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 dioptric power of myopia increased. However, there were no significant correlations found between N1 ($r=0.073$, $P=.30$), P1 ($r=0.071$, $P=.31$), and N2 ($r=0.052$, $P=.46$) amplitudes and the severity of myopia in children. The severity of myopia was also significantly correlated with N1 ($r=-0.750$, $P<.001$), P1 ($r=-0.769$, $P<.001$), and N2 ($r=-0.664$, $P<.001$) implicit times in adults with myopia, however, only the P1 ($r=-0.166$, $P=.02$) implicit time was significantly correlated with children with myopia.

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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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.

STANDARD ERRORS MEASUREMENT

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 of adults and children with myopia were minus 0.666, \( P < .001 \), and minus 0.903, \( P < .001 \), respectively.

<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>Adults with myopia</td>
<td>Amplitude</td>
<td>N1 ( y = 0.23x + 8.12 ), ( r^2 = 0.349 )</td>
<td>0.591</td>
<td>0.264-0.796</td>
<td>.001</td>
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<tr>
<td></td>
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<td>P1 ( y = 0.76x + 22.41 ), ( r^2 = 0.466 )</td>
<td>0.682</td>
<td>0.401-0.846</td>
<td>.001</td>
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<tr>
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<td></td>
<td>N2 ( y = 0.94x + 23.16 ), ( r^2 = 0.535 )</td>
<td>0.732</td>
<td>0.481-0.872</td>
<td>.001</td>
</tr>
<tr>
<td></td>
<td>Implicit time</td>
<td>N1 ( y = -0.26x + 14.88 ), ( r^2 = 0.562 )</td>
<td>-0.750</td>
<td>-0.874-0.534</td>
<td>.001</td>
</tr>
<tr>
<td></td>
<td></td>
<td>P1 ( y = -0.39x + 27.94 ), ( r^2 = 0.592 )</td>
<td>-0.769</td>
<td>-0.884-0.566</td>
<td>.001</td>
</tr>
<tr>
<td></td>
<td></td>
<td>N2 ( y = -0.29x + 42.61 ), ( r^2 = 0.441 )</td>
<td>-0.664</td>
<td>-0.827-0.400</td>
<td>.001</td>
</tr>
<tr>
<td>Children with myopia</td>
<td>Amplitude</td>
<td>N1 ( y = 0.07x + 6.59 ), ( r^2 = 0.006 )</td>
<td>0.073</td>
<td>0.006-0.209</td>
<td>.30</td>
</tr>
<tr>
<td></td>
<td></td>
<td>P1 ( 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>N2 ( y = 0.13x + 18.89 ), ( r^2 = 0.003 )</td>
<td>0.052</td>
<td>-0.086-0.189</td>
<td>.46</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 (\( \mu V \)) of the mfERG response; \( x \) indicates the spherical equivalent refraction.

![Scatterplots showing the relationships of the axial length, spherical equivalent refraction, and vitreous chamber depth in adults and children with myopia. D indicates diopters.](http://archopht.jamanetwork.com/pdftools/image.axd?r=300&x=1400&y=1400&v=1200&z=1200)
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 responses were compared between adults and children with myopia.
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.7,8 Similar findings were reported using the mfERG technique.10,13 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 retinal input.
develop high myopia in later years. A cohort study may be interesting to know whether these subjects will associate with long-standing myopia. It may be owing to retinal function modifications that are associated with the severity of myopia in children suggesting that other mechanisms must be responsible for the reduction in ERG.

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 diseases18 (eg, retinitis pigmentosa) and in diabetic retinopathy19,20. 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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