Myopic Children Have Central Reduction in High Contrast Multifocal ERG Response, While Adults Have Paracentral Reduction in Low Contrast Response

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Purpose. To compare the retinal function of myopic children and young adults using the multifocal electroretinogram (mfERG).

Methods. Fifty-two children (aged 9–14 years) and 19 young adults (aged 21–28 years) with spherical equivalent refractive errors ranging from plano to −5.50 diopter (D) were recruited. They were examined using the global flash mfERG at 49% and 96% contrasts. Each local mfERG response was pooled into five concentric rings for analysis. The amplitudes and implicit times of direct components (DC) and induced components (IC) from the global flash response were analyzed. Hierarchical multiple regressions were used to evaluate the influence of refractive error and axial length on the DC and IC responses.

Results. Compared with the emmetropes of the same age group, myopic children had a significant reduction in central macular DC response at 96% contrast while the IC response was unaffected, but myopic adults showed significant reductions in paracentral IC amplitudes at 49% contrast. Implicit times for DC and IC responses were unaffected for either group.

Conclusions. Retinal function was unaffected in myopic children, except for the outer retina in the central macular region. In contrast, the inner retinal function was substantially reduced in myopic adults, especially in the paracentral region. This study provides further evidence for different retinal, physiological characteristics in myopic children and myopic adults. (*Invest Ophthalmol Vis Sci.* 2012;53:3695–3702) DOI: 10.1167/iovs.11-9379

Clinically, myopes usually show poorer visual performance in a variety of clinical tests such as visual sensitivity,[1,2] peripheral visual acuity,[3] temporal vision,[4] contrast sensitivity[5] and color vision,[6] probably due to retinal stretching associated with the enlarged eyeball. Structurally, the retina is thinner in human myopes,[7] and in the tree shrew with induced myopia.[8] This structural thinning was recently found to link with reduced retinal function in humans.[9]

Retinal function can be assessed by electroretinography. The multifocal electroretinogram (mfERG) can provide an indication of the regional responses of the central retina with a single examination.[10] The first- and second-order kernel mfERG responses, which are mathematically derived from localized retinal responses through a cross-correlation technique,[10,11] predominantly reflect the activity from the outer retina (i.e., photoreceptor, ON and OFF bipolar cells) and the inner retina (i.e., amacrine cells and ganglion cells), respectively.[12–14] Numerous studies have indicated that the first-order kernel mfERG response is reduced and delayed, especially in the paracentral retina in myopic adults,[15–18] suggesting that the outer retinal function of the myopic eye is reduced, and that this alteration in function may be regionally specific.

Most previous studies have focused on investigating retinal function[15–19] or visual function[1–6,20–22] in myopic adults. Luu and his coworkers[18] were the first to study retinal function in myopic children; they found reduced and delayed first-order kernel mfERG response in myopic adults, but only delayed response in myopic children, suggesting a difference in retinal physiology between myopic adults and myopic children. However, the investigation of only the first-order kernel mfERG response, which primarily reflects the activity from the outer retina,[12–14] without the assessment of the inner retina, is not sufficient for an understanding of the detailed functional integrity of the retina in myopia. The authors' recent study has shown that inner retinal function in adults is more susceptible to effect of myopia than is outer retinal function.[19] These findings are in agreement with a histological study, which shows that the inner retina is affected most when the retina thinned in myopic tree shrews.[8]

However, the use of second- or higher-order kernel mfERG response to study the inner retina is limited by its poor signal-to-noise ratio (SNR). Sutter and his coworkers[23] developed the global flash mfERG paradigm to enhance inner retinal activity. This paradigm has been shown to demonstrate reduced global flash mfERG responses in glaucomatous eyes, particularly affecting the inner retina.[24,25] Thus, the mfERG using the global flash paradigm would appear to be a better protocol for examining retinal function in myopes.

The primary purpose of this study was to compare retinal function between myopic children and myopic adults. The secondary purpose was to investigate the functional integrity of the retina in myopic children, especially the inner retina.

Methods

Subjects

Fifty-two children aged from 9 to 14 years (mean = 11.1 ± 1.2 years) and 19 adults aged from 21 to 28 years (mean = 23.4 ± 2.0 years) were

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recruited as subjects. All subjects received a comprehensive eye examination including a cycloplegic subjective refraction, a color vision test with a 16-plate version of the Ishihara Color Vision Test, and an ocular biomicroscopy carried out by an optometrist. All subjects had best corrected visual acuity of logMAR 0.00 or better in both eyes, normal color vision, and good ocular health. Using criteria from previous epidemiological studies, children whose myopia developed after the age of 6 years were classified as acquired myopia.[26,27] Subjects with myopia developed before the age of 6 years (classified as congenital myopia) were excluded, as were subjects with ocular degenerative changes, any ocular disease, any known systemic disease, or history of epilepsy.

