Correspondence

EDITED BY LOUISE HOWARD

Does electroconvulsive therapy lead to changes in cerebral structure?

Sir: Some retrospective imaging studies have reported an association between a history of electroconvulsive therapy (ECT) and cerebral change, particularly affecting the lateral ventricles and/or cerebral cortex (Weinberger *et al*, 1979; Calloway *et al*, 1981; Andreasen *et al*, 1990). We report the results of a small study of the acute cerebral effects of ECT using recently developed highly sensitive image registration and subtraction techniques applied to high-resolution magnetic resonance imaging brain scans.

A prospective study was carried out in which four ECT-naïve patients with depression underwent 3D high-resolution magnetic resonance imaging less than one week prior to the start of bilateral ECT and again within 24 hours of the administration of first treatment. One of the patients was also scanned six weeks after his first ECT. All examinations were performed on a Picker 1.0 T HPQ system using rf spoiled volume acquisition (TR=21 ms, TE=6 ms, flip angle=35°, 1.6 mm nominally isotropic resolution).

Accurate registrations were performed between the baseline and follow-up scans by using an image registration technique producing alignment of images to a fraction of a voxel, typically less than 0.01 mm in each linear dimension (Hajnal *et al*, 1995*a*). Hajnal *et al* (1995*b*) have demonstrated how subtraction of such aligned images can result in virtually complete cancellation of signals from unchanged structures, thereby providing an unambiguous null condition against which much smaller changes to the brain can be detected than has been possible in previous ECT neuroimaging studies.

The anatomical images and the registered subtraction images (n=4) did not reveal any significant difference in cerebral structure following ECT, either within 24 hours or after six weeks. We conclude that use of one of the most sensitive techniques for detecting cerebral change offers no evidence that ECT leads to acute structural brain changes.

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Risperidone-induced rabbit syndrome

Sir: Rabbit syndrome is an uncommon side-effect of neuroleptic treatment. This syndrome consists of tongue-sparing movements of the mouth, usually after long-term treatment (Schwartz *et al*, 1995). Rabbit syndrome has also been reported, in some cases, as an acute complication of therapy (Todd *et al*, 1983). We describe a case of rabbit syndrome in a patient treated with risperidone.

In March 1989, Mrs G., a 68-year-old with no past history of psychiatric disorder, was admitted to the psychiatric unit because of recent symptoms of acute anxiety and paranoid delusions. She was treated with haloperidol and thioridazine but she developed side-effects. She continued treatment with fluphenazine and benzhexol. Four months later she developed a depressive episode and mianserin 30 mg/day was added. Her condition quickly improved. In August 1996 she had a relapse. In September 1996 we stopped the fluphenazine and started risperidone 4 mg/day. Mianserin was continued in the same dose and full remission was achieved again. Four months later involuntary movements of the mouth appeared. The movements were mainly in the jaw, rapid and on a vertical axis, without lingual involvement. Fine tremor of the head was also present. No other extrapyramidal signs were present. Rabbit syndrome was diagnosed and benzhexol 10 mg/day was started orally. One week later the tremor of the head disappeared and two weeks after beginning treatment the movements of the mouth resolved completely. She continues with the same medication, and during follow-up has been free of clinical extrapyramidal symptoms and signs.

Rabbit syndrome is an iatrogenic syndrome induced by neuroleptics. It has not been reported with other psychotropic drugs, such as anxiolytics, sedative hypnotics or antidepressants (Casey, 1992). In most of the case reports the majority of patients with rabbit syndrome also had other Parkinsonian signs such as tremor, rigidity or bradykinesia. Some authors reported this syndrome as a *forme fruste* of drug-induced parkinsonism (Casey, 1992). In spite of that, treatment with dopamine agonists is not effective in rabbit syndrome. In the present case, rabbit syndrome appeared four months after treatment with risperidone and improved

with benzhexol. Risperidone is a new-generation atypical antipsychotic agent with potent dopamine antagonist action (Owens, 1994). Despite this pharmacological effect, a low risk of extrapyramidal side-effects has been reported. To our knowledge, this is the first report of rabbit syndrome caused by risperidone treatment.

