Multifocal Electroretinogram in Adults and Children With Myopia

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**Objective:** To determine the correlation between multifocal electroretinogram (mFERG) parameters and the severity of myopia in adults and children.

**Design:** Observational study.

**Methods:** Multifocal electroretinograms were recorded using the VERIS system from randomly selected eyes of 104 children and 31 adults with various degrees of myopia. Dawson, Trick, and Litzkow fiber electrodes were used and the pupil was dilated with 1% tropicamide. Subjective refraction was performed under cycloplegia and axial length measurement was determined by A-scan ultrasonography. The N1 (first negative trough), P1 (first positive peak), and N2 (second negative trough) components of the first-order kernel response of the mFERG were measured and correlated with the refractive data.

**Main Outcome Measures:** First-order kernel mFERG responses.

**Results:** The N1, P1, and N2 amplitudes were significantly correlated with the severity of myopia in adult subjects (N1, \( r = 0.591, P = .001; P1, r = 0.682, P < .001; N2, r = 0.732, P < .001 \)). The response amplitudes of N1, P1, and N2 decreased as the dioptic power of myopia increased. However, there were no significant correlations found between the implicit time of the N1 response and the refractive error. The results of the current study are presented together with a consideration of the possible factors contributing to this correlation.

**Conclusions:** There is a significant correlation between the refractive error and mFERG amplitude in adults with myopia; however, such a relationship is absent in children with myopia. These findings suggest that the severity of myopia has little influence on the ERG amplitude, at least in children.

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MYOPIA IS A PUBLIC health concern in many parts of the world including Asia, where the prevalence of myopia has been reported to be as high as 80%. Although myopia can be easily managed with an appropriate optical correction, it is a risk factor for a number of retinal pathologies, especially in high myopia (≥ -6.0 dioptries), and may cause permanent visual impairment or even blindness. Reduction of retinal function has also been reported in myopic eyes without myopic retinopathy. It has previously been shown that the amplitude of the b-wave of the electroretinogram (ERG) decreases as a function of increasing axial length or degree of refractive error. Yamamoto et al showed a significant reduction of macular cone function in a group with high myopia compared with groups with low or moderate myopia. Although many studies have shown a strong negative correlation between the severity of myopia and ERG response amplitude in adult subjects, it is still unknown whether a similar correlation occurs in children with myopia. Furthermore, it is still unclear whether the reduction of ERG response in myopia is due to retinal degenerative changes associated with long-standing myopia or a reflection of the myopia itself. To investigate these possibilities, we used the mFERG to assess the central retinal function in adults and children affected by various degrees of myopia. The results of the current study are presented together with a consideration of the cause of reduction in ERG amplitudes associated with high myopia in adults.
this study. All participants had a best-corrected logMAR visual acuity of 0.00 (equivalent to 6/6 on the Snellen chart) or better. Ophthalmoscopic examination showed a normal fundus appearance in all eyes of all children. Two of the adult subjects had tessellated fundi. The optic discs varied from normal to slight crescents. Subjects with a family history of inherited retinal diseases, any eye disease associated with abnormal ERG, and myopia-related retinal changes other than slight crescents at the optic disc or tessellated fundus were excluded.

Informed consent was obtained for all adult participants prior to testing. Parental informed consent was obtained for the children before their participation. The current study was approved by the Human Ethics Committee of the Singapore Eye Research Institute and the research procedures used in this study followed the tenets of the Declaration of Helsinki.

**REFRACTION MEASUREMENT**

Measurement of the refraction was performed under cycloplegia. One drop of 0.4% proparacaine, followed by 3 drops of 1% cyclopentolate at 5-minute intervals, were instilled in each eye. Subjective cycloplegic refraction was performed after at least 30 minutes from the time of the last instillation of cyclopentolate.

**AXIAL LENGTH MEASUREMENT**

Measurement of the axial length of the eye was performed immediately after cycloplegic refraction using A-scan ultrasound echography (Echoscan US-800; Nidek Inc, Tokyo, Japan). Before the measurements were taken, 1 drop of 0.4% proparacaine was instilled into each eye to produce corneal anesthesia. Six reliable readings were taken for each eye and accepted if the standard deviation was less than 0.12 mm. The refraction and axial length measurements were made on a separate day to the mfERG recording.

