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A Basic Investigation of Multifocal Electroretinogram: Reproducibility and Effect of Luminance

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Purpose: To investigate the reproducibility as well as the effect of luminance in multifocal electroretinogram (mERG).

Methods: Multifocal electroretinogram recordings were repeated on different days in 6 normal subjects using the Veris III system. The mean luminance of the monitor displaying the stimuli was randomly varied by five kinds of neutral density (ND) filters.

Results: The standard deviation of mERG amplitude from the macular region was approximately 10% of the mean value for each normal subject. Reproducibility largely depended on the condition of the subject and placement of the contact lens electrode. With decreases in the mean luminance of the monitor, the amplitude of mERG decreased exponentially, whereas the peak latency increased linearly. mERGs elicited from a patient with mild cortical cataract resembled the mERGs obtained from the control group using an ND filter between −0.30 and −0.52 log, whereas two patients with typical retinitis pigmentosa showed much lower response densities in mERGs.

Conclusions: It is necessary to pay attention to the reproducibility and the luminance effect to obtain reliable mERGs. **Jpn J Ophthalmol 2000;44:122–127**

Key Words: Cataract, luminance, multifocal electroretinogram, reproducibility, retinitis pigmentosa.

Introduction

Until now, it has been possible to obtain only a single focal response from the retina. The multi-input stimulus technique[1] of multifocal electroretinogram (mERG) will make it possible to record simultaneously from many focal retinal areas. Each response density can be calculated from the corresponding focal electroretinogram to yield a functional topography. It is important to evaluate the reproducibility of mERGs recorded from healthy subjects before the application of mERG for diagnosis of various ophthalmic diseases. Recently, several basic studies have been reported concerning mERG data taken from normal volunteers.[2–5] It is necessary to accumulate more data on healthy patients to establish criteria for using mERG in the clinic.

We have investigated the feasibility of using mERG to evaluate parafoveal visual field defect.[6] In this study, mERGs were obtained from healthy subjects to evaluate the reproducibility as well as the monitoring of luminance. The original waves were analyzed for peak latency and amplitude. mERGs were also elicited from a patient with cortical cataract and two patients with retinitis pigmentosa. These clinical data were compared with data obtained from a control group to determine the effect of stimulus luminance on mERG.

Materials and Methods

mERGs were recorded using the Veris III system (Tomey, Nagoya). The stimuli displayed on a cath-

Received: July 22, 1998
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Published by Elsevier Science Inc.

