Multifocal Visual Evoked Potential in Eyes With Temporal Hemianopia From Chiasmal Compression: Correlation With Standard Automated Perimetry and OCT Findings

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PURPOSE. To verify whether multifocal visual evoked potential (mfVEP) can differentiate eyes with temporal hemianopia due to chiasmal compression from healthy controls. To assess the relationship between mfVEP, standard automated perimetry (SAP), and Fourier domain-optical coherence tomography (FD-OCT) macular and peripapillary retinal nerve fiber layer (RNFL) thickness measurements.

METHODS. Twenty-seven eyes with permanent temporal visual field (VF) defects from chiasmal compression on SAP and 43 eyes of healthy controls were submitted to mfVEP and FD-OCT scanning. Multifocal visual evoked potential was elicited using a stimulus pattern of 60 sectors and the responses were averaged for the four quadrants and two hemifields. Optical coherence tomography macular measurements were averaged in quadrants and halves, while peripapillary RNFL thickness was averaged in four sectors around the disc. Visual field loss was estimated in four quadrants and each half of the 24-2 strategy test points. Multifocal visual evoked potential measurements in the two groups were compared using generalized estimated equations, and the correlations between mfVEP, VF, and OCT findings were quantified.

RESULTS. Multifocal visual evoked potential–measured temporal P1 and N2 amplitudes were significantly smaller in patients than in controls. No significant difference in amplitude was observed for nasal parameters. A significant correlation was found between mfVEP amplitudes and temporal VF loss, and between mfVEP amplitudes and the corresponding OCT-measured macular and RNFL thickness parameters.

CONCLUSIONS. Multifocal visual evoked potential amplitude parameters were able to differentiate eyes with temporal hemianopia from controls and were significantly correlated with VF and OCT findings, suggesting mfVEP is a useful tool for the detection of visual abnormalities in patients with chiasmal compression.

Keywords: multifocal visual evoked potential, standard automated perimetry, optical coherence tomography, band atrophy of the optic nerve, chiasmal compression, temporal hemianopia
VF defects from previous chiasmal compression and reduced amplitude measurements, finding a good level of agreement with SAP VF defects. Jayaraman\textsuperscript{15} tested four patients with active chiasmal compression and found reduced mfVEP amplitude and prolonged latency in patients compared with controls. Qiao et al.\textsuperscript{18} also found an agreement between mfVEP and VF findings, but sample size and disease status (active compression versus previously treated patients) were not reported.

Another way of evaluating the performance of objective mfVEP perimetry is to correlate mfVEP findings with measurements of structural fundus abnormalities obtained with optical coherence tomography (OCT), as has already been done for patients with glaucoma, optic neuritis, and MS.\textsuperscript{10,23–25} In this regard, in patients with longstanding chiasmal compression, temporal VF defects and normal nasal VF, retinal neural loss is restricted to (or predominant in) the nasal hemiretina, providing a good model for structure–function studies.\textsuperscript{26,27} In such eyes, peripapillary retinal nerve fiber layer (RNFL) loss also occurs in a specific pattern (mostly on the nasal and temporal sides of the optic disc) usually referred to as band atrophy (BA) of the optic nerve.\textsuperscript{28} Retinal and optic nerve neural loss may be adequately quantified with OCT and is well correlated with SAP VF defects.\textsuperscript{1,3,29–32} To our knowledge, only Qiao et al.\textsuperscript{18,20} have evaluated the relationship between mfVEP and OCT-measured peripapillary RNFL loss in patients with pituitary adenoma, but macular thickness measurements were not obtained. Because macular measurements can be averaged in quadrants, they are likely to provide better correlations with mfVEP loss (which can also be averaged in quadrants) than are peripapillary optic disc RNFL assessments; in fact, most sectors of the disc receive fibers from ganglion cells corresponding to both the nasal and the temporal quadrant.\textsuperscript{20,53}

The purpose of this study was therefore to evaluate the ability of mfVEP measurements to differentiate eyes with temporal hemianopia from healthy controls and to evaluate the correlation between mfVEP and VF loss on SAP. In addition, we investigated the spatial correlation between mfVEP and Fourier-domain (FD) OCT quadrantic macular and optic nerve thickness measurements in the same sample of patients.

METHODS

Subjects

Twenty-seven eyes from 21 patients (12 male) with temporal VF defects and 43 healthy eyes from 23 controls (15 male) were studied. All patients had been treated for suprasellar tumors and had stable VF defects at least 1 year prior to study entry. Patients were excluded using magnetic resonance imaging (MRI) to confirm the diagnosis of tumor compressing the optic chiasm and to document effective optic pathway decompression after treatment.

The subjects underwent a complete ophthalmologic examination, including VF evaluation by SAP. Among the inclusion criteria for the study were best-corrected VA of 20/30 or better in the study eye, within ±5 diopters (D) for the most ametropic meridian, and IOP of less than 22 mm Hg, and reliable VE. Patients were required to have complete or partial temporal VF defect and a nasal hemifield within normal limits on SAP.

