

# Multifocal VEP in patients with optic nerve disease

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## Abstract

• **AIM:** To determine whether the multifocal visual evoked potential (mfVEP) can be used as a clinical method to assess the patients with optic nerve disease.

• **METHODS:** Fifteen patients with optic nerve disease were examined in this study. All patients underwent visual acuity examination, slit-lamp inspection, ophthalmoscopy, Goldmann perimeter, fundus fluorescein angiography, visual field and mfVEP. Although these patients with unilateral optic nerve damage, data from both eyes were included in the analysis.

• **RESULTS:** In all patients the visual fields defect was demonstrated on the mfVEP and showed good correspondence in location of the scotoma. However, we also found some slight difference between visual field and mfVEP. In some locations, when the local visual fields were normal, mfVEP showed that its amplitude reduced. In reverse, when the local mfVEP seemed normal, visual field showed abnormality.

• **CONCLUSION:** Multifocal visual evoked potential could be used as a clinical diagnosis option in patients with optic nerve disease. Local monocular damage to the optic nerve can be measured by an interocular comparison of the mfVEP.

• **KEYWORDS:** optic nerve disease; multifocal visual evoked potential

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## INTRODUCTION

The visual evoked potential (VEP) has traditionally been an important method in the diagnosis of optic nerve disease. There have been several reports on VEP abnormalities in optic nerve disease [1-3]. However, the conventional pattern VEP is predominantly generated by cortical elements receiving projections from the central retina. Therefore, it had limited ability to reflect field loss in non-central areas.

One recently proposed candidate is the multifocal visual

evoked potential (mfVEP) technique described by Baseler and his colleagues [4]. They showed that 60 or more local VEP responses could be obtained over a wide retinal area if the stimulus array was scaled. However, they concluded that intersubject variability was too great to make this technique viable for clinical field test.

Klistorner argued that if the recording electrodes were judiciously placed, then mfVEP responses could be recorded from most field locations and the technique could be used to detect local field defects. In particular, they showed that there was qualitative agreement between Humphrey visual field defects and regions of diminished mfVEP responses in patients with ganglion cell and/or optic nerve damage [5-7].

Although the mfVEP responses differ among individuals, the mfVEP responses from both eyes of the same individual should be very similar. It was suggested that interocular comparisons and asymmetry analysis between eyes within subjects to overcome the problem of intersubject variability [8-12].

The development of mfVEP give us a new method to diagnose the optic nerve disease. The purpose of this study was to investigate the ability of mfVEP to identify optic nerve damage and detect the focal visual field loss in patient with unilateral optic nerve disease.

## MATERIALS AND METHODS

**Subjects** The study included 15 patients (8 male, 7 female) ranging in age from 22 to 63 years (mean, 47 years). Of these, 6 had primary open angle glaucoma (POAG), 2 had normal tension glaucoma (NTG), 3 had ischemic optic neuropathy (ION), 2 had optic neuritis, and 2 had optic atrophy. Ophthalmological examinations, besides mfVEP, included assessment of visual acuity, slit-lamp inspection, ophthalmoscopy, Goldmann perimeter, fundus fluorescein angiography (FFA) and visual field. The visual fields were performed with automated perimeter (Octopus 101, Interzegg INC, Switzerland). Although these patients had unilateral optic nerve damage, data from both eyes were included in the analysis (Table 1).

**Stimulus** The stimulus array was produced with VERIS software (Dart Board 60 With Pattern) from EDI (vision 4.0, Electro-Diagnostic Imaging, San Mateo, CA). The stimulus (Figure 1) consisted of 60 sectors, each with 16 checks, 8 white (200cd/m<sup>2</sup>) and 8 black (<1cd/m<sup>2</sup>). The entire display had a diameter of 26°. The stimulus array was displayed on a black and white monitor driven at a frame rate of 75Hz. The

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**Table 1 Clinical characteristics and examination results in 15 monocular patients with different types of optic nerve disease**

<i>n</i>	Age (yr)	Sex	eye	visual acuity	Visual Field (MD)	Diagnosis
1	47	female	OS	20/30	-12.4	POAG
2	40	male	OD	20/60	-8.7	POAG
3	54	female	OS	20/30	-18.4	POAG
4	52	male	OD	20/20	-5.2	POAG
5	62	female	OD	20/25	-9.4	POAG
6	60	female	OS	20/30	-11.9	POAG
7	50	female	OD	20/25	-10.6	NTG
8	34	male	OD	20/100	-12.2	NTG
9	57	female	OD	20/50	-14.5	ION
10	54	male	OS	20/30	-9.8	ION
11	55	male	OD	20/50	-11.5	ION
12	33	female	OD	20/60	-22.5	Optic Neuritis
13	26	male	OS	20/100	-18.8	Optic Neuritis
14	63	male	OD	20/200	-20.5	Optic Atrophy
15	22	male	OD	20/100	-14.4	Optic Atrophy

monitor had a resolution of 1024×3768 pixels, and the check inside the smallest sector had an average of approximately 20 pixels. The 16-element checkerboard of each sector had a probability of 0.5 of reversing on any new frame change and the pattern of reversals for each sector followed a pseudorandom m-sequence with a sequence length of  $2^{14}$  steps.