**STATISTICAL ANALYSIS**

The spherical equivalent refraction (spherical power + 1/2 cylindrical power) of each individual was calculated. The sum of the first-order responses of 37 hexagons were obtained (Figure 1). This response represents the retinal function within the central 38 degrees. The response amplitude and implicit time of the first-order components (N1 [first negative trough], P1 [first positive peak], and N2 [second negative trough]) of the spatial summation response waveform were used for the analysis. There were no significant differences in the spherical
equivalent refraction between the right and left eye (adults, \( P = .75 \); children, \( P = .88 \); paired \( t \) test); therefore, only data from a randomly selected eye of each individual were included in the analysis. Pearson correlation was used to determine the relationship between the spherical equivalent refraction (SER) and the mfERG parameters.

RESULTS

The mean ages (SD) of adults and children with myopia were 24.1±6.4 (range, 20.7-36.4) and 11.5±1.5 (range, 8.3-14.6) years, respectively. The mean logMAR visual acuity was –0.666, \( P < .001 \) for adults, and –0.903, \( P < .001 \) for children.

Table 1. Linear Regression and Correlation Coefficient of the mfERG Parameters and the Spherical Equivalent Refraction for Adults and Children With Myopia

<table>
<thead>
<tr>
<th>Group</th>
<th>mfERG Parameters</th>
<th>Linear Regression Line*</th>
<th>Correlation Coefficient</th>
<th>95% CI</th>
<th>( P ) Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Correlation</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>95% CI</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adults with myopia</td>
<td>Amplitude</td>
<td>( y = 0.32x + 8.12, r^2 = 0.349 )</td>
<td>0.591</td>
<td>0.264-0.796</td>
<td>.001</td>
</tr>
<tr>
<td></td>
<td>P1</td>
<td>( y = 0.76x + 22.41, r^2 = 0.466 )</td>
<td>0.682</td>
<td>0.401-0.846</td>
<td>&lt;.001</td>
</tr>
<tr>
<td></td>
<td>N1</td>
<td>( y = 0.94x + 23.16, r^2 = 0.535 )</td>
<td>0.732</td>
<td>0.481-0.872</td>
<td>&lt;.001</td>
</tr>
<tr>
<td></td>
<td>Implicit time</td>
<td>N1</td>
<td>( y = -0.26x + 14.88, r^2 = 0.562 )</td>
<td>-0.750</td>
<td>-0.874-0.534</td>
</tr>
<tr>
<td></td>
<td></td>
<td>P1</td>
<td>( y = -0.33x + 27.94, r^2 = 0.592 )</td>
<td>-0.769</td>
<td>-0.884-0.566</td>
</tr>
<tr>
<td></td>
<td></td>
<td>N2</td>
<td>( y = -0.29x + 42.61, r^2 = 0.441 )</td>
<td>-0.664</td>
<td>-0.827-0.400</td>
</tr>
<tr>
<td>Children with myopia</td>
<td>Amplitude</td>
<td>N1</td>
<td>( y = 0.07x + 6.59, r^2 = 0.006 )</td>
<td>0.073</td>
<td>0.065-0.209</td>
</tr>
<tr>
<td></td>
<td>P1</td>
<td>( y = 1.66x + 18.09, r^2 = 0.050 )</td>
<td>0.071</td>
<td>0.067-0.206</td>
<td>.31</td>
</tr>
<tr>
<td></td>
<td>Implicit time</td>
<td>N1</td>
<td>( y = 0.13x + 18.89, r^2 = 0.003 )</td>
<td>0.052</td>
<td>0.086-0.189</td>
</tr>
<tr>
<td></td>
<td></td>
<td>P1</td>
<td>( y = -0.003x + 15.52, r^2 = 2.44E^{-6} )</td>
<td>-0.002</td>
<td>-0.140-0.135</td>
</tr>
<tr>
<td></td>
<td></td>
<td>N2</td>
<td>( y = -0.11x + 26.33, r^2 = 0.027 )</td>
<td>-0.166</td>
<td>-0.297-0.030</td>
</tr>
</tbody>
</table>

Abbreviations: CI, confidence interval; mfERG, multifocal electroretinogram; N1, first negative trough; N2, second negative trough; P1, first positive peak.

*\( y \) indicates the amplitude (µV) of the mfERG response; \( x \) indicates the spherical equivalent refraction.

