

Multifocal Electroretinogram in normal subjects

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Abstract

Background: Multifocal electroretinogram (mfERG) is a device for recording the physiological response of multiple retinal areas in short time. Using this technique enables us to detect the spatial extent and severity of the retinal damage. **Objectives:** In this study, we aimed to assess the topographic properties of mfERG in normal subjects to use it as a basic data to evaluate eye disease. **Methods:** We recorded mfERG from 20 eyes of 20 normal subjects. We measured amplitude and latency of recorded waves. We compared between amplitude of these waves between different retinal areas and the same for latency. **Results:** We found mfERG responses in the form of waves, every wave consists of negative wave (N1) followed by positive wave (P1). The amplitude of N1 wave and amplitude of P1 were largest at the fovea and decreased toward periphery. The latency of N1 and P1 were shorter in upper retina than lower retina. The N1 amplitude and P1 amplitude was larger in upper retina than lower retina, which reflex functional superiority of upper retina. There was no statistical difference between nasal and temporal retina in the amplitude and latency. **Conclusion:** Multi-focal ERG would be useful for objective examination of the retinal function.

Key words: *mfERG; retina; topography; functional superiority of upper retina.*

Introduction

The multifocal electroretinogram (mfERG) is a relatively new technique for assessing the local ERG from different regions of the posterior retina. It was developed by Sutter in 1992, which measures the spatial distribution of the central retinal cone function (1). The mfERG extracts many local responses simultaneously by mathematical analysis through pseudorandom light stimuli following binary m-sequence. The result of mfERG is obtained from multiple retinal areas simultaneously in short time and the amplitude of response is reported to correspond to the density of the cones (2). Electrical responses from the eye are recorded with a corneal

electrode just as in conventional ERG recording, but the special nature of the stimulus and analysis produce a topographic map of ERG responses (3). mfERG is a very sensitive tool in detection of localized retinal dysfunction in a patient who had normal full-field ERG (4). In our study, we aimed to analyze the topographical properties of mfERG responses in multiple retinal areas in normal eye to use it as a basic data to evaluate eye with pathology.

Subjects and Methods:

This study was applied to healthy subjects (volunteers) from TOMEY corporation company, Nagoya, Japan. Informed consent was obtained from

each subject after a full explanation of the procedures. This study was approved by the ethical committee review board of Fujita Health University, Nagoya, Japan and Sohag University, Egypt. Multifocal ERGs were recorded in **20** eyes of **20** normal subjects with no ocular disease except for refractive error. The eye of the subject's choice was tested (**11** right eyes and **9** left). Subjects ranging in age from **31–53** years (mean=**42.35** years). All subjects received eye examination including a fundus examination with dilated pupils. The visual acuity was **1.0** or better with correction. Refractive error ranged from **0** to **-6** diopters. The mean spherical equivalent refractive error of these subjects was **-2.94** Diopters (± 1.92 D). All subjects were free of ocular and systemic pathology.

Recording:

All subjects were subjected to full ophthalmological examination including visual acuity, slit-lamp examination, intraocular pressure, and direct and indirect ophthalmoscope. The recordings were performed under room light conditions.

Pupils were dilated with eye drops of **0.5%** tropicamide and **0.5 %** phenylephrine hydrochloride. Subjects sit comfortably in front of the screen. The pupil was centered in the corneal electrode ring using contact lens electrodes. Two drops of topical anesthetic were placed on the eye prior to inserting the contact lens electrode. Celluvisc (Allergan, Irvine, CA) was used to protect the cornea under the contact lens electrode. If more than two blinks were present in a **30** sec segment, the data for that segment were discarded

and the segment repeated. A ground electrode was clipped to the left ear lobe. Good fixation, both central and steady, was done to avoid eccentric fixation. Refraction was corrected by using lenses that was placed in a holder in front of the eye.

Response analysis:

The waveforms in mfERG consist of negative peak called (**N1**) wave and positive peak called (**P1**) wave. The amplitude of the **N1**-wave was measured from the baseline to the bottom of the **N1**-wave, and the amplitude of **P1**-wave was from the trough of the **N1**-wave to the peak of the **P1** wave. The peak latency was defined as the period from the time stimulation was given to the peak of each wave (Figure 1).

