Lithium induced cognitive side-effects in bipolar disorder: a qualitative analysis and implications for daily practice

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Authors' objectives
To investigate whether lithium gives rise to cognitive side-effects and affects the ability to drive a car.

Searching
MEDLINE and PsycLIT were searched from 1977 onwards using the key terms "cognition", "bipolar disorder" and "lithium".

Study selection
Study designs of evaluations included in the review
Articles that scored more than 70 on the quality assessment were included in the review. Controlled and uncontrolled studies were included.

Specific interventions included in the review
Lithium taken for between 2 weeks and 9 years.

Participants included in the review
Patients with manic depressive illness, one trial also included alcoholic patients and people with schizophrenic disorder, another trial included those with depression.

Outcomes assessed in the review
Short term memory, long term memory, vigilance, reaction time, EEG tests, WMS tests (definition not provided), Halstead test, Reitan battery tests, trailmaking, memory tasks, 20 word task, Benton tests, story recall, Stroop 'digit span' test, Tachistoscope, Tapping, Steering task and 14 and 16 word tasks.

How were decisions on the relevance of primary studies made?
The authors do not state how the papers were selected for the review, or how many of the authors performed the selection.

Assessment of study quality
Studies were scored on: the number of individuals included, homogeneity of the research population, use of a standardised diagnostic system, research design (prospective or retrospective), use of a placebo-controlled design, duration of lithium therapy, specificity of tests and tasks and methods used to control for variables that could bias outcome such as blood lithium levels and reporting of mood. A quantitative scoring system was used to score specific aspects of the articles (see Other Publications of Related Interest no.1). The maximum score for each item was 10, the maximum total score was 100. The authors do not state how many of the authors performed the validity assessment.

Data extraction
The authors do not state how the data were extracted for the review, or how many of the reviewers performed the data extraction. Data were extracted on: author, number of subjects, duration of lithium treatment, lithium level, diagnosis, research design, methodology tests and results.

Methods of synthesis
How were the studies combined?
A narrative synthesis is provided.

How were differences between studies investigated?
Differences were discussed in a narrative synthesis.

**Results of the review**
Seventeen studies, only 4 of which met methodological inclusion criteria.

Only four of the 17 studies met the criteria for methodological quality. All of these four studies were placebo controlled and/or double blinded. All studies showed a statistically significant negative effect of lithium on memory, vigilance, reaction time and tracking.

**Authors' conclusions**
Lithium has a negative effect on memory, as concluded from a relatively small number of well designed and controlled studies that showed an improvement of memory functions after temporary discontinuation of lithium. Inconsistent findings concerning memory effects seem to be related to differences in methodology and research designs.

**CRD commentary**
A good review of the area. A reasonably thorough literature search was conducted, however no attempts were made to trace unpublished work and the authors do not state whether there were any language restrictions, thus the results may be subject to publication bias. A thorough quality assessment was conducted, however the authors do not give any methodological details regarding how many reviewers were involved in the process of quality assessment or in screening for inclusion and data extraction. A narrative synthesis appears appropriate given the nature of the data and good study details are provided in the text. The authors' conclusions follow from the results presented.

**Implications of the review for practice and research**
Practice: The authors state that 'separate from normal routine laboratory testing, the serum lithium concentration should be measured in patients with bipolar disorder treated with lithium who present themselves with memory problems and mental slowness in order to rule out lithium intoxication. Patients should be given psycho-education about cognitive deficits in an attempt to make them aware of implications of these deficits for their ability to drive, thereby decreasing the risk of road accidents'.

**Bibliographic details**

**PubMedID**
10435769

**Other publications of related interest**

**Indexing Status**
Subject indexing assigned by NLM

**MeSH**
Antimanic Agents /adverse effects /therapeutic use; Automobile Driving; Bipolar Disorder /drug therapy /psychology;
Clinical Trials as Topic; Cognition Disorders /chemically induced /psychology; Controlled Clinical Trials as Topic; Double-Blind Method; Humans; Lithium /adverse effects /therapeutic use; Longitudinal Studies; Prospective Studies; Psychomotor Performance /drug effects

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**Record Status**
This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.