The mean ages (SD) of adults and children with myopia were 24.1±6.4 (range, 20.7-36.4) and 11.5±1.5 (range, 8.3-14.6) years, respectively. The mean logMAR visual acuity was –0.666, \( P < .001 \) for adults, and –0.903, \( P < .001 \) for children.

Figure 2. Scatterplots showing the relationships of the axial length, spherical equivalent refraction, and vitreous chamber depth in adults and children with myopia. D indicates diopters.
ity was 0.015±0.005 in the adult group and 0.009±0.004 in the children's group. The difference in the mean log-MAR acuity between the 2 groups was not statistically significant (*P* = .722, Mann-Whitney U test).

The axial length was significantly correlated with SER and vitreous chamber depth in both adults and children with myopia (Figure 2), indicating that the nature of myopia in our study subjects was primarily owing to elongation of the vitreous chamber.

The N1, P1, and N2 components of the first-order mfERG response were significantly correlated with the severity of myopia in adult subjects (Table 1). The response amplitudes of N1, P1, and N2 were decreased as the dioptric power of myopia increased (Figure 3). However, no significant correlations between N1, P1, or N2 amplitudes and the SER were found in children with myopia (Table 1).

Similarly, the SER was significantly correlated with N1, P1, and N2 implicit times in adults with myopia (Figure 4). However, only the P1 implicit time was significantly correlated with SER in children with myopia (Table 1).

To determine the relationship between the mfERG parameters and the severity of myopia as a function of retinal eccentricity, the mfERG data of each individual were subdivided into the central and peripheral responses. The central response represented the sum of mfERG responses within the central 2 rings which covered about 10 degrees of the central retina. The peripheral response consisted of mfERG data of the remaining outer 2 rings. Again, the mfERG parameters of the central and peripheral re-

Figure 3. Scatterplots showing the correlations between multifocal electroretinogram amplitude and spherical equivalent refraction in adults and children with myopia. The N1 (first negative trough), P1 (first positive peak, and N2 (second negative trough) components were significantly correlated with spherical equivalent refraction in adults with myopia but not in children with myopia. D indicates diopters.

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responses were significantly correlated with the severity of myopia in the adult group but not in children (Table 2).

**COMMENT**

The reduction in b-wave amplitude of the full-field ERG in adults with myopia has been well documented. Similar findings were reported using the mfERG technique. The first-order kernel of the mfERG responses of all rings are reduced as the severity of myopia increases. Our findings in the adult group concurred with those reported previously. However, we are unaware of any previous publications on the relationship between ERG response and myopia in children. The findings from the current study show that there is no significant correlation between mfERG amplitudes and refraction in children with myopia. These findings suggest that the ERG reduction in subjects with myopia is not directly or solely due to the severity of myopia, at least in children.

Although a reduction in ERG response in adults with myopia has been well recognized, the actual mechanisms of ERG reduction in myopia are still unclear. A number of factors for this reduction have been suggested and in this article, they are broadly divided into 3 main categories, namely optical, electrical, and retinal factors. In relation to optical factors, it has been suggested that the reduction in ERG amplitudes seen in myopic eyes may be owing to a reduced image size and decreased reti-

Figure 4. Scatterplots showing the correlations between multifocal electroretinogram implicit times and spherical equivalent refraction in adults and children with myopia. The N1 (first negative trough), P1 (first positive peak), and N2 (second negative trough) implicit times were significantly negatively correlated with the spherical equivalent refraction in adults with myopia. Only the P1 implicit time was significantly correlated with spherical equivalent refraction in children with myopia.
Peripheral Response (Rings 3-4)

Table 2. Correlation Coefficient of the mfERG Parameters and the Spherical Equivalent Refraction for Adults and Children With Myopia at Different Retinal Eccentricities