All children were accompanied by their parent(s) or guardian(s) throughout the experiment. Before the start of the experiment, the aim of this study was explained. Written consent was obtained from adult subjects, and parents gave consent for their children to participate. All research procedures followed the tenets of the Declaration of Helsinki. The study was reviewed and approved by the human ethics committee of The Hong Kong Polytechnic University.

Refraction and Axial Length Measurement

Before these assessments, each subject had one drop of 0.4% Oxybuprocaine (Agepha Pharmaceuticals, Vienna, Austria) and two drops of 1% Tropicamide (Alcon Laboratories, Inc., Fort Worth, TX) instilled 5 minutes apart, so as to achieve both mydriasis and cycloplegia. Subjective refraction was performed at least 30 minutes after the instillation of the cycloplegic. Axial length was measured using a noncontact optical biometer (IOL master, V.4.08; Carl Zeiss Meditec, Inc., Dublin, CA). The axial length of each tested eye was measured five times to obtain a mean value.

Multifocal ERG Stimulation

The stimulus pattern was presented on a 22-inch liquid crystal display (LCD) (2232GW+; SAMSUNG, Tianjin, China) and was controlled with the Visual Evoked Response Imaging System (VERIS) (Veris Science 6.0.09d19; Electro-Diagnostic Imaging, Inc., Redwood City, CA) run on a computer (Macintosh; Apple Inc., Cupertino, CA).

The pattern for the global flash mfERG paradigm was made up of 61 hexagons, scaled with eccentricity (stretch factor = 12.18). The pattern subtended 39° horizontally and 37° vertically at a working distance of 40 cm. The stimulus sequence started with a multifocal flash frame, followed by a dark frame, a global flash, and a second dark frame in each cycle; the video frame rate was 75 Hz (Fig. 1a).[24,25,28] For the multifocal flash, each hexagon was temporally modulated between bright and dark stimulation, according to a pseudorandom binary maximum-length sequence (m-sequence). The global flash mfERG responses were measured at 49% and 96% contrasts in two separate examinations, and the mean luminance was maintained at 50 cd/m^2; the background was also set at 50 cd/m^2. High and low contrast tests were conducted in random order. The recording time for each stimulation sequence was 3 minutes 40 seconds with a 2^{12} binary m-sequence, and the recording process was divided into 16 slightly overlapping segments.

The 61 scaled hexagonal array used in this study covers the retinal areas that have been shown to be affected in adult myopes (i.e., from 9° to 27° of horizontal visual field).[19] Using a 61 hexagon stimulus field increases SNR, decreases the influence of fixation errors, and, thus, is more suitable when recording with children.

Multifocal ERG Recording

The procedure followed the International Society for Clinical Electrophysiology of Vision guidance for mfERG measurement.[29] Before measurement, all subjects were allowed to adapt to the room luminance for at least 15 minutes. The eye to be measured was randomly selected while the other eye was occluded during recording.

The mfERG examination started only after the pupil of the tested eye was dilated to at least a 7-mm diameter. A Dawson Trick Litzkow (DTL) thread electrode was placed in the inferior fornix of the tested eye as the active electrode. Gold-cup surface electrodes were placed 10 mm lateral to the outer canthus of the tested eye and the central forehead, as reference and ground, respectively. The refractive error of the tested eye was corrected for the working distance of the mfERG stimulator (i.e., 40 cm) with spectacle trial lenses of a 35-mm diameter. To maintain a constant retinal image size among different magnitudes of myopes, the corrective lenses were placed at the anterior focal plane of the eye according to Knapp's law. A chin rest and a lens holder were used to, respectively, control working distance and center the trial lenses properly without blocking the field of view.

To aid fixation, a red fixation cross, which subtended 1.6° in diameter, was incorporated at the center of the central hexagon (i.e., ring one). All subjects were instructed to maintain their fixation at the central fixation cross and avoid blinking during recording. The signals were amplified using a Physiodata Amplifier system (15A54; Grass Technologies, Astro-Med, Inc., West Warwick, RI). The band pass was set at 10 to 200 Hz and the gain was 100,000 times. The measurement was monitored using the real-time response shown by the VERIS program, and any recording segments contaminated with blinks or small eye movements were rejected and re-recorded immediately.

Multifocal ERG Response Analysis

The local mfERG responses were pooled into five concentric rings (Fig. 1b) and averaged for analysis using the system software (VERIS 6.0.09d19; Electro-Diagnostic Imaging, Inc.). Only the first-order kernel response was analyzed. The first and second distinct peaks were defined as direct component (DC) and induced component (IC) respectively (Fig. 1c). The DC amplitude (DC_{Amp}) was measured from the first distinct trough to the following peak, whereas the IC amplitude (IC_{Amp}) was measured from the second distinct peak to the subsequent trough. The DC implicit time (DC_{IT}) was measured from the onset of the multifocal flash frame to the first distinct peak. The IC implicit time (IC_{IT}) was measured from the presentation of the global flash frame (i.e., 26.6 ms) to the second distinct peak.

