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A comparison of the fast stimulation multifocal-ERG in patients with an IOL and control groups of different age

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Abstract

Purpose: It has been shown that a cataract significantly reduces mfERG responses in the central 4–14°. Removing the cataract, leads to a significant increase in the response of the central 4°. In this study we compare the mfERG of Woerdehoff et al.'s patients' [Doc Ophthalmol 2004; 108(1): 67–75] following cataract surgery to a healthy control group in order to assess whether, in the elderly, further influences of age need to be considered in addition to optical effects. *Methods:* Eighteen patients with an IOL following cataract surgery and 29 healthy volunteers (without clouding of the media or retinal changes) underwent testing of the mfERG (103 hexagons stimulating the central 50°, M-sequence 2^{15}, L_{max}: 200 cd/m^2, L_{min} <1 cd/m^2). For the first order response component we compared the latencies of N1,P1 and N2 as well as the natural logarithm (ln) of the amplitudes N1P1 and P1N2 for four group averages: I. the central 4°, II. 4–7°, III. 7–10° and IV. 10–15°. *Results:* Mean age was 67 years (SD 10.1) for the IOL patients, 28.5 years (SD 5.6) for a young group of controls ($n=15$) and 60.2 years (SD 9.2) for the older control group ($n=14$). Patients with an IOL did not differ in latency from either control group (ANOVA, Tukey). Interestingly, at 10–15° eccentricity, the latency of N2 differed significantly between the younger (41.4 ms, SD 1.4) and the older (43.0 ms, SD 1.9) control group. In the central 4° LnN1P1 amplitudes were significantly lower in the IOL group (mean: 3.7, SD 0.2) than either the younger (mean: 3.9, SD 3.3) or the older (mean: 4.0, SD 0.3) control group. In all other amplitude measures, the older control group had slightly larger mean amplitudes than the younger control group and significantly larger amplitudes than the patients with an IOL, whose amplitudes were lowest. *Discussion:* Both, primarily optical but also neural phenomena have been described to affect the mfERG changes observed with age. Our results, are in support of this, as the improvement of the mfERG response following cataract surgery does not seem to reach the level of a healthy control group of equal age. Thus, our results suggest, that a control group with an IOL should be used when retinal function is tested in subjects with an IOL.

Introduction

It has recently been shown that a cataract significantly reduces mfERG responses in the central 4–14° [1, 2]. On the other hand, removing the cataract, leads to a significant increase in the response of the central 4° [1]. This suggests, that following cataract extraction, the mfERG may recover to normal values. If this were the case, the mfERG in patients with a retinal problem who happen to have an IOL might be compared to a healthy control group, although it needs to be determined, whether this control group would have to be age matched, as recent literature contains conflicting reports on the influence of age on the mfERG: While some report no change

with age [3], most studies report a reduction in amplitudes with or without an increase in latencies [4–11]. These age related changes have been thought to occur primarily as a result of an increasing lens opacity with age [7]. However, others have suggested neural changes to be additionally involved in these effects[6].

In this study we therefore compare the mfERG of pseudophake [1] to an age matched as well as to a younger healthy control group in order to assess whether, in the elderly with an IOL, further influences of age need to be considered in addition to optical effects.

Methods

Eighteen pseudophake patients and 29 healthy volunteers underwent testing of the mfERG.

Mean age was 67 years (SD 10.1) for the IOL patients, 28.5 years (SD 5.6) for a young group of controls ($n=15$) and 60.2 years (SD 9.2) for the older control group ($n=14$). Visual acuity was over 0.8 in patients with an IOL and 1.0 in the control group.

In either patients or subjects, inclusion criteria included the absence of clouding of the optic media, other eye disease, such as glaucoma, or systemic diseases that might affect the mfERG recording, such as diabetes mellitus, as well as refractive errors exceeding 6 dioptres spherical correction and 3 dioptres astigmatic correction. No previous eye surgery – other than the cataract surgery in patients- had been performed in the eyes recorded from.

Patients with an IOL were taken from the study of Woerdehoff et al. [1]. In these patients, the mfERG was recorded prior to and at least 6 weeks following cataract surgery. Patient pt15 who suffered from retinal dysfunction secondary to an eye trauma was excluded. Three patients received a multifocal IOL, while the others received a monofocal IOL.

In patients the eye undergoing cataract surgery was included. In 14 patients this was the right eye, in 4 the left eye. In the control subjects the right eye was included, unless it did not fulfil the inclusion criteria. In this case the patients' left eye was included ($n=2$).