In 15 patients, only one eye met the inclusion criteria; in the other six patients, both eyes qualified and were enrolled in the study. The controls consisted of healthy volunteers with normal ophthalmic examination and normal VE. In the first three controls, only one randomly selected eye was included in the study. However, to increase sample size, we decided to include both eyes in the remaining 20 controls and use statistical methods to compensate for intereye dependency. The study followed the principles of the Declaration of Helsinki and was approved by the institutional review board. All participants gave their informed written consent.

Visual Field Testing

Visual field testing was done with the 24-2 SITA-Standard strategy (Humphrey Field Analyzer, Carl-Zeiss Meditec, Dublin, CA, USA) and a Goldmann size III stimulus. The reliability criteria were false-positives and false-negatives or fixation losses of less than 30%. Patients with BA were required to have complete or partial temporal hemianopia and a nasal hemifield within normal limits. The severity of VF defects in patients with BA was estimated for 50 test points (excluding 2 points immediately above and below the blind spot), in an area roughly equivalent to the area tested by mfVEP.

Multifocal Visual Evoked Potential

Multifocal visual evoked potential response was elicited with a pattern stimulus of 60 cortically scaled sectors and recorded using checkerboard screens with a 27° visual angle and the RETiscan System (Roland Consult, Wiesbaden, Germany) and a Goldmann size III stimulus. The reliability criteria were false-positives and false-negatives or fixation losses of less than 30%. Patients with BA were required to have complete or partial temporal hemianopia and a nasal hemifield within normal limits. The severity of VF defects in patients with BA was estimated for 50 test points (excluding 2 points immediately above and below the blind spot), in an area roughly equivalent to the area tested by mfVEP.

Multifocal VEP and OCT in Chiasmal Compression

METHODS

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complete the acquisition protocol. The total time of attendance was between 45 and 90 minutes for each subject.

The patient was instructed to look at a target (a text) at the center of the screen during acquisition. The mfVEP responses were recorded in four channels (BC-CD-AD-BD) with gold disc electrodes, as described by Hood et al., except for the position of the ground electrode.

One of the recording electrodes (reference) was placed at the inion, the other (active) 4 cm above the inion, in the vertical midline. Two lateral electrodes were placed along a line 1 cm above the inion, at 4 cm to the left or right of the vertical midline. The ground electrode was placed on the Cz anatomic location in the midline, as described by the International Society for Clinical Electrophysiology of Vision.34

With impendence below 5 kΩ. Using the best responses from four channels, the equipment’s software mathematically generated a fifth channel plot response filtered using digital signal processor. The responses from this channel were then analyzed. No follow-up visits were required; all recordings were made during a single session.

The 60 waveforms of mfVEP response obtained in our study were characterized by two negative peaks, N1 (at 75 ms) and N2 (at 135 ms), and one positive peak, P1 (at 100 ms), similar to the pattern of VEP response, although of smaller amplitude. In order to correlate mfVEP response with VF data, after exclusion of the 12 peripheral sectors, the amplitude and latency of the average mfVEP response were determined for 48 responses, subdivided into groups of 24 sectors for the nasal hemifield (NH) and temporal hemifield (TH), and groups of 12 sectors for the superotemporal (ST), supenorinal (SN), inferotemporal (IT), and inferonasal (IN) quadrants (Figs. 2A-B) and plotted for comparison with the 24-2 SAP test points (Figs. 2C-D). These measurements were labeled ‘global mfVEP parameters’. We also assessed mfVEP responses in a 10° central circle (the 24 central responses of the mfVEP) corresponding to an area of 8° containing 24 central mfVEP responses. Labeled ‘central mfVEP parameters’, these were also estimated in quadrants and hemifields (Figs. 2D, 2F). Finally, we calculated the intraocular temporal/nasal response ratios using both the TH and the NH as well the temporal and nasal hemifield 10° central responses. Figures 3A and 3B show the response disposition for 24-2 SAP and mfVEP represented in the fundus photography. Amplitude and peak time measurements were automatically calculated by the equipment’s software after detection of the potential with the most significant amplitude at a peak time of roughly 100 ms. Manual adjustment of the automatic peak selection was used when needed. The values of the above mentioned quadrants and hemifields were averages calculated by the equipment based on our selection of individual responses for each set of measurements.

### Fourier-Domain OCT Scanning

On the same day of the ophthalmic evaluation, the subjects underwent FD-OCT raster scanning of the ONH region and macular area using a three-dimensional (3D) OCT-1000 (Topcon Corp., Tokyo, Japan). The scanning protocol used in this study involved the acquisition of a set of three high-definition OCT images of the ONH and macula in a raster pattern covering a 6 × 6-mm area (Figs. 3C-D) with a scan density of 512 × 128 pixels in approximately 3.5 seconds (27,000 A-scans/sec). To be deemed acceptable, images should display consistent signal intensity across the scan and include no large eye movements (defined as an abrupt shift completely disconnecting a large retinal vessel) or black bands (result of blinking) throughout the scan.