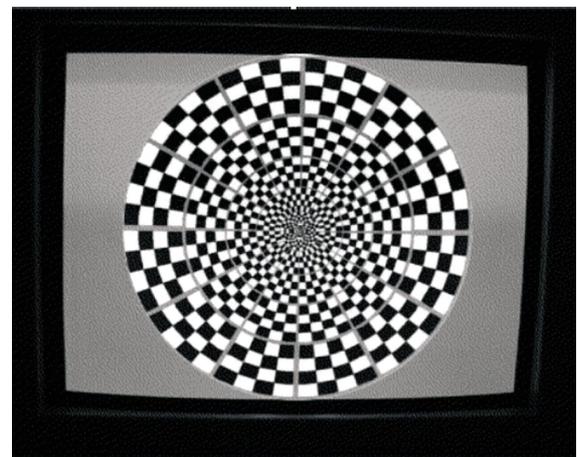
**Recordings** A bipolar electrode (Figure 2) was placed 2cm above the inion described by Klistoner *et al* [5]. To obtain a mfVEP, the continuous VEP record was amplified with the low- and high-frequency cutoffs set at 3 and 100 Hz and it was sampled at 100 000 times. The m-sequence had  $2^{14}$ -1 elements and required approximately 13.3 minutes for a single run. The records presented in the figures are the average of two of these runs. To improve the subject's ability to maintain fixation, the run was broken up into overlapping segments, each lasting approximately 27 seconds. Second-order local response components were extracted by using VERIS4.0 software from EDI.

**Analysis** For the purpose of the analysis, the results of mfVEP and visual field from two eyes were compared and analyzed.

### RESULTS

In our study, we observed that mfVEP could detect local optic nerve damage and resemble the local visual field defects. We also observed that in some regions the results of mfVEP were not always consistent with the visual field. In some locations, when the local visual fields were normal, mfVEP showed that its amplitude reduced. In reverse, when the local mfVEP seemed normal, visual field showed abnormality. However, when we performed asymmetric analysis, there were clear differences between the mfVEP responses of the two eyes and correspondence with the visual field defects.

