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. 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 provides only a single waveform for analysis. For the mfVEP, employing cortical-ly 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 26º eccentricity. Many investigators have now verified this capability using different recording systems and techniques, and they have shown good correlation with subjective perimetric defects.

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 the inion, 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 90º (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 VEP but is readily identified on a multichannel mfVEP.

The mfVEP provides an objective assessment of visual field loss and is still evolving with newer stimulus techniques.
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 system 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, $2.3 \pm 1.9$ 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, whereas the more peripheral points remain unaffected. 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 MF VEP**

The possibility of simultaneous binocular (dichoptic) mfVEPs was recently realized using virtual reality goggles or with twin LCD screens split by 45º mirrors. 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 stimulation 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 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).
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 importantly, 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.

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