Asymmetry of Focal ERG in Human Macular Region

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Electroretinograms (ERGs) were elicited by hemicircular (half-disc) stimuli to the upper, lower, temporal and nasal maculas of 26 normal subjects, and the amplitudes and implicit times of the ERGs from opposing macular regions were compared. The amplitudes of a-wave, b-wave and oscillatory potentials (OPs) were significantly larger in the upper macular region than in the lower macular region \( (P < 0.05) \). The amplitudes of a- and b-waves did not differ significantly between temporal and nasal macular regions, but OPs showed enormous asymmetry, with significantly larger amplitudes in the temporal retina than in the nasal retina \( (P < 0.001) \). The implicit times of a-waves, b-waves and OPs did not differ significantly between upper and lower retina, or between temporal and nasal retina. These findings aided analysis of the ERG of a patient with a retinal defect. Invest Ophthalmol Vis Sci 30:1743-1749, 1989

A functional asymmetry between upper and lower or between nasal and temporal areas of the human retina has been reported. The upper–lower differences have been studied by visual evoked potentials (VEP),1,2 motor reaction time,3 temporal sensitivity,4 visual acuity,5 visual field,6,7 contrast sensitivity8 and standing potentials of the eye.9 These studies suggest superior visual function in upper hemiretina over the lower hemiretina.

Attempts to study possible nasal–temporal differences by critical flicker fusion frequency and/or performance in a double-flash discrimination task6,7 have had conflicting results.

It is unknown whether such differences originate within the retina itself or are due to higher visual processing. Although some answers to this question have been suggested by studying the standing potential of the eye12 or the anatomical asymmetry of the human retina,13,14 no statistical report employing the flash electoretinogram (ERG) has dealt with this subject.

We have succeeded in recording oscillatory potentials (OPs) as well as a- and b-waves in human focal macular ERGs.15 Results of our previous study suggested that the distribution of OPs is different from that of a- and b-waves, when ERGs from the fovea, parafovea and perifovea are compared. We wished to extend our investigations to a comparison of a-waves, b-waves and OPs in opposing halves of the human macula.

Materials and Methods

Twenty-six normal subjects ranging in age from 16 to 62 years (mean, 41 years) were tested. Refractive error ranged from +1.0 to —2.5 diopters (mean, —0.75 diopters). Informed consent was obtained from each subject after the procedures had been explained.

Our system for recording focal macular ERG has been described previously.15-17 Briefly, an infrared television fundus camera monitors the exact locus of stimulation on the fundus. The stimulus light (29.46 cd/m²), background illumination (2.84 cd/m²), and fixation target (16' in diameter) were incorporated in the fundus camera. 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 light adaptational changes of amplitude of focal ERG during recordings were proved negligible in our relatively low level of background illumination,18 although we reported that the full-field cone ERG changes significantly in amplitude during intense light adaptation in normal subjects.19 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. After the subjects' pupils were fully dilated 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. Hemicircular stimuli (15°...
Fig. 1. Hemicircular stimuli for recording focal ERG. The center point of the straight edge was on the foveola.

in diameter) were used as shown in Figure 1, and 512 responses were averaged by a signal processor. A small fixating target (16' in diameter) was always at the middle of the straight border of the hemicircle during recordings.

Two recordings were made simultaneously; a time constant (TC) of 0.003 sec with a 300 Hz high-cut filter on the amplifier (frequency range from 50 to 300 Hz with 30% reduction rate) was used to record the OPs, and a time constant of 0.03 sec with a 100 Hz high-cut filter (frequency range from 5.0 to 100 Hz with 30% reduction rate) recorded a- and b-waves. An artifact clearer system eliminated sweeps having a baseline fluctuation larger than 40 µV from the summation. The responses were recorded on an X–Y plotter. In order to negate any trend that might favor one region over another, the order of recording the ERG in the four macular regions was randomly decided in each subject.

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 b-wave (b-wave amplitude). The amplitude of each OP wavelet (designated O1, O2, O3 and O4) was measured from a baseline, drawn as a first order approximation between the troughs of successive wavelets, to its peak. Since the fourth wavelet (O4) was missing in some instances, we limited measurement to the constantly recordable O1, O2 and O3.

