ECT in hospital with a degree of improvement but administrative problems precluded further treatments." This experience was early in the course of treatment; the patient went on to lengthy hospitalisation and eventual resolution. It is difficult to envisage what administrative problems could have been so compelling as to preclude the further administration of a treatment which seemed useful. ECT is an effective treatment for NMS (Davis *et al*, 1991); is safely administered under the most complex conditions of systemic disease (Abrams, 1992); and is reported as life-saving in similar cases of NMS or malignant catatonia (Mann *et al*, 1990; Rummans & Bassingthwaighte, 1991).

Could the administrative problems that precluded the continued administration of such a life-saving treatment as ECT reflect a prejudice against the use of ECT or a lack of training and experience?

The authors also make much of the surprising outcome – the patient's state changed for the better after prolonged hypoxia, artificial intubation, and ventilation. Such 'surprising' changes in behaviour were commonplace when both insulin coma and leucotomy were accepted medical psychiatric treatments. The frequent appearance of behavioural improvement after prolonged insulin coma or induced severe seizure states after leucotomy led many to suggest that the beneficial effects of these treatments on behaviour was the consequence of prolonged organic mental syndromes. Such observations became the basis for hypotheses of the mode of action of these somatic treatments (APA, 1978). While the present experience does not justify a recall of these therapies, the common thread makes the change in this patient's behaviour more understandable.

ABRAMS, R. (1992) *Electroconvulsive Therapy*. New York: Oxford University Press.

AMERICAN PSYCHIATRIC ASSOCIATION (1978) *Electroconvulsive Therapy*. Task Force Report 14. Washington DC: American Psychiatric Association.

DAVIS, J. M., JANICAK, P. G., SAKKAS, P., *et al* (1991) Electroconvulsive therapy in the treatment of the neuroleptic malignant syndrome. *Convulsive Therapy*, **7**, 111–120.

MANN, S. C., CAROFF, S. N., BLEIER, H. R. *et al.* (1990) Electroconvulsive therapy of the lethal catatonia syndrome. *Convulsive Therapy*, **6**, 239–247.

RUMMANS, T. & BASSINGTHWAIGHTE, M. E. (1991) Severe medical and neurologic complications associated with near-lethal catatonia treated with electroconvulsive therapy. *Convulsive Therapy*, **7**, 121–124.

MAX FINK

Departments of Psychiatry and Neurology
SUNY at Stony Brook
Long Island, New York 11794–8101
USA

B37 repeats are normal in most schizophrenic patients

SIR: Two groups recently reported abnormal expansions of the CAG repeats in the brain transcript B37, in patients with dentatorubral-pallidoluysian atrophy (DRPLA). Normal chromosomes had 7–34 repeats while DRPLA was associated with 49–75 repeats (Koide *et al*, 1994; Nagafuchi *et al*, 1994). Both groups stressed the clinical heterogeneity of this condition and Koide *et al* (1994) reported two patients who had been diagnosed by psychiatrists as schizophrenics, who also had expansions of the B37 CAG repeats. These patients had 57 repeats, at the lower end of the abnormal range.

Schizophrenia is a disease in which genetic factors play a significant role. However, no linkage studies have been successfully replicated (Kendler & Diehl, 1993). The inheritance patterns of this disease show features compatible with variable penetrance and anticipation (reviewed by Ross *et al*, 1993). These features and the finding of B37 expansions in 'schizophrenic' individuals implicated B37 as a possible candidate gene for schizophrenia. We examined 55 unrelated schizophrenic patients from the USA, UK and Italy for abnormal expansions at this locus (Fig. 1). Unrelated families in which there were at least two siblings with schizophrenia were identified from three main sources: a USA national registry of families identified from treatment centres within a NY county catchment area (Suffolk county) and throughout the USA (40 families); a cohort of cases receiving clinical care at a district hospital in northwest London and its surrounding regions and other cases associated with the National Schizophrenia Fellowship (12 families); families recruited in a similar manner by

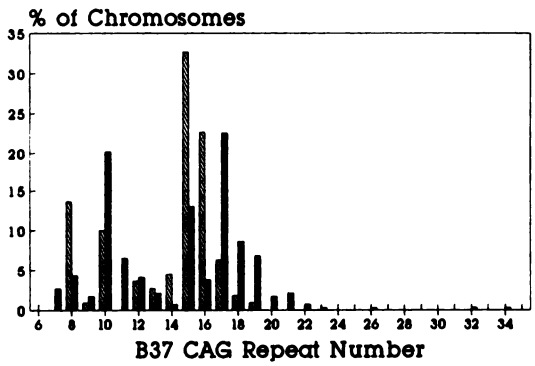

Fig. 1 B37 CAG repeat numbers in schizophrenic patients (hatched bars) (this study) and normal Japanese (solid bars) (data from Koide *et al*, 1994).

