There were no neuropsychological correlates of specific psychiatric symptoms in this study, and indeed this seems to be a common negative finding in schizophrenia research. While only 67% of schizophrenic subjects demonstrated impaired WCST performance, using cut-offs generated from this study, it is to be remembered that WCST performance is not the only measure of pre-frontal functioning. The pre-frontal cortex is a large area of the brain!

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Computerised tomography in schizophrenia

SIR: In the article entitled "Computerised tomography in schizophrenia, 15 years on" by Lewis (*Journal*, 1990, **157** (suppl. 9), 16–24) there is one statement that I feel is unnecessarily dogmatic and probably wrong. Lewis states that "the degree of ventricular enlargement is convincingly not a function of how long a patient has been ill". In a recent review of this issue (Miller, 1989) over 30 studies were considered which contained data on the statistical relationship between abnormalities of CT findings in schizophrenia and age, duration of illness, duration of hospital stay, or number of episodes. The majority of these studies found no relationship with duration of illness, but a few did show increased abnormalities in those patients who had been ill longer. The latter group of papers generally studied younger patients with shorter durations of illness.

Ventricular enlargement occurs to some extent with increasing age in normal persons, and this correlation might explain those cases where CT abnormalities in schizophrenia increase in magnitude with increasing duration of illness. However, in two studies, the appropriate statistical analyses were performed to show that duration of illness *does* have a correlation with degree of CT abnormality, independent of the age correlation.

More recent scanning studies have supported the suggestion that, at least in the first few years of a schizophrenic illness, there is a progressive increase in brain abnormalities. For instance, a one to four and a half year CT follow-up study by Woods *et al* (1990) showed progressive enlargement between the two scans. Of all follow-up scanning studies carried out to date, this study used the youngest, and probably the least chronic patients. DeLisi *et al* (1991) carried out a NMR study of very early-stage schizophrenic patients and found significant correlation between some measures of loss of brain substance and duration of illness. Thus, in contrast to the statement by Lewis, this issue is by no means settled.

In my own article, I suggested that there is progressive loss of brain substance during the manifest illness, which occurs mainly in the first few years of the illness, particularly when there are episodes of unchecked psychosis. This hypothesis could be of considerable significance, if correct. It may mean that, once a diagnosis has been made, very careful attention to antipsychotic medication to prevent, as far as possible, all further episodes of psychosis, can to some extent prevent progressive brain cell loss, and perhaps also the tendency towards progressive decline in mental function over the years of the illness.

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Tardive dyskinesia and HLA

SIR: I read with interest Brown & White's report (*Journal*, February 1991, **158**, 270–272) of their study on the possible association between tardive dyskinesia (TD) and the human leucocyte antigen (HLA), B44. However, I do not think that the methods and results reported either replicate or extend Canoso *et al*'s (1986) work, their stated aim, or support their conclusion that HLA B44 is not useful as a predictor of neuroleptic-induced TD.

Canoso *et al*'s 66 patients were all male, and no indication is given of their ethnic origin. Drs Brown & White included both male and female subjects, and although of a "similar ethnic origin", their exact ethnicity is not stated. It is very unlikely that 40 long-term patients of a Scottish psychiatric hospital could be reasonably compared with 66 patients at a Massachusetts Veterans Administration facility for something as ethnically dependent as HLA haplotype.

Unlike the Scottish sample, Canoso's patients did not all suffer from schizophrenia; 19 of the 66 had other diagnoses. Furthermore, Canoso used Research Diagnostic Criteria and not DSM–III (American Psychiatric Association, 1980) for diagnosis. The difficulty in comparing the two studies is further compounded by Canoso assessing only orofacial movements, and using a score of 14 on the Rockland scale to separate moderate/severe, from mild, TD; the Scottish group used the same scale without qualification of the score accepted as indicating the presence of TD, and included an assessment of all body areas. The use of an arbitrarily high or low score would inadvertently consign TD patients to the non-TD group, or vice versa, respectively, and thus cancel out any real differences in haplotype between the two.

Hence, on the basis of differences in ethnicity and gender, and the use of various diagnostic criteria for both psychiatric illness and TD, comparisons between the Scottish and American results are, at best, difficult.

Turning to the conclusions of Drs Brown & White; the sample is clearly not large enough to confirm or refute an association between HLA B44 and TD, such is the degree of polymorphism at the HLA locus. Again, the comparison of their group with 500 British subjects tissue-typed for other reasons, is not tenable, as no indication is given of the sex, age or ethnicity of the latter.

It is interesting to note that one other study (Metzer *et al*, 1990) failed to replicate Canoso's findings in 58 patients at an Arkansas Veterans Administration facility, but did find that possession of the DR4 antigen increased the relative risk for TD to 3.04, and that all patients with the extended haplotype B44–DR4 had neuroleptic-induced movement disorder. Drs Brown & White's suggestion of an association between schizophrenia and B44, although not supported by research to date, perhaps indicates that the extended B44–DR4 haplotype predisposes to both schizophrenia and TD, or that the latter is yet another symptom of the former as some authors suggest (Crow *et al*, 1983). The A1–B37 extended haplotype has already been implicated in increasing the relative risk for schizophrenia to 15.87 (Metzer *et al*, 1988).

Clearly, further research is needed to determine the evasive links that exist between schizophrenia, TD and HLA haplotype.

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Menopausal depression

SIR: Much of Dr Wheatley's letter (*Journal*, March 1991, **158**, 431–432) on menopausal depression is a criticism of the study by Montgomery *et al* (1987) in which I carried out the psychiatric assessments, and there are several misunderstandings in what he says.

His main concern is that the instrument used to detect emotional symptoms was not specific to depression and did not enquire about 'biological' and some other symptoms. This was because our interest was not confined to depression. We preferred to assess all neurotic symptoms because this patient group, like many other out-patient populations, does not fall conveniently into one diagnostic category. Menopausal women experience a mixture of neurotic and physical symptoms, but few biological features of depression, hence the use of the SRD–30 (Kellner & Sheffield, 1973), which had sub-scales for anxiety, depression and somatic complaints and which has frequently been used in studies of a similar kind. Despite this, Dr Wheatley believes that psychopharmacologists have not heard of the SRD–30. They may however, have heard of the Clinical Interview Schedule (Goldberg *et al*, 1970) which we used to validate the SRD–30 scores.

His letter also manages to miss out our main finding: that psychological disorders responded to HRT in peri-menopausal but not post-menopausal women. The implication is that a hormonally sensitive sub-group may exist – although this is not to say that HRT is the treatment they need – but post-menopausal women who are depressed should be treated like anyone else, i.e. pharmacologically and, equally important, psychologically.

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