0021-5155/00/$–see front matter
PII S0021-5155(99)00189-6

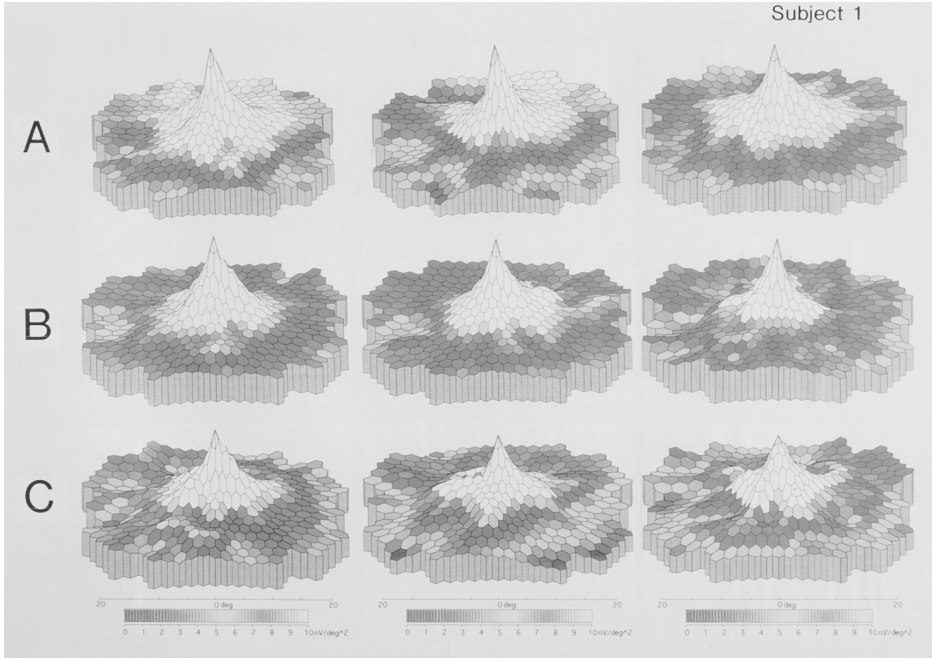

Figure 1. Multifocal electroretinograms recorded from a well-trained normal younger subject in control group A (subject 1). Three series of three consecutive trials on different days (**A**, **B**, and **C**) are depicted.

ode-ray tube (CRT) monitor (Sony, Tokyo) consisted of densely arranged arrays of 103 hexagonal elements. The size of the CRT monitor was 42° high by 45° wide. Three healthy younger patients (27, 28, and 35 years of age: control group A) and an older group (60, 64, and 68 years of age: control group B) participated in this study after giving their informed consent. Their refractive errors were between −0.5 D and −3.0 D.

Each hexagonal element was independently altered between brightness and darkness according to a special scheme using binary M-sequences at a frequency of 75 Hz. The mean luminance was 91 cd/m^2 (L max = 178 cd/m^2, L min = 4 cd/m^2) without a neutral density filter. The contrast was 95%. The pupils were fully dilated by drops of 0.5% tropicamide and 0.5% phenylephrine · HCl solution. mERGs were recorded using a bipolar contact lens electrode after corneal anesthesia was induced with two drops of oxybuprocaine chlorohydrate solution. One or more drops of artificial tears (sodium hyaluronate) were instilled before lens insertion. A ground electrode was placed at the ipsilateral earlobe. Each subject was seated comfortably with chin and forehead immobilized, wearing a bipolar contact lens electrode. Subjects were asked to fixate monocularly on a point in the center of CRT monitor. The distance between the tested eye and the CRT monitor was 32 cm. Signals were amplified using model 12-4 Neurodata Acquisition System (Astro-Med, Glass Instrument Division, West Warwick, RI, USA) and band-pass filtered from 10 to 300 Hz. It took 4 minutes (eight 30-second sessions) to obtain one mERG recording for one subject. To study the reproducibility of mERGs recorded from normal subjects, recordings were repeated on 3 different days.

To create various levels of mean luminance, five different neutral density (ND) filters, which correspond to −0.15 log, −0.30 log, −0.52 log, −1.0 log, and −2.0 log, were randomly used. Multifocal electroretinograms were recorded with these ND filters fixed to the spectacle frame, and the responses obtained from the center region were analyzed.

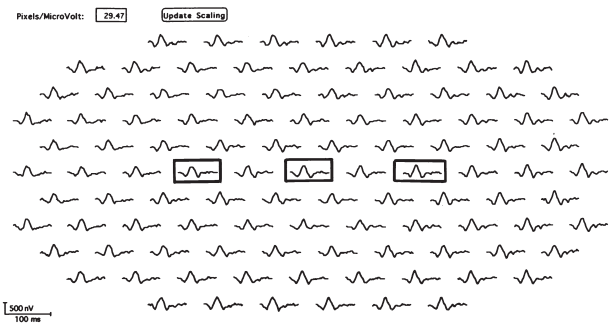

Figure 2. Multifocal electroretinogram original waves elicited from 103 hexagonal stimulus elements in subject 1. After enlargement of each wave amplitude between initial negative and initial positive peaks was measured for center, nasal, and temporal responses enclosed by squares in this figure.

