While we applaud the approach taken, we find it difficult to interpret the reported results. We are wary of significance levels uncorrected for multiple comparisons, and of the use of controls screened to exclude those with cerebral abnormality as a comparison for scans without such screening. We are particularly concerned by the varying proportion of male and female subjects in the groups compared. Although the VBR measure attempts to correct for varying brain sizes by constructing a ratio of ventricular size to brain size, VBR varies positively as a function of brain size, which is in turn positively related to overall body size. Male subjects, generally larger than female subjects, have significantly larger VBR measures as well (Bridge *et al*, 1985).

An examination of the results of Dr Kaiya *et al* reveals that where differences in VBR are found between groups, there are also differences between the proportion of male subjects in these groups, with a larger proportion of males associated with larger VBR. The strength of this possible confound is indicated by calculating the correlation between the ratio of male to female subjects in a subgroup and the mean $VBR_l$ (lateral ventricles VBR) reported for that subgroup; here $r=0.994$, $P<0.005$ for the non-familial, familial (horizontal), familial (vertical), and familial (mix) subgroups, and remains high ($r=0.963$, $P<0.005$) after including the control subjects.

It is my hope that by controlling intersubject variability due to gross physical differences such as height, continuing investigation of subtle differences between subgroups of schizophrenic individuals will reveal robust cerebral morphometric differences useful in elucidating the pathophysiological bases of schizophrenic illness.

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SIR: We were interested to read the study by Kaiya *et al* (*Journal*, October 1989, **155**, 444–450). In common with similar studies, the use of high technology in psychiatric research seems to have excused the authors from sticking to the scientific conventions of a plausible, testable hypothesis which is adequately tested. Firstly, the hypothesis of three genetically distinguishable sub-groups in the aetiology of schizophrenia has little or no precedent to our knowledge, nor much in the way of rationale. Secondly, the hypothesis is not tested properly. The control group was not, as might be expected, healthy volunteers, but neurology patients. They were collected retrospectively, were not matched for age or sex, and most surprisingly were not psychiatrically assessed. In addition, there is nothing to indicate that the multivariate analysis was performed with the intention of making planned comparisons. Consequently, the suggested associations between the CT findings in schizophrenic sub-groups may well be accidental.

It is a pity that with such a topical subject the study failed to be rigorous enough.

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### Age of onset of depression in the elderly

SIR: The interesting papers by Musetti *et al* (*Journal*, September 1989, 330–336) and Burvill *et al* (*Journal*, November 1989, 673–679) concerning depression in later life and age of onset prompted me to examine, in the light of their findings, data from a previously described cohort of elderly patients with major depression (Baldwin & Jolley, 1986).

Details of whether the age of onset was before or after the age of 60 was available for all but two patients: 77 were late onset and 21 early onset. Late-onset patients were significantly older at the index admission than the early-onset group: 74.7 years compared with 71.5 years ($t$-test, $P<0.01$). Unlike Dr Burvill *et al* I did not find that early-onset patients were more depressed, although the cohort as a whole were more severely depressed than theirs (Hamilton Rating Scale for Depression (17 item) scores: late-onset 27.8, early-onset 27.2; NS). However, like them, I found no significant differences in family history of depression. Twenty-three percent of the late-onset group ($n=62$) and 21% ($n=19$) of the early-onset group had a positive history, although this data was missing on 17 patients. Likewise, there were no differences in the numbers dying or developing dementia during the follow-up period or in the overall outcome using the classification of Post (1972). Although adverse life events occurring in the previous 12 months were more common compared with the cohort of Dr Burvill *et al*, as in their study, the proportions did not differ significantly between the groups. Bereavement was the commonest event

in both early-onset and late-onset cases. Also, like Dr Burvill *et al* I found an excess of physical health problems, notably chronic, active disease, among the late-onset group, but similarly these differences were not statistically significant. Using a simple health rating (Baldwin & Jolley, 1986) the late-onset group scored a mean of 2.25 compared with 2.00 for the early-onset group (NS).

This data supports the findings of Dr Burvill *et al*. Their paper and that of Dr Musetti *et al* suggest that perhaps the adage "depression is depression at any age" is largely true. Although the findings of a positive family history of depression were in the expected direction, surprisingly high rates were found for the late onset groups – two-fifths in the study of Dr Burvill *et al* – thus challenging another conventional myth that a positive family history of depression is rare in depression arising in later life.

Does this mean that the search for specific aetiological factors in late-life depression is fruitless? I think not. The limited evidence we have suggests that aetiological differences between late- and early-onset depressions are subtle – see for example the pioneering work of Jacoby *et al* (1981) concerning biological factors. Unravelling aspects of biological, genetic, and life event factors in the genesis of depression in old age, not to mention the tantalising but neglected area of personality and temperament touched on by both sets of authors, will necessarily require studies involving much larger numbers of elderly patients than those to date – surely a strong argument in favour of collaborative research.

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## Who benefits from lithium?

SIR: Markar & Mander (*Journal*, October 1989, **155**, 496–500) report the outcomes of a selected group of bipolar patients on lithium as only marginally superior to those of a group not taking lithium, but as the subjects were not randomised the validity of the outcome comparison is dubious. The efficacy of lithium prophylaxis is well established, but clearly not all patients benefit from lithium (Priern *et al*, 1984) and certain characteristics are associated with a better response (Abou-Saleh & Coppen, 1986; Bouman *et al*, 1986). Until predictors of treatment response are more refined and reliable, practice should remain initially to treat all bipolar patients. The crucial question for the clinician is whether the course of an individual's illness is beneficially affected by the introduction of lithium, and this cannot be answered without detailed data collected longitudinally. Studying the outcome of a cohort of patients that will include good and poor responders will minimise a lithium effect and fail to address the problem facing the clinician, where the 'before and after' design has more relevance to the ordinary clinical situation.

A recent prescribing survey of lithium clinic attenders (Anderson, 1989) included 61 bipolar patients whose past records were available for study. Patients had a mean duration of illness of 21 years (13.5 years pre-lithium) requiring a mean of 7.6 admissions (5 pre-lithium) with a range of illness duration of up to 47 years, the maximum number of admissions being 33 over 28 years. When the whole group ($n=61$) was considered regarding relapse rate (relapses per unit time) there was no significant difference between the periods before and after the start of lithium treatment. However, this concealed a sub-group ($n=27$) who had no admissions following lithium prophylaxis yet were statistically indistinguishable from lithium relapsers in terms of duration of illness before lithium, relapse rate before lithium, and time on lithium (mean 7.1 years). This study design also tends to bias against a lithium effect (Hullin *et al*, 1972).

The problem facing the clinician is that of not having easy access to this sort of data that will allow the identification of poor responders who are not benefiting from long-term prophylaxis but whose psychiatric histories are buried in the depths of multiple case notes.

Lithium clinics and registers should create continuity of care, allow collation of the data necessary for informed clinical judgements about continued treatment, and provide valuable populations for research. Case notes and clinical memory cannot handle and organise the amount of longitudinal data needed to objectively evaluate treatment response in the normal clinical setting, and computerisation is essential to store, organise, and retrieve information used to chart progress and assist the clinician, researcher and auditor.

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