<table>
<thead>
<tr>
<th>Group</th>
<th>mfERG Parameters</th>
<th>Central Response (Rings 1-2)</th>
<th>Peripherel Response (Rings 3-4)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Correlation</td>
<td>P Value</td>
</tr>
<tr>
<td>Adults</td>
<td>Amplitude</td>
<td>N1</td>
<td>0.313</td>
</tr>
<tr>
<td></td>
<td></td>
<td>P1</td>
<td>0.455</td>
</tr>
<tr>
<td></td>
<td></td>
<td>N2</td>
<td>0.487</td>
</tr>
<tr>
<td></td>
<td>Implicit time</td>
<td>N1</td>
<td>-0.677</td>
</tr>
<tr>
<td></td>
<td></td>
<td>P1</td>
<td>-0.453</td>
</tr>
<tr>
<td></td>
<td></td>
<td>N2</td>
<td>-0.471</td>
</tr>
<tr>
<td>Children</td>
<td>Amplitude</td>
<td>N1</td>
<td>0.074</td>
</tr>
<tr>
<td></td>
<td></td>
<td>P1</td>
<td>0.031</td>
</tr>
<tr>
<td></td>
<td></td>
<td>N2</td>
<td>0.026</td>
</tr>
<tr>
<td></td>
<td>Implicit time</td>
<td>N1</td>
<td>-0.015</td>
</tr>
<tr>
<td></td>
<td></td>
<td>P1</td>
<td>-0.117</td>
</tr>
<tr>
<td></td>
<td></td>
<td>N2</td>
<td>-0.025</td>
</tr>
</tbody>
</table>

Abbreviations: mfERG, multifocal electroretinogram; N1, first negative trough; N2, second negative trough; P1, first positive peak.

By examining the stimulus intensity response function, Kawabata and Adachi-Usami\(^{10}\) claimed that decreased retinal illuminance did not explain the reduced ERG response because the responses of the high-myopic eye had much lower saturated amplitudes than for the emmetropic eye. Second, the electrical factor is the increased distance between the electrical source (ie, the retina) and the electrode. Finally, decreased retinal photoreceptor density,\(^{14}\) morphological changes in the photoreceptor outer segment,\(^{15,16}\) and photoreceptor dysfunction\(^{17}\) have been considered as retinal factors. Morphological changes in the photoreceptor outer segment in myopic eyes have been reported in chick models but it is unknown whether a similar alteration occurs in humans.

In light of the results obtained from this study, the optical and electrical factors are unlikely to be the cause of the ERG reduction because of the absence of any relationship between ERG amplitudes and the severity of myopia in children. Similarly, with photoreceptor morphological and functional changes in myopic eyes, a good correlation between ERG amplitude reduction and severity of myopia would be expected irrespective of the subject’s age. However, the current study shows that ERG reduction is not significantly correlated with the degree of myopia in children suggesting that other mechanisms must be responsible for the reduction in ERG.

The mfERG is a sensitive electrophysiological technique for early detection of retinal changes. Increased implicit time with normal amplitude has been reported in the early stages of degenerative retinal diseases\(^{18}\) (eg, retinitis pigmentosa) and in diabetic retinopathy.\(^{19,20}\) Based on the findings that only the implicit time, not the amplitude, of the P1 response was significantly associated with the severity of myopia in children, it is postulated that the reduction in ERG response seen in the adult group may be owing to retinal function modifications that are associated with long-standing myopia.

It is also noted that a number of subjects with a mild degree of myopia had very delayed P1 implicit time. It would be interesting to know whether these subjects will develop high myopia in later years. A cohort study may help to identify possible mfERG parameters that would enable us to predict which children will develop high myopia.

There are some important limitations of this study. First, because the analyses were cross-sectional, it is impossible to determine cause (eg, myopic degeneration) and effect (eg, ERG reduction). Availability of prospective data will resolve this problem. It is intended to repeat the mfERG recordings in children with myopia and the correlation between ERG amplitude and to reexamine the severity of myopia. Second, there may be differences in the levels of attention, cooperation, and fixation behavior between the adults and children, indicating that the mfERG recordings in children may have been contaminated. We attempted to control this factor by dividing the recording time into smaller segments of 14 seconds each. Segments contaminated by eye movements or blinking artifacts were discarded and the recording was repeated. The children were well behaved and cooperative during the recordings. The recorded mfERG traces of the children were as clean as those of the adults. Finally, there seems to be more scatter in the mfERG data of the children than in that of the adults. We do not think that the increased variability was due to the lack of attention or cooperation for the reasons mentioned earlier. We suspect that the variability may represent the normal variation in children. It would be interesting to know if this variation is associated with the rate of myopia progression.

In summary, the findings from the current study show that there is a significant correlation between the refractive error and ERG amplitude in adults with myopia; however, such a relationship is absent in children with myopia. Based on these findings, it is postulated that the reduced ERG response in myopia is not directly due to the severity of myopia but more likely to be related to myopic retinal changes.

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REFERENCES


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