Oscillatory Potentials in Electroretinograms of the Human Macular Region

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Using focal stimuli, we successfully recorded oscillatory potentials (OPs) in electroretinograms of the macular regions of 72 normal volunteers. The OPs consisted of three to four wavelets with a mean peak interval of approximately 6.5 msec, consistent with that recorded with conventional full-field stimuli over the entire retina. The changes of amplitude in response to the spot sizes and ring stimuli suggested that the distribution of OPs is different from that in a- and b-waves in human macular region. Invest Ophthalmol Vis Sci 29:1631-1635, 1988

Oscillatory potentials (OPs) are the wavelets superimposed on the ascending slope of the conventional electroretinogram (ERG).1-3 OPs are seen as a series of three to four rhythmic wavelets having almost equal amplitude and an interpeak interval of about 6.5 msec in humans.1-3 OPs have clinical values in the assessment of retinal function. In the early stage of diabetic retinopathy, for example, the a- and b-waves of the ERG may be of normal amplitude, whereas OPs may be selectively abnormal.1-3 In one kind of X-linked congenital stationary night blindness, OPs are absent or have extremely reduced amplitude, and the female carrier may show reduction in the amplitude of OPs, while other components of her ERG remain normal.6 This selective abnormality of OPs is considered to be indirect evidence that OPs are generated independently from a- and b-waves. The site for generation of OPs is not yet known, but experimental evidence indicates that OPs reflect activity of inhibitory feedback synaptic circuits within the retina.7-9

Although many studies have dealt with their physiological properties and clinical value, OPs in humans have, until now, been evaluated as components of total ERGs recorded with a full-field stimulus over the entire retina. Although a- and b-waves in local macular ERGs have been successfully recorded by many authors, attempts to record OPs in human macular region by using a focal stimulus light have not been reported.

By improving the signal to noise (S/N) ratio of our previously reported system for recording local macular ERG,10-12 we have successfully recorded OPs in human macular region.

Materials and Methods

Seventy-two normal subjects ranging in age from 18 to 62 years (mean, 36 years) were tested. They had refractive error ranging from +1.5 to —3.5 diopters (mean, —1.0 diopters). Informed consent was obtained from each subject after the procedures had been explained.

Our system for recording local macular ERG has been described in detail.10-12 An infrared television fundus camera was mounted to monitor the exact locus of stimulation on the macula. The stimulus light, background illumination and fixation target were incorporated in the fundus camera. The size, frequency and intensity of the stimulus spot were changeable, and so was the level of background illumination. The stimulus spot and fixation target could be moved independently over the entire 25° area of central fundus to be examined. A background field of 45° visual angle was projected to the eye from the fundus camera. Additional background illumination outside the central 45° was provided to produce homogeneous illumination across the entire visual field. The Burian-Allen bipolar contact lens electrode used for ERG recording allowed only an extremely low noise level and permitted clear fundus observation with the television monitor. The intensity of the white stimulus light and background light were 29.46
cd/m² and 2.84 cd/m², respectively. After the subjects' pupils were fully dilated for testing with a combination of 0.5% tropicamide and 0.5% phenylephrine hydrochloride, ERGs were recorded with 5 Hz rectangular stimuli, administered as 100 msec of light on and 100 msec of light off. The center of the stimulus spot was on the fovea, and 512 responses were averaged by a signal processor. Two recordings were made simultaneously; a time constant of 0.003 second with a 300 Hz high-cut filter on the amplifier (frequency range from 53 to 300 Hz with a reduction rate of 30%) was used to record the OPs, and a time constant of 0.03 seconds with a 100 Hz high-cut filter (frequency range from 5.3 to 100 Hz with a reduction rate of 30%) recorded the a- and b-waves.