https://doi.org/10.1192/bjp.164.6.851 Published online by Cambridge University Press

psychiatrists from the University of Milan from surrounding northern Italian communities (3 families). All individuals were evaluated by a trained clinician. Subjects were interviewed using a modified SADS structured format (Schedule for Affective Disorders and Schizophrenia; Endicott & Spitzer 1978). Records from previous hospitalisations and of psychiatric treatments were obtained, and further information was collected on each individual from reliable family members. Diagnoses were made, based on information from these multiple sources, using DSM-III-R (American Psychiatric Association, 1987) criteria. None of these patients had any atypical movements. Ethical approval has been granted for the use of these samples for linkage analysis and for the investigation of candidate genes. The CAG repeats in the B37 genes from 55 affected probands were measured. Polymerase chain reactions were performed essentially as described by Koide *et al* (1994) except that 25 ng of each primer was used and 64°C was used as the annealing temperature.

These patients had between 8 and 19 repeats, clearly within the reported normal ranges (Koide *et al*, 1994; Nagafuchi *et al*, 1994), and had an observed heterozygosity of 73% that was significantly different to that observed in Japanese (88% ($\chi^2=6.502$, $P<0.025$); Koide *et al*, 1994). It is possible that some of the patients who appeared to be homozygotes for these B37 repeats were in fact heterozygotes with very large mutant alleles that were not successfully amplified by our PCR – however, we have been able to amplify 60 repeats at this locus and see the results after an overnight exposure of the autoradiograph. In addition, a nuclear family with two schizophrenic brothers was analysed separately for B37 expansions. Both brothers had severe abnormal choreiform movements of unknown aetiology and were thus candidates for DRPLA. However, they too had normal numbers of B37 repeats. Thus, we conclude that abnormal expansions in the B37 gene are not found in most schizophrenic patients.

We thank Drs N. Bass, G. Shields, A. Boccio-Smith, C. Morganti and A. Vita for helping with family evaluations. Funding for the clinical collections of families and preparation of DNA was provided by a NIMHR01-844245 in the USA and the Medical Research Council in the UK. We are also grateful to the Huntington's Disease Association (UK) for research funding.

ENDICOTT, J. & SPITZER, R. L. (1978) A diagnostic interview: the SADS. *Archives of General Psychiatry*, **35**, 837–853.

KENDLER, K. S. & DIEHL, S. R. (1993) The genetics of schizophrenia: a current, genetic-epidemiologic perspective. *Schizophrenia Bulletin*, **19**, 261–285.

KOIDE, R., IKEUCHI, T., ONODERA, O., *et al* (1994) Unstable expansion of CAG repeat in hereditary dentatorubral-pallidoluysian atrophy (DRPLA). *Nature Genetics*, **6**, 9–12.

NAGAFUCHI, S., YANAGISAWA, H., SATO, K., *et al* (1994) Dentatorubral and pallidolusian atrophy expansion of an unstable CAG trinucleotide on chromosome 12p. *Nature Genetics*, **6**, 14–18.

ROSS, C. A., MCINNIS, M. G., MARGOLIS, R. L., *et al* (1993) Genes with triplet repeats: candidate mediators of neuropsychiatric disorders. *Trends in Neurosciences*, **16**, 254–260.

D. C. RUBINSZTEIN
J. LEGGO
S. GOODBURN
D. E. BARTON
M. A. FERGUSON-SMITH
East Anglian Regional Genetics Service
Box 158, Addenbrooke's NHS Trust
Cambridge CB2 2QQ

C. A. ROSS
S. H. LI
Ross 618, Johns Hopkins University
720 Rutland Avenue
Baltimore
Maryland 21205-2196, USA

R. LOFTHOUSE
T. J. CROW
Clinical Research Center
Watford Road
Harrow

L. E. DELISI
Health Sciences Center
State University of New York at Stonybrook
New York 11794, USA

Fluvoxamine – prescription event monitoring

SIR: Edwards *et al* (*BJP*, March 1994, **164**, 387–395) provided valuable additional safety data for fluvoxamine in their prescription event monitoring (PEM) study.

Fluvoxamine has been available in the UK since 1987 and an estimated 6 million patients have been treated worldwide. Data from 10 401 patients in the PEM study gave a side-effect profile comparable with the Duphar clinical trials safety database of 24 624 patients (Wagner *et al*, 1992), recently updated to a total of 34 587 patients (unpublished). Gastrointestinal side-effects predominated in both data sets with only nausea/vomiting reported at an incidence greater than 10%, diminishing rapidly after the first month. No new adverse effects were identified and the incidence of seizures was shown to be no higher on than off treatment. This should provide considerable reassurance to prescribers.