Peripapillary RNFL and macular thickness parameters were automatically calculated with the software provided by the manufacturer. Macular thickness measurements were registered according to an overlaid OCT-generated checkerboard with 36 checks. The macular thickness parameters were subsequently averaged separately for each of the four quadrants (9 checks per quadrant) of the macular area: average ST, IT, SN, and IN response (Fig. 3E). The average thickness of the macula and of each hemiretina (18 nasal and 18 temporal checks) and a ratio between the nasal and the temporal hemiretina measurements were also calculated. In addition, thickness measurements were taken using a circular (0 = 3.4 mm) RNFL peripapillary map drawn around the ONH when measuring the average thickness (360°), and the ONH measurements divided into 12, 30° sectors (Fig. 3F). Based on earlier studies correlating the VF with the position of the RNFL in the optic disc head, we expected the retinal ganglion cell (RGC) axons in the areas stimulated by mfVEP to enter the optic disc in the 270° sector comprised of the nine 30° segments between the 5 o’clock meridian and the 1 o’clock meridian.

### Data Analysis and Statistics

The descriptive statistics included mean values ± SD for normally distributed variables and median, first quartile, third quartile, and interquartile ratio (IQR) for nonnormally distributed variables. The distribution of the data was tested using the Kolmogorov-Smirnov test for normality.

The mfVEP and FD-OCT parameters of the two groups of eyes were compared with generalized estimating equation (GEE) models to compensate for the fact that some patients and controls had both eyes included. As eyes of the same individual were expected to have some degree of intercorrelation with respect to VF, mfVEP, and OCT parameters, GEE models were used to adjust for within-patient intereye correlations. Receiver operating characteristic (ROC) curves were used to describe the diagnostic power of mfVEP and OCT parameters. DeLong et al.’s method35 was used to compare the areas under the ROC curves (AROCs).

Visual field loss on the SAP 24-2 test was calculated as mean deviation based on the average total deviation plot of each quadrant (12 test points for temporal quadrants and 13 test points for nasal quadrants) and hemifield (26 test points for the nasal and 24 for the temporal hemifield) in the logarithmic (dB) scale (Figs. 1D–E). The average mean deviation parameters from the 24-2 test were subdivided into temporal mean defect (TMD), nasal mean defect (NMD), ST mean defect, IT mean defect, SN mean defect, and IN mean defect.

To investigate peripapillary RNFL loss in a disc area corresponding to the area stimulated by mfVEP and SAP, we calculated the average FD-OCT–measured RNFL thickness for four disc sectors. The average thickness of the superior + temporal sectors (10, 11, 12, and 1 o’clock meridians) and the inferior + temporal sectors (8, 7, 6, and 5 o’clock meridians) were expected to correlate with the mfVEP and VF measurements of the quadrants nasal to the fovea. The average RNFL thickness measurements of the superotemporal (but closer to the horizontal meridian) area (the average of the 9, 10, and 11 o’clock meridians) and the inferotemporal area (the average of the 9, 8, and 7 o’clock meridians) were expected to correlate with the mfVEP and VF measurements of the quadrants temporal to the fovea. We also determined the FD-OCT parameters of the four macular quadrants. To better assess the correlation between OCT-measured macular thickness parameters and mfVEP, the 24 central responses were averaged for the 12 central nasal hemifield (cNH) responses and the 12 central temporal hemifield (cTH) responses, the central...
FIGURE 2. Top row: representation of the 50 test points (excluding one above and one below the blind spot) evaluated on SAP and averaged for each quadrant (A) and hemifield (B). Middle row: schematic indication of 48 mfVEP responses averaged for each quadrant (C) and hemifield (D). Bottom row: representation limited to the central 24 mfVEP responses averaged for each quadrant (E) and hemifield (F). Quadrants and hemifields are represented in different shades of gray.
FIGURE 3. Top row: Demarcation of points read on 24-2 SAP (A) and 60 responses scaled approximately on mfVEP (B). Middle row: demarcation of areas in the macula (C) and optic nerve (D) scanned by FD-OCT. Bottom row: schematic representation of a macular thickness map (left) and RNFL thickness (right) of a normal individual.
**RESULTS**

A total of 27 eyes with temporal hemianopia and 43 control eyes were studied. The mean age ± SD was 52.5 ± 8.6 years for BA patients, and 50.1 ± 6.0 years for healthy subjects (P = 0.28; Student’s t-test). All patients had pituitary adenoma. On SAP 24-2, 10 eyes had complete temporal hemianopia, 15 had partial temporal VF defects greater than one VF quadrant, and 2 had a defect of less than one quadrant. The mean SAP 24-2 MD, TMD, and NMD ± SD were -7.22 ± 4.90, -15.09 ± 2.08, and -1.04 ± 0.18, respectively. The ST mean defect, SN mean defect, IT mean defect and IN mean defect in the different quadrants were -16.60 ± 1.98, -0.93 ± 0.19, -13.57 ± 2.25, and -1.16 ± 0.21, respectively. A comparison between VF parameters of BA eyes and controls revealed a significant difference in all parameters (P < 0.01). Fundoscopic examination revealed signs of BA of the optic disc in all 27 eyes with temporal VF defect.