Results

We proved that the ERGs in our system were generated by the cone system and our stimuli were focal.10-12 We improved S/N ratio significantly to record OPs in this study. Namely, under the present conditions, responses could be detected if they equailel or exceeded 0.23 μV in a- and b-waves, and 0.1 μV in OPs. Therefore, additional attempts were made to prove that our ERG responses in the present system were still local. When a stimulus spot of 5° in diameter was on the optic disc, ERG was nonrecordable in four normal subjects. Figure 1 shows the results of local ERG in three patients with unilateral macular coloboma having three different sizes. The size of macular coloboma was approximately 5.5°-6.5° (case 1), 10°-12° (case 2) and 16°-18° (case 3) in diameter. The roughly corresponding stimulus sizes were used to record the local ERG under fundus monitor. All patients showed nonrecordable ERG in the affected eye (left) and the responses were normal when the stimulus spot was on the macula in the normal fellow eye (right). Two recordings were made simultaneously; a time constant (T.C.) of 0.03 seconds was used to record the a- and b-waves (left in each case), and a T.C. of 0.003 seconds recorded the OPs. The bottom tracings indicate the responses from photocell.

Figure 1. Local ERG in three patients with unilateral macular coloboma having three different sizes. The size of macular coloboma was approximately 5.5°-6.5° (case 1), 10°-12° (case 2) and 16°-18° (case 3) in diameter. The roughly corresponding stimulus sizes were used to record the local ERG under fundus monitor. All patients showed nonrecordable ERG in the affected eye (left) and the responses were normal when the stimulus spot was on the macula in the normal fellow eye (right). Two recordings were made simultaneously; a time constant (T.C.) of 0.03 seconds was used to record the a- and b-waves (left in each case), and a T.C. of 0.003 seconds recorded the OPs. The bottom tracings indicate the responses from photocell.

Areas of macular coloboma showed an absolute scotoma, while the outside of coloboma showed no scotoma in cases 1, 2 and 3. Above results indicate that our ERG responses were essentially local.

Figure 2 shows the local ERGs in a normal subject recorded with variable diameters of stimulus spot. The OPs consisted of three to four wavelets (O1-O4) and were clearly observed for all stimulus spots. Table 1 shows a mean (±SD) of implicit time of O1, O2 and O3, and interpeak interval of O1-O2 and O2-O3 in 72 normal subjects. Since the fourth wavelet (O4) was missing in some instances, we limited the
The mean (±SD) amplitudes of a-waves, b-waves, and OPs for the three different spot sizes, 5°, 10° and 15°, in 72 normal subjects are shown in Table 2. The amplitudes were measured from the isoelectric line to the trough of the a-wave (a-wave amplitude) and from the trough of the a-wave to the peak of the b-wave (b-wave amplitude). The amplitude of each OP wavelet was measured from a baseline, drawn as a first order approximation between the troughs of successive wavelets, to its peak. The OPs became proportionately smaller than the a- and b-waves as the stimulus diameter is decreased. We calculated the a-wave to b-wave (a/b) ratio, and OPs (O1 + O2 + O3)/b ratio in three spots. The mean a/b ratios for the 5°, 10° and 15° spots were 0.37, 0.42 and 0.42, respectively. There were no statistically significant differences between these ratios. The mean OPs/b ratios for the 5°, 10° and 15° spots were 0.27, 0.39 and 0.50, respectively. The differences between these ratios were statistically significant (P < 0.01, t-test, two-tailed comparison).

In order to further investigate the special distribution of OPs in the macular area, we made two ring stimuli as shown in Figure 3. One was a 10° stimulus with 5° of its central field taken away (5°-10° spot), and the other was a 15° stimulus with 10° of central field taken away (10°-15° spot). The 5°-10° spot elicits potentials between 5° and 10° of the visual angle (parafovea), and the 10°-15° spot elicits those between 10° and 15° of the visual angle (perifovea). The responses recorded with these two ring stimuli were compared with those recorded with a central 5° (fovea) stimulus to the retinas of eleven normal subjects. Figure 3 shows the comparison of a/b ratio and OPs (O1–O4)/b ratio between 5°, 5°-10° and 10°-15° stimuli. The mean a/b ratios for the 5°, 5°-10° and 10°-15° stimuli were 0.46, 0.41 and 0.41, respectively. There were no statistical differences between them. The mean OPs/b ratios for 5°, 5°-10° and 10°-15° stimuli were 0.25, 0.49 and 0.64, respectively. The OPs/b ratio was significantly smaller (P < 0.01) for the 5° than for the 5°-10° stimulus, and was significantly smaller (P < 0.05) for the 5°-10° than for the 10°-15° stimulus (t-test, two-tailed comparison).

