Double-blind trials

SIR: Oxtoby *et al* (*Journal*, November 1989, **155**, 700–701) draw attention to the serious difficulties entailed in ensuring that a therapeutic trial achieves the intended ideal of 'double-blindness'. In a double-blind study the identity of the treatment administered to an individual patient is concealed from both the patient and the assessing clinician, in an attempt to disentangle a 'true' therapeutic effect from any prejudice arising on account of the reputation of a recognised treatment. Ensuring concealment in this way is regarded as particularly important in psychiatric research, in that it would otherwise be impossible to obtain objective evidence (Pocock, 1983) – although conversely it may be argued that in some cases in which the aim is purely to provide symptomatic relief, a placebo effect could be construed as validly beneficial.

'Double-blindness' is one of several attributes a trial may exhibit which are unequivocally desirable, other things being equal, but which may not in every instance be feasible. For example, it can be argued that the principle that adequately informed consent on the part of the patient and 'therapeutic equipoise' on the part of the clinician are prerequisites for ethicality would, if taken literally, preclude the majority of studies actually performed. Similarly, not all types of trial can aspire to double-blindness. The comparison of a surgical treatment with a conservative, medical one cannot ethically be made in a double-blind manner. In psychiatry, the 'non-blindness' that can arise from recognition of a drug from its taste or side-effects is a problem only because recognition leads to imputation of the characteristics the drug is believed to have.

The suggestion that the ability of participants to guess the patients' drug status should be used as a retrospective criterion to exclude certain results is likely to replace one problem with several others.

(a) A phase III drug trial is normally construed as 'pragmatic' in the sense of Schwartz & Lellouch (1967) and analysed according to the 'intention-to-treat' principle. Retrospective exclusion of some results because in those cases compliance with the principle of 'blindness' could not be obtained is as alien to this scenario as exclusion on account of any other non-compliance or co-intervention.

(b) Some questions could never be answered. In the case of many drugs, such as those with anticholinergic effects, the treatment taken would be 'blind' to the patient in few instances. In the case of less recognisable treatments, retrospective exclusion of a substantial proportion of patients would lead to a serious shortfall in statistical power.

(c) Inappropriate significance testing: to advocate discrimination between the discerning patient and the undiscerning by use of a significance test comparing correct guesses or surmises with chance expectation betrays a misunderstanding of the meaning of significance testing and type I and type II errors – the setting of the boundary for such a selection rule is essentially arbitrary, and is made no less so by invoking permutational probabilities under a null hypothesis.

(d) Exclusion of some patients will upset the randomisation and might introduce a selection bias; any observed difference in outcome could be spurious; or conversely, an apparently null difference could be observed because the selection bias masks a true difference. Since we do not know in what respects the undiscerning would differ from the discerning in their susceptibility to (truly) respond to one treatment rather than another, the results of a trial based on the undiscerning could not reasonably be expected to transfer to a target patient population that was not selected in this way.

A more appropriate conclusion to draw from the great difficulty of ensuring 'double-blindness' is that studies sufficiently well planned to be definitive (in particular, heeding the points I raised recently (Newcombe, 1988)), and also as well masked as possible, should be carried out very early in the career of a treatment, before myths concerning its efficacy become widely disseminated.

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Carbamazepine in affective disorders

SIR: We expected that the paper by Lusznat *et al* (*Journal*, August 1988, **153**, 198–204) would give rise to immediate and vigorous comment. As this did not materialise, we wish to record our reservations about the study.

This double-blind trial allocated 54 acutely manic patients to treatment with either carbamazepine or lithium carbonate, and the effects were monitored in