the columns

correspondence

Sodium valproate or valproate semisodium?

I read with interest the article by Fisher & Broderick regarding the differences between sodium valproate and valproate semisodium in the management of bipolar disorder (*Psychiatric Bulletin*, December 2003, **27**, 446–448). I would like to comment on both the accuracy of the information presented and highlight important information not included in the article.

The vast majority of trials use valproate semisodium, with over 4000 bipolar patients involved in these studies. The authors erroneously state that the Pope *et al* (1991) study used sodium valproate, when in fact valproate semisodium was used in this placebo controlled trial.

The search criteria used did not include data published in 2003 and consequently missed a further large, randomised, controlled trial which compared valproate semisodium with olanzapine in the management of bipolar disorder, and showed no difference in rates of bipolar relapse between both agents (Tohen *et al*, 2003).

With regard to tolerability, it should be noted by the authors that the most commonly used preparation of sodium valproate in the UK, Epilim Chrono, is not enteric coated and will therefore break down to valproic acid in the stomach and small intestine. The studies showing improved tolerability of valproate semisodium *v.* valproic acid therefore have some particular relevance to the UK.

Finally, the National Institute for Clinical Excellence (2003) has recently reviewed extensively the evidence regarding the use of valproate semisodium in the management of bipolar disorder, and the guidelines specifically state that this compound is recommended for the treatment of acute mania associated with bipolar I disorder.

NATIONAL INSTITUTE FOR CLINICAL EXCELLENCE (2003) Olanzapine and valproate semisodium in the treatment of acute mania associated with bipolar disorder I disorder. Technology Appraisal 66. www.nice.org.

POPE, H., McELROY, S. L., KECK, P., *et al* (1991) Valproate in the treatment of acute mania. A placebo-controlled study. *Archives of General Psychiatry*, **46**, 62–68.

TOHEN, M., KETTER, T., ZARATE, C., *et al* (2003) Olanzapine versus divalproex sodium for the treatment of acute mania and maintenance of remission: a 47 week study. *American Journal of Psychiatry*, **160**, 1263–1271.

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Authors' response

We would wish to thank Dr Mackin for pointing out our error in stating that the Pope *et al* (1991) study used valproate semisodium and not sodium valproate. He also draws attention to a possible misinterpretation in our section on tolerability. We did not wish to imply that Epilim Chrono, a combination formulation of sodium valproate and valproic acid, was enteric coated. However we believe this does not alter our underlying opinion that US data derived from non-enteric coated forms of valproate should not be extrapolated in relation to the general use of valproate in the UK, unless interpreted cautiously. Epilim Chrono by nature of its modified release formulation does not release a bolus of valproate in the stomach and based on the assumption that gastric side effects are concentration related, cannot be regarded as the same as non-enteric coated valproate with respect to gastric side effects. Although Epilim Chrono may be the most commonly used preparation in the UK, figures from the Prescription Pricing Bureau in England show that it only accounts for around 30% of valproate items dispensed in tablet form.

At the time we submitted our paper, 2003 data mentioned by Dr Mackin were not available to us. Dr Mackin mentions the NICE (2003) Technology Appraisal, number 66. We were surprised by the government-directed remit for this particular appraisal, set out in section 3.1; that only medicines with a licence for the treatment of bipolar disorder were to be considered. This is in contrast to other areas of medicine where NICE have clearly felt 'off licence' use was within their remit. One effect of this was to exclude drugs with an established 'off licence' use and create a spurious belief among many psychiatrists that valproate semisodium had to be used in preference to other forms of valproate because it was the only form approved of by NICE. Local Drug and Therapeutics Committees were left to struggle with this issue.

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Risperidone long-acting injection

We were pleased to read of the positive experience with long-acting risperidone by Paton & Okocha (*Psychiatric Bulletin*, January 2004, **28**, 12–14). The abstract, however, appeared inconsistent with the data describing generally positive patient outcomes. From the abstract alone, the findings with long-acting risperidone sound more negative than they actually were.

Specifically, the authors studied a difficult-to-treat population (42 of 50 patients with histories of non-compliance or unacceptable extrapyramidal side-effects). Even in this population, a majority (54%) had at least minimal improvement, with 40% (20 of 50 patients) being seen as 'much or very much improved'. This is impressive considering the population examined, but the authors do not mention this context when drawing their conclusions.

Further, one might view a 40% attrition rate to be a positive outcome given that patients were selected largely on the basis of noncompliance. Comparison with a published one-year trial (Fleischhacker *et al*, 2003) may not be entirely appropriate as patients in the latter were selected on the basis of clinical stability, not noncompliance, and most were switched from oral atypical, not depot, antipsychotics.

We agree with Paton & Okocha about the need for additional information regarding long-acting risperidone, including mention that at least 6 months of therapy are needed before assessing outcome. However, we interpret their findings as supportive of the potential for

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