

corrected 793.5 at risk. The morbid risk to siblings of male probands was thus 5.60%.

Among the siblings of female probands, 40 were affected out of an age-corrected total of 651 siblings, giving a morbid risk of 6.14%. Thus Rüdin found a slightly increased risk of dementia praecox in the relatives of women with dementia praecox, although his excess was in the order of 10% and considerably less striking than that reported in recent papers.

CASTLE, D. & MURRAY, R. M. (1991) The neurodevelopmental basis of sex differences in schizophrenia. *Psychological Medicine*, **21**, 565–575.

GOLDSTEIN, J. M., FARAONE, S. V., CHEN, N. J., *et al* (1990) Sex differences in the familial transmission of schizophrenia. *British Journal of Psychiatry*, **156**, 819–826.

PAUL CRICHTON
SHÓN LEWIS

*Department of Psychiatry
Charing Cross and Westminster Medical School
St Dunstan's Road
London W6 8RP*

Absence of prion protein mutation in bipolar manic-depressive patients

SIR: Creutzfeldt-Jakob disease (CJD) is a neurodegenerative disease once felt to be due to slow virus infection and now associated with an altered host protein encoded by the PRNP gene (Brown *et al*, 1991). Several genetic mutations in the gene coding for this protein have been found to be linked to the genetic form of CJD (Carlson *et al*, 1991). A high prevalence of CJD, including its familial form, occurs among Libyan Jews in Israel (Chapman & Korczyn, 1991). Recently a point mutation in codon 200 of the PrP gene (resulting in a change from glutamic acid coded by GAG to lysine coded by AAG) was described in some Libyan Jewish patients with familial CJD (Goldfarb *et al*, 1990).

We recently identified a large pedigree of Libyan Jews in Israel with a high prevalence of bipolar manic-depressive illness. Crow (1987) has speculated that psychosis with genetic transmission may involve incorporation of transmissible retroviruses into the human genome. Since CJD in its early stages has behavioural and emotional symptoms and particularly depression (Behar *et al*, 1969), we hypothesised that manic-depressive illness might involve a pleiotropic expression of the PrP gene mutation.

Blood samples were obtained by informed consent from two bipolar manic-depressive patients and one schizoaffective patient from different branches of the same large kindred of Libyan origin, and also from three unrelated bipolar manic-depressive patients of

non-Libyan origin. All six patients were euthymic on lithium therapy. The PRNP genes of these patients were examined for the existence of the codon 200 mutation by means of a polymerase chain reaction followed by restriction enzyme digestion as previously described (Goldfarb *et al*, 1990). Two patients known to be positive for the mutation as well as two negative controls were analysed at the same time. The three patients of Libyan origin and the three manic-depressive patients of other ethnic background were all negative for the PrP codon 200 mutation. The two positive controls were found to carry the mutation.

The complexity of molecular genetic pathophysiology unveiled in CJD presents new models for psychiatric research. As the border between viral and genetic illness is blurred it is possible to envisage disease processes that are similar in sporadic and familial forms of the same illness. While the particular mutation studied here was not present in our patients, further studies for possible mutant DNA sequences should be performed in sporadic and particularly in familial forms of psychosis.

BEHAR, M., SROKA, C., ELIAN, M., *et al* (1969) Creutzfeldt-Jakob disease and its relation to pre-senile dementia. *Harfuah*, **67**, 275–279.

BROWN, P., GOLDFARB, L. G. & GAJDUSEK, D. C. (1991) The new biology of spongiform encephalopathy: infectious amyloidoses with a genetic twist. *Lancet*, **337**, 1019–1022.

CARLSON, G. A., HSIAO, K., OESCH, B., *et al* (1991) Genetics of prion infections. *Trends in Genetics*, **7**, 61–65.

CHAPMAN, J. & KORCZYN, A. D. (1991) Genetic and environmental factors determining the development of Creutzfeldt-Jakob disease in Libyan Jews. *Neuroepidemiology*, **10**, 228–231.

CROW, T. J. (1987) Integrated viral genes as potential pathogens in the functional psychoses. *Journal of Psychiatric Research*, **21**, 479–485.

GOLDFARB, L. G., KORCZYN, A. D., BROWN, P., *et al* (1990) Mutation in codon 200 of scrapie amyloid precursor gene linked to Creutzfeldt-Jakob disease in Sephardic Jews of Libyan and non-Libyan origin. *Lancet*, **336**, 637–638.

AMOS D. KORCZYN
JOAB CHAPMAN

*Department of Neurology
Ichilor Hospital
6 Weizmann Street
Tel-Aviv 64239
Israel*

R. H. BELMAKER
HEDY SHIMON

*Ben Gurion University Medical School
Beer Sheva
Israel*

MIRON BARON

*New York State Psychiatric Institute
New York, USA*