varied nature of studies included in the meta-analysis we did not feel it appropriate to calculate specificity and sensitivity in the traditional way.

It was not stated in Prasher *et al*'s (1997) paper which 31 patients (15 with and 16 without dementia) out of 40 patients with Down's syndrome, presented in Wisniewski *et al*'s (1995) study, were included in their meta-analysis. The age of death of patients reported in Wisniewski *et al*'s study ranged widely between 15 and 69 years. They mentioned at the bottom of their table that "The presence of dementia is defined as a deterioration of competence, as judged by the physician following the patient". No detail

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