
Effects of lithium on cognitive performance: a meta-analysis

Wingo AP, Wingo TS, Harvey PD, Baldessarini RJ

CRD summary

This review found lithium carbonate had mild negative effects on cognitive performance in immediate verbal learning and memory and creativity. Some methodological flaws and the lack of information about the quality of the included studies means that the reliability of the results is unclear and the authors' conclusions should be interpreted with caution.

Authors' objectives

To assess the effects of lithium on cognitive performance in the treatment of recurrent affective disorders.

Searching

MEDLINE, EMBASE and PsycINFO were searched from inception to December 2008 for relevant English-language studies; search terms were reported. Bibliographies of the included studies were also cross-referenced by hand.

Study selection

Comparative studies that evaluated treatment with lithium compared with no lithium treatment on the cognitive performance of either healthy volunteers or patients with affective disorders were eligible for inclusion. Studies were excluded if patients: had co-morbid neurocognitive disorders; had substance abuse or dependence within 30 days; had received lithium carbonate for less than one week; were receiving anticonvulsants concurrently; were younger than 17 years of age. Reviews, editorials, letters, case reports and dissertations were also excluded.

The included studies were conducted between 1977 and 2000. In most of the included studies, participants were their own control and there were washout periods between the time on lithium and the time not taking lithium. The affective disorders of the included patients were bipolar disorder, recurrent unipolar major depressive disorder, and cycloid or schizoaffective disorders. The mean age of the enrolled participants was 37.4 years (± 12.6 years). The included affective disorder patients were required to be in remission at the time of the study; these patients received a mean serum lithium carbonate concentration of 0.82mEq/L for a mean of 3.9 years (± 3.5 years). The healthy volunteers received mean serum levels of lithium concentrate of 0.78mEq/L for 2.52 weeks (± 1.05 weeks). Concurrent medication in a minority of studies included anti-depressants and/or anti-psychotic medications.

Outcomes were measured using neurocognitive tests. Nine cognitive domains were examined: immediate verbal learning and memory, delayed verbal learning; immediate visual memory; delayed visual memory; attention; processing speed; executive function; creativity; and psychomotor performance.

Two reviewers independently performed the study selection; any disagreements were resolved by consensus.

Assessment of study quality

The authors did not state that they formally assessed methodological quality, but blinding and comparability of patients were evaluated.

Data extraction

Two reviewers independently extracted data on measures of cognitive performance to calculate unbiased standardised effect sizes (mean differences) using the Hedges and Olkin method. When means and standard deviations were not provided, the effect size (ES) was calculated using the methods of Rosnow and Rosenthal. Similar neurocognitive tests were grouped a priori based on the cognitive domains under assessment.

Any discrepancies between the reviewers were resolved by consensus.

Methods of synthesis

Pooled effect sizes and 95% confidence intervals (CIs) were calculated using a fixed-effect model, and were also

reported separately for healthy volunteers and patients with affective disorders. The Q-statistic was used to assess statistical heterogeneity. If statistical heterogeneity was significant, the effect sizes were pooled using a random-effects model. For each study, only one neurocognitive test per domain was used for the pooled analyses.

Publication bias was evaluated through visual inspection of funnel plots.

Results of the review

Twelve studies (n=539 participants) were included in the review, comprising six studies of 213 healthy volunteers and six studies of 326 patients with affective disorders. Eight studies used double-blind designs. Nine studies compared cognitive performance of individuals who received lithium with the cognitive performance of the same individuals when not taking lithium.

The meta-analysis of both healthy volunteers and patients with affective disorder showed small, but statistically significant impairments with the use of lithium in immediate verbal learning and memory (ES 0.24, 95% CI 0.05 to 0.43; 10 studies) and creativity (ES 0.33, 95% CI 0.02 to 0.64; three studies). There were no significant differences between participants who received lithium and those not receiving lithium in delayed verbal memory, immediate and delayed visual memory, attention, processing speed, executive function or psychomotor performance. There was evidence of statistical heterogeneity for immediate and delayed memory, processing speed and psychomotor performance.

For the analysis of patients with affective disorders, statistically significant impairments were observed with the use of lithium in immediate verbal learning and memory (ES 0.29, 95% CI 0.07 to 0.51; six studies), creativity (ES 0.34, 95% CI 0.00 to 0.68; two studies) and psychomotor performance (ES 0.62, 95% CI 0.27 to 0.97; two studies). There was no evidence of statistical heterogeneity.

There were no significant differences between healthy volunteers who received lithium and those who received a placebo for any of the cognitive domains examined, although there was some evidence of statistical heterogeneity for processing speed.

The authors stated that visual appraisal of the funnel plots showed no evidence of publication bias.

Authors' conclusions

Lithium carbonate had only mild negative effects on immediate verbal learning and memory and creativity, and a moderate adverse effect on psychomotor performance in patients with euthymic affective disorders.

CRD commentary

The review addressed a defined question and criteria for the inclusion of studies were stipulated. Appropriate databases were searched, but there were no attempts to identify unpublished literature, and dissertations were excluded from the review. This meant that there was a risk of publication bias. The restriction of the review to English-language studies meant that there was also the risk of language bias. Steps were taken to minimise errors and bias for study selection and data extraction.

There was a limited assessment of methodological quality, but it was unclear how this was undertaken, so the reliability of the results was not clear. There was some clinical heterogeneity in the enrolled population, which comprised both healthy volunteers and patients with affective disorders. In addition, the patients with affective disorder received treatment with lithium for longer durations than the healthy volunteers (for who the exposure to lithium was very short). For these reasons, pooling of the results across the trials may not have been appropriate. Patients with comorbid conditions were excluded from the review which raised questions about the applicability of the results to the general population of patients with affective disorders. The sample sizes in the included studies were small. Only one dose of lithium was used, so the findings may not be generalisable to other doses.

Some methodological flaws and the lack of information about the quality of the included studies means that the reliability of the results is unclear and the authors' conclusions should be interpreted with caution.

Implications of the review for practice and research

Practice: The authors did not state any implications for practice.

Research: The authors stated that research is required to evaluate the cognitive effects of other mood stabilisers, especially interactions with aspects of bipolar disorder itself including illness duration, episode counts and effects of acutely abnormal states and clinical euthymia.

Funding

American Psychiatric Institute of Research and Education; Bruce J Anderson Foundation; McLean Private Donors Research Fund.

Bibliographic details

Wingo AP, Wingo TS, Harvey PD, Baldessarini RJ. Effects of lithium on cognitive performance: a meta-analysis. *Journal of Clinical Psychiatry* 2009; 70(11): 1588-1597

PubMedID

19689922

DOI

10.4088/JCP.08r04972

Original Paper URL

http://article.psychiatrist.com/dao_1-login.asp?ID=10006163& amp;RSID=31044124315465

Indexing Status

Subject indexing assigned by NLM

MeSH

Cognition /drug effects; Cognition Disorders /diagnosis /drug therapy; Humans; Lithium Carbonate /pharmacology /therapeutic use; Neuropsychological Tests /statistics & numerical data; Psychomotor Performance /drug effects; Treatment Outcome

AccessionNumber

12010000725

Date bibliographic record published

23/06/2010

Date abstract record published

18/05/2011

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.