Table 1 shows 24-2 mfVEP median, first quartile, and third quartile amplitudes in eyes with BA and controls, both as global mfVEP response (average of 24 responses) and as central mfVEP response (average of 6 responses). In all temporal mfVEP parameters (both global and central hemifields as well as in temporal quadrants), the mean P1 and N2 amplitude was significantly smaller in BA patients than in normals. No significant difference was observed between the two groups regarding mfVEP recordings in the nasal parameters. The ROC curve analysis indicated that the three best-performing mfVEP amplitude parameters were the TH/NH N2 amplitude ratio (AROC = 0.92), the cTH/cNH N2 amplitude ratio (AROC = 0.92), and the TH/NH P1 amplitude ratio (AROC = 0.89).

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### TABLE 1. Median Values (IQR) of mfVEP Amplitude in 27 Eyes With BA of the Optic Nerve and 43 Healthy Control Eyes With ROC Curves

<table>
<thead>
<tr>
<th>Parameter</th>
<th>BA Eyes, n = 27</th>
<th>Controls, n = 43</th>
<th>P Value*</th>
<th>ROC Area (SE)</th>
<th>Abnormal/Normal Eyes†</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Global mfVEP Amplitude (µV)</strong></td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>NH P1</td>
<td>0.15 (0.09-0.22)</td>
<td>0.16 (0.12-0.22)</td>
<td>0.273</td>
<td>0.57 (0.07)</td>
<td>5/27</td>
</tr>
<tr>
<td>(24 responses) N2</td>
<td>0.27 (0.18-0.37)</td>
<td>0.30 (0.23-0.39)</td>
<td>0.259</td>
<td>0.57 (0.07)</td>
<td>6/27</td>
</tr>
<tr>
<td>TH P1</td>
<td>0.10 (0.06-0.15)</td>
<td>0.15 (0.11-0.22)</td>
<td>0.002</td>
<td>0.75 (0.06)</td>
<td>11/27</td>
</tr>
<tr>
<td>(24 responses) N2</td>
<td>0.15 (0.08-0.21)</td>
<td>0.27 (0.20-0.36)</td>
<td>0.001</td>
<td>0.79 (0.06)</td>
<td>15/27</td>
</tr>
<tr>
<td>ST quadrant P1</td>
<td>0.10 (0.06-0.13)</td>
<td>0.13 (0.10-0.18)</td>
<td>0.003</td>
<td>0.73 (0.06)</td>
<td>10/27</td>
</tr>
<tr>
<td>(12 responses) N2</td>
<td>0.13 (0.08-0.18)</td>
<td>0.25 (0.18-0.32)</td>
<td>&lt;0.001</td>
<td>0.81 (0.06)</td>
<td>14/27</td>
</tr>
<tr>
<td>IT quadrant P1</td>
<td>0.09 (0.07-0.17)</td>
<td>0.17 (0.13-0.25)</td>
<td>0.003</td>
<td>0.74 (0.06)</td>
<td>14/27</td>
</tr>
<tr>
<td>(12 responses) N2</td>
<td>0.15 (0.07-0.25)</td>
<td>0.30 (0.23-0.43)</td>
<td>0.002</td>
<td>0.79 (0.06)</td>
<td>17/27</td>
</tr>
<tr>
<td>SN quadrant P1</td>
<td>0.10 (0.09-0.19)</td>
<td>0.14 (0.10-0.18)</td>
<td>0.475</td>
<td>0.93 (0.07)</td>
<td>4/27</td>
</tr>
<tr>
<td>(12 responses) N2</td>
<td>0.24 (0.15-0.32)</td>
<td>0.27 (0.18-0.35)</td>
<td>0.306</td>
<td>0.57 (0.07)</td>
<td>5/27</td>
</tr>
<tr>
<td>IN quadrant P1</td>
<td>0.17 (0.10-0.23)</td>
<td>0.18 (0.14-0.25)</td>
<td>0.183</td>
<td>0.59 (0.07)</td>
<td>5/27</td>
</tr>
<tr>
<td>(12 responses) N2</td>
<td>0.32 (0.18-0.43)</td>
<td>0.32 (0.24-0.45)</td>
<td>0.238</td>
<td>0.57 (0.07)</td>
<td>7/27</td>
</tr>
<tr>
<td><strong>Amplitude ratio</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Temp/Nasal P1</td>
<td>0.68 (0.50-0.81)</td>
<td>0.95 (0.84-1.08)</td>
<td>&lt;0.001</td>
<td>0.89 (0.04)</td>
<td>18/27</td>
</tr>
<tr>
<td>(24 responses) N2</td>
<td>0.53 (0.36-0.71)</td>
<td>0.94 (0.82-1.06)</td>
<td>&lt;0.001</td>
<td>0.92 (0.04)</td>
<td>21/27</td>
</tr>
<tr>
<td><strong>Central mfVEP Amplitude (µV)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>cNH P1</td>
<td>0.18 (0.09-0.25)</td>
<td>0.21 (0.16-0.29)</td>
<td>0.09</td>
<td>0.62 (0.07)</td>
<td>8/27</td>
</tr>
<tr>
<td>(12 responses) N2</td>
<td>0.32 (0.19-0.45)</td>
<td>0.38 (0.26-0.50)</td>
<td>0.10</td>
<td>0.62 (0.07)</td>
<td>9/27</td>
</tr>
<tr>
<td>cTH P1</td>
<td>0.12 (0.06-0.19)</td>
<td>0.19 (0.13-0.28)</td>
<td>&lt;0.001</td>
<td>0.80 (0.05)</td>
<td>12/27</td>
</tr>
<tr>
<td>(12 responses) N2</td>
<td>0.13 (0.07-0.24)</td>
<td>0.34 (0.23-0.47)</td>
<td>&lt;0.001</td>
<td>0.82 (0.05)</td>
<td>15/27</td>
</tr>
<tr>
<td>cST quadrant P1</td>
<td>0.12 (0.06-0.14)</td>
<td>0.19 (0.12-0.24)</td>
<td>&lt;0.001</td>
<td>0.79 (0.05)</td>
<td>12/27</td>
</tr>
<tr>
<td>(6 responses) N2</td>
<td>0.14 (0.09-0.23)</td>
<td>0.34 (0.22-0.43)</td>
<td>&lt;0.001</td>
<td>0.84 (0.05)</td>
<td>15/27</td>
</tr>
<tr>
<td>cIT quadrant P1</td>
<td>0.10 (0.06-0.19)</td>
<td>0.22 (0.15-0.31)</td>
<td>&lt;0.001</td>
<td>0.80 (0.06)</td>
<td>14/27</td>
</tr>
<tr>
<td>(6 responses) N2</td>
<td>0.13 (0.06-0.26)</td>
<td>0.37 (0.28-0.54)</td>
<td>&lt;0.001</td>
<td>0.81 (0.06)</td>
<td>17/27</td>
</tr>
<tr>
<td>cSN quadrant P1</td>
<td>0.16 (0.11-0.24)</td>
<td>0.39 (0.20-0.45)</td>
<td>&lt;0.001</td>
<td>0.87 (0.06)</td>
<td>14/27</td>
</tr>
<tr>
<td>(6 responses) N2</td>
<td>0.26 (0.18-0.45)</td>
<td>0.37 (0.23-0.45)</td>
<td>0.18</td>
<td>0.58 (0.07)</td>
<td>7/27</td>
</tr>
<tr>
<td>cIN quadrant P1</td>
<td>0.20 (0.11-0.26)</td>
<td>0.23 (0.17-0.32)</td>
<td>0.05</td>
<td>0.65 (0.07)</td>
<td>5/27</td>
</tr>
<tr>
<td>(6 responses) N2</td>
<td>0.36 (0.20-0.45)</td>
<td>0.40 (0.29-0.55)</td>
<td>0.07</td>
<td>0.63 (0.07)</td>
<td>9/27</td>
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<td><strong>Amplitude ratio</strong></td>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T/N ratio P1</td>
<td>0.61 (0.46-0.83)</td>
<td>0.95 (0.80-1.09)</td>
<td>&lt;0.001</td>
<td>0.87 (0.04)</td>
<td>18/27</td>
</tr>
<tr>
<td>(12 responses) N2</td>
<td>0.55 (0.32-0.70)</td>
<td>0.92 (0.78-1.07)</td>
<td>&lt;0.001</td>
<td>0.92 (0.03)</td>
<td>20/27</td>
</tr>
</tbody>
</table>

