Cognitive side-effects of chronic antiepileptic drug treatment: a review of 25 years of research
Vermeulen J, Aldenkamp A P

Authors' objectives
To assess the cognitive side effects of long-term anti-epileptic drug treatments.

Searching
Computerised and manual searches of English language literature between January 1970 and December 1994 were made. DIMDI database (keywords 'AEDs' and 'anti-epileptic drugs') was searched; and bibliographies of several reviews were examined. The article had to be a report of original research in a peer reviewed journal or proceedings.

Study selection
Study designs of evaluations included in the review
Post-test only, single-group pre-test-post-test, parallel groups, crossover (with or without randomised treatment allocation).

Specific interventions included in the review
Long-term treatment with currently used anti-epileptic medication either in monotherapy or polytherapy modalities.

Participants included in the review
Patients with epilepsy receiving long-term anti-epileptic drug (AED) treatment (participants ranged from school age children to adults) and healthy volunteers.

Outcomes assessed in the review
Psychometrically-assessed cognitive functions were assessed.

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
The minimum methodological criteria were: the design of the study should be transparent; total number of participants assigned to each treatment group and number and type of cognitive variables should be given; statistical tests and data should be reported clearly. Studies failing to meet these criteria were included, but their findings were generally not given weight in the study. The authors do not state how the papers were assessed for validity, or 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 authors performed the data extraction.

Methods of synthesis
How were the studies combined?
The studies were combined in a narrative review, with tables giving the main characteristics of each study.

How were differences between studies investigated?
Different groups of study types were examined and reported separately: healthy volunteer studies, monotherapy studies,
polytherapy studies, studies with a non-randomised post-test only design, studies providing insufficient information. No
tests for heterogeneity were used, methodological and statistical issues were discussed.

Results of the review
Ninety-four articles representing 89 non-overlapping studies were included. The total patient numbers were not given.

No clear results were shown on the cognitive side-effects of chronic anti-epileptic drug treatment. This is due to the
paucity of studies meeting fairly basic standards of methodology, design and analysis that apply to the evaluation of any
clinical research. This severely limits the precision of statements regarding cognitive AED effects. If the available
database is reduced to monotherapy studies in epilepsy using control group data for comparison, employing an
appropriate form of repeated measures analysis and providing sufficient information, very few studies remain that are
directly relevant. This in itself precludes definitive conclusions. However, the tentative overall picture emerging from
the best of the research on cognitive AED effects is that differences in cognitive profiles may not be very large.

Authors’ conclusions
There is little reason to recommend any of the first-line AEDs as the AED of choice from the standpoint of cognitive
side-effects. The present review does not provide a straightforward answer as to whether AEDs in therapeutic doses
have any cognitive effects at all, good or bad. Any effects that may have been detected, however, appear to be small but
may be worth detecting as patients receive these drugs for years or decades. Ten recommendations are made by the
authors on improvement of methodology for future cognitive AED research.

CRD commentary
The review adequately states its objectives, interventions, participants, outcomes, search strategy, inclusion and validity
criteria, assessment of differences between the studies and results. The review lacks sufficient detail on the process by
which inclusion and validity criteria were applied and methods of data extraction. The results appear to accurately
reflect the evidence presented.

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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.