Statistical Analysis

Compared with emmetropes, myopes have an increase in myopic refractive status, and are usually accompanied with an increase in axial length.[30] Both refractive error[17,18] and axial length[15] can affect the mfERG response in myopic adults. In essence, compared with axial length, refractive error was found to account for a greater proportion of the variability in mfERG response measured with conventional stimulation in myopic adults.[16] The authors hypothesize that these two factors will also operate similarly in children. A hierarchical regression model not only evaluates the potential effects of sets of independent variables (i.e., refractive error and axial length) on dependent variables (i.e., mfERG response), it also evaluates the individual effect of each independent variable. Since refractive error has a greater impact than axial length on the mfERG response in adults,[16] a hierarchical regression model was used to first evaluate the effect of refractive error on the global flash mfERG response; then, the combined effect of refractive error and axial length on the global flash mfERG response was evaluated.[19] Bonferroni correction was used to correct the level of significance due to multiple comparisons across different retinal regions; that is, the level of significance was set at 0.01. Because there was a substantial correlation between refractive error and axial length, these two factors have been tested and passed for the assumption of multicollinearity and the variance inflation factor of the multiple regression models.[31] These tests were used to avoid any redundant, independent factors put into the models. Statistical Package for the Social Sciences (SPSS 15.0; SPSS Inc., Chicago, IL) was used to perform all statistical testing.

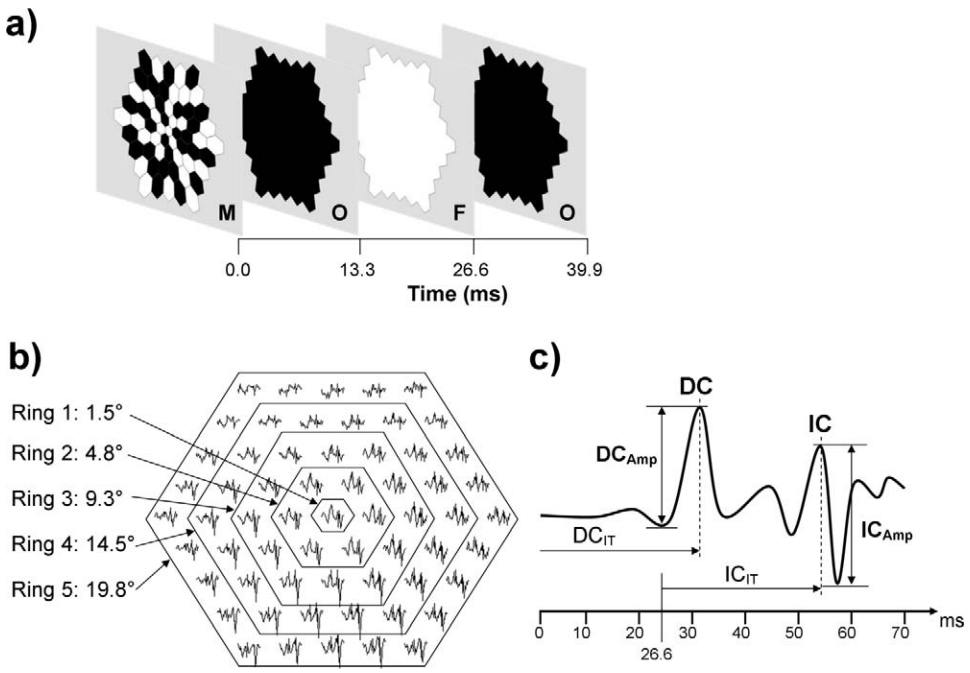

Figure 1. (**a**) Schematic diagram showing the video frames of the global flash mfERG paradigm. The stimulus consisted of four video frames in each cycle with this sequence: a multifocal flash frame ("M" 61-scaled hexagonal array), a dark frame ("O" 1 cd/m^2), a global flash ("F" 100 cd/m^2), and a second dark frame. The video frame rate was 75 frames per second, with a frame interval of 13.3 ms. (**b**) The 61 local responses were pooled into five concentric rings and were averaged. The eccentricity boundary of each ring is shown. (**c**) Schematic diagram showing a typical waveform of the first-order kernel global flash mfERG response, together with measured parameters.

Results

Table 1 summarizes the refractive error and axial length of two groups of subjects. There was no difference in refractive error (spherical equivalent) ($P > 0.05$) or axial length ($P > 0.05$) between adults and children. For both groups of subjects, there was a significant correlation between refractive error and axial length, with longer eyes being more myopic ($P < 0.001$ for children; $P = 0.008$ for adults) (Fig. 2).