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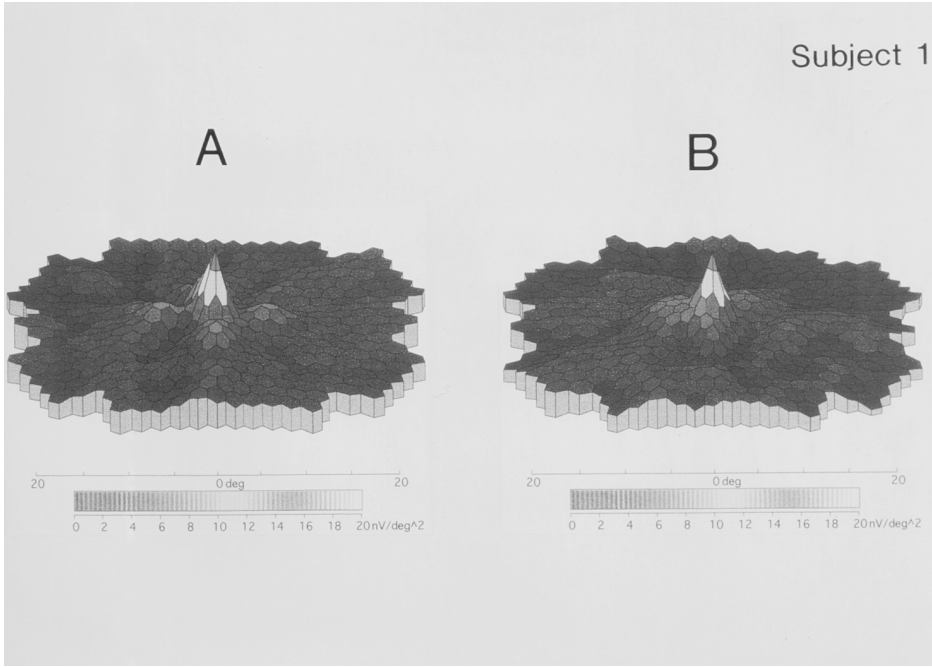

Figure 3. Multifocal electroretinograms recorded when subject 1 was in less than optimal condition (**A**), or when an air bubble formed between the cornea of the tested eye and the contact lens electrode (**B**).

mERGs were also recorded from one patient with mild cataract and two patients with typical retinitis pigmentosa. The patient with cataract (66 years of age) had no systemic disease and showed no fundus abnormality. His best-corrected visual acuity was 1.2 with a refraction of −1.75 D–0.50 DAx60° OD and 1.2 with a refraction of −1.75 D OS. The severity of cataractous lens transparency was evaluated by an anterior eye segment analysis system (EAS-1000; NIDEK, Tokyo). The response densities were compared with normal data to determine the effect of the ND filter. The mERGs recorded from the 3 normal older subjects (group B) were combined using the Veris Science software program. No lens opacity around the visual axis was observed in these group B subjects. The best-corrected visual acuities of the two patients with retinitis pigmentosa (47 and 35 years of age, respectively) were 1.2, with refractions of −1.75 D OS for case 1 and −1.25 D–1.25 DAx130° OS for case 2. No abnormality of the optic media was observed for either retinitis pigmentosa patient. The fundus examination revealed the typical bony corpuscle appearance, and Goldmann visual field testing for both cases showed markedly restricted fields with targets V-4 and I-4. These findings were similar in both the right and left eyes of each patient.

Results

Multifocal electroretinograms recorded in a well-trained normal younger subject (subject 1) are shown in Figures 1A–C. These recordings (Figures 1A–C) were performed on different days. The nine mERGs (Figure 1 in three-dimensional color map mode) are quite similar. The amplitude of each wave that is enclosed by a square in Figure 2 was measured between the initial negative and the initial positive peaks, as indicated by arrowheads in Figure 4B. The waveform of mERG consists of an initial negative, an initial positive, and an after-negative component. The standard deviations calculated from at least six mERG trials in group A subjects were approximately equivalent to 10% of the mean amplitude value (Table 1). These findings were the same in each of the 3 normal younger subjects. Even for a well-trained subject 1, much lower response densities of mERG were obtained when the subject was in less than optimal condition just after his night duty as a resident physician (Figure 3A). The intrusion of a large air bubble between the cornea and the inner surface of the contact lens electrode (Figure 3B) also contributed to lower response densities.

