An Attempt to Detect Glaucomatous Damage to the Inner Retina with the Multifocal ERG

Donald C. Hood, Vivienne C. Greenstein, Karen Holopigian, Rebecca Bauer, Babar Firoz, Jeffrey M. Liebmann, Jeffrey G. Odel, and Robert Ritch

PURPOSE. To detect glaucomatous damage to the inner retina using the multifocal electroretinogram (mERG).

METHODS. The stimulus array consisted of 103 hexagons with a mean luminance of 100 cd/m² and a contrast of 50%. The mERG was recorded from 13 control subjects, 18 patients with open-angle glaucoma (OAG), 4 glaucoma suspects, and one patient with ischemic optic neuropathy (ION). Individual responses, as well as responses summed within quadrants or across the entire array, were measured in a number of ways. Humphrey visual fields were obtained for all patients, and the mean total deviation (MD) values for the 18 patients with OAG ranged from −2.2 to −18.2 with a mean (SD) of −7.3 (4.5).

RESULTS. The mERG measure that best discriminated between the patients and the control subjects was the ratio of the amplitude at 8 msec after the peak response to the amplitude at the peak. Although the value of this ratio fell below the median of the control group for 16 of the 18 OAG patients, only 6 of these patients had ratios that fell below the normal range. Other measures of first- and second-order kernels did not do as well. Both within and across patients, the correlation between local field loss and the mERG ratio measure was poor. Furthermore, although in some patients the mERG waveform is clearly different from normal, in other patients (including the patient with ION) the waveform approximates the normal even in visual field areas with substantial sensitivity loss.

CONCLUSIONS. Because glaucomatous damage is known to affect the ganglion cell axon, these data suggest that damage to ganglion cell axons is not a sufficient condition to produce changes in the mERG as measured here and that in patients with clear changes in mERG waveforms, these changes do not appear to be well localized and local waveforms are poorly correlated with local changes in field sensitivity. (Invest Ophthalmol Vis Sci. 2000;41:1570–1579)

Glaucoma is thought to affect primarily the inner retina (the connections of the inner plexiform layer and the ganglion cells). Because glaucomatous damage can be controlled with medication and/or surgery, it is important to detect early signs of inner retinal damage. The most widely used procedure for detecting early damage is the behaviorally measured visual field. Unfortunately, significant ganglion cell fiber loss can occur before there is a reliable change in the visual field.1 For this reason, considerable attention has been paid to other measures; one such measure is the pattern electroretinogram (PERG). Numerous studies have documented that the PERG is abnormal in patients with ocular hypertension and glaucoma2–12 (for review see Refs. 5 through 7, 9, and 12). Although some of these studies report that abnormalities in the PERG can precede visual field defects, the PERG technique has limitations. For example, PERG amplitudes obtained from control subjects are small; they can be less than 2 µV.10 In addition, changes in the amplitude of the PERG do not correlate well with visual field measures. Furthermore, the PERG must be obtained with a relatively large stimulus, yet early retinal damage can be restricted to relatively local regions in patients with glaucoma. Thus, there continues to be a need for a reliable measure of early retinal damage to the inner retina. The multifocal ERG (mERG) has been suggested as a candidate.

The mERG technique, developed by Sutter and colleagues,13,14 allows for multiple local retinal responses to be recorded in a few minutes. Sutter and Bearse15,16 have argued that ganglion cells contribute to the human mERG and have provided preliminary indications in a few patients that glaucomatous damage can be identified with this technique.17,18 Recently, a number of studies, most in abstract form, have examined mERGs from patients with glaucoma. Considerable disagreement exists among these studies about both the degree to which glaucomatous damage can be detected in the mERG and the measure of the mERG to be used to detect such damage.19–24

Recently, the mERG was recorded from monkeys before and after intraretinal injections of n-methyl DL aspartate...
studies in cats and monkeys. Thus, the firing of action results of these studies were consistent with full-field ERG due to action potential activity in the retina. Hood et al. 25 26 had the effect of removing perhaps interplexiform cells generate sodium-based action potentials. Tetrodotoxin and NMDLA had the effect of removing a substantial component from the mERG response.25,26 The particular, the mERG waveform from monkeys exhibits considerable nasotemporal variation, and this variation is removed if the nasotemporal variation was markedly decreased in some of these patients. These observations provided the motivation for the present study.