* GEE, Significant values are in italics.
† BA eyes below the lower 10th percentile.

Supertemporal (cST) quadrant, the central superonasal (cSN) quadrant, the central inferotemporal (cIT) quadrant, and the central inferonasal (cIN) quadrant (6 responses each).

Spearman rank correlation coefficients were used to assess possible associations between mfVEP, OCT, and VF parameters. To compare the diagnostic power of mfVEP and OCT, we investigated eyes labeled as normal or abnormal in each test. The proportion of eyes defined as abnormal (below the lower 10th percentile of normal eyes) was calculated for each measurement for both mfVEP and OCT and compared using McNemar’s test. Because both multiple comparisons and correlations were performed, the level of statistical significance was set at a conservative less than 0.01. Significance at P < 0.001 was also estimated. The statistical analyses were performed with the software SPSS v.20.0 (SPSS Inc., Chicago, IL, USA) and MedCalc v.17.5.3 (MedCalc Software, Mariakerke, Belgium).
Peak time was also calculated for patients and controls. In eyes with BA, the average peak time (ms) ± SD for P1 in the average 24 nasal (NH) and temporal subsets (TH) and the 12 average responses of the ST, IT, SN, and IN subsets were 100.83 ± 6.12, 103.02 ± 1.12, 104.25 ± 1.27, 101.79 ± 1.21, 101.51 ± 1.36, and 100.16 ± 1.46, respectively. The corresponding values for control eyes were 100.78 ± 1.00, 100.71 ± 0.99, 102.22 ± 1.21, 99.20 ± 0.91, 101.30 ± 1.27, and 100.26 ± 0.90. No significant difference was found between the two groups. Average peak time measurements (ms) ± SD for N2 in the average 24 nasal and temporal subsets and the 12 average responses in the ST, IT, SN, and IN subsets in BA eyes were 151.03 ± 1.55, 154.87 ± 1.35, 155.77 ± 1.22, 153.97 ± 1.85, 151.11 ± 1.65, and 150.96 ± 1.71, respectively. The corresponding values for controls were 151.41 ± 1.17, 150.87 ± 1.24, 152.27 ± 1.38, 149.46 ± 1.24, 151.60 ± 1.17, and 151.23 ± 1.35. No significant difference was found in N2 peak time values between control eyes and eyes of patients with BA in any comparison. Nor were any significant differences observed between patients and controls when central mfVEP responses in quadrants and hemifields were analyzed.