### Discussion

To our knowledge, these are the first recordings that isolate macular OPs from the total ERG. The amplitude of local ERG of the macular is extremely low (Table 2), while the peak frequency of the OPs is quite typical (130–150 Hz). The OPs in such small ERGs are therefore easily buried unless the noise...
Table 2. Mean amplitude (±SD) of a-waves, b-waves and OPs elicited by focal stimuli of different sizes from maculas of 72 normal volunteers

<table>
<thead>
<tr>
<th>Spot size</th>
<th>a-wave</th>
<th>b-wave</th>
<th>O1</th>
<th>O2</th>
<th>O3</th>
<th>Sum</th>
</tr>
</thead>
<tbody>
<tr>
<td>5°</td>
<td>0.46 ± 0.19</td>
<td>1.27 ± 0.35</td>
<td>0.07 ± 0.06</td>
<td>0.11 ± 0.07</td>
<td>0.16 ± 0.10</td>
<td>0.33 ± 0.19</td>
</tr>
<tr>
<td>10°</td>
<td>1.19 ± 0.33</td>
<td>2.88 ± 0.70</td>
<td>0.21 ± 0.10</td>
<td>0.46 ± 0.19</td>
<td>0.41 ± 0.17</td>
<td>1.09 ± 0.38</td>
</tr>
<tr>
<td>15°</td>
<td>2.12 ± 0.50</td>
<td>4.96 ± 1.07</td>
<td>0.56 ± 0.20</td>
<td>1.09 ± 0.35</td>
<td>0.81 ± 0.27</td>
<td>2.46 ± 0.73</td>
</tr>
</tbody>
</table>

level is extremely well suppressed. In our previous results with this recording system,10-12 the S/N ratio was not sufficient to record OPs. Now that we have improved the S/N ratio, increased the number of averaging responses and used a suitable frequency range of the amplifier, we succeeded in recording OPs. In

Fig. 3. Local ERGs recorded with a 5° spot stimulus and two ring stimuli in a normal subject (top), and a/b ratios (bottom, left) and OPs/b ratios (bottom, right) in three stimuli. Ratios are means ± SD in 11 normal subjects. OPs: O1 + O2 + O3.
addition to this, the suitable combination of stimulus and background light intensity may have contributed to successful recordings of OPs.

The OPs in local macular ERG consisted of three to four wavelets with a mean of interpeak interval of approximately 6.5 msec (Table 1). This interval is consistent with that of OPs recorded with conventional, full-field stimuli, indicating that the wavelets seen in macular ERGs were not noise but OPs. Comparison of OPs with simultaneously recorded a- and b-waves can provide clues to the physiology of the macula and confirm the clinical usefulness of OPs in evaluating macular diseases—for example, diabetic maculopathy.

Our results suggest that the distribution of OPs is different from those of a- and b-waves in human macular region. The changes of amplitude in response to the spot sizes and ring stimuli indicated that the distribution of OPs is relatively sparse in the fovea. However, it becomes relatively more dense than those of a- and b-waves from the fovea toward the parafovea, and even more strikingly toward the perifovea. The different distribution may result from different generating sites of OPs. The OPs reflect neuronal activity in the inner nuclear layer of the retina and are probably mediated by the amacrine cell or the interplexiform cells. Both cells contain dopamine and demonstrate alteration of dopaminergic metabolism to changes in illumination. Application of dopamine to the retina in vivo will also alter the OPs. It has also been suggested that dopamine modulates OPs biogenesis in human retina. Thus, we expected the OPs reflect dopaminergic neuronal activity. In macaque, the density of dopamine-containing amacrine cells was minimal in the fovea, and it gradually increased as the counts proceeded peripherally to reach maximum at a distance of 3 mm from the foveal center (perifovea). It is interesting that there is some correlation between the distribution of dopamine-containing amacrine cells in macaque and that of OPs in human macular region.

Key words: oscillatory potentials, local ERG, macular region, human, distribution

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References