

The Multifocal Pattern Visual Evoked Potential

The mfVEP provides an objective assessment of visual field loss and is still evolving with newer stimulus techniques.

BY STUART L. GRAHAM, MBBS, PhD, MS, FRANZCO, AND ALEXANDER KLITORNER, MD, PhD

The objective assessment of visual function remains a primary goal in glaucoma research due to the limitations of subjective tests. To date, the multifocal pattern visual evoked potential (mfVEP) is the only electrophysiological test capable of topographically mapping glaucomatous visual field defects.¹ Although the pattern electroretinogram (PERG) has been extensively studied and certainly reflects ganglion cellular loss, it tests only the central visual field and does not provide any topographic information. The photopic negative response has also recently been shown to be reduced in glaucoma, but it also provides only a single waveform for analysis.² For the mfVEP, employing cortically scaled pattern stimuli with appropriate electrode positions and multiple channels enables visual evoked potential (VEP) responses to be recorded from small areas of the field as far as 26° eccentricity. Many investigators have now verified this capability using different recording systems and techniques, and they have shown good correlation with subjective perimetric defects.³⁻⁷

The mfVEP technique has been refined during the last 15 years, with the addition of multiple channels, adjusted filter settings, electrode positions, different types of stimuli, and analysis of resulting waveforms. The goal has been to maximize signals and improve interpretation. Bipolar electrodes, placed near or straddling theinion, allow a larger response to be recorded than the conventional fronto-occipital electrode placements (where the upper hemifield responses are consistently smaller). Adding at least one pair of electrodes oriented at 90° (ie, horizontally) from the first pair allows detection of additional signals that are otherwise very small for the vertically oriented pair. Conventional VEPs have previously shown variable results in glaucoma patients, depending on the distribution of the field loss. An upper field defect, for example, may not produce a significant change in the signal on a conventional VEP² but is readily identified on a multichannel mfVEP.

RECORDING SYSTEMS

The electrophysiological method used is now similar in most systems. Investigators have used the VERIS Scientific system (Electro-Diagnostic Imaging, Redwood City, CA), the AccuMap (ObjectiVision, Sydney, Australia; no longer available commercially), the Retiscan system (Roland Instruments, Wiesbaden, Germany), MetroVision (MetroVision, Perenchies, France), or the SHIL Multifocal Imager (Scottish Health Innovations, Ltd., Glasgow, Scotland, United Kingdom). The visual stimulus is usually generated on a CRT screen (eg, 22-inch high-resolution display), but with faster refreshing rates, flat screens (LCD and plasma) can now be used. The most common stimulus consists of a dartboard pattern of 60 close-packed segments, the sizes of which are cortically scaled with eccentricity to stimulate approximately equal areas of cortical (striate) surface.⁸ The scaling would therefore be expected to produce a signal of a similar order of amplitude from each stimulating segment. I consider it essential to include in the analysis a means for removing the effects of alpha rhythm on the signal-to-noise ratio and to adjust for interindividual variability. Otherwise, specificity is reduced.

SENSITIVITY/PERFORMANCE

Sensitivity of the mfVEP in established glaucoma has been reported to be greater than 90%, depending on the criteria used to define abnormality and the degree of the glaucoma's severity.^{4,6,9-13} Signal amplitude is reduced in glaucoma, but mfVEP latency shows only minimal changes. Inter-eye asymmetry analysis is a useful technique for detecting early changes.^{9,14} The close proximity in the striate cortex of the signal generators for the right and left eyes' visual fields means that the signals are normally almost identical for the two eyes, assuming no other pathology or amblyopia. Interocular asymmetry analysis will not be reliable, however, in patients where symmetric field loss occurs between both eyes or for

