

There can surely be no doubt that new putative antidepressant compounds require testing against placebo in properly controlled double-blind studies before their efficacy can be regarded as established. Comparative trials against other 'established' antidepressants can never prove the efficacy of a new compound (although studies against the standard may have a place later in a compound's development). The main problem with trials against a standard antidepressant is that the investigators predict no difference between the two groups of patients. However, there is no way of testing the absence of a difference between groups. In contrast, testing a compound against a placebo leads to the prediction of a difference which can be tested by ordinary statistical techniques. Indeed, it is extremely easy to obtain a result of no difference between two treatment groups. One simply enters too few patients for statistical significance or makes any of the other design errors which beset even the best psychopharmacology trialists.

To take an example from the Levine *et al* study, patients in the imipramine comparison group were treated with 75–150 mg/day. In the event seven patients were treated at the 75 mg dose. This is well accepted to be inadequate, and a recent study (Thompson & Thompson, in preparation) confirms the inefficacy of 75 mg of a tricyclic antidepressant. Thus, one-third of the standard treatment group received a treatment which was no better than placebo, and a fluoxetine-treated group fared no better in terms of outcome than the imipramine-treated group. I would suggest that this study does not provide evidence of the effectiveness of fluoxetine as an antidepressant, and that only studies against placebo can do this.

There is one point on which I would disagree with Dunn. The use of atropine as a comparison treatment in antidepressant studies is in doubt, as it induces not only the side-effects of the older antidepressants but also may have some intrinsic antidepressant activity. The more appropriate "active placebo" would be methscopolamine, which has peripheral anticholinergic effects but does not pass the blood-brain barrier. Unfortunately, this compound is difficult to obtain and is thus not frequently used. However, in view of the relative lack of anticholinergic effects in the newer generation of antidepressants which are currently being tested, this may not be such a major flaw in current antidepressant trial design.

If psychopharmacologists are shying away from placebo-controlled antidepressant studies for ethical reasons, or if ethical committees are refusing to pass placebo-controlled studies, then they should

consider the ethical implications of allowing a potentially ineffective antidepressant or any other compound onto an already overcrowded market.

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### **The Symbolic Significance of Munchausen's Syndrome**

SIR: Cremona-Barbaro's paper on the symbolic significance of Munchausen's syndrome (*Journal*, July 1987, **151**, 76–79) prompts comment. Fanciful, dramatic and grandiose presentation is the hallmark of the Munchausen patient, and there may be some relationship between feigned bereavement and the syndrome, but it is by no means "the most common story" (Scoggin, 1983). There has been no previous mention of preoccupation with opera and operatic themes in the literature. Certainly none of our patients exhibited any such interest in the arts (O'Shea, 1987: personal communication).

The aetiology of Munchausen's syndrome would seem to be multifactorial, but there is growing evidence to support a transgenerational learning theory of maladaptive communication patterns with roots in early childhood (O'Shea, 1982; Meadow, 1982).

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### **References**

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SIR: It is difficult to know exactly what is "the most common story" given by Munchausen patients presenting with psychosocial symptomatology. Feigned bereavement is commonly accepted to be a very frequent presentation (Simpson, 1978; Snowdon *et al*, 1978), and will be familiar to psychiatrists and to those working in A & E departments. It is overwhelmingly the commonest story given in my own small series of Munchausen patients presenting with psychiatric symptoms.

I would agree that there has been no previous mention of a preoccupation with the opera in the