Responses from all elements of the stimulus were grouped to learn the topographical properties of retinal responses as follows: (a) fovea and its outer portions, (b) upper and lower retina, and (c) nasal and temporal retina. The amplitude (nv/deg^2) and the latency (milliseconds) of the first negative wave (**N1A** and **N1L**, respectively), and the first positive wave amplitude and latency (**P1A** and **P1L**, respectively) were recorded. The data obtained were exported to excel sheet. Statistical analysis was carried out using the excel **2013**. Analysis of variance (ANOVA) was used to correlate the change in mfERG responses with increasing eccentricity from the fovea, paired t -tests for the upper and lower retina, and the nasal and temporal retina. **P < 0.05** was considered statistically significant.

Results

Comparison between the Fovea and Its Outer Portions:

We grouped responses in a trace array into four areas and named the areas **1** to **4**, respectively, from the center to the periphery (Figure 2). Responses were summed and averaged in each area. A negative wave (N1-wave) and a positive wave (P1-wave) were found in all areas. Statistical difference was found, but there was a tendency for N1 latency to be long at the fovea, shorter at the parafovea, and again longer at the perifovea ($P = 0.01$) (Table 1, Figure 3A). Also The P1 latency was long at the fovea, shorter at the parafovea, and again longer at the perifovea ($P = 0.5$) (Figure 3C). The N1 and P1 amplitudes decreased from the fovea outward ($P < 0.0001$) (Figures 3).

Comparison between the Upper and Lower Retina

Each wave grouped in the upper and lower retina as shown in (Fig.4) and summed and averaged focal ERGs in each group. The latency of the N1 wave was statistically shorter in the upper retina than in the lower retina (Table 2, $P < 0.0001$). The N1 amplitude was statistically larger in the upper than in the lower retina (Table 2, $P = 0.0008$). The P1 amplitude was statistically larger in the upper than in the lower retina (Table 2, $P = 0.0001$). The latency of the P1 wave was statistically shorter in the upper retina than in the lower retina (Table 2, $P < 0.0001$).

Comparison between the Temporal and Nasal Retina

We grouped each wave in the nasal and temporal retina as shown in (Figure 5) and totaled and averaged focal ERGs in each group. The portion including the optic disc was excluded from the summation. No statistical difference was found in N1 latency ($P = 0.04$), N1 amplitude ($P = 0.32$), P1 latency ($P = 0.13$), or P1 amplitude ($P = 0.12$) as shown in (Table 3).

Discussion

ERG response amplitudes are widely used to quantify retinal activity (5). In this study, the amplitudes of N1-waves and P1-waves were the largest in the fovea, and they decreased toward periphery. Song et al. (6) reported that with the increasing of eccentricity, P1 amplitude (all $p = 0.0000$ in ring 1 -5) of each group decreased. Azad et al. (7) reported that the amplitudes of the N1 and P1 waves also were largest in the fovea (area 1) and decreased progressively with increasing eccentricity. This observation may be explained anatomically by the cone density distribution, as demonstrated by Curcio et al. (8) from cadaveric retinas. Sutter and Tran (2) reported before that the multifocal ERG responses fell with eccentricity. Nagatomo et al (9) recorded multifocal ERGs from 20 eyes

of 20 normal subjects and analyzed the topographical properties of the responses and reported that the mean amplitudes were largest in foveal area and decreased with eccentricity by using a 61 element stimulus pattern. Hood et al (10) reported that the latencies can be a sensitive index of retinal damage in some eye disease. In our study, the latencies (Implicit Times) of N1-waves tended to be long in the fovea, become shorter in the parafovea, and again longer in the periphery. Also Implicit times for P1-waves show a slight tendency for foveal responses to be longer than parafoveal. Nagatomo et al. (9) reported the same findings. But the underlying physiologic mechanism remains unknown.

In contrast, Azad et al. (11) reported that the latencies of the P1 and N2

waves were longest in the central ring and progressively shortened with eccentricity. A similar finding was however not obtained in the latencies of the N1 wave.

It is noticed that the N1 and P1 amplitude were larger in the upper retina than in the lower retina. The N1 and P1 latencies were shorter in the upper retina than in the lower retina. Also Nagatomo et al. (9) have reported shorter latencies and larger amplitudes of upper over lower retina in the average of 20 eyes. A functional asymmetry between the upper retina and lower retina has been reported by visual acuity, and the standing potential

of the eye (12). These reports suggest a superior visual function in the upper retina over the lower retina. This proved that the new technique of multifocal ERG indeed reflects the local function of the outer retina.

No statistical difference was found between latency and amplitude of the nasal and temporal retina. But Sutter and Tran (2) reported that there was asymmetry between the nasal and temporal areas in every subject and the nasal retina showed higher response density. Nagatomo et al (9) and Wane et al (5) reported no statistical difference between the nasal and temporal areas which is the same in the present study.