Table 2 shows the results of the comparison between OCT RNFL and macular thickness measurements in BA and normal eyes. All measurements were significantly smaller in BA eyes than in normals. The ROC curve analysis indicated that the best-performing OCT parameter was the nasal/temporal macular ratio for the average macular thickness measurements (AROC = 1.0) followed by the macular SN quadrant (AROC = 0.98) and average nasal macular thickness (AROC = 0.98).

A comparison between the AROCs with mfVEP and OCT parameters showed no significant difference (P > 0.01) between the three largest AROCs of the two devices except for the comparison between the nasal/temporal macular thickness ratio and the TH/NH P1 amplitude ratio (P = 0.008).

Tables 1 and 2 also show the proportion of eyes labeled as abnormal eyes based on the normative average estimated using the 10th percentile of normal on mfVEP and OCT. Under these conditions, the best discrimination of abnormality on mfVEP was the nasal/temporal ratio of 24 N2 (21/27) and P1 (18/27) amplitude responses, the temporal/nasal ratio of 12 central N2 (20/27) and P1 (18/27) amplitude responses, the average of 12 N2 amplitudes in the IT quadrant (17/27), the average of six N2 amplitudes in the cIT quadrant (17/27) and the average of six P1 amplitudes in the cIT quadrant (17/27). On OCT, nasal/temporal macular thickness measurements ratio (27/27), average macular thickness in the SN quadrant (26/27), the IN quadrant (24/27), and the nasal average (24/27) provided the best discrimination of abnormality. No significant difference was observed between the above-mentioned best-performing mfVEP and OCT parameters (P > 0.05, McNemar’s test). Because VD defect was an inclusion criterion in the study, the ability of mfVEP and OCT to detect it was not evaluated.

Table 3 shows the associations between global mfVEP amplitude measurements and VF loss based on the 50 points of the subjective VF (in dB). Statistically significant correlations were found for most temporal VF and mfVEP parameters, especially between temporal hemianopic or quadrantic mfVEP N2 amplitude measurements and temporal VF deviations from normal (range, 0.42–0.60). The most significant correlation was found between IT N2 amplitude and the VF deviation from normal in the IT quadrant (P = 0.60; P < 0.001), followed by the correlation between N2 amplitude in the TH, and VF deviation from normal in the IT quadrant (P = 0.59; P < 0.001), or VF TMD (P = 0.58; P < 0.001) (Table 3; Fig. 4).

Table 4 shows the correlations between peripapillary RNFL thickness measurements and mfVEP P1 and N2 responses based on the 48 points and the correlation between quadrantic or hemianopic macular thickness and mfVEP amplitude measurements based on the 24 central mfVEP responses. Statistically significant correlations were found for most average temporal and macular N2 amplitudes on mfVEP and temporal RNFL thickness (range, 0.32–0.54) and average nasal macular thickness parameters (range, 0.31–0.54). Highly significant correlations were found between TH/NH or cTH/NH P1 and N2 amplitude responses and peripapillary RNFL thickness measurements (range, 0.37–0.58) or the nasal macular thickness parameters or the nasal/temporal thickness ratio (range, 0.50–0.58). When mfVEP and OCT parameters were compared, the most significant correlations were found between the TH/NH amplitude N2 wave (P = 0.58; P < 0.001), average central temporal N2 amplitude on mfVEP and SN macular thickness (P = 0.46; P < 0.001), followed by the correlation between central ST quadrant or temporal hemifield N2 amplitude and average nasal macular thickness (P = 0.45 for both; P < 0.001) (Table 4; Fig. 4).
DISCUSSION

Our results show that several mfVEP amplitude parameters were significantly reduced in the temporal hemifield and quadrants in eyes with BA and VF than in normal control eyes. Because all eyes had permanent temporal VF defects and established BA of the optic nerve, the finding of reduced mfVEP P1 and N2 responses indicates that mfVEP was effective...
at detecting visual abnormalities in this group of patients. The absence of abnormality in nasal hemifield and nasal quadrant mfVEP measurements is consistent with the SAP findings because our patients were required to have a normal nasal VF examination to be included in the study. Our results confirm the findings of previous investigations showing reduced mfVEP amplitude responses in patients with VF defects from compressive optic pathway disease, 13–18 and are supported by studies showing reduced mfVEP amplitude measurements in eyes with VF defects from glaucoma, 37,8,24,56 ischemic optic neuropathy, 37 and optic neuritis 3–11,38 reinforcing the notion that objective perimetry with mfVEP is a useful method of visual assessment, particularly in uncooperative or inattentive patients in whom SAP VF testing may yield unreliable results.