The purpose of the present study was to use the mERG to identify local damage to the inner retina. Humphrey visual fields and mERG recordings were obtained from all patients. In an attempt to improve the efficacy of the mERG in detecting local changes, the display for the mERG was set to a contrast of 50%.

### METHODS

**Subjects**

Eighteen patients with open-angle glaucoma, ranging in age from 29 to 72 years (mean, 55.8 ± 13.0 years), and four glaucoma suspects, ranging in age from 46 to 67 years, participated in this study. Table 1 shows further categorization of the patients and their ages, visual acuities, Humphrey visual field indices, and cup-to-disc ratios. In all but two patients, only one eye was tested. In two patients, P6 and P14, the mERG was recorded from both eyes. In addition, mERGs were obtained from both eyes of a 61-year-old patient with unilateral ischemic optic neuropathy (ION), 8 months after his ischemic attack.

Thirteen control subjects, with no known abnormalities of the visual system, also participated in the study. They ranged in age from 35 to 72 years (mean, 52.7 ± 10.9 years). Informed consent was obtained from all subjects before their participation. Procedures followed the tenets of the Declaration of Helsinki, and the protocol was approved by the committee of the Institutional Board of Research Associates of New York (NMDLA) and/or tetrodotoxin (TTX). Tetrodotoxin blocks the sodium-based-action potentials of ganglion and amacrine cells, and NMDLA depolarizes the postsynaptic membranes of these cells (e.g., see Ref. 27 for a review). As far as is known, only ganglion cells, some subclasses of amacrine cells, and perhaps interplexiform cells generate sodium-based action potentials. Tetrodotoxin and NMDLA had the effect of removing a substantial component from the mERG response.25,26 The results of these studies were consistent with full-field ERG studies in cats and monkeys. Thus, the firing of action potentials by amacrine, ganglion cells, or both has a large effect on the mERG.

This recent work with monkeys suggests that a simple change in the mERG procedure might improve the sensitivity of the technique for detecting glaucomatous damage. In particular, the mERG waveform from monkeys exhibits considerable nasotemporal variation, and this variation is removed by TTX. That is, the nasotemporal variation in waveform is due to action potential activity in the retina. Hood et al. found that the human mERG had a qualitatively similar nasotemporal variation, but this variation was more prominent if the contrast of the stimulus display was decreased to 50% as opposed to the generally used maximum contrast. This may be explained, at least in part, by an increase in the proportion of the responses coming from the outer retina as opposed to the inner retina, as contrast is increased. Additional support for the presence of a large inner retinal component in the human mERG comes from the same study. The mERG records obtained from a patient with glaucoma resembled those of the monkey treated with TTX and NMDLA, and a preliminary analysis of the records of other patients with glaucoma revealed that the nasotemporal variation was markedly decreased in some of these patients. These observations provided the motivation for the present study.

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### Table 1. Characteristics of Study Subjects

<table>
<thead>
<tr>
<th>Subject</th>
<th>Age</th>
<th>Visual Acuity</th>
<th>Visual Field (MD)</th>
<th>Visual Field (CPSD)</th>
<th>Cup/Disc Ratio</th>
<th>Diagnosis</th>
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<tr>
<td>P1</td>
<td>39</td>
<td>20/20</td>
<td>−7</td>
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<td>35hk</td>
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<td>pgOAG</td>
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<td>48</td>
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<td>5</td>
<td>0.4</td>
<td>pgOAG</td>
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<td>0*</td>
<td>0.8</td>
<td>POAG</td>
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<td>−4.4</td>
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<td>59</td>
<td>20/25</td>
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<td>GLS</td>
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<td>20/25</td>
<td>−0.5*</td>
<td>1.2*</td>
<td>0.4</td>
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</tr>
</tbody>
</table>