Our previous work showed that ERGs produced by this method are generated by the cone system,16,18 and that responses elicited by spot stimuli with sizes ranging from 5° to 15° are local.15,18

Results

Upper and Lower Retina

Figure 2 shows examples of focal ERGs recorded from upper and lower retinal areas in four subjects. Figure 3 shows the mean (±SD) amplitudes of a-waves, b-waves, and OPs (O1 + O2 + O3) for the upper and lower retina in all 26 subjects. The mean (±SD) amplitudes (µV) of upper and lower retinal ERGs were 1.02 ± 0.36 and 0.71 ± 0.28 (a-waves), 2.59 ± 0.67 and 2.18 ± 0.64 (b-waves), and 1.20 ± 0.48 and 0.80 ± 0.34 (OPs), respectively. The amplitudes of a-waves, b-waves, and OPs were statistically
Fig. 2. Samples of focal ERGs recorded from upper (left) and lower (right) retinal areas in four normal subjects. Two different time constants (TC) were used simultaneously in each recording. The a- and b-waves were evaluated by a 0.03 sec TC, and oscillatory potentials by a 0.003 sec TC. The bottom tracings are the response from the photocell.

Fig. 3. Mean (±SD) amplitudes of a-wave, b-wave and OPs (O1 + O2 + O3) for the upper (open circle) and lower (closed circle) retina in 26 normal subjects.

larger in the upper than in the lower retina ($P < 0.05$) (t-test, two-tailed comparison).

The mean (±SD) implicit times (msec) of upper and lower retinal ERGs were 22.1 ± 1.1 and 22.2 ± 1.5 (a-waves), 42.9 ± 2.6 and 42.8 ± 2.6 (b-waves), 26.2 ± 1.0 and 26.0 ± 0.7 (O1), 32.6 ± 1.2 and 32.6 ± 1.3 (O2), and 39.0 ± 1.6 and 39.4 ± 1.4 (O3), respectively. For each component, the differences of implicit time in upper and lower retinal ERGs were not statistically significant.

Temporal and Nasal Retina

Figure 4 shows an example of focal ERGs recorded from temporal and nasal retina with the hemicircular stimuli and with the circular stimulus (15° in diameter). (A small black dot indicates the fixating point at the foveola.) Amplitudes and implicit times of a- and b-waves in nasal retina were almost identical with results from temporal retina; however, the amplitudes of OPs were much larger in temporal than in nasal retina. The focal ERG recorded with the circle stimulus (Fig. 4, lower) showed an amplitude which was nearly the summation of the amplitudes of the temporal and nasal ERGs (Fig. 4, upper).

Temporal and nasal ERGs in four subjects are compared in Figure 5. In all subjects, only the amplitudes of OPs are larger in temporal than in nasal retina. Figure 6 presents a comparison of temporal and nasal focal ERGs in all 26 subjects. The mean (±SD) amplitudes ($\mu$V) of temporal and nasal retinal ERGs were 0.95 ± 0.24 and 0.96 ± 0.22 (a-wave), 2.37 ± 0.58 and 2.45 ± 0.58 (b-wave), and 1.76 ± 0.66 and 0.90 ± 0.46 (OPs), respectively. The am-
amplitudes of a- and b-waves did not differ significantly between temporal and nasal retina, but OPs showed significantly larger amplitudes in the temporal retina than in the nasal retina ($P < 0.001$).

No significant difference between temporal and nasal retina was found for the implicit times of a-waves, b-waves, and OPs (O1, O2, O3). The mean ($\pm$SD) implicit times (msec) of temporal and nasal retinal ERGs were 21.7 ± 0.9 and 22.0 ± 1.1 (a-wave), 42.8 ± 2.6 and 43.4 ± 1.8 (b-wave), 25.8 ± 1.0 and 26.3 ± 1.5 (O1), 32.4 ± 1.4 and 32.6 ± 1.2 (O2), and 39.3 ± 1.5 and 38.8 ± 2.2 (O3), respectively.

Case Report

The following case report demonstrates the importance of horizontal asymmetry of OPs to the analysis of the focal macular ERG. A 14-year-old girl had a unilateral coloboma-like region in the posterior pole of her right eye. The region was approximately 17° (vertical) by 20° (horizontal) and was located on the temporal side of the fovea (Fig. 7A). The foveola was spared from the region, and visual acuity was 0.9. The region showed an absolute scotoma in subjective scotometry, and the focal ERG from the region was nonrecordable with a 15° spot.

We stimulated the fovea with a 15° spot, centered on the foveola as shown in Figure 7B. The focal macular ERG recorded under this stimulus condition is shown in Figure 8A. The ERG was elicited only from the normal nasal retina, resembling results obtained with the nasal hemicircular stimulus spot in normal eyes. We compared the focal ERGs...
recorded from nasal (Fig. 8B) and temporal retina (Fig. 8C) with hemicircular stimuli to the normal left eye. The a- and b-waves were slightly larger in temporal retina than in nasal retina; however, as was seen in normal subjects (Fig. 6), the OPs were much larger in temporal than in nasal retina. The focal macular ERG in the right eye with the 15° spot (Fig. 8A) showed amplitude similar to that recorded with the nasal hemicircular stimulus in the left eye (Fig. 8C).

