Drug-induced dysphoria

SIR: In the paper "Antipsychotic drug-induced dysphoria" (King *et al*, 1995), the authors refer to our report (Anderson *et al*, 1981) on "Prolonged adverse effects of haloperidol in normal subjects".

Prior to our small study there were only two case reports in the literature regarding normal subjects' response to haloperidol (Kendler, 1976; Belmaker & Wald, 1977). These case reports involved a medical student and a physician who took haloperidol 1 mg intramuscularly and 5 mg intravenously, respectively. Both experienced akathisia and dysphoria lasting 5 and 36 hours respectively.

King *et al* claim that our three subjects had side-effects for 6 weeks. In our study 3 normal healthy volunteers were given oral haloperidol 5 mg, not to assess side-effects, but to look at another aspect of the drug, i.e. its effects on serum beta endorphin levels, and the fourth subject was a resident physician who independently self-administered haloperidol 5 mg orally to test for dysphoria, a frequent complaint of her patients. These four subjects reported dysphoria and akathisia commencing around 3–6 hours after ingestion and lasting 36 hours, 4 days, 5 days and 14 days respectively. One subject reported temporarily experiencing similar symptoms after he drank coffee 6 weeks after the experiment.

The chief disparity between our brief report and that of King *et al*'s much larger study concerns the duration of side-effects. King *et al* describe a 50% dropout rate, mainly due to subjective complaints of dysphoria or agitation, between 3–8 hours after dosing in their first group of 26 subjects. Dropouts apparently fled the laboratory – "I'll have to get out of here . . .". No apparent evaluation of side-effects lasted longer than 8 hours. If the authors have any follow up data on the dropouts, this might be valuable in assessing the safety and duration of effects of single dose haloperidol in normal subjects. In our study one of us (BGA) re-interviewed subjects between 1 and 4 weeks after ingesting 5 mg haloperidol. Also, King *et al*'s assertion that two of our three subjects experiencing side-effects were not helped by diphenhydramine or benztropine is untrue. They both gained at least temporary relief from these compounds.

If our report, as suggested by King *et al*, did deter researchers from giving haloperidol to normal healthy volunteers, then hopefully it also alerted physicians to the prevalence of dysphoria and akathisia as side-effects of these drugs. Interestingly, in the U.S. Physician's Desk Reference (1996), for haloperidol the word akathisia is mentioned once, but the term dysphoria is never used.

King *et al* have contributed important information regarding the disturbing incidence of dysphoria without akathisia in normal subjects given oral haloperidol 5 mg.

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B.G. ANDERSON
NYU at Manhattan Psychiatric Center
Ward's Island
NY 10035

D. REKER
Greenville, NC

T. COOPER
Nathan Kline Institute
Orangeburg
NY 10962

Low incidence of mania in northern Finland

SIR: Daly *et al* (1995) reported that the first admission rate of mania was higher in Dublin than in London or Aarhus, Denmark. The study confirmed the clinical impression of psychiatrists of a high incidence of mania in Dublin.

We have an ongoing prospective follow-up study of an unselected birth cohort. The study population is composed of 6007 men and 5757 women who were born in northern Finland in 1966 (Rantakallio, 1988). The psychiatric morbidity has been followed from Finnish Hospital Discharge Registers. By the end of 1993 a total of 515 subjects had been admitted in psychiatric hospitals. The data of that register have demonstrated good accuracy in research (Keskimäki & Aro, 1991). The case records of all registered patients were re-checked against clinical records by two senior researchers, who made the final DSM–III–R diagnoses.

In our sample there have been only two cases of bipolar disorder (mania) before the age of 28 years. On the other hand, during the same follow-up time, there have been 76 cases of schizophrenia. This finding is in line with the clinical impression of a low admission rate of mania in northern Finland.