Figure 3 shows the typical global flash mfERG waveforms recorded from a child and an adult subject with a low magnitude of myopic refractive error. The waveforms have been normalized to facilitate comparisons of the contours of the waveforms at different eccentricities and between the two subjects. For all regions examined, the mfERG waveforms had a first positive peak at approximately 35 ms and a second positive peak at approximately 63 ms in both the child and adult. Also, there were some oscillatory potentials between the two main peaks in both subjects. The waveform recorded from both groups of subjects with higher magnitude of myopia also demonstrated similar pattern. The overall contour of the global flash mfERG waveforms at 49% contrast, which was similar to those recorded at 96% contrast, also consisted of two distinct peaks at approximately 35 ms and 63 ms, corresponding to the DC and IC responses respectively (waveform not shown).

The global flash mfERG response data were log transformed to meet the normality and linearity requirements of the hierarchical regression models applied to these findings. Table 2 summarizes the results of the hierarchical regression model from the effect of refractive error, and the combined effects of refractive error and axial length on the logarithm of DC amplitude in both child and adult groups. For the children, refractive error accounted for approximately 8% of the change in log-DC amplitude of ring one at 96% contrast ($P < 0.05$), this just failed to reach statistical significance after Bonferroni correction. The addition of axial length as a second independent variable accounted for an extra 10% of the change in log-DC amplitude (F change = 6.16; $P < 0.05$). Thus, refractive error and axial length combined, accounted for approximately 18% of the reduction in the log-DC amplitude of ring one at 96% contrast ($P < 0.01$). Neither refractive error nor axial length contributed to any variance in log-DC amplitude from rings two to five at 96% contrast; they did not contribute to any change in log-DC amplitude of any rings at 49% contrast in the group of myopic children (all $P > 0.05$).

Table 1. The Characteristics of Refractive Error and Axial Length in Children and Adults

			Range			
	Mean	**SD**	**Minimum**	**Maximum**	**Median**	**Unpaired *t*-Test**
Refractive error (D)						
Children	−2.43	1.47	−5.50	−0.13	−2.25	$t < 0.01$, $P > 0.05$
Adults	−2.43	1.75	−5.50	−0.13	−2.25	
Axial length (mm)						
Children	24.36	0.76	22.79	26.01	24.39	$t = -0.01$, $P > 0.05$
Adults	24.37	1.14	22.83	26.66	23.91	

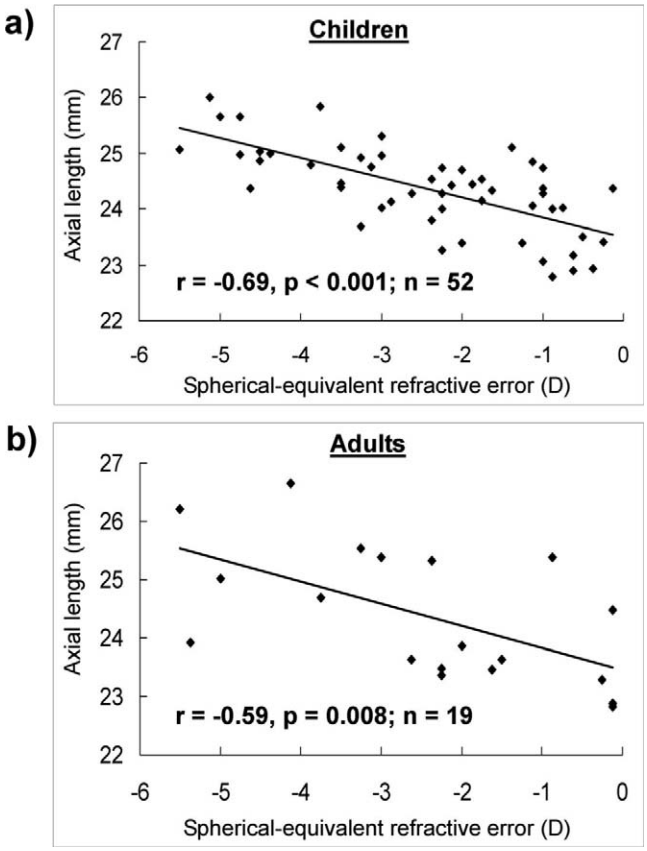

Figure 2. Correlation between refractive error and axial length in (**a**) children and (**b**) adults.