Table 1. Multifocal Electroetinograms (mERG) in Different Retinal Positions

Subject	Nasal	Center	Temporal
1	436.5 ± 43.4	442.8 ± 46.0	428.7 ± 41.2
2	333.3 ± 38.5	364.6 ± 34.4	316.7 ± 36.1
3	339.4 ± 27.8	383.7 ± 36.5	348.5 ± 26.2

Note: Mean amplitudes ± standard deviations measured from 103 original mERG waves depicted in Figure 2. Data for 3 normal younger subjects in control group A.

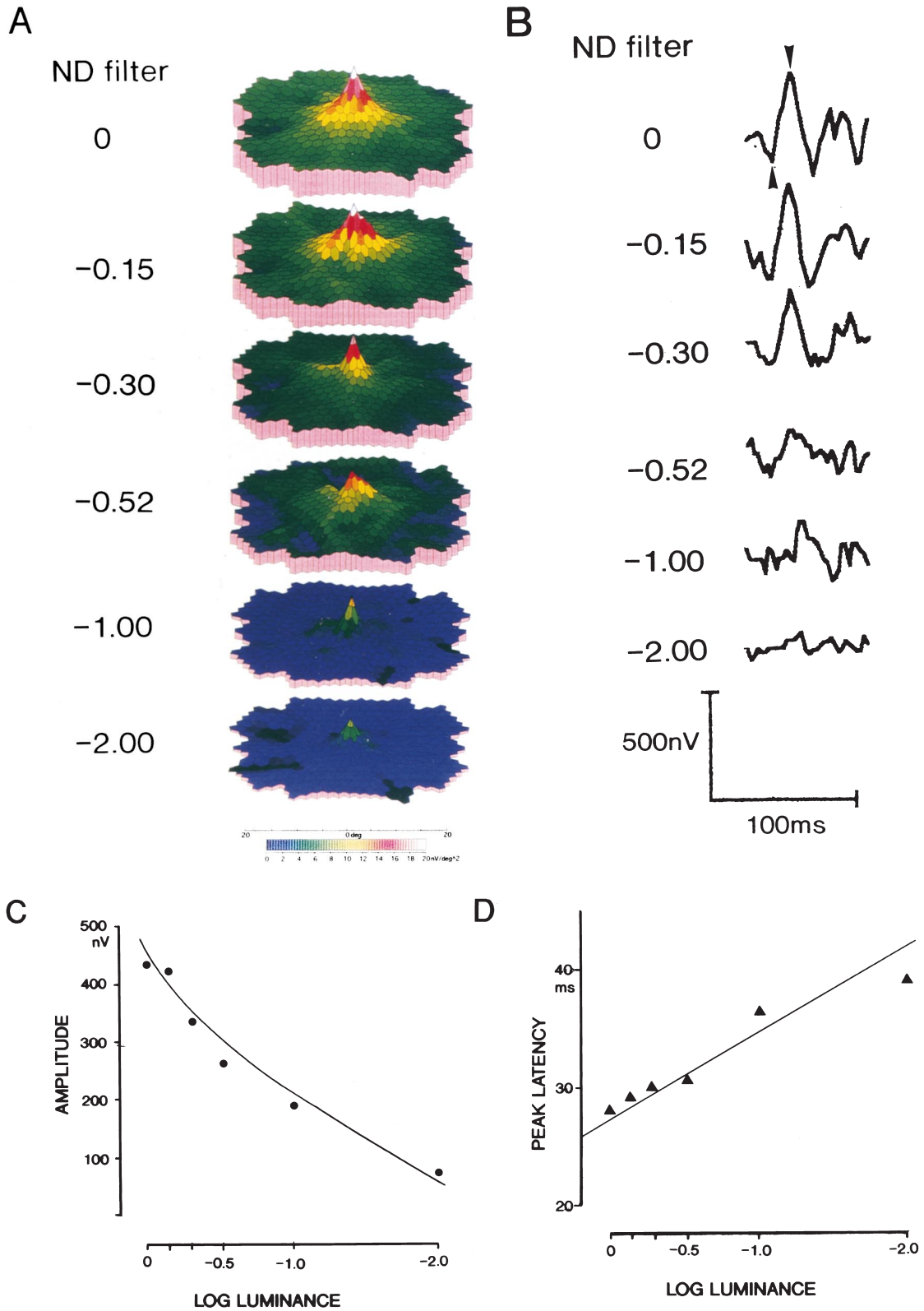