In agreement with the declaration of Helsinki, approval from the ethic comittee had been obtained and participants had given their informed consent in writing.

MfERGs were recorded with VERIS science^{TM} (EDI, San Mateo, California) using a Burian- Allen bipolar contact lens electrode. The stimulus was presented on a monochrome monitor. During recording, 103 hexagons stimulated the central 50° of the retina. Hexagons were scaled with eccentricity to take into account the distribution of retinal cones in this area. Hexagons flickered between light (L_{max}: 200 cd/m^2) and dark ($L_{min}<1$ cd/m^2) according to an M-sequence of 2^{15} [12]. An artefact elimination technique was applied once [12]. Individual responses were not additionally averaged with their neighbouring responses.

For the first order response component we compared the latencies of N1, P1 and N2 as well

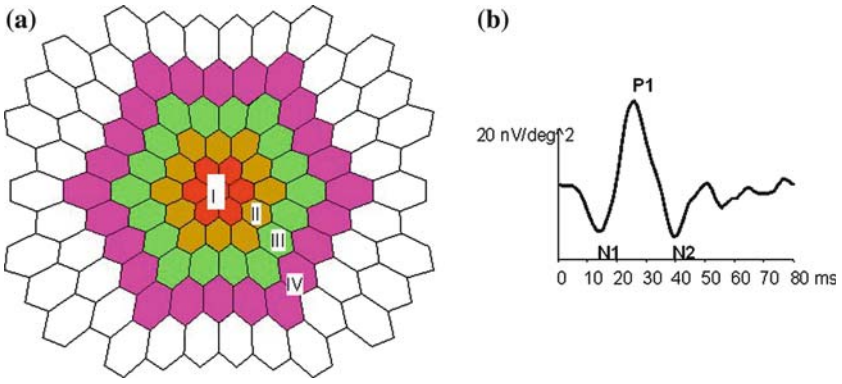

Figure 1. (a) Shows the area of the responses that were averaged for analysis: I. the central 4°, II. 4–7°, III. 7–10° and IV. 10–15°. (b Depicts a typical waveform of the first order response. For the first order response component we compared the latencies of N1,P1 and N2 as well as the natural logarithm (ln) of the amplitudes of N1P1 and P1N2 for the four group averages shown in 1a.

as the amplitudes of N1P1 and P1N2 for four group averages: I. the central 4°, II. 4–7°, III. 7–10° and IV. 10–15°. Figure 1 demonstrates the area of the responses that were averaged for analysis (Figure 1a) as well as a waveform showing N1, P1 and N2 (1b). As amplitudes are not normally distributed, they were normalized using the natural logarithm (ln).

For statistical analysis an ANOVA was performed, followed by a Tukey post hoc test. The resulting p-value was considered significant if it was below 0.05.

Results

Tables 1 and 2 show the resulting mean amplitudes and latencies and their corresponding standard deviation, while Figure 2 allows comparison of the ln amplitudes (Figure 2a and b) as well as of the latencies (Figure 2c).

Latencies did not differ between the pseudophake patients and the control groups (ANOVA, Tukey). Interestingly, between the younger and the older control group the latency of N2 differed significantly at 10–15° eccentricity ($p = 0.032$). Here the mean latency of N2 was 41.4 ms (SD 1.4) in the younger control group and 43.0 ms (SD 1.9) in the older control group (Table 2. Figure 2c). This compared to a mean latency of N2 of 42.5 ms (SD 1.7) in the pseudophake patients.

Amplitudes in the central 4° LnN1P1 (natural log) were lower in the IOL group (mean: 3.7, SD 0.2) than either the younger (mean: 3.9 (SD 3.3), $p = 0.043$) or the older control group (mean: 4.0 (SD 0.3), $p = 0.006$).

In all other amplitude measures, the older control group had slightly larger mean amplitudes than the younger control group and significantly larger amplitudes than the patients with an IOL, whose amplitudes were lowest (Table 1,

Table 1. Shows the mean amplitudes and their corresponding standard deviation for a young control group aged 20–40 years, for an older control group aged 41–72 years and for the patients with an IOL