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Jet lag and relapse of schizoaffective psychosis despite maintenance clozapine treatment

Sir: Jet lag is a transient disorder of the sleep–wake schedule which results from rapid multiple time zone changes, affects only east–west travel and is worse after eastward travel. Its symptoms, which may last 7–10 days, include sleepiness, fatigue, exhaustion with insomnia during sleep period (Karacan *et al*, 1992).

There has been no report of *de novo* psychosis or relapse of a stabilised psychotic disorder following an acute jet lag. Tec (1981) reported a case of relapse of endogenous depression following jet lag. I present the case of a young man whose schizoaffective psychosis, stabilised on clozapine for five years, relapsed during an eastward transatlantic flight, despite continued compliance.

Mr A., a 26-year-old man, was first hospitalised in 1991 for a psychotic episode later diagnosed as schizoaffective disorder. Following failed trials of conventional neuroleptics he commenced clozapine on 3 December 1992. The Positive and Negative Syndrome Scale (PANSS; Kay *et al*, 1987) total score was 104. He was stabilised on clozapine 400 mg per day and by early 1996 worked part-time in a grocery store. In December 1997, he left for Lebanon for a visit. Total PANSS score was 46, and maintenance dose of clozapine was 400 mg h.s. After a six-hour flight to London, England, and before boarding the plane to Lebanon that day, he became guarded, suspicious and apprehensive. On arrival in Lebanon he became psychotic, with auditory hallucinations, ideas of reference and persecutory delusions that the police were after him. He saw a psychiatrist who increased clozapine to 500 mg h.s., with benefit after two weeks.

His westward return trip to Canada a month later was uneventful. However, on arrival in Canada, the dose of clozapine had to be decreased to 450 mg h.s. because of over-sedation.

This is the first case of psychotic relapse following acute jet lag. The dose of clozapine that controlled his psychosis in Lebanon (eastward travel) was excessive on return to Canada (westward travel). The clinical implication of this report is that such patients travelling eastward across time zones may need a slight dose increase to prevent a relapse.

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Testicular pain and swelling on withdrawal of imipramine

Sir: We present an unusual occurrence of testicular pain and swelling on withdrawal of imipramine. Testicular pain and swelling is noted in the package insert as an adverse reaction to the drug and it has been described in the literature with the use of desipramine (Deicken & Carr, 1987; Thienhaus & Vogel, 1988). A.B. is a 61-year-old, married, unemployed male with major depression and generalised anxiety and had been treated with imipramine 150 mg daily for the past eight years. He decided to stop imipramine because of prolonged adverse reactions. The medication was withdrawn over a two-week period. At the end of the first week he complained of bilateral pain, tenderness, swelling of testes and difficulty with micturition of gradual onset. The symptoms coincided with withdrawal.

Physical examination revealed bilateral swelling, redness and tenderness on palpation of testes. There was no history of being exposed to sexually transmitted diseases. On examination, his pulse and temperature was normal, there was no lymphadenopathy, no parotid swelling and no hypertrophy of prostate gland on rectal examination. Full blood count, erythrocyte sedimentation rate, urea, creatinine and electrolytes, prostate specific antigen, the tumour marker for beta human chorionic gonadotrophin, and alpha-fetoprotein, were all within normal limits. Urine microscopy was unremarkable and culture did not reveal any significant growth. Testicular ultrasound was not performed.

All of the genital symptoms and the other adverse symptoms subsided by the end of the fourth week and he remained symptom-free during regular follow-up over six months. The testicular pain and swelling may be due to an infection, but the laboratory findings did not support this hypothesis. There was a strong relationship between the time course of the withdrawal and the emergence of testicular pain and swelling. We postulate that a decline in level of the drug and/or its metabolite, possibly acting via an endocrine imbalance, gave rise to a hypersensitivity-type reaction and these symptoms subsided with restoration of equilibrium.

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Adults with Williams syndrome

Sir: I read with interest the preliminary report on Williams syndrome (Davies *et al*, 1998). I feel that the omission of significant behavioural phenotypes and the ascertainment bias has marred an otherwise