This study fails to confirm previous findings of a maternal age effect on the risk of AD. The average age of the parents at birth of the subjects was, if anything, slightly lower in the patients than in the controls. This study differs from others in that it is considerably larger, and employed randomly selected population controls.

Two methodological issues have to be discussed. Firstly to reduce misclassification of Alzheimer patients as much as possible we applied the diagnostic criteria suggested by McKhann *et al* (1984) rigorously and restricted our study to patients in whom the diagnosis was made before the age of 70 years. However, we cannot rule out that some misclassification has occurred and as in other studies this tends to dilute a true difference in maternal age between the study groups. Secondly, this study was performed in early-onset Alzheimer patients. We do not know to what extent the present findings apply to AD with a later onset.

In conclusion, we suggest that parental age at birth of the subject is not likely to be a risk factor for AD.

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*A. Hofman, MD, PhD, *Professor of Epidemiology, Department of Epidemiology and Biostatistics, Erasmus University Medical School, PO Box 1738, 3000 DR Rotterdam, The Netherlands*; Cornelia M. van Duijn, MSc, *Resident in Epidemiology*; Willem Schulte, MD, *Social Geriatrician*; Teun A. Tanja, MD, *General Practitioner*; Robert Haaxma, MD, PhD, *Lecturer in Clinical Neurology*; Arie J. Lameris, MD, *General Practitioner*; Rolf J. Saan, MSc, *Reader in Neuropsychology*

*Correspondence

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The Effects of Chronic Lithium Treatment on Psychomotor Performance Related to Driving

SIMON HATCHER, RUTH SIMS and DAVID THOMPSON

A group of 16 psychiatric out-patients in remission, who had been taking lithium carbonate as their sole medication for at least three months, were compared with a control group of

22 healthy volunteers. On a computerised driving simulator which produced measures of reaction time, tracking ability and mistakes made, the patient group had a significantly slower reaction time. Patients should be warned therefore that lithium may affect their ability to drive or operate machinery and that psychomotor impairment and sedation are not synonymous.

Medical Aspects of Fitness to Drive (Raffle, 1985) published by the Medical Commission on Accident Prevention, states that patients "should be advised of the effects of [prophylactic] medication" in relation to driving ability. Previous work on relating lithium to driving skills has involved either normal volunteers given medication for a short period (Linnoila *et al*, 1974) or small numbers of patients taking other medication concurrently (Hobi *et al*, 1982). These studies have come to different conclusions concerning the safety of driving while taking lithium.

The validity of using laboratory tests to relate drug effects to driving skills has been demonstrated by prospective follow-up studies (Haakinen, 1976) and by comparing laboratory tests with other tests of driving skills (Sivak *et al*, 1981). This study aimed to examine the effects of chronic treatment with lithium carbonate on the driving skills of psychiatric out-patients in remission, using a computerised driving simulator.

Method

Patients were entered into the study if they were out-patients, were taking lithium as their sole psychotropic medication, had been on lithium for at least three months, and were between the ages of 18 and 65 years. They were excluded if they were actively psychiatrically ill or had any concurrent neurological disease. In practice, all the patients included in the study had previously been diagnosed as suffering from manic–depressive psychosis – circular type.

The controls were volunteers recruited from health authority domestic, secretarial, medical and nursing staff who were not on any medication and did not have any concurrent physical or psychiatric illness. Their occupations were as follows: four doctors; eight psychiatric nurses; four secretaries; two medical students; one domestic; one social worker; one salesman; and one research assistant. They were matched for age, sex, and driving experience with the patient population. All the drivers in the control and patient group were currently driving.

The null hypothesis was that there was no difference in psychomotor abilities between the two populations. All investigations, with the exception of those two patients who were tested in the afternoon, were performed in the morning in order to control for circadian variation in reaction time.