hk, H-K loop electrode used; MD, the mean deviation in decibels; CPSD, corrected pattern standard deviation in decibels; POAG, primary open-angle glaucoma; jPOAG, juvenile primary open-angle glaucoma; pgOAG, pigmentary open-angle glaucoma; xSOAG, open-angle glaucoma exfoliation syndrome; NTG, normal tension glaucoma; GLS, glaucoma suspect (includes both ocular hypertensives and those with suspect Cup/Disc ratio).

*Not significant at the 0.05 level or better.
mERG Technique

mERGs were recorded using the VERIS technique (for details see Refs. 13 and 14). Figure 1A shows the stimulus array used in this study. The visual stimulus consisted of 103 hexagonal areas scaled with eccentricity (VERIS stimulus “Hexagon 103”). The stimulus array was displayed on a high-resolution black and white monitor driven at a frame rate of 75 Hz. The contrast of the display was set at 50% (see note 1). Each hexagonal area was modulated independently from a darker gray (50 cd/m²) to a lighter gray (150 cd/m²), according to a binary m-sequence. The luminance of the surround was 100 cd/m² (see Ref. 31 for details).

Before recording, the pupil was dilated with 1% tropicamide and 2.5% phenylephrine hydrochloride, and the cornea was anesthetized with proparacaine hydrochloride.

mERGs were recorded monocularly with a bipolar contact lens electrode (Burian–Allen), and the subject was corrected for best acuity for the viewing distance after insertion of the contact lens. The fellow eye was occluded.

To obtain mERGs, the continuous ERG record was amplified with the low- and high-frequency cutoffs set at 10 and 300 Hz (Grass preamplifier model P511J; Quincy, MA), and it was sampled at 1200 Hz (every 0.833 msec) with an A/D board. The m-sequence had 2¹⁵-1 elements and required approximately 7 minutes of recording for a single run. To improve the subject’s ability to maintain fixation, the 7-minute recording was broken up into 32 overlapping segments by the VERIS program, each lasting less than 14 seconds. The results from two 7-minute runs were combined. Stimulus control and data collection were performed with VERIS Scientific software from EDI (Electro-Diagnostic Imaging, San Mateo, CA). The quality of the recordings was controlled by real time display, and contaminated segments were rejected and repeated. Local retinal response components were extracted using the fast m-transform algorithm. The first- and second-order components were analyzed.

Visual Fields

To compare multifocal data with visual field data, both standard and modified visual fields were obtained from each patient using a Humphrey Visual Field Analyzer. A 24-2 Humphrey visual field was obtained as part of the patient’s routine visit to the ophthalmologist, and a modified Humphrey visual field was obtained on the day of the mERG testing. For the modified Humphrey visual field, thresholds were measured at 103 locations corresponding to the centers of the 103 hexagonal areas in the multifocal display. The mean deviation (MD) and corrected pattern standard deviation (CPSD) values for the 24-2 Humphrey visual field are shown in Table 1.

RESULTS

Measurement of Inner Retinal Activity Based on Previous Experiments with Monkeys

Figure 1B shows the responses from one of the control subjects. The sum of all 103 individual responses is shown in Figure 2 as the upper curve. To obtain a measure of inner retinal activity we examined the waveforms from monkeys in which inner retinal activity had been blocked.25,26 Figure 2A shows the sum of all 103 multifocal responses from a monkey before (control) and after injections of TTX and then NMDLA (from Figs. 1 and 2 in Ref. 25). The lowest record (dashed) is the difference between the control and the TTX records. The inner retinal component removed by these drugs has a complex waveform with a number of positive and negative peaks. Thus, there is no single aspect of the control
response that provides a simple measure of the underlying inner retinal activity. However, the maximum of the negative trough of the inner retinal component occurs at approximately 25 msec, close to the first positive peak of the control record, and after the negative trough, the first large positive peak occurs 8 to 10 msec later. Thus, we devised a measure that could be objectively determined. In particular, a ratio measure is obtained by dividing the amplitude at 8.3 msec after the first positive peak, P1, by the amplitude of P1. This produces a normalized estimate that does not depend on the absolute mERG amplitude, which can show fairly large intersubject variation. The ratio measure in Figure 2A does well in distinguishing the monkey’s control records from those after the retinal drug treatments. The value of this ratio is 0.86 for the control condition, 0.18 after TTX, and −0.03 after TTX + NMDLA.

