The role of 1H magnetic resonance spectroscopy in pre-operative evaluation for epilepsy surgery: a meta-analysis

CRD summary
This review found that magnetic resonance spectroscopy showing an abnormality on the same side as the epileptogenic zone has a good association with outcome following surgery. The review suffers from a number of methodological limitations, therefore these findings should be interpreted with extreme caution.

Authors' objectives
To determine the additional pre-operative value of $^1$H magnetic resonance spectroscopy (MRS) in identifying the epileptogenic zone (EZ) for epilepsy surgery.

Searching
MEDLINE (PubMed) was searched; the search terms were reported. Journals in which identified articles had been published were screened for additional studies, as were the reference lists of retrieved studies. Studies published in English between 1992 and July 2003 were eligible for inclusion. Studies published in paediatric journals were excluded.

Study selection
Prospective and retrospective studies that provided original data on the performance of proton interictal MRS, reported test results in detail for each individual patient, and that reported on surgical outcome based on the Engel classification or closely related criteria, were eligible for inclusion. Studies exclusively in children, patients with proven brain tumours, or patients with 'foreign tissue lesions' detected by magnetic resonance imaging (MRI) or proven by pathology, were excluded.

The studies used either chemical shift imaging or single-voxel spectroscopy, mostly at 1.5 tesla (T) although 2.0 and 4.1 T were also reported. Time of echo ranged from 50 to 272 milliseconds and time of repetition from 1.5 to 6 seconds. Chosen ratios or asymmetry indices were N-acetyl-aspartate (NAA)/choline (Cho) plus creatine-phosphocreatine (Cr), NAA/Cr, NAA/Cho, Cr/NAA and NAA alone. The reference standard was either site of surgery, Engel criteria, pathology, invasive electroencephalography (EEG), Engel criteria and MRI, or Engel criteria and invasive EEG. Classification for outcome following surgery was based on the Engel criteria, percentage reduction in seizure frequency, percentage reduction in seizures, or seizure frequency score. The duration of follow-up post surgery ranged from 3 to 78 months and the participants were aged from 3 to 66 years. All of the studies included patients with intractable temporal lobe epilepsy. Study design was either prospective or not reported.

The authors did not state how the papers were selected for the review, or how many reviewers performed the selection.

Assessment of study quality
The authors did not state that they assessed validity.

Data extraction
Data were extracted on the proportion of patients with ipsilateral MRS decrease concordant with the EZ and the proportion of patients with ipsilateral MRS decrease concordant with the EZ, who had a good outcome following surgery. Where possible, a 2x2 table was constructed, showing the number of patients with unilateral and bilateral MRS decreases against the number with Class I (seizure free) or Class II to IV (not seizure free) outcome following surgery. Odds ratios (ORs) were calculated from this table. Unilateral findings were defined as exclusively ipsilateral (presumable to the EZ, although this was not stated) or clearly lateralised. Patients showing normal or non significant results, bilateral results lateralised to the surgical side, or no changes on MRS were grouped as bilateral.

The authors did not state how many reviewers performed the data extraction.
Methods of synthesis
The proportion of patients with ipsilateral MRS decrease concordant with the EZ and the proportion of patients with ipsilateral MRS decrease concordant with the EZ who had a good outcome following surgery was summed across studies. Pooled ORs with 95% confidence intervals (CIs) were estimated across studies. Heterogeneity was assessed using the Q statistic.

Results of the review
Twenty-two studies were included in the review (596 patients of which 445 underwent surgery).

The proportion of patients with an ipsilateral MRS abnormality was 64% (13 studies, 267 patients) and the proportion with an ipsilateral MRS abnormality and a good outcome following surgery was 72% (12 studies, 201 patients).

The odds of being seizure free was almost five times greater among those with an ipsilateral MRS abnormality compared with those with bilateral MRS abnormalities (OR 4.89, 95% CI: 1.97, 12.17; based on 6 studies). The p-value for heterogeneity was not reported.

Authors' conclusions
MRS remains a research tool but has clinical potential. The review shows the relationship between ipsilateral MRS abnormality concordant with EZ and a good outcome following surgery.

CRD commentary
The review addressed a broad objective and inclusion criteria were not defined in terms of the population or reference standard. The electronic literature search was limited to MEDLINE/PubMed and the review was restricted to studies published in English. It is therefore possible that relevant studies have been missed and the review may be subject to language and publication bias. In addition, since the quality of the included studies was not assessed, their reliability is unclear. Details of the review process were not reported, so it is not possible to determine whether appropriate steps were taken to minimise bias and error. The analysis was confusing and difficult to interpret. Some relevant study details were tabulated, but there were very few details about the patients included in the primary studies or how the EZ was identified. Given the limitations highlighted, the authors' conclusions should be interpreted with extreme caution.

Implications of the review for practice and research
Practice: The authors stated that MRS remains a research tool.

Research: The authors stated the need for larger prospective studies in patients with non-localised ictal scalp EEG or in MRI-negative patients.

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