Psychomotor ability was assessed using a BBC micro-computer and a simple driving simulator. This consisted of a steering wheel and two foot pedals positioned to replicate the brake and accelerator pedals in a car. The screen display consisted of a roadway with two traffic lights either side of the road and two arrows at the bottom of the screen. The traffic lights changed colour at random time intervals 11 times a minute. The top arrow was moved by the computer in a horizontal plane according to a complex sine wave and the bottom arrow by the subject using the steering wheel. Subjects were instructed to follow the computers' arrow using the steering wheel and at the same time, if either of the traffic lights changed from green to red, to take their foot off the accelerator pedal and press the brake pedal as fast as possible. This generated an accuracy or tracking score, which reflected how closely the subjects followed the computers' arrow, a brake reaction time and a record of how many lights the subject had failed to respond to (lights missed). The closer the match between the computers' arrow movement and that of the subject the lower the accuracy score, i.e. low scores represented higher accuracy (the score was derived from the inverse of a root mean square measure of the deviation of the subject's arrow from the computer-generated track).

Subjects were given a five-minute practice period on the simulator during which 55 changes of the lights were made. They were then tested for three minutes when there were 33 changes of the lights.

To confirm that they were in remission, patients also completed a Hospital Anxiety and Depression Rating Scale (HAD scale) and were interviewed using the Montgomery-Asberg Depression Rating Scale (MADRAS scale). Patients were excluded if they scored seven or more on the MADRAS scale, which corresponds to a 'mild depressive disorder' (Snaith *et al*, 1986), and eight or more on the HAD depression subscale, which indicates a probable case of depression (Zigmond & Snaith, 1983). Blood samples were collected for serum lithium measurement, thyroid function tests and blood alcohol. Patients were excluded if their thyroxine levels were outside the normal range of 60–140 nmol/l or if there was any alcohol in their blood.

Results

A comparison of some of the demographic features of the two groups is shown in Table I. The patients were taking a mean dose of lithium carbonate of 809 mg daily (range of 400–1250 mg daily), and had been on this medication for a mean of 4.36 years. At the time of taking the test the mean serum lithium was 0.61 mmol/l (range 0.27–1.04 mmol/l). Two patients were included with serum lithium levels below the usually accepted minimum of 0.40 mmol/l who had been successfully maintained on a low dose of lithium for some years.

A comparison of the two groups on the driving simulator is shown in Table II. This shows that the patients had a significantly slower reaction time than controls. The difference in accuracy approached significance while there was no significant difference in the number of mistakes (lights missed). However, because of the numbers involved, the power of the statistical tests to detect a significant difference is probably low.

TABLE I
Composition of control and patient groups

	Controls (n = 22)	*Patients (n = 16)*
Age range: years	21–58	18–63
Mean age: years	37.8	36.0
Females/males	12/10	8/8
Non-drivers (%)	5 (23)	4 (25)

TABLE II
Comparison of control and patient groups on the driving simulator (all statistical tests are two-tailed Mann–Whitney U-tests)

	Controls	*Patients*
Median reaction time: seconds (range)	0.58 (0.46–0.82)	0.72* (0.50–1.01)
Median accuracy[1] (range)	27.5 (16–51)	32** (24–75)
Median lights missed: *n* (range)	0.00 (0–8)	0.00*** (0–4)

*$P<0.05$, **$P=0.052$, ***$P=0.23$.
1. Score derived from inverse of a root mean square measure of the deviation of subjects' arrow from computer-generated track.

Within the patient group there was no significant correlation between age and accuracy (Spearman's $r=-0.08$, $P=0.75$), reaction time ($r=0.30$, $P=0.27$) or lights missed ($r=0.30$, $P=0.27$) or between anxiety scores from the HAD and reaction times ($r=0.18$, $P=0.53$). Serum lithium and total thyroxine (T_4) level were not significantly correlated with any of the variables measured on the driving simulator. In an attempt to further examine the effects of the serum lithium level the patients were divided by means of the median lithium level into a high and a low group. There were no significant differences between either group on any of the variables. Excluding non-drivers from the analysis confirmed a significant difference in reaction time ($P<0.05$) with the difference in accuracy approaching significance ($P=0.53$).

Discussion

Lithium carbonate is a commonly used drug in psychiatric out-patients and yet, like most drugs, its effects on everyday activities such as driving have received little attention. This study has shown that compared to a normal population, patients taking lithium have an increased reaction time. Is this a true difference?