For the myopic adults, refractive error accounted for 23% to 25% of the reduction of log-DC amplitude of ring five at both 49% and 96% contrasts ($P < 0.05$), but it did not reach the statistically significant level after Bonferroni correction. The addition of axial length as a secondary independent variable failed to account for further changes at ring five. Refractive error contributed to 17% to 19% of reduction of the log-DC amplitude at both contrasts at ring four, which was not statistically significant (all $P > 0.05$). However, the addition of axial length as a secondary variable accounted for an additional 22% of the reduction of log-DC amplitude at 49% contrast (F change = 5.83; $P < 0.05$). So, the combined effects of refractive error and axial length contributed to 39% of the reduction of response ($P < 0.05$), but it just failed to reach the Bonferroni corrected significance level. Neither refractive error nor axial length explained any significant changes in log-DC amplitude at 49% or 96% contrast from rings one to three (all $P > 0.05$).

Table 3 summarizes the results of the hierarchical regression model from the effect of refractive error alone, and the combined effects of refractive error and axial length on log-IC amplitude for myopic children and myopic adults. For adults, refractive error contributed to 41% to 45% of the reduction in log-IC amplitudes from rings four to five at 49% contrast (all $P < 0.01$), but not the other regions examined (Fig. 4). It did not account for any change in log-IC amplitudes at 96% contrast for any regions examined. The addition of axial length did not explain additional variance in log-IC amplitudes of any region examined for either contrast (all $P > 0.05$). For the children, refractive error or axial length did not contribute to any change in log-IC amplitudes of any region examined at either 49% or 96% contrast (all $P > 0.05$).

Refractive error, and refractive error combined with axial length, made no contribution to any significant change in either DC or IC implicit times at either of the contrast levels examined in either group (all $P > 0.05$).

The second independent variable (i.e., axial length) had a greater effect than the first independent variable (i.e., refractive error) on the DC amplitude at 96% contrast at ring one in the hierarchical regression models of the children group. This violated the basic assumption of this model; that is, the impact of each independent variable at each level on the dependent variable reduced successively. Thus, simple linear regression models for refractive error and axial length on the response were performed separately for further verification. Refractive error and axial length accounted for, respectively, 8% and 18% of the reduction of log-DC amplitude at 96% contrast for this region (Fig. 5), indicating that axial length had a greater effect than refractive error on the response in myopic children.

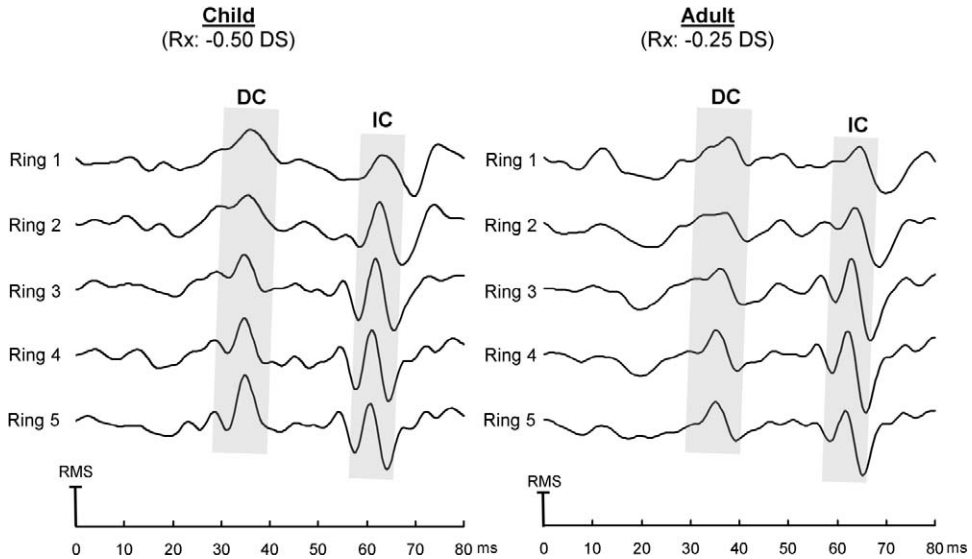

Figure 3. The typical ring-averaged global flash mfERG waveform at 96% contrast recorded from a low myopic child (*left*) and a low myopic adult (*right*). The shaded areas indicate the DC (first distinct peak) and IC (second distinct peak) responses.

Table 2. Hierarchical Regression Analysis of Refractive Error and Combined Refractive Error and Axial Length on $\log_{10}$ of DC Amplitude in Children and Adults