Amplitudes (nV/deg^2)									
		Group average I		Group average II		Group average III		Group average IV	
		N1P1	P1N2	N1P1	P1N2	N1P1	P1N2	N1P1	P1N2
Control 20–40	Mean	57.5267	60.2667	37.8067	40.1400	29.0133	30.6533	22.7467	23.4933
	SD	21.8772	24.4176	17.7857	19.7598	13.6608	15.3024	11.5265	12.7517
Control 41–72	Mean	63.6214	74.5357	41.4357	49.1643	31.6000	38.0429	26.9357	30.4000
	SD	25.2789	32.8338	14.4032	18.9055	10.9400	13.9845	8.5732	10.6426
IOL	Mean	41.7294	46.8176	28.3059	31.1353	22.4882	24.1353	18.6118	18.9000
	SD	9.2089	12.8117	6.7110	8.3192	5.6337	6.5400	5.2315	5.5677

Table 2. Depicts the mean latencies and their corresponding standard deviation for a young control group aged 20–40 years, for an older control group aged 41–72 years and for the patients with an IOL

Latencies (ms)												
		Group average I			Group average II			Group average III			Group average IV		
		N1	P1	N2	N1	P1	N2	N1	P1	N2	N1	P1	N2
Control 20–40	Mean	15.2333	28.4867	44.2067	14.4933	27.5600	41.9800	14.2733	27.1067	41.4067	14.5000	27.1667	41.4267
	SD	1.1574	1.3907	1.4602	0.9331	1.3984	1.5758	0.9903	1.3392	1.6455	0.8194	1.4505	1.4210
Control 41–72	Mean	15.9000	29.3357	45.6714	14.7429	28.5071	43.4214	14.6429	28.1071	42.6500	15.1071	28.4500	43.0643
	SD	1.3342	1.5805	1.8433	1.1921	1.3205	1.5846	1.1036	1.6836	1.4179	1.0299	1.5356	1.9274
IOL	Mean	15.2941	28.6647	44.7824	14.1176	27.8412	42.5294	13.8647	27.2588	41.8824	14.7529	27.9824	42.4765
	SD	1.0201	1.1152	1.8294	0.9983	1.3933	1.7367	1.0612	1.5500	1.8256	0.8581	1.8782	1.7452