While mfVEP amplitude responses were significantly reduced in temporal areas of the VF in our patients, no significant difference in peak time response was observed between patients and controls. Prolonged mfVEP latencies have been observed in patients with optic neuritis and demyelinating disease 3–11,38 and active compressive lesions affecting different regions of the optic 12,14,15,17,21. We believe the normal latencies observed in active compressive lesions affecting different regions of the Nerve and 43 Healthy Control Eyes

### Table 4. Correlation Between mfVEP Amplitude and Peripapillary RNFL or Macular Thickness Measurements in 27 Eyes With BA of the Optic

<table>
<thead>
<tr>
<th>Average Peripapillary RNFL Thickness</th>
<th>NH P1</th>
<th>NH N2</th>
<th>TH P1</th>
<th>TH N2</th>
<th>TH/NH Ratio P1</th>
<th>TH/NH Ratio N2</th>
<th>SN Quadrant P1</th>
<th>SN Quadrant N2</th>
<th>IN Quadrant P1</th>
<th>IN Quadrant N2</th>
<th>ST Quadrant P1</th>
<th>ST Quadrant N2</th>
<th>IT Quadrant P1</th>
<th>IT Quadrant N2</th>
</tr>
</thead>
<tbody>
<tr>
<td>10, 11, 12, and 1 o’clock</td>
<td>0.11</td>
<td>0.16</td>
<td>0.35</td>
<td>0.46</td>
<td>0.52</td>
<td>0.58</td>
<td>0.02</td>
<td>0.13</td>
<td>0.19</td>
<td>0.17</td>
<td>0.27</td>
<td>0.44</td>
<td>0.40</td>
<td>0.48</td>
</tr>
<tr>
<td>8, 7, 6, and 5 o’clock</td>
<td>0.20</td>
<td>0.23</td>
<td>0.13</td>
<td>0.52</td>
<td>0.51</td>
<td>0.57</td>
<td>0.16</td>
<td>0.24</td>
<td>0.21</td>
<td>0.21</td>
<td>0.41</td>
<td>0.54</td>
<td>0.42</td>
<td>0.52</td>
</tr>
<tr>
<td>9, 10, and 11 o’clock</td>
<td>0.18</td>
<td>0.22</td>
<td>0.32</td>
<td>0.41</td>
<td>0.37</td>
<td>0.43</td>
<td>0.15</td>
<td>0.23</td>
<td>0.19</td>
<td>0.21</td>
<td>0.29</td>
<td>0.42</td>
<td>0.34</td>
<td>0.42</td>
</tr>
<tr>
<td>9, 8, and 7 o’clock</td>
<td>0.19</td>
<td>0.19</td>
<td>0.34</td>
<td>0.41</td>
<td>0.41</td>
<td>0.49</td>
<td>0.15</td>
<td>0.19</td>
<td>0.19</td>
<td>0.19</td>
<td>0.32</td>
<td>0.43</td>
<td>0.34</td>
<td>0.42</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Average Macular Thickness</th>
<th>cNH P1</th>
<th>cNH N2</th>
<th>cTH/cNH Ratio P1</th>
<th>cTH/cNH Ratio N2</th>
<th>cSN Quadrant P1</th>
<th>cSN Quadrant N2</th>
<th>cIN Quadrant P1</th>
<th>cIN Quadrant N2</th>
<th>cST Quadrant P1</th>
<th>cST Quadrant N2</th>
<th>cIT Quadrant P1</th>
<th>cIT Quadrant N2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Temporal half</td>
<td>0.21</td>
<td>0.21</td>
<td>0.35</td>
<td>0.37</td>
<td>0.32</td>
<td>0.36</td>
<td>0.17</td>
<td>0.22</td>
<td>0.21</td>
<td>0.22</td>
<td>0.31</td>
<td>0.36</td>
</tr>
<tr>
<td>Nasal half</td>
<td>0.25</td>
<td>0.26</td>
<td>0.47</td>
<td>0.51</td>
<td>0.52</td>
<td>0.58</td>
<td>0.18</td>
<td>0.22</td>
<td>0.29</td>
<td>0.25</td>
<td>0.44</td>
<td>0.52</td>
</tr>
<tr>
<td>ST quadrant</td>
<td>0.20</td>
<td>0.20</td>
<td>0.34</td>
<td>0.35</td>
<td>0.32</td>
<td>0.43</td>
<td>0.16</td>
<td>0.21</td>
<td>0.22</td>
<td>0.17</td>
<td>0.29</td>
<td>0.34</td>
</tr>
<tr>
<td>IT quadrant</td>
<td>0.21</td>
<td>0.22</td>
<td>0.34</td>
<td>0.35</td>
<td>0.30</td>
<td>0.45</td>
<td>0.18</td>
<td>0.24</td>
<td>0.18</td>
<td>0.20</td>
<td>0.52</td>
<td>0.36</td>
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<tr>
<td>SN quadrant</td>
<td>0.22</td>
<td>0.25</td>
<td>0.44</td>
<td>0.48</td>
<td>0.51</td>
<td>0.58</td>
<td>0.15</td>
<td>0.20</td>
<td>0.26</td>
<td>0.22</td>
<td>0.41</td>
<td>0.50</td>
</tr>
<tr>
<td>IN quadrant</td>
<td>0.26</td>
<td>0.26</td>
<td>0.48</td>
<td>0.51</td>
<td>0.50</td>
<td>0.57</td>
<td>0.20</td>
<td>0.23</td>
<td>0.28</td>
<td>0.25</td>
<td>0.46</td>
<td>0.54</td>
</tr>
<tr>
<td>Temp/nasal ratio</td>
<td>0.20</td>
<td>0.23</td>
<td>0.44</td>
<td>0.49</td>
<td>0.53</td>
<td>0.58</td>
<td>0.14</td>
<td>0.17</td>
<td>0.25</td>
<td>0.23</td>
<td>0.43</td>
<td>0.52</td>
</tr>
</tbody>
</table>

