Low-contrast multifocal visual evoked potentials

Identifying more shades of gray in MS

Matthew J. Thurtell, MBBS, FRACP
Steven L. Galetta, MD

Correspondence & reprint requests to Dr. Thurtell: mj.thurtell@gmail.com

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For 40 years, visual evoked cortical potentials (VEPs) have been used to aid in the diagnosis of demyelinating optic neuropathy.[1] Early studies demonstrated an increased latency of the positive peak normally seen at about 100 msec—the P100—in patients with optic neuritis.[1] Since the P100 often remains prolonged following recovery from the acute episode, the VEP is useful to detect optic nerve involvement in patients with suspected multiple sclerosis (MS).[2] One might posit that the VEP would be useful in the identification of subclinical optic neuropathy, in which the demyelination is so mild as to give no abnormal physical examination findings.[3]

Since many patients with MS have impaired contrast vision,[4] a modification of the traditional VEP technique has been proposed wherein the contrast between the shaded and white checks is reduced (figure).[5] One recent study comparing VEPs in response to 100% and 10% contrast pattern-reversal checkerboard stimuli found that P100 latencies were increased in response to low- vs high-contrast stimuli in patients with MS compared with normal controls.[5] VEP latencies correlated with low-contrast letter acuities and retinal nerve fiber layer (RNFL) thickness as measured by optical coherence tomography (OCT).[5] Of note, several patients had a VEP latency increase with only the low-contrast stimulus in an eye without a history of optic neuritis, suggesting that low-contrast VEPs might be more sensitive than conventional high-contrast VEPs for detecting subclinical optic neuropathy.[5]

The conventional "full-field" VEP provides a summed response from all neuronal elements stimulated and is dominated by the response from the macular region of the retina, due to its large cortical representation. Consequently, the full-field VEP is of limited value in detecting optic neuropathy in patients with small or more peripheral visual field defects. To overcome this limitation, "multifocal" techniques have been developed, allowing responses from multiple individual segments of the visual field to be evaluated simultaneously.[6] The central 24°–32° of the visual field is divided into 58–60 segments, each of which contains a 4 × 4 grid of black-and-white checks that reverse according to a pseudorandom sequence (figure). Analysis of the segmental waveforms allows for a topographic study of optic nerve function, whereby the latency and amplitude of the VEP in response to focal visual field stimulation can be evaluated. The multifocal VEP technique is sensitive and specific for the detection of demyelinating optic neuropathy.[6] Furthermore, the finding of multifocal VEP latency delays in patients with a history of optic neuritis predicts progression to MS.[7]

In this issue of *Neurology*®, Frohman et al.[8] describe a further refinement of the VEP paradigm, wherein multifocal VEPs were evaluated at 3 contrast levels: high contrast (100%), low contrast (33.3%), and very low contrast (14.2%). Normal subjects and patients with MS were studied. About half of the patients with MS had a history of unilateral optic neuritis, with a corresponding intereye asymmetry in low-contrast letter acuity and RNFL thickness. When compared with the multifocal VEP obtained using the 100% contrast stimulus, the amplitude obtained with the lower contrast stimuli was reduced in the patients with MS who had a history of optic neuritis.[8] Intereye asymmetry in multifocal VEP latency using the lower contrast settings was also increased in the patients with MS who had a history of optic neuritis.[8] The findings confirm that, in patients with a history of optic neuritis, the multifocal VEP amplitude and latency is contingent upon contrast level. The findings also suggest that low-contrast multifocal VEPs might identify subclinical optic neuropathy better than conventional VEP techniques.

Prior studies have compared the efficacy of several tests for identifying subclinical optic neuropathy in MS (including formal perimetry, contrast vision testing, MRI, optical coherence tomography, and high-contrast VEPs), but found that none of these reliably identified all eyes with subclinical optic neuropathy.[3]

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From the Departments of Ophthalmology and Visual Sciences (M.J.T.) and Neurology (M.J.T.), University of Iowa, Iowa City; and Department of Neurology (S.L.G.), University of Pennsylvania School of Medicine, Philadelphia.

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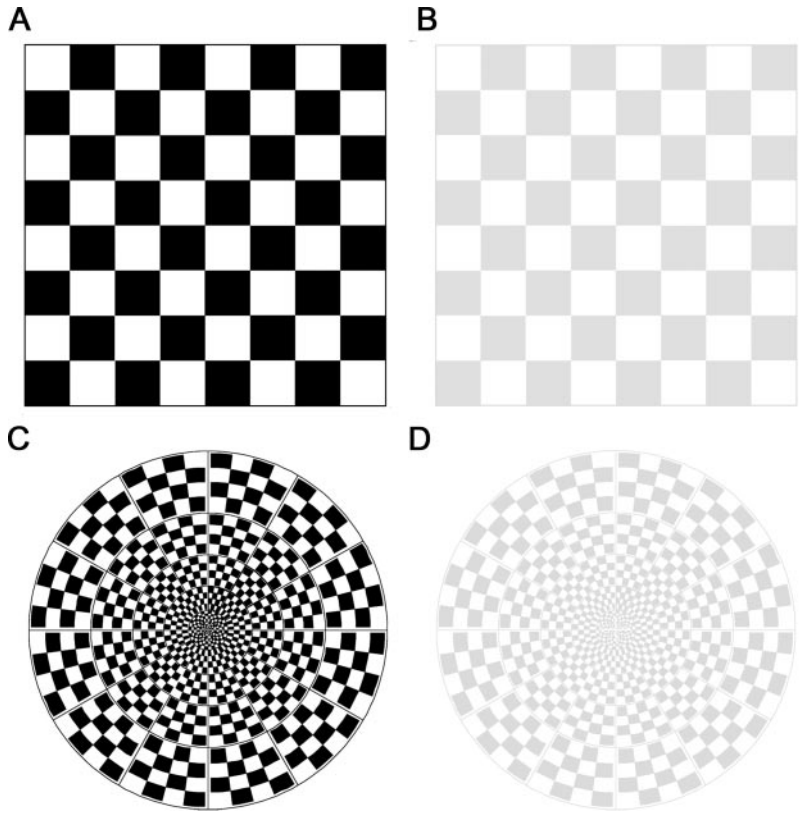
Figure Full-field and multifocal visual evoked potential stimuli



(A) High-contrast (100%) full-field pattern-reversal checkerboard stimulus. (B) Low-contrast (10%) full-field pattern-reversal checkerboard stimulus. (C) High-contrast (100%) multifocal dartboard pattern-reversal stimulus. Each segment is scaled according to cortical representation and contains a 4 × 4 checkerboard grid. (D) Low-contrast (10%) multifocal dartboard pattern-reversal stimulus.

Low-contrast multifocal VEPs may prove to be more sensitive than these other investigations for detecting subclinical optic neuropathy, but direct comparisons are required to clarify their role. Nonetheless, tests of structure and function may provide complementary information about the integrity of the optic nerve. A number of other issues remain unclear. One study reported that the magnitude of high-contrast multifocal VEP latency prolongation and amplitude decline in the fellow eye 12 months following an attack of optic neuritis was proportional to the risk of developing MS.[9] Low-contrast multifocal VEP latency prolongation and amplitude decline may prove to be even more predictive, but further study is necessary. In addition, low-contrast multifocal VEPs need to be studied longitudinally in patients with optic neuritis, to clarify the time course of improvement.[10] In recent years, new techniques have greatly augmented our ability to detect structural and functional changes in the eyes of patients with MS. Low-contrast multifocal VEPs may provide yet another quiver to our evolving visual testing armamentarium.

DISCLOSURE

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