Discussion

Our finding that the amplitude of focal ERG was slightly, but significantly, larger in the upper than in the lower retina is consistent with previous reports that variable visual function tests suggest functional superiority of the upper retina. Analyses of the standing potential have led to the suggestion that these differences arise from the retina itself, since the standing potential primarily reflects the function of retinal pigment epithelium. However, there has been no statistical comparison of focal ERGs (using flash stimuli) of the upper and lower retina.

Our results indicated that the asymmetry of the upper and lower retina is based, at least in part, on retinal function, as demonstrated by flash ERG. Flash ERGs differed in amplitude, but not in implicit time. Reduced amplitude without prolonged implicit time is also observed in cases of patchy destruction of the retina, such as localized choroidal scar. The difference of amplitude without difference of implicit time in upper and lower hemiretina may be the result of anatomical differences in the regional distribution of rods and cones; a higher density of photoreceptors has been reported for upper retinal areas. Although there was no difference of implicit time in flash ERG, shorter latencies of VEP components have been suggested for the upper than the lower hemiretina. These inconsistent results for ERG and VEP timing may suggest that the asymmetry in the vertical merid-
The enormous asymmetry found only in OPs from temporal and nasal retina was surprising. Since a- and b-waves did not show any asymmetry, it is unlikely that the asymmetry of OPs is caused by artifacts, such as inharmonious stimulus intensity or stimulus size. We previously reported that the distribution of OPs in the fovea is relatively sparse compared with that of a- and b-waves; closer to the parafovea, however, OPs become more dense than a- and b-waves, and become even denser in ERGs taken closer to the perifovea. The current study describes an additional feature of the distribution of OPs, as distinct from a- and b-waves, in the human macular region.

We are very interested in the relation of the selective asymmetry of OPs to psychophysical visual function. Payne reported that visual reaction time is faster on the nasal side than on the temporal side. Similarly, critical flicker fusion and double flash discrimination have indicated superior visual function in the nasal over the temporal retina. The larger amplitude of OPs that we observed in the temporal retina is not inconsistent with these findings, because OPs may not be related directly to such psychophysical visual functions; rather, OPs may reflect activity of inhibitory feedback synaptic circuits within the retina. Indeed, as we previously reported, the distribution of OPs in the central fovea is relatively sparse in comparison with a- and b-waves, even though the fovea is the most sensitive in some visual functions. Although the correlation between psychophysical visual function and OPs remains obscure, the significant asymmetry of OPs in the human macular region may provide useful evidence in the search for electroretinographical and psychophysical correlations.

Since it has been suggested that OPs arise from the amacrine or interplexiform cells, we checked the published literature of human or primate retinal histology, expecting to find an asymmetry of these cells between nasal and temporal retina. However, we could find no report on such a comparison. Some reports have indicated the nasotemporal difference in the number of cones and ganglion cells or in the optical density of foveal cone photopigments. Perry and associates reported that the ganglion cell soma diameter and dendritic field size tend to be larger in the temporal retina in monkey. Larger OPs from the temporal retina might be related to the functional segregation of axons within the optic nerve and differences in the retinal distribution of X and Y cells. It has also been suggested that dopamine modulates the biogenesis of OPs in human retina. Since amacrine and interplexiform cells contain dopamine, we thought that OPs might reflect dopaminergic neuronal activity. We did, in fact, find some correlation between the distribution of dopamine-containing amacrine cells in the macaque and that of OPs in the human macular region, when we compared both distributions in fovea, parafovea and perifovea. However, Mariani and associates found little difference in the distribution of dopamine-containing amacrine cells between the nasal and temporal retina of the macaque.

Although we found no previous report that suggests reasonable correlation with the OP asymmetry, we believe that this finding provides useful evidence in the investigation of the retinal neural network as well as in analysis of the macular ERG of some diseases, as illustrated by the case report.

Key words: functional asymmetry, focal macular ERG, upper and lower retina, nasal and temporal retina, oscillatory potentials.
Acknowledgments

The authors thank Prof. Shinobu Awaya for revision of our manuscript. We are grateful to Dr. Kazuo Kawasaki, Dr. Hiroshi Shirao and Dr. Toshiro Tamura at Kanazawa University for their useful suggestions in this study.

References