N = 70. The data are expressed as Spearman’s correlation coefficients. Italics, $P < 0.05$; bold type, $P < 0.01$; bold and italic type, $P < 0.001$. A comparison of the discrimination ability between mfVEP and OCT parameters shows that, although no significant difference was found in the proportion of abnormal eyes based on the normative average estimated using the 10th percentile of normal, the performance of OCT based on ROC curve analysis (ranging from 0.88–1.00) were slightly superior than that of mfVEP (ranging from 0.75–0.92, in the affected field of vision) (Tables 1, 2). However, it is important to consider that we have selected patients with permanent visual deficits (already treated for chiasmal compression), somewhat favoring OCT performance that detects structural damage. The fact that despite this potential source of bias mfVEP parameters performed similar to OCT underscores its potential clinical utility, particularly in patients with active chiasmal compression when structural abnormalities are usually not so prominent.

In the current study, we also evaluated the relationship between mfVEP and OCT parameters. In investigations of visual pathway diseases, it is of great importance to understand the correlation between structural and functional testing with different technologies. While functional evaluations of the VF...
Multifocal VEP and OCT in Chiasmal Compression

with subjective or objective (mfVEP) perimeter reveal a deficit, which is potentially reversible after visual pathway decompression, structural evaluations of abnormalities on FD-OCT point to a certain degree of permanent dysfunction. Therefore, understanding the precise correlation between functional and structural measures is of great help in estimating the chances of visual recovery after optic pathway decompression. Previous studies have evaluated the structure-function correlation between Humphrey VF sensitivity and mfVEP or OCT parameters in patients with glaucoma. Moschos et al. and Weizer et al. reported a moderate correlation between mfVEP and RNFL thickness on OCT in a group of patients with glaucoma. Kanadani et al. found a good correlation between 10-2 Humphrey VF central mfVEP, and structural measures of the macular area on OCT in glaucoma patients. Also, in a study by Laron et al. on patients with optic neuritis, a moderate agreement between mfVEP and RNFL thickness on OCT was observed.

To our knowledge, this is the first study to evaluate the relationship between macular mfVEP parameters, FD-OCT measurements of RNFL thickness, and VF sensitivity loss in patients with chiasmal compression. Recently, in a study on the association between RNFL thickness OCT, mfVEP, and VF loss sensitivity, agreement was only 21.5% between OCT and SAP, and 24.2% between OCT and mfVEP. However, the authors did not evaluate the association between macular OCT measures and mfVEP responses and failed to inform the number of eyes studied. The findings of the current study indicate a moderate correlation between mfVEP amplitudes and macular and peripapillary RNFL FD-OCT measurements. Because our patients had established structural damage and permanent VF loss from previous (already treated) chiasmal compression, we expected a stronger correlation between mfVEP and FD-OCT measurements. Though significant, the values ranged between 0.32 and 0.58, indicating a slightly weaker correlation than that observed between SAP VF and FD-OCT measurements (range, 0.32-0.78) in a previous study using the same FD-OCT analysis in a similar set of patients. However, it should be kept in mind that our patients were selected based on established SAP VF defects. The results might have been different had the patients been selected based on mfVEP findings. Humphrey VF analysis, which was used as the standard for selecting patients in our study, is based on a threshold test, whereas mfVEP is an objective measure of the amplitude and latency detected at the visual cortex, reflecting the integrity of the visual pathways. The fact that the correlation between mfVEP and VF defects in our patients was moderate indicates that while both approaches may be used to evaluate visual deficit, there are important differences to take into account and the two methods should be regarded as complementary rather than alternative. On the other hand, the selection of patients based on subjective VF defects may be responsible for the moderate agreement observed and may be viewed as a weakness of the study design.

Our study was also limited by the relatively small number of patients included and by the fact that the mfVEP software did not include a signal-to-noise averaging protocol. Nevertheless, careful measurement of mfVEP responses and avoidance of noise interference allowed us to record mfVEP data accurately enough for the purposes of comparison and correlation with VF and FD-OCT measurements.

In conclusion, mfVEP amplitude measurements were able to differentiate eyes with temporal hemianopia due to chiasmal lesions from normal controls, and were moderately though significantly correlated with SAP-measured VF defect severity and retinal axonal loss expressed as FD-OCT peripapillary RNFL and macular thickness. In other words, mfVEP appears to be a useful and objective tool for the quantification of visual function in chiasmal diseases. However, further studies are necessary to confirm our findings and to better understand how electrophysiological and anatomic measurements relate to each other in chiasmal compressive diseases.

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References


