Neuropsychological outcomes after epilepsy surgery: systematic review and pooled estimates

CRD summary
The review concluded that epilepsy surgery was associated with specific cognitive changes, but may also improve cognition in some patients. Given the possibility of bias, limited and variable evidence of unknown quality and major methodological shortcomings in the review, the authors' conclusions should be treated with caution.

Authors' objectives
To assess the effects of epilepsy surgery on neuropsychological function.

Searching
PubMed, EMBASE and The Cochrane Library were searched for relevant studies published in English up to June 2008; search terms were reported. The reference lists of retrieved studies were also searched for additional studies. A second search of PubMed and PsycINFO was conducted in 2009.

Study selection
Eligible studies included a pre-post design of resective epilepsy surgery and contained original neuropsychological data with 20 or more participants; outcomes were measured by standardised tests. Studies were required to use empirically based methods for determining change (either reliable change index or standardised regression-based change scores) and to contain information on the percentage of patients that experienced outcomes. Studies interpreting significant changes based directly on the standard error of the mean or the standard deviation were excluded.

In the included studies, almost all studies involved patients with childhood-onset epilepsy and almost all involved surgical series with seizure-free rates approximating 70%, where reported. Most patients were adults, but two studies involved only children. The surgical approach included standard anterior temporal lobectomy, Spencer-type lobectomies, lobectomies sparing or removing superior temporal gyrus, hippocampus or lateral neocortex, selective amygdalohippocampectomy and lesionectomies with or without tailoring by language mapping or they were otherwise reported as temporal lobectomy. Studies used either standardised regression-based or the reliable change index; confidence intervals varied in the individual studies. Controls were either normative data, patients with intractable epilepsy, matched healthy controls, non operated epilepsy controls, patients on epilepsy surgery wait list or medically treated temporal lobe epilepsy patients. Cognitive domains included intelligence quotient (IQ; either full scale, verbal or performance), verbal memory, visual memory, naming, receptive language, executive functioning (either mental flexibility or word fluency), attention and overall multiple cognitive abilities.

The authors did not state how many reviewers selected studies for the review.

Assessment of study quality
The authors did not state whether studies were assessed for quality.

Data extraction
Data were extracted on the proportion of participants experiencing gains or losses in each individual cognitive domain, with separate estimates made for left and right surgery. Self reported subjective changes in cognitive domains were also extracted.

The authors did not state how many reviewers extracted data.

Methods of synthesis
Studies were pooled in meta-analyses using a random-effects model and summary weighted estimates for gains and losses and for left and right surgery for individual cognitive domains were calculated together with 95% confidence intervals (CIs). Where data were heterogeneous, medians were derived; these medians were found to be comparable to weighted averages. Self reported subjective changes in cognitive domains were described in narrative format and presented in a table. Heterogeneity was assessed with the Q statistic.
Results of the review
Twenty-three studies (2,012 patients) were included in the review.

IQ (four studies): Epilepsy surgery was associated with an average 11% loss and 16% gain in IQ for combined left and right surgical groups.

Memory (12 studies): In studies that reported results by side of surgery (eight studies), in left operated patients, the average rate of verbal memory decline was 44% (95% CI 34 to 55) versus 20% (95% CI 14 to 28) in right sided patients. Gains in verbal memory (seven studies) were 7% (95% CI 3 to 16) in left sided surgery and 14% (95% CI 7 to 27) in right sided surgery. For visual memory (six studies), average loss was 21% (95% CI 13 to 31) for left sided surgery and 23% (95% CI 18 to 29) for right sided surgery and average gain was 15% (95% CI 10 to 21) in left sided surgery and 10% (95% CI 7 to 13) in right sided surgery. In one study involving children where side of surgery was not reported, gains in verbal and visual memory were 10% and 25% of children, respectively and risks of loss were 5%.

Language (five studies): Average risk of decline in naming (four studies) was 39% (95% CI 32 to 47) for left sided surgery. Gain (one study) for right sided surgery was 4%. A loss of 4% in receptive comprehension of language was reported in one study of left sided surgery.

Executive functioning and attention outcomes (four studies): Left and right sided surgery were associated with a loss of 1% and 0% respectively (one study) and a gain of 9% and 4% (one study) in mental flexibility. Left and right sided surgery were associated with an average loss of 10% (95% CI 4 to 23; 3 studies) and 21% (two studies) respectively and an average gain of 27% (95% CI 10 to 55; 2 studies) and 16% respectively (two studies) in word fluency. In left and right sided surgery, two studies reported an average loss of 6% and 2% respectively and an average gain of 10% and 15% respectively in attention.

Overall subjective change in multiple abilities (three studies): Regardless of side of surgery, average overall loss was 9% and average overall gain was 18%.

Substantial heterogeneity was identified in all pooled estimates of verbal memory, average loss in left sided surgery for visual memory and most measures of word fluency.

Authors' conclusions
Epilepsy surgery was associated with specific cognitive changes, but may also improve cognition in some patients.

CRD commentary
The research question was clearly stated and was supported by appropriate inclusion criteria. A range of relevant sources was used to find studies published in English which increased the risk of language bias. No attempts were made to find unpublished studies, so studies may have been missed. The methods for data extraction and selection of studies were not reported, so reviewer error and bias could not be ruled out.

It appeared that studies were not assessed for quality, which makes it difficult to determine the reliability of the results. The methods used for measurement of outcomes were appropriate as they attempted to take into account test reliability and/or practice effects. The studies mostly had small sample sizes, none were randomised and the precision around the estimates (confidence intervals) not always reported, making it difficult to make comparative judgments on the effects of surgery. There was wide variation in the types of participants, controls, and surgical techniques used. The authors presented results as the average weighted change (either gain or loss) in a number of cognitive domains compared to control. The presentation of results in this way does not make it easy to reach conclusions on risk or benefit of epilepsy surgery.

Given the possibility of bias, limited and variable evidence of unknown quality and major methodological shortcomings in the review, the authors’ conclusions should be treated with caution.

Implications of the review for practice and research
Practice: The authors stated that, as epilepsy was a heterogeneous condition, an individualised approach was required for defining the risks and benefits of surgery that take into account both neurologic and neuropsychological risk factors. They also stated that screening with objective tests should be undertaken as surgical follow-up.
Research: The authors stated that multi centre outcome studies were needed of head to head comparisons of surgical techniques and more studies were required that assess attention, executive functioning and receptive language.

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