Figures:

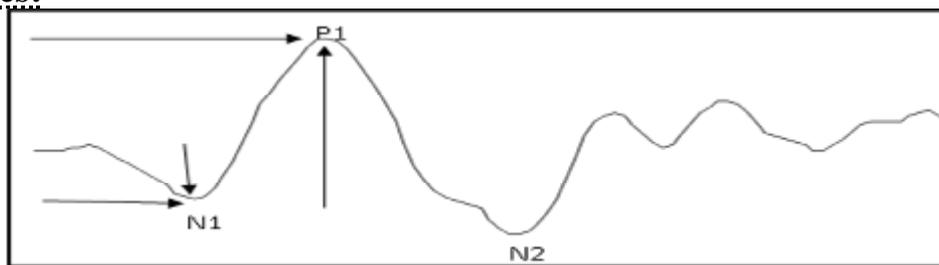


Fig. 1: Diagram of mfERG response to show the designation of the major features of the waveform. The arrows show the trough-to-peak amplitude (vertical arrow) and the implicit time (horizontal arrow) from the onset of the stimulus to the peak of the waveform.

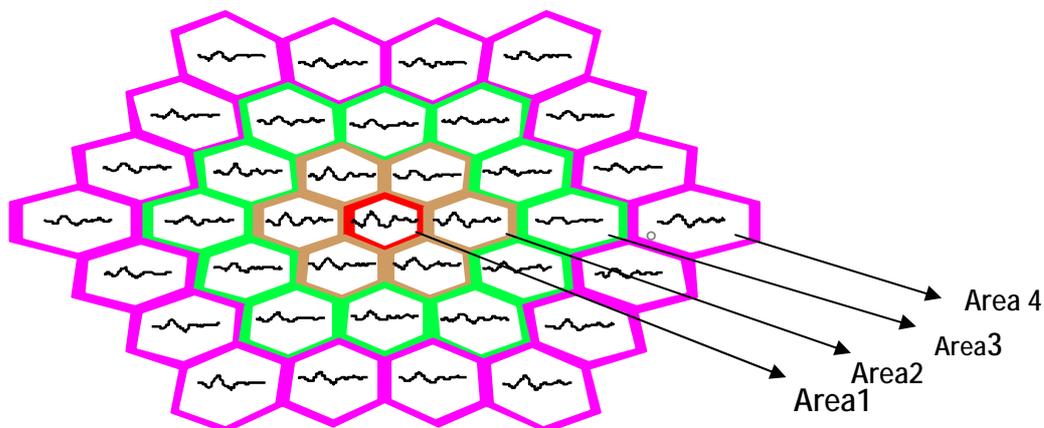


Fig. 2: Comparison between fovea and its outer portions. Area 1 corresponds to fovea, area 2 to parafovea, areas 3 and area 4 to the outer portions.

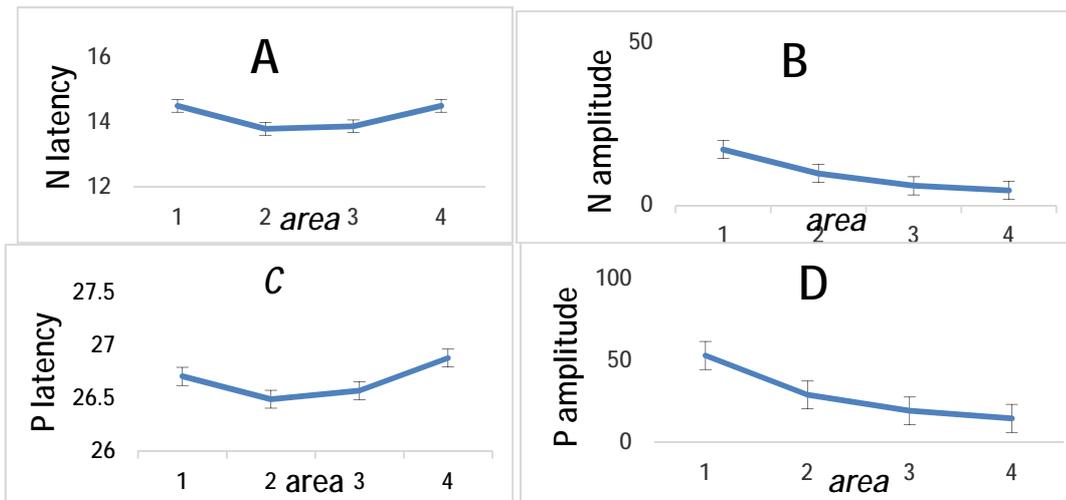


Fig.3. Comparison between fovea and its outer portions. Mean and standard error of N1 latency (A), N1 amplitude (B), P1 latency (C), and P1 amplitude (D) at four different stimulus sites illustrated in Figure 2.

