Evoked potentials are of little use in the diagnosis or monitoring of MS: Yes

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Proposal

The diagnosis of multiple sclerosis (MS) remains a clinical one but as no single presenting symptom is disease specific, evidence from paraclinical tests are generally sought to support the diagnosis. Evoked potentials (EP) once provided valuable information on dissemination in time and space when clinicians had few alternatives, but advances in neuroimaging and emerging technologies have made them of little use in the diagnosis and management of MS in the 21st century.

The diagnostic criteria for MS have evolved to reflect the utility and accuracy of emerging diagnostic tests. The Schumacher criteria1 were based primarily on clinical considerations. The later Poser criteria2 included paraclinical evidence: cerebrospinal fluid IgG, oligoclonal bands and EP. As a result, EP gained prominence in the diagnosis of MS, which was appropriate for the time. Advances since then, particularly in magnetic resonance imaging (MRI), mean that the role of EP in diagnosing and monitoring MS has greatly diminished.

In 2000 the Quality Standards Committee of the American Academy of Neurology published a practice parameter paper about the usefulness of EP in identifying clinically silent lesions and concluded that only visual evoked potentials (VEP) were ‘probably’ useful in this context, but found insufficient evidence to support the use of other types of EP.3 In July of the same year, the International Panel on MS Diagnosis, led by Professor W. Ian McDonald, first met to recommend updated guidelines for diagnostic criteria in MS, which acknowledged the contribution of MRI.4 It was proposed that the usefulness of VEP was restricted to those patients with insidious neurological progression suggestive of primary progressive MS (PPMS). Therefore, as this group accounts for only 10–15% of prevalent cases of MS, by the turn of this century, EP were already considered by this expert group of ‘little use’ in the majority of patients diagnosed with the condition. Subsequent revisions of these criteria in 20055 and 20106 have further relegated use of EP to very specific instances where the diagnosis is not secured using other clinical and paraclinical measures. In these later criteria the presence of disseminated lesions in space and asymptomatic gadolinium-enhancing lesions on the baseline MRI scan of a patient presenting with a clinically isolated syndrome (CIS) suggestive of a demyelinating event is sufficient for the diagnosis of MS, avoiding the need for any further investigations.

The counter argument is that these criteria apply only to ‘typical patients’ – those who present with the classical MS symptoms as a CIS – but that other investigations will be necessary to establish the diagnosis in the context of vague, atypical or multifocal symptoms, or in some uncommon MS subtypes such as PPMS. I agree that, in the scenarios described, current MRI protocols alone, even with additional evidence from positive oligoclonal bands in cerebrospinal fluid, may not be sufficient. Identifying clinically silent lesions, particularly in the visual pathway, would be valuable; however, as we gain more experience with the use of MRI to identify optic nerve lesions and optic atrophy this information should be available from a baseline MRI. The more widespread use of MRI techniques to identify grey matter lesions will, I believe, also assist in establishing the diagnosis in many of these cases.

Optical coherence tomography also appears to provide us with a reliable, cost-effective way of detecting clinically silent optic nerve involvement,7 but has the advantage over VEP of also providing longitudinal information on retinal nerve fibre layer thickness, which appears to correlate with brain volume loss.8

Perhaps the focus of the proposal thus far has been too narrow and limited to discussion of the use of VEP. Is there more to gain from utilizing multiple EP such as brainstem auditory and somatosensory (SSEP) evoked potentials early in the diagnostic work up? The role of a multimodal approach to evoked potentials (MMEP) has been studied. Pelayo et al.,9 in this journal, hypothesized...
that the use of MMEP in patients with CIS would provide further information on conversion risk to clinically definite MS and time to Expanded Disability Status Scale (EDSS) 3.0. In a sample of 245 CIS patients, only 8% had abnormalities identified in all three EP at baseline, which limited interpretation of the predictive value of MMEP in identifying patients at risk of developing disability, making it of ‘little’ use. Furthermore, when MRI was used as a covariate the study failed to identify a relationship between the number of abnormal EP and conversion to CDMS.

Therefore, as a clinician, I am convinced that EP are of little value in the diagnosis of MS, but those who feel strongly about continued use of the techniques will, I suspect, argue that EP will have an increasing role in monitoring or prognostication in patients with MS.

The addition of motor evoked potentials (mEP) to aid prognostic utility of MMEP has been evaluated in several studies. In a group of 50 patients with early relapsing–remitting MS, Schlaeger and colleagues\textsuperscript{10} correlated a study. In a group of 50 patients with early relapsing–remitting MS, Schlaeger and colleagues\textsuperscript{10} correlated a study failed to identify a relationship between the number of abnormal EP and conversion to CDMS.

The same group recently replicated this work in 22 patients with PPMS\textsuperscript{11} and demonstrated similar correlations. However, in the latter study the use of only upper limb mEP and tibial SSEP gave the same predictive value. These measurements were acknowledged by the authors to be markers of spinal cord pathology. We accept that spinal cord lesions on MRI correlate well with disability progression in this group, so I do not see this as a prognostic advance. Whilst producing interesting results, neither of these studies provides a strong argument for the use of MMEP in helping individualised disease progression. The number of patients in these studies was small and the results need to be replicated by larger groups. Also, one would like to see a direct comparison with the predictive value of measures of grey matter lesions and brain and spinal cord atrophy on MRI before recommending that time-consuming, labour-intensive, electrophysiological studies such as MMEP be used as outcome measures in therapeutic trials or as prognostic tools in clinical practice.

To conclude, having reviewed the evidence for EP both in the diagnosis and monitoring of MS, I propose that they are currently of little use.

**Conflict of interest**

Dr McGuigan has participated in advisory panels for Biogen Idec, Novartis and Genzyme and received honoraria from Bayer, Serono and Teva Pharmaceuticals.

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**References**