Figure 2B shows the same analysis for the human mERGs previously published for one control subject and one patient (Fig. 3 in Ref. 25). The value of the ratio is 0.45 for the control record and −0.03 for the patient’s record. The patient’s value provides a quantification of the earlier observation that some patients with glaucoma have waveforms similar to those from monkeys in which inner retinal activity has been removed.25 Although the patient’s value is close to the value for the treated monkey, the value for the control subject is lower than the monkey’s control value. In fact, the mean value of 0.44 (median, 0.43) for our controls is lower than the mean value of 0.72 (median, 0.54) for a group (n = 6) of monkeys. We believe that we are measuring the same inner retinal activity in monkey and human controls because both show very similar nasotemporal waveform differences for the conditions used here. (Compare the responses in Figs. 1 and 6 in this article to the responses from the monkey in Refs. 25 and 26.) However, our quantitative measure of inner retinal activity suggests that the monkey mERG has a larger inner retinal contribution. In any case, no matter what we are assessing with our ratio measure, we will show below that it does distinguish our glaucoma group from our control group and does so better than other measures we have tried.

Figure 3A shows the value of the ratio for all subjects in the present study. The average ratio for the 13 control subjects was 0.44 (SD = 0.15), the median was 0.43, and the range was 0.20 to 0.70. The top three records in Figure 2C are the summed mERGs for three control subjects. Control C2 has a ratio value near the mean for the control group, and C9 and C4 are the control subjects with the largest and smallest ratios, respectively. For the 18 glaucoma patients, the average value was 0.21 (SD = 0.23), whereas the four suspects had an average ratio of 0.49, close to that of the control group. Figures 1C and 1D show the responses from two of the patients, one, P5, with one of the two largest ratios and one, P16, with a ratio near the median of the two glaucoma groups. Figure 2C shows the summed mERG for these two patients and the summed mERG for P13, the patient with the lowest ratio.

The mean ratio for the 18 patients with glaucoma was significantly different from the values for the control group (f = 3.05, P < 0.005). Furthermore, 16 of the 18 patients with glaucoma had values that fell below the median value of the control group (see Fig. 3A). However, only 6 patients had ratios that fell outside the normal range. Thus, the ratio does not do a good job of predicting who has glaucoma.

Figure 3B shows these ratios for all subjects, plotted against MD, one of the Humphrey visual field indices. MD represents the average elevation of the patient’s visual field in decibels compared with an age-related control group. The control subjects are shown at the 0 db point because we do not have 24-2 fields for them. For the patients, there was no correlation between the severity of the field loss and the ratio measure. In an attempt to find some correlation, field losses in MD and mERG ratios were determined for each of the four quadrants (see Fig. 3C). To obtain a MD for each quadrant of the modified Humphrey field for each patient, the deviations from thresholds obtained from a group of control subjects were determined for all 103 locations of the modified Humphrey, and the mean value for each of the four quadrants was calculated. The largest negative correlation (−0.4) was found for the superior nasal retina (inferior temporal field), and these results are shown in Figure 3D. However, even here many of the ratios
for the 18 patients, including those with extreme field losses, fell within the normal range. Examining more local sensitivity measures using the modified visual field data did not improve the correlation.

