interaction between mental handicap and a double-blind design might have undertones is conceded in the statement, "The nature of the trial and the procedures involved were explained to each patient (at an appropriate level) and to a relative or responsible guardian". Just how much each participant actually understood is unknown, however, because of the lack of operational criteria showing that they understood, as distinct from being in receipt of an explanation. It appears that an opportunity to establish such criteria was lost; for example, each participant should be able to explain the procedure back to the researcher.

However, the more compelling scientific issues concern the other half of the "double-blind" design, the researchers. The outcome variable, levels of aggression, was assessed daily by the nursing staff on duty, who differed during the study; none of them were asked to guess the allocation of the patients. This would have been a prudent precaution given that, "The initial daily dose of 800 mg lithium carbonate was not sufficient, in most cases, to bring the serum lithium concentrate above 0.7 mmol/litre, and subsequently dosage adjustments were needed . . .". But we are not told that equivalent adjustments were made for the patients receiving placebo, so that one wonders what the nursing staff made of a group of patients who were having their medication adjusted and another group who were not having such adjustments.

Also, side-effects may have betrayed treatment allocation. Although the medical officer assessed each patient for the occurrence of possible side-effects of lithium treatment both before the trial and after one, two, three, six, nine, and twelve weeks, it is naive and unnecessary to suppose that these results, arising as they do out of interviews at specific points of time, generalised to what may have passed between the patients and the nurses who look after them 24 hours a day. It would have been easy to test the nurses themselves. Again, what was the mnesic ability of these patients? How reasonable was it to suppose that at an interview at a given point in time they would recall what had happened in between those points in time?

With this perspective, the authors' claim that blindness was maintained because classical side-effects were noted in 36% of the lithium patients and 20% of placebo patients is unwarranted, particularly as the exact means whereby the side-effects were detected remain apocryphal. Did the medical officer await spontaneous complaints? Did he or she ask a direct question, and if so what question? Was a check-list used?

Why were the measures of aggression made by different members of nursing staff? Given that they were, why was there not a reliability study of these staff? Given that there wasn't such a study, why were the results not analysed for individual nurses? The five-point scale whereby level of aggression was assessed is, on paper, no better than ordinal, the more so given that it may have been used in different ways by the different nursing staff; there was therefore good reason to suppose that the scale did not have interval qualities, and no evidence was presented to gainsay that, so how do the authors justify the use of parametric statistics?

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SIR: According to the Declaration of Helsinki, "In any research on human beings each potential subject must be adequately informed of the aims, methods, anticipated benefits and potential hazards of the study and the discomfort it may entail . . . . Where physical or mental incapacity makes it impossible to obtain informed consent . . . permission from a responsible relative replaces that of the subject in accordance with national legislation". Thus it is not necessary for a mentally handicapped patient to be able to understand a double-blind design in order to participate in such a trial.

Regarding blindness, in the method section of our paper we described how dummy results for serum lithium concentrations were provided for placebo patients. The medical officer responsible for each patient adjusted the dosage of trial medication accordingly, so that both he and the nursing staff remained unaware of whether the patient was being treated with lithium or placebo.

Records were kept by the nursing staff of the type, duration, and severity of side-effects, as and when they occurred, using a check-list of common lithium side-effects.

It cannot be possible in a hospital to have daily assessments carried out by the same person over a 16-week period. Before undertaking this trial we carried out a reliability study, using the same 5-point rating scale for aggression, to assess the correlation between scores given by different nurse assessors. Statistical analysis of the results showed that while the score of 2 (mood uncertain) was the least reliable, scores of 1 (well-behaved) and 3 or more (overt aggression) achieved satisfactory levels of correlation between separate assessors. For this reason the analysis of our trial results concentrated on these scores.

In our trial it seemed reasonable to use parametric methods for analysis of the scores obtained with the

5-point scale because the data being analysed were themselves summary statistics. However, due to the discrete nature of the data, and to the question of how different intervals on the fixed point scales related to each other, it would, alternatively, have been appropriate to adopt a non-parametric approach.

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Gilles de la Tourette's Syndrome in Down's Syndrome

SIR: We recently documented the occurrence and treatment of Gilles de la Tourette's syndrome (GTS) in an individual with Down's syndrome (*Journal*, May 1986, **148**, 601–604). Corbett (*Journal*, April 1987, **150**, 569) suggests that carbamazepine may have accounted for the late onset of GTS in this patient. However, as we indicated in the case report, the patient had been observed by nursing staff to have consistently displayed motor and phonic tics since the age of 11, when she was first institutionalised. We also mentioned that GTS had been diagnosed according to DSM–III criteria, which stipulate that age of onset must occur between 2 and 15 years. In contrast, carbamazepine had only first been used by this patient when she was aged 24, following the onset of a possible seizure disorder.

Corbett correctly points out that pharmacological compounds are increasingly being recognised as precipitants of tics. As indicated in the case report, although we attempted to correlate the presence and frequency of tics to the patient's previous use of medication we felt unable to do so accurately in view of the limited information available. However, tics appeared to have been continuously present since at least the age of 11, an interval that spanned the non-continuous use of several medications specified in the case report, and antedated the introduction of carbamazepine by 13 years. Although carbamazepine possibly exacerbated her symptomatology, it was clearly not responsible for the onset of GTS manifestations in this patient.

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Onset of Schizophrenia in Men and Women

SIR: Stromgren has referred to studies indicating that onset of schizophrenia occurs later in women (*Journal*, January 1987, **150**, 1–7). Our experience in India is different.

We have been engaged in a multicentre 5-year follow-up study of schizophrenia, sponsored by the Indian Council of Medical Research, to find out factors associated with the course and outcome of schizophrenia. The centres selected for this study were Lucknow, Madras, and Vellore. All patients who attended psychiatry clinics in the participating centres between 15 October 1981 and 15 October 1982 and who satisfied a modified form of Feighner's criteria for the diagnosis of schizophrenia were included in the study (245 men and 141 women) (Verghese *et al*, 1985). The age of onset was calculated from the age of the patient at the time of inclusion and the time when the earliest abnormality was noticed (duration of illness). Both these pieces of information were given by the close relatives of the patients. Age of onset was found to be 25.87 ± 6.67 years for men and 25.89 ± 7.33 years for women, which suggests that age of onset of schizophrenia is not later in women in all parts of the world.

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