	Group	Children						Adults					
	Contrast	49%			96%			49%			96%		
Region	Model	R^2	F	P	R^2	F	P	R^2	F	P	R^2	F	P
Ring 1	RE†	0.038	1.928	0.171	0.077	4.150	0.047	0.050	0.902	0.356	0.069	1.260	0.277
	RE + AL‡	0.056	1.411	0.254	0.180§	5.370*§	0.008§	0.180	1.751	0.205	0.134	1.241	0.315
Ring 2	RE	0.056	2.909	0.094	0.033	1.723	0.195	0.050	0.886	0.360	0.011	0.190	0.668
	RE + AL	0.056	1.427	0.250	0.057	1.473	0.239	0.160	1.526	0.247	0.018	0.151	0.861
Ring 3	RE	0.016	0.797	0.376	0.012	0.629	0.431	0.036	0.639	0.435	0.001	0.020	0.890
	RE + AL	0.022	0.540	0.586	0.072	1.893	0.162	0.158	1.500	0.253	0.019	0.156	0.856
Ring 4	RE	0.002	0.101	0.751	0.002	0.089	0.766	0.167	3.403	0.083	0.187	3.899	0.065
	RE + AL	0.072	1.857	0.167	0.078	2.079	0.136	0.389	5.100	0.019	0.213	2.170	0.147
Ring 5	RE	0.010	0.475	0.494	0.024	1.242	0.271	0.248	5.593	0.030	0.227	4.990	0.039
	RE + AL	0.048	1.209	0.307	0.103	2.828	0.069	0.248	2.632	0.103	0.302	3.469	0.056

† Refractive error.
‡ Combined refractive error and axial length.
§ Bonferroni-corrected statistically significant values.

Discussion

Unlike myopic adults, who showed reduced mfERG response in the paracentral region (i.e., rings four to five, eccentricity from 9.3° to 19.8°), myopic children showed attenuated mfERG responses from the central retina examined (i.e., ring one, within 1.5° eccentricity) (Tables 2 and 3). Several studies performed on myopic adults have noted reduced retinal function measured electrophysiologically[15–17,19] and visual function examined psychophysically.[1–6,20–22] However, there is a paucity of data in the literature regarding retinal or visual function in myopic children. Luu and his coworkers[18] reported that the mfERG response, measured with conventional mfERG stimuli, is reduced and delayed in myopic adults, but is only delayed in myopic children. The authors have found a reduction in central, high contrast, DC response amplitude of mfERG in myopic children, but no effect on implicit time of the response.

Depending on the age groups, various parameters (i.e., refractive error and axial length) have different effects on the mfERG responses. In myopic adults, refractive error contributed more to the delay in conventional mfERG response when compared with axial length.[16] This study showed that refractive error contributed 41% to 45% of the reduction in response, but axial length did not account for additional change; this substantiates the findings of the authors' recent study.[19] Both Chen et al.,[16] and the current study, show that refractive error has a strong effect on the mfERG response in myopic adults. However, in children, axial length explains a greater amount of the reduction of the DC response at 96% contrast than refractive error does in both the hierarchical regression (Table 2) and simple regression analyses (Fig. 5). The findings show that the effect of axial length on mfERG response is stronger in myopic children than in adults. Also, the investigation of the effect of refractive error on the mfERG response alone may not be sufficient to understand the characteristics of retinal electrophysiology in myopic children; axial length needs to be taken into consideration, since it is an important determinant of retinal illuminance. This study shows that the effect of increases in both refractive error and axial length on the mfERG response was different between children and adults with myopia.

Fixation instability has been reported to cause reduced central mfERG response.[32] The authors believe that the

Table 3. Hierarchical Regression Analysis of Refractive Error and Combined Refractive Error and Axial Length on $\log_{10}$ of IC amplitude in Children and Adults

	Group	Children						Adults					
	Contrast	49%			96%			49%			96%		
Region	Model	R^2	F	P	R^2	F	P	R^2	F	P	R^2	F	p
Ring 1	RE*	0.001	0.049	0.825	0.001	0.029	0.865	0.073	1.345	0.262	0.003	0.044	0.837
	RE + AL†	0.003	0.073	0.930	0.019	0.481	0.621	0.086	0.749	0.489	0.006	0.048	0.953
Ring 2	RE	0.011	0.556	0.459	0.019	0.994	0.324	0.056	1.007	0.330	0.014	0.236	0.634
	RE + AL	0.021	0.516	0.600	0.101	2.741	0.074	0.205	2.063	0.160	0.014	0.116	0.891
Ring 3	RE	0.003	0.154	0.696	0.019	0.977	0.328	0.059	1.074	0.315	0.087	1.618	0.220
	RE + AL	0.004	0.087	0.917	0.062	1.614	0.209	0.221	2.265	0.136	0.087	0.765	0.482
Ring 4	RE	0.012	0.616	0.436	0.032	1.664	0.203	0.447‡	13.755‡	0.002‡	0.098	1.856	0.191
	RE + AL	0.032	0.804	0.453	0.049	1.255	0.294	0.498‡	7.922‡	0.004‡	0.104	0.932	0.414
Ring 5	RE	0.016	0.779	0.382	0.050	2.635	0.111	0.407‡	11.659‡	0.003‡	0.152	3.057	0.098
	RE + AL	0.025	0.614	0.545	0.084	2.259	0.115	0.513‡	8.440‡	0.003‡	0.159	1.512	0.250

* Refractive error.
† Refractive error and axial length.
‡ Bonferroni-corrected statistically significant values.