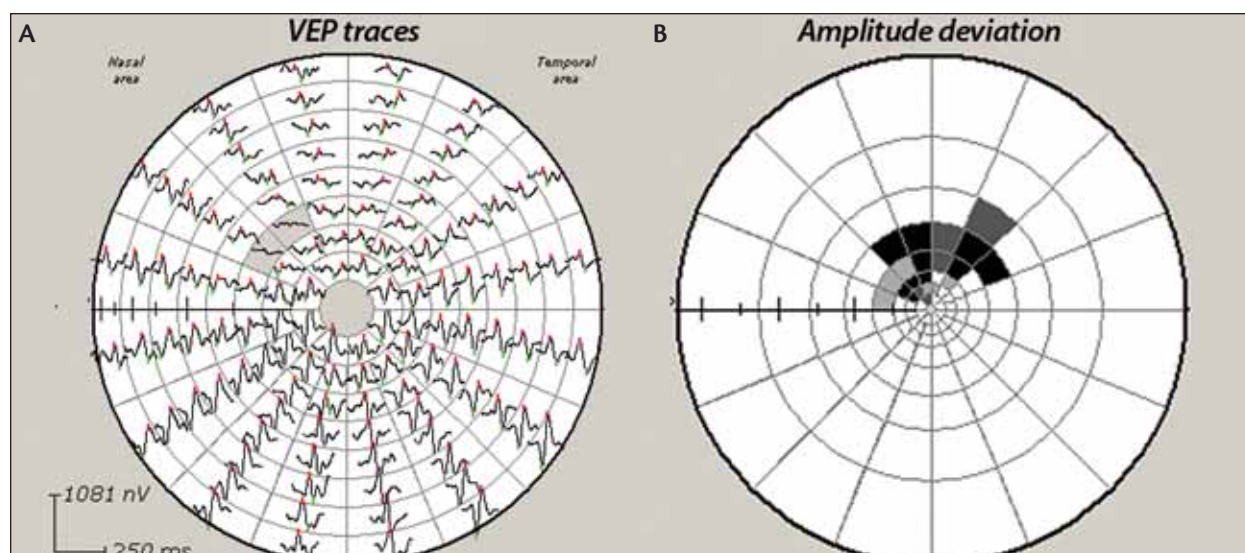


Figure 1. An example of a high-resolution mfVEP recorded with 120 test points from a patient with glaucoma who has a superior paracentral scotoma. A trace array (A). Preliminary amplitude deviation plot based on a sample of 30 normal subjects (B).

detecting damage in the less affected eye when one eye has more advanced loss. It is therefore necessary to examine both the monocular amplitude deviation and the interocular asymmetry in combination.

In a study by Fortune et al using the VERIS system¹⁵ of 185 individuals with high-risk ocular hypertension or early glaucoma (average standard automated perimetry [SAP] mean deviation, $+0.3 \pm 2.1$ dB; average point standard deviation, 2.3 ± 1.9 dB), the diagnostic performance of mfVEP was similar to that of SAP. This was true whether the diagnostic standard was a masked evaluation of stereo optic disc photographs or the HRT Moorfields Regression Analysis (Heidelberg Engineering GmbH, Heidelberg, Germany). SAP and mfVEP agreed in only approximately 80% of eyes, however, suggesting that these testing strategies may detect slightly different functional deficits.

Currently, the between-test amplitude variability of the mfVEP is 10% to 16%, and it is greatest in the zones with smaller signals. This limits the application of the data to progression analysis. Improved signal-to-noise ratios are needed to enable better reproducibility and the potential for serial analysis. Several studies are looking at repeatability, and they have implications for the technique's ability to be used in some form of progression analysis.^{16,17}

The mfVEP is not invasive, with only scalp electrodes required. No pupillary dilation, light adaptation, or shielding is required. Testing time is around 8 minutes per eye, with additional setup time for the electrodes' application. Cataract and visual blur can reduce central amplitudes,¹⁸ whereas the more peripheral points remain unaf-

fected. As for the PERG, the resultant mfVEP signal can be affected by other pathology, and an exclusion of retinal pathology is therefore needed. Clinicians must remember the mfVEP is not a specific test for glaucoma; it is effectively a field test with latency information.

NEW STIMULI FOR mfVEP

The possibility of simultaneous binocular (dichoptic) mfVEPs was recently realized using virtual reality goggles¹⁹ or with twin LCD screens split by 45° mirrors.²⁰ The advantage of a simultaneous binocular technique is that inter-eye comparisons are more valuable due to the identical recording and noise conditions for each eye. Limitations will remain, however, with patients who have underlying strabismus or another disparity in the fixation angle between their eyes. The use of a spatially sparse stimulation²¹ pattern has the potential to provide better signal-to-noise ratios, at least in the central field, and possibly greater sensitivity to early glaucoma.

Along with our colleagues, we recently reported on a high-resolution stimulus recording with 120 test zones of 3 X 3 checks arranged in eight rings (vs 4 X 4 checks in five rings for conventional mfVEP).²² The recordings showed slightly reduced variability across the field and improved scotoma definition (but not initial detection). Figure 1 shows a high-resolution mfVEP recording. We were pleased to find no loss of sensitivity despite the lower signal-to-noise ratio with small testing zones. The testing time was longer, however, so this technique may be reserved for eyes with small focal or paracentral defects due to its much better topographic definition.