Figure 4. Three-dimensional color maps of multifocal electroretinograms recorded with varying neutral density filters (**A**) in subject 2 in group A. Range of density scale, 0–20 nV/deg^2. These amplitudes obtained from center region (**B**) were measured and potentials between initial negative (▲) and the initial positive (▼) components (**C**) and positive peak latencies (**D**) were calculated. ND: Neutral density.

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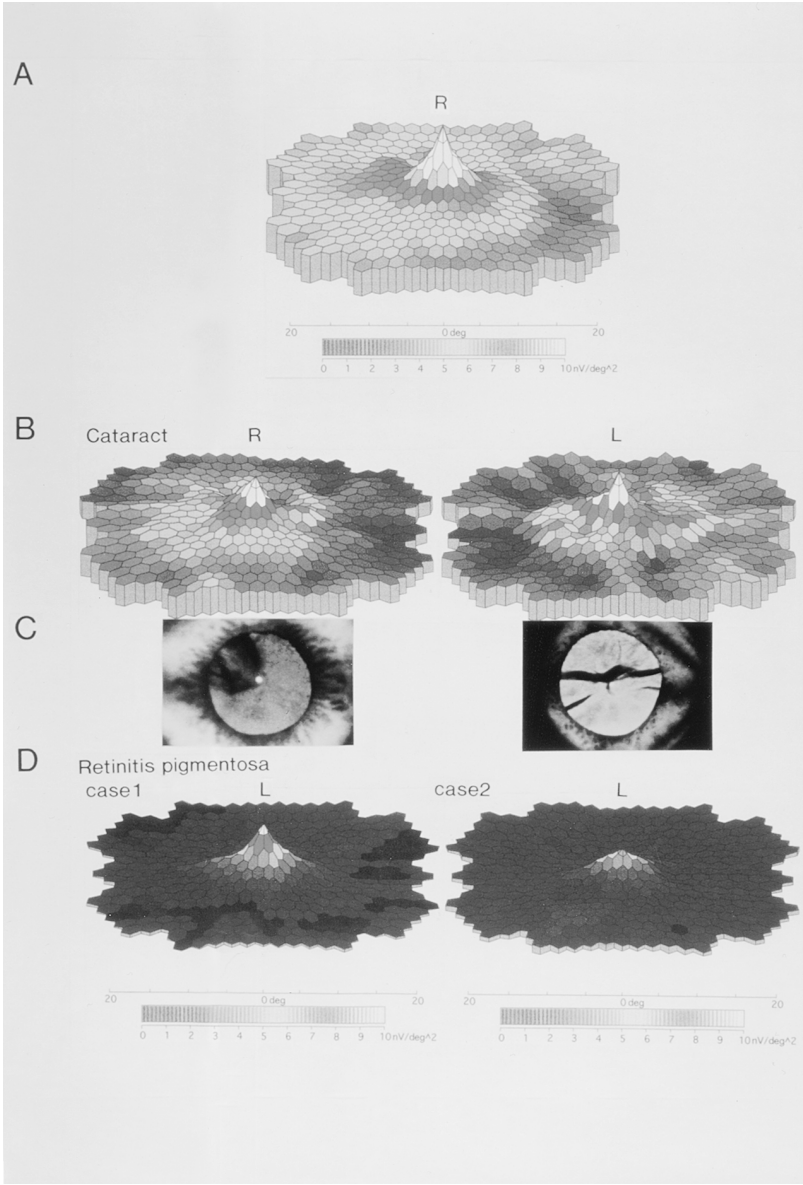

