Authors' objectives
To determine the effectiveness of evoked potential (EP)-identified silent lesions in diagnosing multiple sclerosis (MS).

Searching
MEDLINE was searched for articles published between 1966 and January 1998, using the terms 'multiple sclerosis' and 'evoked potential'. The bibliographies of retrieved articles were also examined.

Study selection
Study designs of evaluations included in the review
No a priori inclusion criteria regarding the study design appears to have been used. However, the studies were graded according to the study design and other methodological characteristics. All included studies were graded as either II or IV: grade II incorporated a prospective design, while grade IV corresponded to expert opinion or case series without controls. The mean duration of follow-up varied from 12 to 36 months.

Specific interventions included in the review
EPs. Studies that did not employ standard EP techniques were excluded. All of the included studies appeared to use standard EP techniques, although the reviewers could not determine if they used institutionally established normal values or a 95 or 99% cut-off for abnormal.

Reference standard test against which the new test was compared
Any criteria used to measure clinically definite MS (CDMS) appears to have been considered for inclusion. Where stated, the criteria used by the included studies were those described by McDonald and Halliday (see Other Publications of Related Interest no.1), Schumacher et al. (see Other Publications of Related Interest no.2), McAlpine (see Other Publications of Related Interest no.3), or Poser et al. (see Other Publications of Related Interest no.4).

Participants included in the review
Studies of patients suspected of having MS were eligible for inclusion. The mean age of the included participants ranged from 27.5 to 43 years. One study excluded patients aged less than 15 or greater than 60 years. All studies describing gender reported a predominance of females.

Outcomes assessed in the review
No a priori inclusion criteria relating to the outcome measures appear to have been used. The outcome measures calculated in the review were the sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV).

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 reviewers performed the selection.

Assessment of study quality
The studies were graded from class I to IV using a diagnostic strength-of-evidence rating scheme, which was appended to the report. The authors do not state how the papers were assessed for validity, or how many of the reviewers 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.

The following information was abstracted from each study: reference details; the method and setting of the cohort assembly; the number of patients studied; duration of follow-up; the proportion (%) of patients developing CDMS; spectrum of disease; patient demographics (age and gender); and the criteria used to define CDMS. For each EP technique studied, the following parameters were calculated: sensitivity, specificity, PPV, NPV, the relative risk of developing CDMS (by dividing the PPV by the NPV) and its associated 95% confidence interval. An overall measure of the strength of the association between EP results and eventual CDMS was calculated using Goodman and Kruskal's tau (See Other Publications of Related Interest no.5).

Methods of synthesis
How were the studies combined?
The studies were combined in a narrative summary.

How were differences between studies investigated?
Differences between the studies were investigated in a narrative summary.

Results of the review
Nine studies with 892 patients were included.

The cohort assembly methods of studies varied: two studies selected consecutive MS suspects from patients referred to EP laboratories; one study was population-based; and the method could not be determined in another two studies. The number of MS suspects enrolled ranged from 21 to 222. The spectrum of the disease varied considerably.

The prospective design meant that the EPs in all studies were interpreted without knowing which patients develop CDMS. However, none of the studies were described as having used techniques to ensure that the EPs were interpreted without knowledge of the patients' clinical presentations. Many articles did not discuss the patients lost to follow-up.

The criteria used to diagnose CDMS appeared similar in most studies. The percentage of MS suspects that developed CDMS during the follow-up period ranged from 17 to 51%. There was a trend for studies with longer follow-up periods to have a higher frequency of CDMS.

Five studies were classed as Grade IV because it was not possible to determine if an acceptable 'gold' standard for diagnosing MS had been used, and/or it was not possible to calculate the strength of the EP-CDMS association and other parameters describing diagnostic accuracy. These studies were not considered in further analyses because of these serious methodological limitations.

Visual EPs (3 studies): an association between abnormal visual EPs and an increased risk of CDMS has been established with moderate clinical certainty.

Somatosensory EPs (4 studies): the evidence describing the relationship between abnormal somatosensory EPs and the development of CDMS was inconclusive and conflicting.

Brainstem auditory EPs (3 studies): the absence of a useful association between abnormal brainstem auditory EPs and an increased risk of CDMS has been established with moderate clinical certainty.

Multimodal EPs (2 studies): a slight gain in sensitivity from using multimodal EPs was offset by a greater loss in specificity.

Authors' conclusions
The impact of EPs on patient outcome remains unknown. No study demonstrated improved outcomes in MS suspects who receive EPs compared with MS suspects who do not.
CRD commentary
This was a diagnostic review of moderate quality. The objectives were clearly stated, but there were few details of any pre-specified inclusion or exclusion criteria. The literature search was very limited in that one electronic database was searched using only two search terms. This means that some important information may have been missed. In addition, there was no attempt to find unpublished data. Information about the methodology of the review process was not reported; for example, how decisions on the relevancy of the primary studies were made, whether more than one reviewer extracted the data, and how any discrepancies were resolved. The validity of the included studies was incorporated into a grading system, and poor-quality studies were excluded from the main analyses on which the conclusions were based. A narrative synthesis of the results was appropriate in view of the clinical heterogeneity between the included studies.

The authors’ conclusions appear to follow from the results.

Implications of the review for practice and research
Practice: The authors state that visual EPs are probably useful, and somatosensory EPs possibly useful, in identifying patients at increased risk for developing CDMS. The current evidence is insufficient to recommend brainstem auditory EPs as a useful test to identify patients at increased risk of developing CDMS.

Research: The authors state that current studies do not provide sufficient information to determine the independent contribution of diagnostic modalities employed in MS suspects. Future studies could include:

- longitudinal design with the development of CDMS, independent of paraclinical tests, as the independent 'gold' standard of MS;
- patients with possible and probable MS by clinical criteria, and patients with isolated optic neuritis;
- follow-up periods of at least 5 years;
- multivariate analyses to assist in determining the optimal combination and sequence of tests that best predict the development of CDMS; and
- subgroup analyses of MS suspects to determine which EPs are useful in which patients.

Bibliographic details

PubMedID
10802774

Other publications of related interest

Indexing Status
Subject indexing assigned by NLM
MeSH
Brain /physiopathology; Electroencephalography; Evidence-Based Medicine; Evoked Potentials /physiology; Humans; Multiple Sclerosis /diagnosis /physiopathology; Predictive Value of Tests

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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.