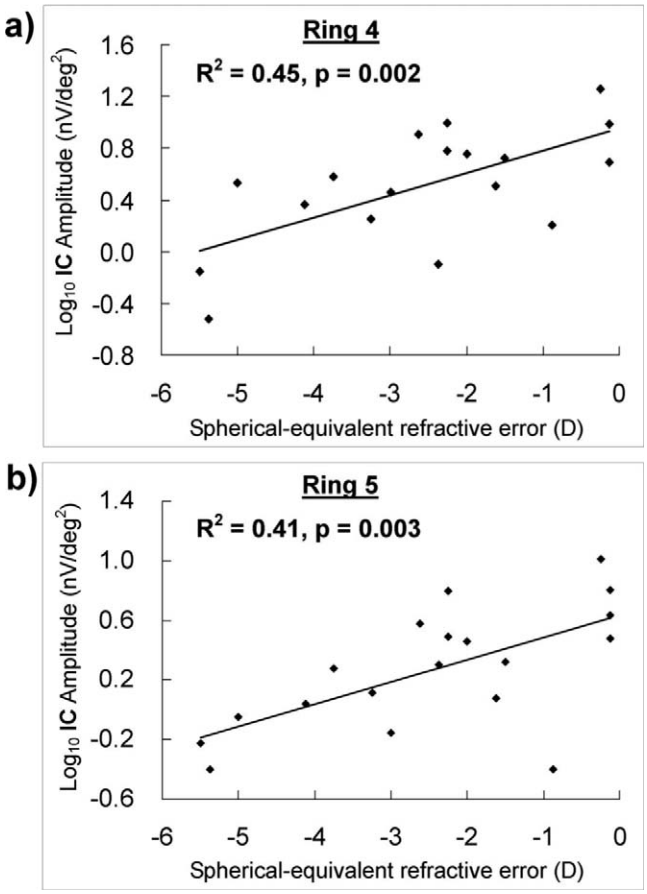

Figure 4. The scatter plots show the change in logarithm of IC amplitude as a function of refractive error for (**a**) ring four and (**b**) ring five at 49% contrast in the adults.

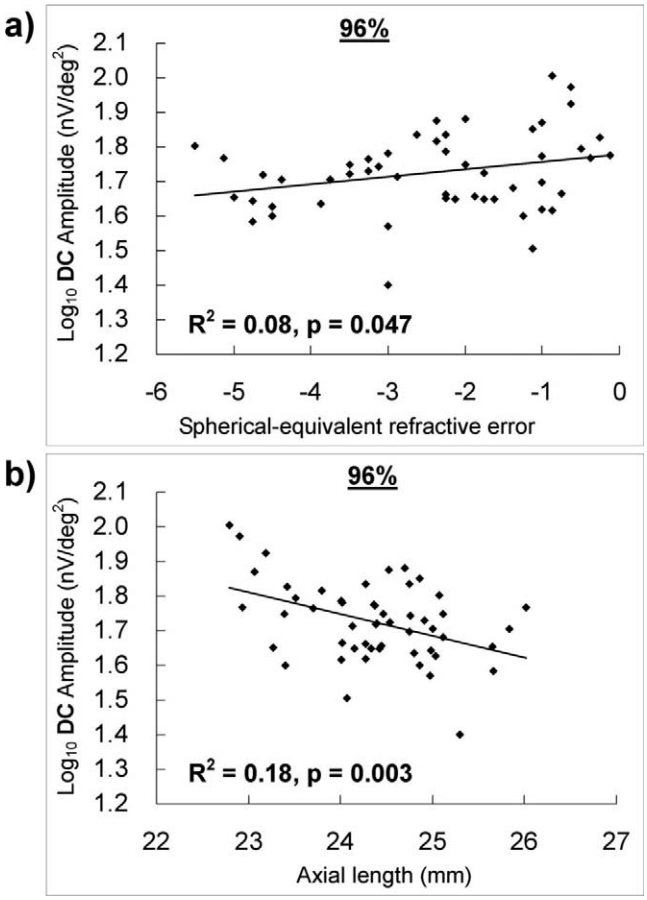

Figure 5. The logarithm of DC amplitude at 96% contrast reduced with increasing (**a**) refractive error and (**b**) axial length for ring one in the children.

reduction of central macular response in the children group is unlikely to be a consequence of fixation instability. To monitor the fixation stability, the depth of depression of the mfERG response at the blind spot has been used as an indicator of fixation stability in a previous study from the authors' laboratory.[32] Using this strategy, the depression of the mfERG response at the blind spot in both the children and adults groups was analyzed. The results showed that the depression of the mfERG response at the blind spot in the children group was not statistically significant different from that of the adult group (unpaired *t*-test; all $P > 0.05$) (data not shown), indicating that the fixation stability was not the key factor to account for the attenuated central mfERG response in the children group.