A blue-on-yellow mfVEP has also been described using

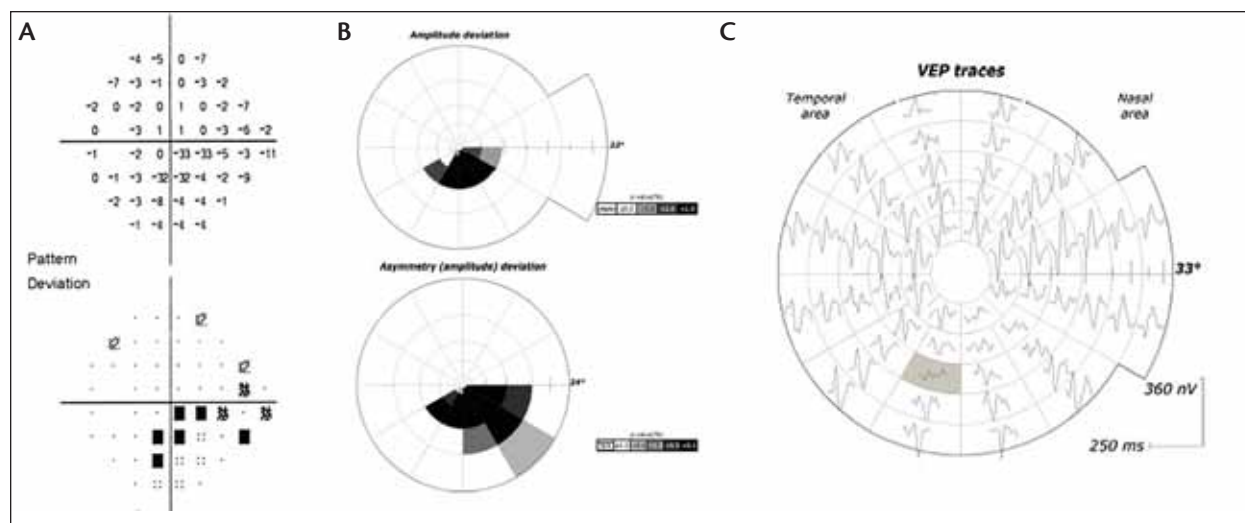


Figure 2. For this patient with glaucoma, an inferior paracentral scotoma is seen on pattern deviation of a Humphrey visual field test (Carl Zeiss Meditec, Inc., Dublin, CA) (A) and is shown on amplitude and asymmetry deviation plots of mfVEP (B). The raw mfVEP traces (combined multichannel recording) are shown (C).

a sparse blue pattern-onset stimulus (instead of pattern reversal) on a yellow-adapting background. The goal was to target the koniocellular pathway. This approach showed good sensitivity and displayed more extensive scotomata than the conventional black-white mfVEP (92.2% sensitivity), and it correlated well with SAP.^{23,24} The advantage of the blue-on-yellow stimulus over standard mfVEP, however, was probably more likely related to the fact that the pattern-onset stimulus was spatially sparse²⁵ (likely due to less lateral inhibition) and was of low luminance, both of which we have demonstrated may increase sensitivity.²⁶

CLINICAL APPLICATION

Unfortunately, no international standards are yet defined for the mfVEP (nor for any other forms of VEP other than transient flash and pattern). Moreover, a recent review somewhat negatively stated that the mfVEP “is perhaps best regarded as a promising research tool.”²⁷ We have been using the mfVEP regularly in our clinic for the last 8 years, however, and although it does not replace SAP in routine testing, the modality has several useful roles. Figure 2 provides an example of an inferior field defect that is confirmed on mfVEP testing.

In clinical assessment, the mfVEP supports the subjective field findings and is most helpful in equivocal or variable cases. It helps to rule out excessive field loss in patients who have trouble with perimetric testing (false positives). In some early or high-risk glaucoma cases, mfVEP may detect functional damage earlier than other measures. Less commonly but very impor-

tantly, when the results of both subjective and objective tests are out of proportion to changes in the optic disc, alternative pathology may be at play. The physician should therefore consider obtaining magnetic resonance imaging. The mfVEP is very helpful in non-organic vision loss and medicolegal cases. It can also be extremely useful in other optic neuropathies such as optic neuritis,²⁸⁻³¹ where the test has been used to monitor outcomes and the likelihood of progression to multiple sclerosis.

The mfVEP is easy for patients to perform, even the first time, and it has a high level of acceptance among patients. It is likely that mfVEP testing will continue to evolve in the future as an objective means of monitoring individuals with glaucoma. With improved signal detection, greater reproducibility, and shortened testing times, mfVEP will provide clinicians with a valuable adjunct for assessing visual function in glaucoma. □

Stuart L. Graham, MBBS, PhD, MS, FRANZCO, is a professor of ophthalmology and visual science at the Australian School Advanced Medicine, Macquarie University, and the Save Sight Institute, Sydney University. He holds patents for technology licensed to Objectivision Pty Ltd. Dr. Graham may be reached at +61 2 98123933; stuart.graham@asam.mq.edu.au.



Alexander Klistorner, MD, PhD, is an associate professor of visual science at the Australian School Advanced Medicine, Macquarie University, and the Save Sight Institute, Sydney University. He holds patents for technology licensed to Objectivision Pty Ltd.

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COVER STORY

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