Two Other Measures of Inner Retinal Activity

Figure 4 contains the results for two other measures that have been proposed as possible ways to differentiate between patients and control subjects. The first is the implicit time of the first positive peak of the first-order kernel (1K) of the summed mERG. Figure 4B shows that the implicit times of five of the patients fell outside the range of normal values. (Note that the vertical axis in Figure 4B has been inverted so that the predicted direction for the patients is always lower than the normal values in all panels of Figs. 3 and 4.) As in Figure 3, the dashed, horizontal lines mark the median and extreme of the range of values of the control group. The mean of the glaucoma group (26.1 msec; SD = 1.3 msec) was significantly longer than the values (24.8 msec; SD = 0.9 msec) for the control group (t = 2.91, P < 0.005). However, as was the case for the ratio measure used in Figure 3, many of the implicit times for the 18 patients, including those with extreme field losses, fell within the normal range. Furthermore, examining regions smaller than the quadrants did not substantially improve the correlation between implicit time and field loss.

It has also been suggested that the second-order kernel (2K) has a larger inner retinal component than does the first-order kernel and that patients with glaucoma show a differential loss of this component. Figure 4A, lower tracing, shows the second-order kernel for the summed response of C2. This response has a clear negative potential at around 26 msec. The peak-to-trough amplitude of this potential was measured as shown. The amplitude of this response (2K) was divided by the peak-to-trough amplitude of the first-order response (1K) measured as shown in Figure 4A, to obtain a measure of the relative size of the second-order response. The mean value of this ratio for the 18 patients with glaucoma was 0.25 (SD = 0.07) and was not significantly different from the mean ratio of 0.29 (SD = 0.09) for the control group. Although four of the patients’ values fell outside the normal range, half of the values fell above the median (0.27) for the control group (see Fig. 4C). The mean value for the four suspects was 0.35.

Finally, the correlation between our ratio measure and the patients’ cup-to-disc ratio was near zero (0.12).

Individual Cases in which Fields Show Regions of Good and Poor Sensitivities

Although a number of measures were tested, there are many others we could have explored. However, a close examination of individual cases suggests that no measure of these particular data will provide a clear differentiation of patients from controls. In particular, we examined the records from patients who had modified Humphrey visual fields with large regions of both high (e.g., normal) and low sensitivities. The top panels of Figure 5 show the modified Humphrey fields for the two patients whose records are presented in Figure 1. The dark areas indicate thresholds that were more than 4 SD greater than the control group mean, and the white areas indicate thresholds within 2 SD of the control values. The waveform of the mERG in regions with poor sensitivity was compared with the mERG from regions at a comparable eccentricity but with good sensitivity. For example, the responses in the region of P16’s field labeled 2 in Figure 5 were summed and are shown as the solid curve in the lower panel of Figure 5 (left column). The accompanying dashed curve is the summed response from the upper field from a comparable region (area 1) with excellent sensitivity. The variation in the waveform of the mERG in normal subjects is largely a difference between nasal and temporal responses; responses from superior and inferior regions tend to be similar, see Ref. 25 and Fig. 6.)
for four regions of P5's field (right column). In all cases, the better region is shown as the dashed lines. It is difficult to discriminate the good from the poor regions of the visual field based on the summed mERG responses in these patients.

This is not to say that one cannot find patients who do show regional differences in mERG waveform. However, even in these patients, the correlation of local changes, as measured with the modified Humphrey visual field, to changes in the mERG, is not good. In any case, the results in Figure 5 suggest that further attempts to improve on our measures of inner retinal activity in this data set are not likely to substantially improve our ability to detect local damage.

**Interocular Comparison**

Normal subjects may differ in the relative contribution that the inner retina makes to the mERG. Recording a mERG from both eyes of a subject can substantially reduce this source of variability. Figure 6A shows the mERG from both eyes of a control subject, with the mERG from the right eye “reversed” so that the temporal and nasal fields of each eye coincide. The mERG records in Figure 6C are responses summed from each of the four quadrants as indicated in Figure 6B. There is a nasotemporal difference in each eye as previously reported. The responses for the two eyes, however, are reasonably similar when responses from similar retinal regions are superimposed.