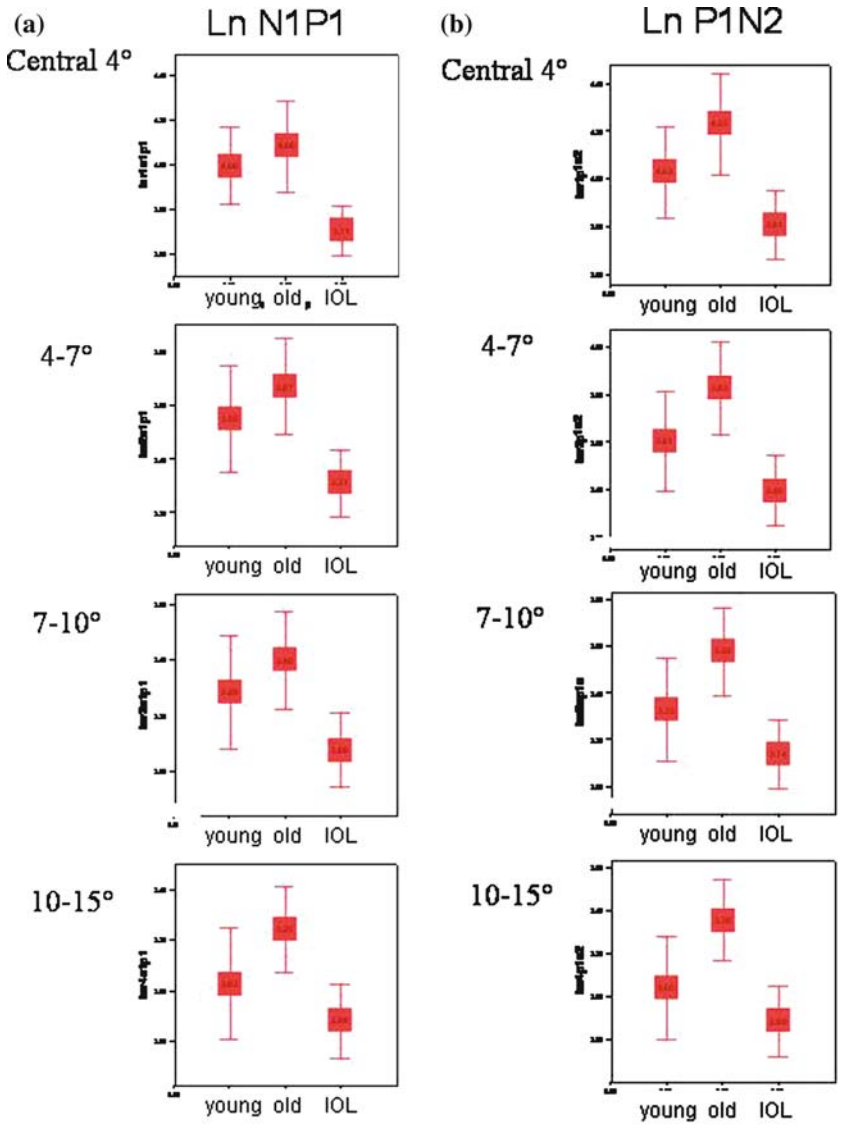

Figure 2. The boxplots in (a–c) show the ln amplitudes of N1P1 (a) and P1N2 (b) as well as the latencies of N1, P1 and N2 (c) for a young control group aged 20–40 years, an older control group aged 41–72 years and for the patients with an IOL. The error bars represent ±2 standard errors of the mean. Non-overlap between 2 SEs of adjacent means implies a significant difference at the 5% level ($p < 0.05$). The values in the ln amplitude plots are the mean ln amplitude values.

Figures 2a and b). Significant amplitude differences are listed below: In the central 4°, mean LnP1N2 was 4.23 in the older control group and 3.81 in the IOL patients ($p = 0.005$, Tukey). Between 4 and 7° mean LnN1P1 was 3.67 in the older control group and 3.31 in the IOL patients ($p = 0.013$, Tukey), while mean LnP1N2 was 3.83 in the older control group and 3.4 in the IOL patients ($p = 0.005$, Tukey). From 7 to 10° mean LnN1P1 was 3.4 in the older control group and 3.08 in the IOL patients ($p = 0.029$, Tukey), while mean LnP1N2 was 3.58 in the older control group and 3.14 in the IOL patients ($p = 0.005$, Tukey). In the outer 10–15° mean LnN1P1 was 3.25 in the older control group and 2.88 in the IOL patients ($p = 0.022$, Tukey), while mean LnP1N2 was 3.36 in the older control group and 2.89 in the IOL patients ($p = 0.006$, Tukey).

The slight difference in age had no significant influence on the statistical outcome (ANOVA).