It could be argued that lithium slows down the learning process. Therefore, what this study measures is reaction times at different points on the same learning curve and, given sufficient practice, both groups would eventually reach the same level. However, the tasks on the simulator were easy to learn and after the initial instructions, all the subjects could be left to operate the simulator on their own. It has also been shown that reaction time measurements are stable and reproducible after the first 18 trials in a series (Hamsher & Benton, 1977). Subjects in this study had 55 trials before measurements were taken.

Is the difference in reaction time due to the underlying disease process or an effect of the drug? Lithium does have specific psychomotor effects (Shaw *et al*, 1987). Elsass *et al* (1981) found a significant impairment in reaction times comparing lithium-treated patients who had 'manic-melancholic' disorder with patients who had the same diagnosis but were not being treated with lithium. However, these results have to be treated with caution because no allowance was made for the affective state of the subjects or any other medication that they might have been taking. In the present study a better experimental design would have been to use the patients as their own controls (i.e. take measurements both on and off lithium). However, this has obvious ethical problems. Whether the difference was due to the disease or the drug, the important point is that it exists. What is also important is that a drug which does not cause sedation at therapeutic levels does have an effect on psychomotor abilities. Sedation and psychomotor impairment are not synonymous.

Does a difference of 0.14 s really matter? Driving at 30 m.p.h. the 'thinking distance' is 9.1 m according to the Highway Code. An increase in thinking time of 0.14 s results in an increase of about 2 m or a 22% rise. It may be argued that patients adopt alternative strategies to cope with this change and are therefore perfectly safe. However, first they must be aware of the change and it is the prescribing doctor's duty to warn patients given lithium that their ability to drive may be affected.

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*Simon Hatcher BSc, MBBS, *Tutor in Psychiatry and Honorary Registrar in Psychiatry, Department of Psychiatry, University of Leeds, Leeds*; Ruth Sims, MBChir, MRCPsych, *Tutor in Psychiatry and Honorary Registrar in Psychiatry, High Royds Hospital, Menston, Ilkley*; David Thompson MBBS, MRCPsych, MSc, *Consultant Psychiatrist, Malham House Day Hospital, Leeds*

*Correspondence: *Department of Liaison Psychiatry, Leeds General Infirmary, Great George Street, Leeds LS1 3EX*

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Do-Do Abuse

S. LOOSMORE and D. ARMSTRONG

Three cases of prolonged abuse of Do-Do tablets, an over-the-counter remedy for "coughs, wheezing and breathlessness", are reported. They have an amphetamine-like action and were used as easily obtained amphetamine substitutes, in one case to relieve social anxiety. Withdrawal symptoms similar to those following cessation of amphetamines occurred in two cases. Do-Do tablets are CNS stimulants and their abuse may be accounted for by the fact that they perhaps affect amine neurotransmitters.

Many over-the-counter remedies for coughs and colds contain one or more central nervous system (CNS) stimulants. Abuse of such medication is recognised, but, until recently, infrequently reported in the medical literature. Most previous reports have concentrated on the acute sequelae of long-term use or abuse.

Do-Do tablets, containing ephedrine hydrochloride (222 mg), caffeine (30 mg), and theophylline sodium glycinate (50 mg), are widely available over the counter and marketed for the relief of "bronchial coughs, wheezing and breathlessness". The packet instructions are brief, stating that no more than three tablets should be taken in twenty-four hours. There is no comment on possible side-effects or the consequences of exceeding the stated dose.

We report, in detail, three cases of prolonged abuse of Do-Do tablets.

Case 1

A 33-year-old, separated, unemployed man was referred to the addiction services with a 15-year history of abuse of Do-Do tablets. He feared that his drug use would prevent access to his children. His stated aim was to abstain.

His mother and maternal grandfather have suffered endogenous depression. His father and paternal uncle are withdrawn, inaccessible individuals and his paternal grandfather, although not formally diagnosed, was an odd man.

Since childhood he had been reclusive with difficulty in forming stable relationships. At school he would sit curled up in a corner with gaze averted, and without speaking. Because of his evident oddness he was bullied.