Figure 5. Combined multifocal electroretinograms (mERGs) recorded from 3 normal older subjects in control group B (**A**), mERGs recorded from patient with mild cataract (**B**) and results of lens transparency evaluation by EAS-1000 (**C**). mERGs elicited from left eye of each of 2 cases of retinitis pigmentosa (**D**). Range of density scale, 0–10 nV/deg^2.

No significant difference in the three-dimensional color map mode was observed between mERG recorded without an ND filter and that recorded with a −0.15 log ND filter. As the mean luminance decreased, mERG response was gradually reduced (Figures 4A,B). The amplitude of m-ERG (Figure 4C) decreased exponentially with the decrements of mean luminance, while the peak latency of m-ERG was prolonged linearly (Figure 4D).

The response densities of mERGs recorded from the patient with mild cortical cataract (Figure 5B) were lower than those obtained after the combination of the data from the normal older subjects (group B) (Figure 5A). The cataract patient's examination using EAS-1000 equipment revealed that mild lens opacity was located near the visual axis (Figure 5C). The 2 patients with retinitis pigmentosa without cataract demonstrated much lower response densities of mERG (Figure 5D) in comparison with those elicited from the cataract patient.

Discussion

Multifocal electroretinograms recorded from the 3 normal younger subjects in control group A demonstrated good reproducibility; the three sets of three consecutive recordings were similar. The standard deviation value of mERG response density obtained from the center region was approximately equivalent to 10% of the mean amplitude value for each normal

subject (Table 1). This 10% of mean amplitude value might be a good indicator for assessing reproducibility when making a basic study of mERG with normal volunteers. According to another report,[7] the ratio of the standard deviation to the mean response density obtained from a normal subject after 10 continuous recordings was 14.9%.

The mERG recording largely depends on the physical condition of the subject as well as the placement of the electrode. It is very important to have the tested eye fixate on the center of the stimulus pattern during stimulation, and to take strict care to place the bipolar electrode accurately during attachment on the cornea.

The early stage of cataract is usually when the opacification involves the equatorial cortex. Our case showed mild cortical opacity around the visual axis. mERGs elicited from this cataract patient resemble those obtained using an ND filter between −0.30 log and −0.52 log if mERGs obtained from the normal older subjects in control group B are assumed to be comparable to that recorded without ND filter in Figure 4A. Because the lens opacity of the mild cataract patient is unusually homogeneous, there may be no way to quantify the filter effect of the lens opacity correctly, and the effect of the ND filter on mERG cannot be directly applied to assessing the visual function of this case. However, the functional difference between the mERGs of the cataract patient and those of the control group B may be equal to the difference between 0.30 and 0.52 log ND filters, if we state the functional difference only in terms of the effect of the luminance. Likewise, the functional differences between the retinitis pigmentosa cases without cataracts and the normal older group B may be interpreted between 1.0 and 2.0 log ND filters. Hood et al[8] recorded mERGs from retinitis pigmentosa patients. They used spatial annular summation for mERGs without proof of whether the first order response component of mERG truly shows linearity in terms of spatial summation. They also compared the total mERGs for all 103 responses with those for the central 7 responses. Because some waves in their Figure 4 do not start at zero time, their discussion of the implicit time is not convincing.

Our patient with cataract demonstrated that it is necessary to pay attention even to mild senile cataract when studying the relationship between aging and mERG response. It should be understood that the loss of visual function in the patients with typical retinitis pigmentosa having good visual acuities partly reflects the influence of the ND filter on the results of mERG.

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