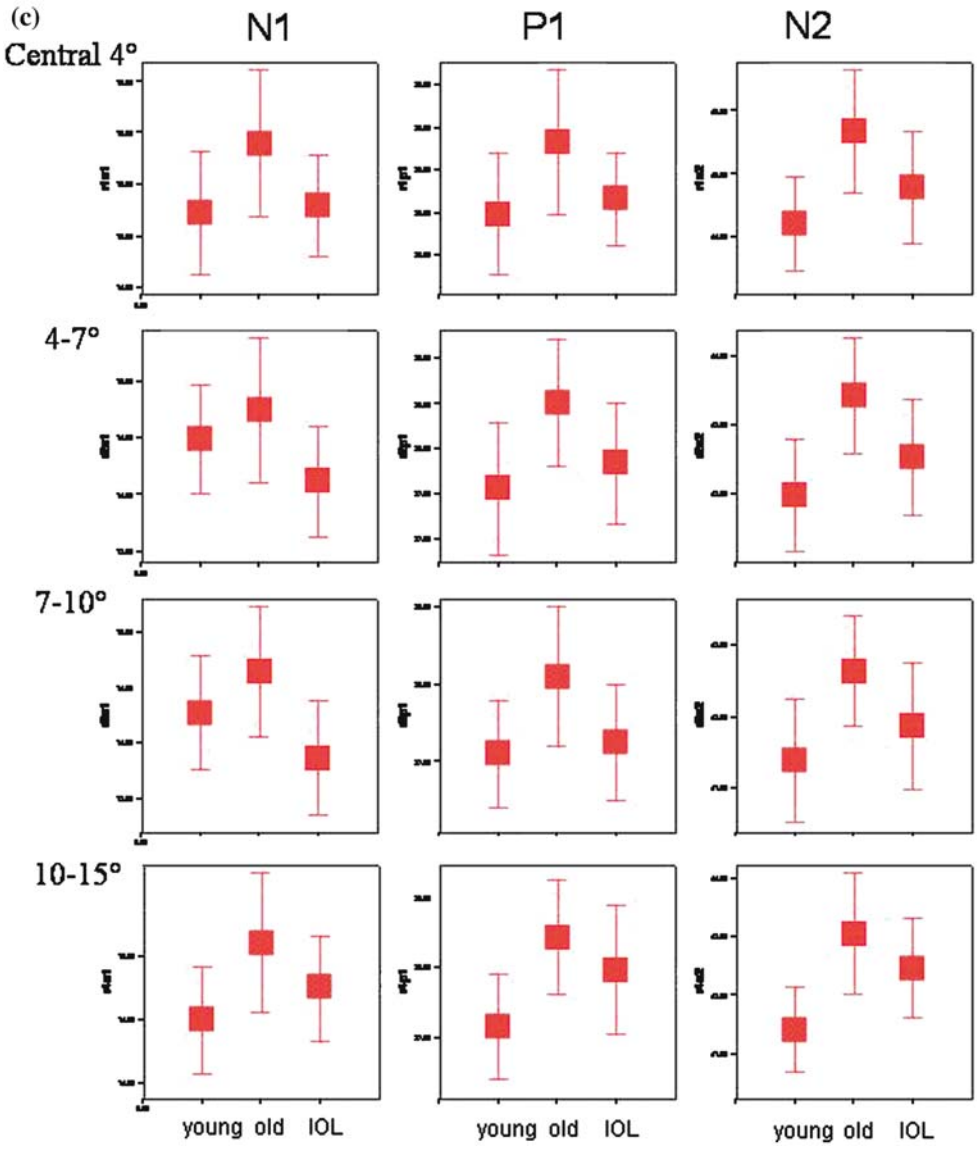

Figure 2. Continued

Discussion

Both, primarily optical but also neural phenomena have been described to affect the mfERG changes observed with age [6, 7]. In this context, response density is thought to be more influenced by optical factors while P1 implicit time changes are more influenced by neural factors [6].

If clearness of the optical axis alone were to account for the changes in the mfERG observed with age [4–11], patients with clear optical media should have mfERG responses comparable to a young healthy control group. Thus, with an IOL, the responses should also be better (amplitudes higher and latencies longer) than those of an age matched control group, where the lens is known to increase in density with age [13].

Another optical factor that needs to be taken into account is that IOLs generally transmit more blue light than the natural lens [14]. The phosphor used in our monochromatic monitor has a double peaked spectral energy distribution with one peak at around 450 nm and a second peak at around 550 nm. A recent study showed that flashes of

blue, green or white light produce a photopic hill response with an almost identical amplitude (V_{max}) [15]. Thus it might be expected that following cataract surgery, the increase in blue light transmittance would cause an increase in amplitude in the patients with an IOL. However, the improvement seen in the central mfERG response following cataract surgery [1] did not even reach the level of a healthy control group of equal age.

Recently intravitreal surgery with peeling of the internal limiting membrane has been shown to have no effect on inner or outer retinal function of the mfERG [16]. Therefore, a reduction in macular function secondary to the surgical light exposure also seems unlikely as a cause of the reduction in amplitude observed in this study.

The slight difference in visual acuity alone would also not account for the reduced amplitudes seen in the pseudophakes. A previous study showed that optical degradation through plus- or minus-lenses did not result in changes in the mfERG of healthy subjects [17]. Also, there is no direct relation between visual acuity and the amplitudes of the mfERG, as the mfERG responses are an averaged response over a retinal area of various size, whereas visual acuity is defined by the function of a few central photoreceptors.

Thus, as optical factors alone cannot explain the mfERG changes observed, our results, are in support of neural factors in addition to optical factors influencing mfERG changes in patients with an IOL.

In our study, amplitudes tended to be slightly higher in our older than in our younger control group. This may present either a selection bias or represent a biological advantage in these older subjects without age related diseases.

Our findings of high amplitudes in the elderly is in contrast to previous findings that show amplitudes to decrease with age [4–11]. However, the inclusion criteria for elderly subjects differ between these studies. As an example, patients with upto five small drusen were included in one study [11], while another allowed a visual acuity of 0.8 or higher [10]. This makes it difficult to compare subject populations, as it is known, that for example drusen affect the mfERG response [18, 19]. Thus the population in elderly control subjects may differ between studies.

Patients with a cataract are known to have an increased risk of developing other age related diseases such as artherosclerosis [20] or age related macular degeneration [21], suggesting that patients with a cataract may age faster and thus have a greater likelihood of being affected by subclinical retinal pathology. In comparison, this would mean, that older patients without a cataract are likely to age slower. Thus our elderly control group consisting of subjects with clinically very clear lenses and no retinal abnormalities may have a biological advantage.

Thus, our results suggest, that a control group with an IOL should be used when retinal function is tested in subjects with an IOL.

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