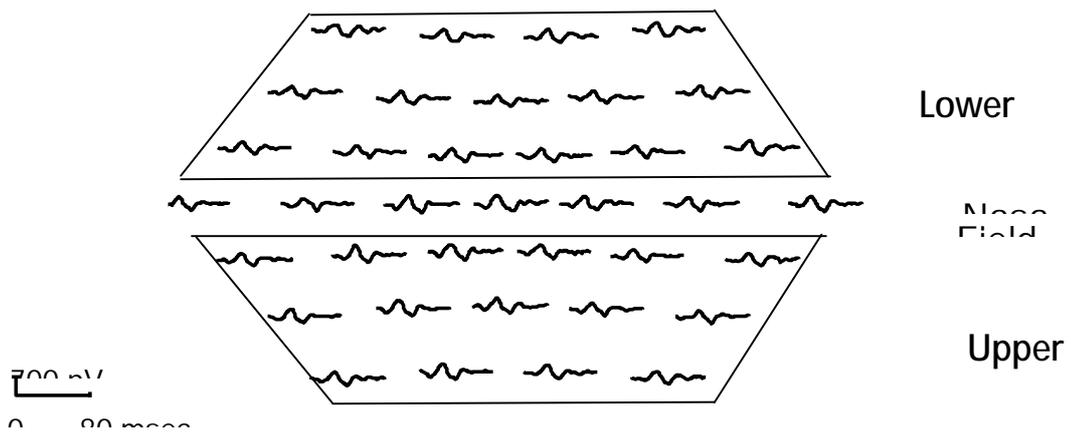


Fig.4. Comparison between the upper retina (lower half array) and lower retina (upper half array).

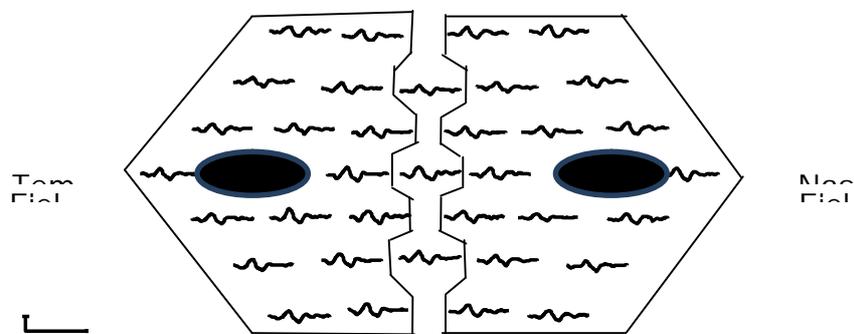


Fig.5. Comparison between the nasal and temporal retina, the portion that included the optic disc and the nasal portion corresponding to this black circular portion was excluded from the summation.

Tables

Table 1. Latency (msec) and Amplitude (nV/deg²) (Mean± Standard Error) of the N1 and P1-Waves at Four Different Stimulus Sites Illustrated in Figure 2.

	area1	area2	area3	area4
N1 Amplitude	17.13±1.58	9.80±0.69	6.03±0.44	4.61±0.34
N1 Latency	14.50±0.28	13.79±0.18	13.87±0.18	14.50±0.17
P1 Amplitude	53.28±4.64	29.19±21.99	19.39±1.32	14.82±0.93
P1 Latency	26.70±0.20	26.49±0.22	26.57±0.24	26.88±0.23

Table 2. Latency (msec) and Amplitude (nV) (Mean ±Standard Error) of the N- and P1-Waves at the Upper and Lower Retina.

	Upper Retina	lower Retina
N1 Amplitude	6.13±0.41	5.24±0.44
N1 Latency	13.58±0.16	14.98±0.14
P1 Amplitude	18.67±1.17	17.04±1.10
P1 Latency	25.66±0.80	26.70±0.76

Table 3. Latency (msec) and Amplitude (nV) (Mean ±Standard Error) of the N- and P1-Waves at the Temporal and Nasal Retina.

	temporal Retina	Nasal Retina
N1Amplitude	5.62±0.42	5.85±0.41
N1 Latency	14.15±0.16	14.41±0.15
P1Amplitude	17.45±1.45	18.40±1.13
P1 Latency	26.37±0.74	26.16±0.20

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