**Comparison between mfVEP and Visual Fields** Figure 3 shows the mfVEP records from a 47-year-old female with

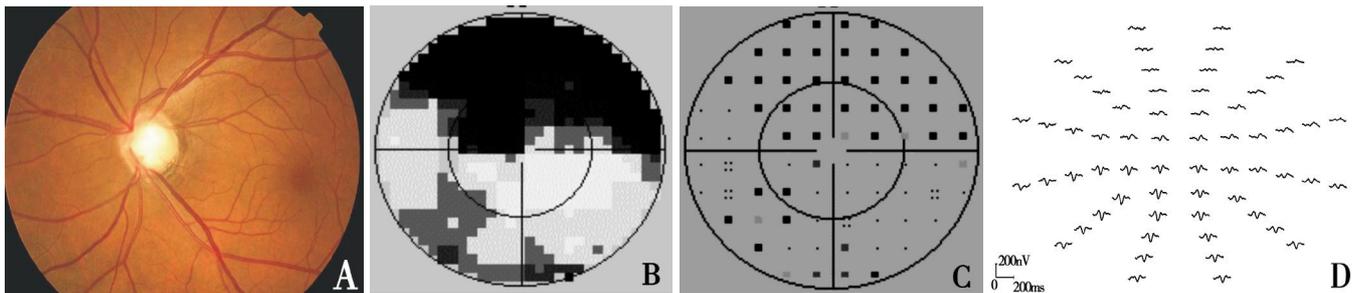


**Figure 1 Photograph of the stimulus display for the mfVEP recordings**

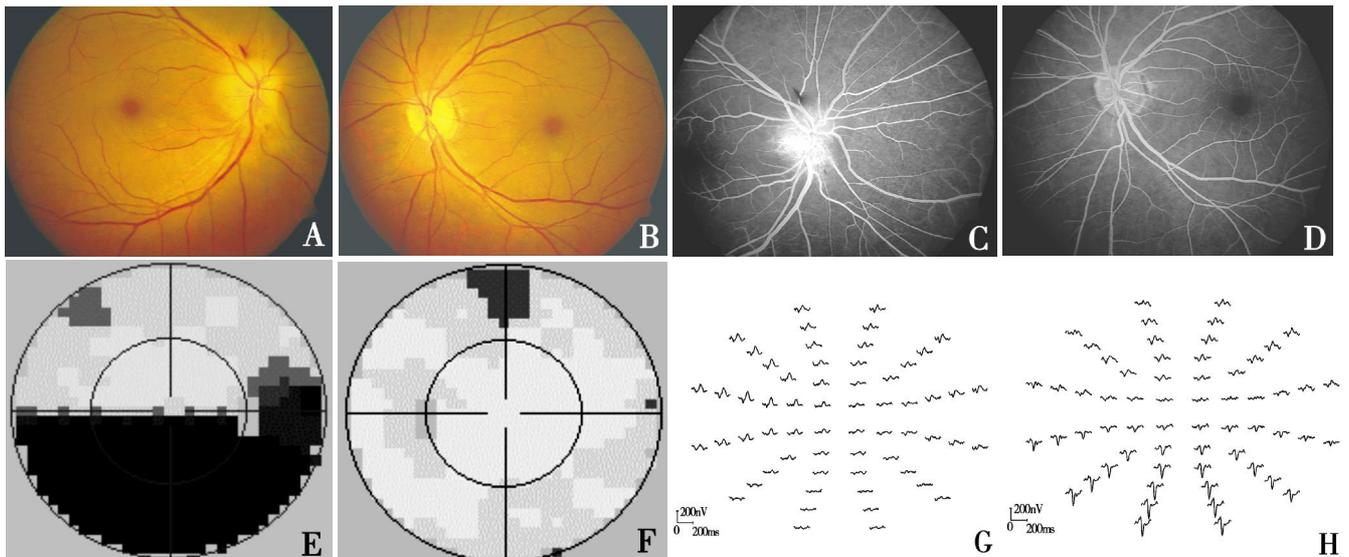


**Figure 2 Photograph of a 30 years control performing the mfVEP test**

primary open angle glaucoma (POAG). Her visual acuity was 20/20 in the right eye and 20/30 in the left eye. She was performed fundus photography (Figure 3A), subjective perimetry (Figure 3B,C), and mfVEP (Figure 3D). Her mfVEP waves were compared and analyzed with visual field. A reproducible absolute mfVEP defect involving the superior



**Figure 3** There is good correspondence between mfVEP and visual field defects A:The fundus picture of left eye; B:The visual field of left eye; C:The visual field of left eye; D:The mfVEP of left eye



**Figure 4** A reproducible absolute mfVEP defect involving the inferior field of the right eye was noted comparing with the left eye, which was consistent with the findings of the visual field A:The fundus picture of right eye; B: The fundus picture of left eye; C: Early-phase fluorescein angiography showed a delay of dye filling in the superior part of the right optic discs; D: The fluorescein angiography of left eye is normal; E: The visual field of right eye; F: The visual field of left eye; G:The mfVEP of right eye; H: The mfVEP of left eye

field of the left eye was noted (Figure 3D), which was consistent with the findings of the visual field (Figure 3B,C).

**Comparing the mfVEP from Two Eyes** Figure 4 shows the mfVEP records from a 57-year-old female with ischemic optic neuropathy (ION). Her visual acuity was 20/50 in the right eye and 20/20 in the left eye. She was performed fundus photography and FFA (Figure 4A-D), subjective perimetry (Figure 4E,F), and mfVEP (Figure 4G,H). Her mfVEP waves from two eyes were compared and analyzed with visual field. A reproducible absolute mfVEP defect involving the inferior field of the right eye was noted comparing with the left eye (Figure 4G,H), which was consistent with the findings of the visual field (Figure 4E,F).

#### DISCUSSION

As a new clinical electrophysiology technique, mfVEP can detect and resemble local field defects secondary to disease of the ganglion or optic nerve. It had been reported in much clinic study.

However, the intersubject variability of mfVEP was limited to make this technique viable for clinical field test. There are many aspects resulting in the variability such as age and sex,

cortical convolution, position of the calcarine fissure relative to external landmarks (inion), conductivity of underlying tissue, general level of brain activity, and stimulus conditions. The major source of variability among individual is cortical anatomy<sup>[4,5,13,14]</sup>.

Although the mfVEP responses differ among individuals, Hood argued the mfVEP responses from both eyes of the same individual should be very similar if both eyes are healthy. The points in the visual field fall on different hemi-retinas of the two eyes, and they project to the same cortical location. If the monocular mfVEP responses from the two eyes of control subjects are reasonably similar, then a comparison of the two monocular mfVEP recordings from patients may allow the detection of early and localized damage of the ganglion cells or optic pathway<sup>[8,15]</sup>. In our study, we observed that mfVEP can detect local optic nerve damage and resemble the local visual field defects. It confirmed this conclusion.

In conclusion, mfVEP can detect local VEP changes and resemble visual field defects. It is advantageous to study optic nerve disease and glaucoma that affect local regions of

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ganglion cells [15-18]. However, individual variations are so great that the mfVEP technique would not be useful for clinical field test by comparing monocular mfVEP responses. In the future, we should conduct study to a large cluster to help define abnormal regions and develop specially designed indices to help in identifying results that are not verified. We still have to overcome problems of variability of signal with different electrode placements, determine normal population variability, and assess the effect of visual acuity, age, and other diseases on the responses [19-24]. Of course, mfVEP provides a breakthrough in assessing the optic nerve disease and is a major advance toward our goal of objective mapping of the visual field.

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