While ICD–10 may be a nightmare for one, it provides clinicians and research workers with a nosology based on international consensus and accord.

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A. S. HENDERSON
NH&MRC Social Psychiatry Research Unit
The Australian National University
Canberra ACT 0200
Australia

A. JABLENSKY
University Department of Psychiatry
Royal Perth Hospital
Western Australia

N. SARTORIUS
University of Geneva
Switzerland

A catecholamine model of fatigue

SIR: The chronic fatigue syndrome (CFS) has been proposed as a clinical disorder characterised by prolonged, excessive fatigue and concurrent neuropsychiatric disturbance (Lloyd *et al*, 1988). Phenomenologically, similarities exist with another proposed neuropsychiatric entity, 'atypical depression'. The latter is also characterised by anergia, limb heaviness or weakness and hypersomnia; its clinical validity is argued largely on its preferential response to monoamine oxidase (MAO) inhibitors (Quitkin *et al*, 1988).

To date, no studies have shown that patients with CFS respond to antidepressants. Given the prominence of muscle pain, sleep and mood disturbance in these patients, the proposed role of serotonin in the production of such symptoms (Lopez-Ibor, 1988) and patients' reported sensitivity to the side-effects of tricyclic agents, we chose initially to evaluate fluoxetine. Given the syndromal overlap between CFS and 'atypical depression', we also evaluated the novel reversible inhibitor of MAO-A, moclobemide.

In the first phase of this open evaluation, 15 CFS patients were treated with 20 mg fluoxetine daily for four to six weeks. The dose was increased to 40 mg daily in two patients, as they had reported a partial response. Sixteen other patients were later treated with moclobemide, started at 150–300 mg per day and increased to 450–600 mg. Response was rated 1–5 on a global outcome scale assessing both overall symptom severity and consequent disability. Ratings were made at 4–6 weeks of treatment, or at therapy cessation due to adverse effects.

Of the 15 patients treated with fluoxetine (7 men, 8 women, mean age 40.5 years, range 18–67), 47% (7/15) reported at least some improvement, though only 27% (4/15) showed a significant clinical response (rating $\geqslant 4$). Four patients (27%) stopped the medication because of side-effects (agitation in two). By contrast, 69% (11/16) of patients treated with moclobemide (8 men, 8 women; mean age 34.7 years, range 16–45) experienced at least some improvement, with 56% (9/16) experiencing a significant clinical response. In two patients the rapid development of severe agitation resulted in cessation of therapy.

Treatment trials in patients with CFS have emphasised a significant non-specific treatment effect (Lloyd *et al*, 1993). Caution is therefore required in the interpretation of uncontrolled studies. The trend towards a difference in clinical response rates between the two antidepressants (56% v. 27%; $\chi^2=2.78$, $P=0.095$) cannot be easily explained by non-specific effects. The response rate to fluoxetine would seem to approximate that of placebo in controlled trials. If further studies confirm a reduction in symptoms in response to agents such as moclobemide, which have their principal effects on noradrenaline and/or dopamine levels (as distinct from serotonin) in the central nervous system, then this would support a catecholamine model for fatigue. Further, it would lend support to the hypothesis that CFS differs at a biochemical level from typical mood disorders, which characteristically respond well to selective serotonin reuptake inhibitors such as fluoxetine.

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I. HICKIE
A. WILSON

School of Psychiatry
University of NSW
Mood Disorders Unit
Prince Henry Hospital
Little Bay, Sydney
Australia 2036

Dystonia induced by amphetamine and haloperidol

SIR: As part of a long-term study of the neuropharmacology of latent inhibition, two healthy volunteers received amphetamine (5 mg) and haloperidol (5 mg). Both developed marked dystonic reactions, such as would be unusual following the administration of haloperidol (5 mg) alone.

The first subject, a 24-year-old woman, 1.7 m tall and weighing 54 kg, was treated with 5 mg haloperidol and 5 mg dexamphetamine at 10.00 a.m. Twenty-nine hours later she telephoned to report stiffness in her neck. Half an hour later she was examined and found to have increased muscle tone, with neck and limb stiffness and Parkinsonian facies. Her jaw was stiff and her tongue protruded. She had oropharyngeal spasm. She was treated with 10 mg intramuscular procyclidine and the symptoms resolved.

The second subject, a 20-year-old woman, 1.7 m tall and weighing 63.2 kg, was treated with 5 mg haloperidol and 5 mg dexamphetamine at 10.00 a.m. She telephoned 34 hours later to say that her eyes were rolling upwards. When examined 30 minutes later she was in oculogyric crisis, with acute dystonia of the neck (her head being dorsoflexed against her shoulders) and her back slightly arched – although not in opisthotonos. She was given 10 mg intramuscular procyclidine and her symptoms resolved over 30 minutes.

The pathogenesis of acute dystonia is not fully understood, but Marsden & Jenner (1980) have argued that it is due to the combined effects of acute dopamine receptor blockade with secondary increase in dopamine turnover followed by a delayed supersensitivity of postsynaptic dopamine D_2 receptors. Dystonia they argue is caused by the effects of increased dopamine release on supersensitive receptors, as the latter become exposed by drug wash-out. In support of their view, Meldrum *et al* (1977) have shown that in baboons drug-induced dystonia can be prevented by depleting presynaptic dopamine. In our two healthy volunteers the opposite may have happened, and the combination of amphetamine with haloperidol may have caused marked dystonia by potentiation of dopamine release.

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CLAIRE CAPSTICK
STUART CHECKLEY
JEFFREY GRAY
SHARON DAWE

Institute of Psychiatry
London SE5 8AF

Adrenoceptor activity and adenylate cyclase inhibition in depression

SIR: The human platelet has been extensively used as a model of monoaminergic neurons in the investigation of the amine hypotheses of depression and the effects of antidepressant treatment. Platelet α_2 adrenergic receptors (AR) are coupled in an inhibitory manner to membrane-bound adenylate cyclase (AC), the effector second messenger system. Platelet α_2 AR desensitisation has been reported in drug-free depressed patients, expressed as low agonist-receptor affinity or impaired AC inhibition (Siever *et al*, 1984).

We report the results of two studies which investigated platelet α_2 AR receptor function and AC inhibition in depressed patients. The first study involved eight patients with DSM–III–R major depression, of mean age 55.4 (s.d. 11.1) years, and 18 normal subjects (hospital personnel) (mean age 49.2 (13.8) years). Blood samples were extracted at 9.00 a.m. for the α_2 adrenoceptor assay (Doyle *et al*, 1985). This was done at baseline and at the end of four weeks' treatment with amitriptyline (5 patients) and fluparoxan (an α_2 adrenoceptor inhibitor) (3 patients). Results were expressed as K_d (nm) and B_{max} (fmol/mg protein). In the second study, eight depressed patients were compared with 11 normal controls (laboratory personnel). Blood samples were extracted at 9.00 a.m. for adenylate cyclase assay (Schultz *et al*, 1987) at baseline and at weeks 1, 2, 3 and 4 of antidepressant therapy.

The results showed no significant differences in K_d or B_{max} of α_2 AR between depressed patients and normal controls at baseline. At the end of four weeks, the mean value of K_d of α_2 AR was not significantly different between depressed patients and normal controls. B_{max} of α_2 AR at the end of treatment, however, was significantly lower in