We were able to retest two patients, in whom the eye initially tested was far more severely affected, so as to test their companion eye. The summary statistics for these eyes can be found in Table 1. The 24-2 Humphrey fields for these two patients are presented in Figures 6E and 7A. Nearly all the regions tested in the right eye of P6 fell within the normal limits, whereas most regions tested in her left eye fell outside the normal limits (Fig. 6E). The difference between the eyes is especially marked in the superior nasal field (quadrant 2). Figure 6D shows the mERG responses from her two eyes plotted together, and Figure 6F shows the summed responses for the four quadrants (grouped as in Fig. 6B). The differences between the mERG responses of the two eyes are minor and do not correspond to the differences seen in the visual fields.

The mERG responses of P14, however, show some difference between the two eyes (Fig. 7B). In three of the four quadrants shown in Figure 7B (the three that differ most in sensitivity between the two eyes), the ratio measure used in Figures 2 and 3 is lower in the more affected eye. However, beyond this general level of agreement, the correspondence with visual field losses is not good. In any case, the records from P6 (Figs. 6D, 6F) indicate that whatever encouragement we can take from the records from P14 will not extend to all patients.

Figure 8 shows the same analysis as seen in Figures 6 and 7 for a patient with ION (see the Methods section). Again the differences between the mERG responses from the two eyes are subtle. The ratio measures used in Figures 2 and 3 are slightly smaller in the affected eye. However, the difference is small and both eyes show clear nasotemporal variations in waveform (an indicator of inner retinal contribution to the mERG).

**DISCUSSION**

The purpose of this study was to detect glaucomatous damage to the inner retina using the mERG. The stimulus conditions (50% contrast) were chosen because they produced nasotemporal variations in the human mERG that resembled those in the monkey mERG. Previous work had shown that block-
Figure 5. **Upper panels:** Modified Humphrey visual fields for two patients. The values shown are in log units (dB/10) and represent the difference from a group of control subjects (see Ref. 32). **White** indicates that the value is within 2 SDs of normal, and **black** indicates more than 4 SD from normal. **Middle panels:** mERG responses were grouped within regions of relatively high and relatively low sensitivity, as shown. **Lower panels:** Summed mERG responses for the groupings shown in the middle panel. See text for more detail.
ing action potentials with TTX removed these nasotemporal variations from the monkey’s mERG and that these variations were missing in some patients with glaucoma.25,26 A measure of inner retinal activity was devised on the basis of work with monkeys. The values of this measure for the patient and normal groups were significantly different. Furthermore, the measure distinguished between the two eyes in some patients (see Fig. 7) with different degrees of monocular damage. Although it is unlikely that either our stimulus conditions or data analysis will prove the best for detecting glaucomatous damage, a better method has yet to be reported. However, although we find that changes in the mERG are present in many of our patients with glaucoma, they are not present in all patients. Furthermore, attempts to relate local changes in the mERG to local visual field defects were largely unsuccessful. These findings raise a number of questions.

First, why are changes in the mERG present in some patients but not in others? Some patients have a reasonably normal mERG even in the presence of substantial visual field losses and presumably substantial optic nerve damage (e.g., Figs. 6D through 6F). It would appear that damage to the ganglion cell axons is not sufficient to produce a large change in the mERG at least under the conditions used here. Further evidence for this conclusion comes from the mERG responses from the patient with ION. Given the extent of the field loss in this patient 8 months after the ischemic attack, it is reasonable to assume that substantial numbers of ganglion cell axons have degenerated. Yet, the mERG responses from the affected eye show only minor changes when compared both with the patient’s better eye and with responses from the control subjects (Fig. 8). On the other hand, some patients with glaucoma show noticeable changes in their mERG responses (e.g., Fig. 7), although these changes do not appear to accurately reflect local changes in the visual field.