Luu and his colleagues[18] could not find any reduction in the central mfERG response in myopic children, whereas this study detected a retinal functional change in the central region with the global flash mfERG paradigm. The discrepancy in results may be associated with the difference in the stimulation sequence as well as with differences in the analytical method. Firstly, the global flash mfERG paradigm is a protocol that incorporates a dark frame between the multifocal flash frame and the global flash. It allows for better separation of the retinal responses from the outer and inner retina, without the overlapping of those responses due to subsequent flashes.[23,33] Secondly, a scaled 61-hexagon array was used, while Luu et al.[18] used a scaled 37-hexagon array as the stimulus; the 61-hexagon array provides better resolution of response topography for identifying localized functional changes. Thirdly, the regression analyses showed that axial length explained a significant reduction of the DC response in myopic children, while refractive error did not, which probably explains why Luu and his coworkers[18] could not find any reduction in mfERG response.

The paracentral (i.e., rings four to five, eccentricity from 9.3° to 19.8°) IC amplitudes at low contrast (i.e., 49% contrast) were reduced in myopic adults (Fig. 4), while the IC responses of all regions were unaffected in myopic children. The IC amplitudes at 96% contrast of all regions were not changed among the range of refractive error examined in either the children or adults. It has been reported that the IC response primarily reflects the activity from the inner retina (i.e., retinal ganglion cells and amacrine cells) in porcine eyes.[34] In addition, IC amplitude has been shown to be reduced in human glaucomatous eyes,[24,25] in which the response of the inner retina is believed to be impaired. The authors' findings suggest that the inner retinal function in the paracentral region is weakened in myopic adults, but inner retinal function within the central region (~40° of visual angle) is virtually unaffected in myopic children.

The effect of myopia on the mfERG response varies in terms of the regions and retinal components affected between children and adults. The central (i.e., ring one, within 1.5° eccentricity) DC amplitude at high contrast was reduced in myopic children, but the DC responses of all regions examined were almost unaffected in myopic adults. The DC response has been reported to mainly reflect activity from outer retinal layers (i.e., photoreceptors and bipolar cells), with some

activity from inner retinal layers (i.e., retinal ganglion cells and amacrine cells), in the porcine eye.[34] Reducing the contrast of the multifocal stimulus increases the relative contribution of inner retinal activity to the DC response of the global flash mfERG.[34] Thus, the DC response at high contrast is believed to include a greater contribution from outer retinal activity. The central macular DC amplitude was reduced at high contrast, but unchanged DC amplitude at low contrast in myopic children indicates that the functional change mainly occurs at an outer retinal level.

On the other hand, the reduced central DC amplitude at high contrast found only in myopic children, but not in adults, is in need of further study. It may be a cause of ocular growth during progression of myopia. Intact retinal function is essential for emmetropization. Early disruption of normal retinal function with neurotoxic agents during postnatal development in animal studies was reported to cause myopia development.[35–37] Furthermore, a reduction in foveal mfERG response was associated with a higher rate of myopia progression later in children.[38] The authors, therefore, speculate that the reduced central macular DC amplitude at high contrast in myopic children may be related to the process of ocular development, and is a cause of rapid myopia progression in this age group.[26] Additionally, the difference in the central mfERG response between children and adults with myopia may be related to the age-related physiological changes at macular region. Further study is necessary to investigate the changes in mfERG response during myopia development from childhood to adulthood in order to understand the underlying cause of regional variations in retinal function between children and adults with myopia.

The mfERG examines the temporal interactive response between continuous flashes.[39] While the flash stimulus impulse of a cathode ray tube (CRT) monitor may take a few milliseconds, those of a LCD may take relatively longer decay time. Due to the different temporal characteristics of the stimulator, the mfERG response would also be different.[40] According to the manufacturer's user manual, the response time of the LCD used in this study was 2 ms (grey-to-grey response). Thus, the authors believe that only a very small overlapping of flashes happened between the fade out of stimulus and the onset of subsequent stimulus. It allows for measurement of interaction between flashes. Consistent with the previous study using a CRT monitor,[19] reduced IC amplitudes at 49% contrast were found in myopic adults, suggesting that the adaptive response at the inner retinal level was likely to be impaired.

In conclusion, only the central macular DC amplitude at high contrast was reduced in myopic children. The fact that paracentral IC amplitudes were reduced at low contrast in myopic adults indicates that inner retinal function is reduced in these subjects. This study demonstrated the difference in retinal electrophysiological activity between children and adult myopes in terms of regions and retinal components affected.

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