These findings raise questions about the nature of the retinal damage that is producing the changes in those patients with an abnormal mERG. Where is the site(s) of this damage and why don’t we see the effects of local damage on the mERG? Before considering an answer to these questions, let’s review the monkey experiments that motivated the present study. The patients showing the largest effects have mERG responses that resemble the monkey treated with TTX or TTX1 NMDLA.25,26 In particular, the patients’ mERG responses are similar in waveform to those from the treated monkey and, like those from the monkey, show reduced nasotemporal variations in waveform. It is important to remember that most of the
change seen in the monkey’s mERG after treatment is due to TTX, which removes all sodium-based action potentials. In addition to ganglion cells, some subclasses of amacrine cells and probably the interplexiform cells carry action potentials.33–35

One possible explanation is that the major effects of both TTX and glaucoma on the mERG are mediated by the action potentials carried by cells other than the ganglion cells. The implication here is that the nasotemporal variations seen in both human and monkey control records are attributable to activity in amacrine and/or interplexiform cells. Furthermore, with this explanation the abnormal responses seen in some patients are due to damage distal to the ganglion cells. Among the possible sites of damage are the amacrine or interplexiform cells themselves or the gap junctions that connect some of these cells. The amacrine cells carrying action potentials are likely to be large cells with relatively long axon-like processes. In addition, the influence of these cells can be extended via gap junctions. These wide-ranging connections supply at least two possible explanations for the lack of local correspondence between changes in the mERG and in the visual field. Relatively local damage may disrupt these circuits and give the appearance of global damage when measured with the mERG. On the other hand, relatively diffuse (global) disruption of gap junctions and/or amacrine cells may not be reflected in the behaviorally measured visual field.

However, we are still faced with evidence for a ganglion cell contribution to both the monkey29 and human mERGs. For example, Sutter and Bearse15–18,30 have presented evidence of an optic nerve head component in the human mERG. Perhaps this component makes a relatively subtle contribution to our records and other paradigms will be more effective in revealing ganglion cell and/or optic nerve contributions.36 But, a second possible explanation is that action potentials generated by ganglion cells are necessary, but not sufficient, to produce the TTX-sensitive contribution to the monkey mERG and that this contribution somehow depends on the integrity of the glial cells or myelin sheaths near the optic disc. According to this second explanation, glaucoma must damage either these structures or a sufficient numbers of ganglion cells for us to see effects on the mERG. This might explain why we observe changes in some patients but not others and why these changes do not appear to be localized. Of course, it is entirely possible that the necessary damage in glaucoma includes both cells distal to the ganglion cell and glial cells near the optic disc.

In summary, glaucomatous damage can be detected in the mERG. However, with the mERG stimulus used here, it is not detectable in some patients, and in others the changes in the mERG are not related to local field losses. Thus, we are not optimistic that a measure of the mERG will prove useful in detecting local, or early, glaucomatous damage. For this reason, we have turned to the multifocal visual evoked potential.37

**Authors’ Notes**

1. Saying that the stimulus was 50% contrast oversimplifies the potential differences that may occur when using it as opposed to the 100% contrast stimulus. In theory the response to the 100% stimulus will be the difference between the response to the local flash and the “response” to darkness (or at least the minimum of the screen). And, the response to the 50% contrast will be the difference between the responses to two local flashes of different intensities. It is not clear why the responses from the monkey to the 100% stimulus resemble the responses to the human with 50%. Perhaps the response to the lower luminance in the case of the human mERG is very small. It appears to be the case that using 100% contrast and a lower luminance also produces similar nasotemporal variations in humans (authors’ unpublished observations, July 1998). On the other hand, the 100% stimulus in the case of the monkey and the 50% stimulus in the case of humans

![FIGURE 7.](image_url) (A) The Humphrey 24-2 total deviation fields for P14, a patient with normal tension glaucoma (NTG). (B) The responses for P14 grouped by quadrant as shown in Figure 6B.

![FIGURE 8.](image_url) (A) The Humphrey 24-2 total deviation fields for P23, a patient with ischemic optic neuropathy (ION). (B) The responses for P23 grouped by quadrant as shown in Figure 6B.
may each be accentuating, perhaps via different mechanisms, nonlinearities that are the signature of the inner retina.

References


