Full-field electroretinogram findings in children in the Atropine Treatment of Myopia (ATOM2) study

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Abstract

Background: The aims of this study were to determine the longitudinal effects of myopia on full-field electroretinogram (ffERG) in children, and whether there were any effects due to atropine treatment.

Methods: Fifty children, enrolled in the Atropine Treatment of Myopia study, were randomly selected and 35 children consented to undergo ffERG at baseline (prior to atropine treatment), 24 months (at end of treatment) and 32 months (8 months after cessation of treatment). An extended ISCEV ffERG protocol was used for all recordings. The relationship between axial length (AL) and the following scotopic and photopic ffERG responses were analyzed: a- and b-wave amplitude and implicit time, saturated amplitude (Vmax) and retinal sensitivity (logK).

Results: Reliable ffERG recordings with acceptable level of noise were obtained on all 3 visits from 29 children (mean age: 9.5±0.8 years and mean spherical equivalent: -5.0±1.6 D). At baseline, the correlation detected between AL and logK was 0.37 ($p=0.047$). There was no significant correlation between AL and Vmax or any scotopic and photopic ffERG amplitude and implicit time measures. Longitudinal data suggested a reduction in photopic a- and b-wave and 30Hz flicker response amplitudes over time. Multivariate analysis showed that the change in 30Hz flicker response amplitude was likely to be associated with AL change. There was no evidence that changes in other responses were associated with age, baseline AL or atropine dose used.

Conclusion: Retinal sensitivity was reduced in myopic children. There was a gradual decline in cone function over time which was not influenced by atropine treatment.

Keywords: electrophysiology, electroretinogram, myopia, refractive error, atropine

Introduction:

Previous studies on the effect of axial myopia on retinal function using full-field electroretinogram (ffERG) demonstrated a strong negative correlation between ERG response amplitude and axial length in adult subjects [1-3]. Similar effects were also noted when macular function was assessed with multi-focal electroretinogram (mfERG) with reduced amplitudes, lower saturation amplitudes and increased implicit time being associated with increased myopia [4-7].

While there is a strong association between ERG responses and myopia in adults, it is uncertain if such a relationship is also present in children with myopia. Luu et al (2006) found no significant correlation between increasing myopia and mfERG amplitude in young myopic children (age 11.5+/-4.5 years) but there was a significant correlation between myopia and mfERG amplitude in myopic adults (age 24.1+/-6.4 years) [6]. These findings suggested that the changes in retinal function seen in adults may have not yet occurred in young children. It is still unclear if and when changes in retinal function occur, particularly in children with high myopia.

To determine whether myopia affects retinal function, in this exploratory study, we recorded longitudinal ffERG in children with varying degrees of myopia. We also evaluated whether atropine treatment had any effect on the ffERG.

Methods:

This study is a subset of the second Atropine Treatment of Myopia Study (ATOM2). The aims of the ATOM2 study were to determine the safety and efficacy of reduced atropine concentration in slowing myopia progression in children [8]. In the ATOM2 study, 400 children aged 6 to 12 years, with myopia of at least 2.0 Diopter (D), were randomized to either one of 3 atropine groups (atropine 0.01%, 0.1% or 0.5%) in 1:2:2 ratio. These drops were administered bilaterally every night for 24 months after which the drops were stopped and

children were followed for a further 12 months. Parental/guardian written informed consent was obtained for all subjects, and the study followed the tenets of the Declaration of Helsinki, with ethics approval obtained from the Singapore Eye Research Institute Review Board. The study was registered with the ClinicalTrial.gov website (registration no: NCT00371124).

Children were followed every 4 months over 36 months. Cycloplegic refraction and axial length (AL) measurements were performed at each visit. Cycloplegia was achieved by administering 3 drops of cyclopentolate 1% (Cyclogyl, Alcon-Convreur) at 5 minutes intervals. Cycloplegic refraction was measured 30 minutes after the first eyedrop using a Canon RK-F1 autorefractor (Canon Inc. Ltd, Tochigiken, Japan). Five readings, all of which had to be less than 0.25D apart, were obtained and averaged. Spherical equivalent (SE), sphere plus half cylinder power, were then calculated from autorefractor readings. The non-contact Zeiss IOL Master (Carl Zeiss Meditec Inc, CA, USA) was used to measure the axial length (AL) of the eye. Five readings, all of which had to be less than 0.05mm apart, were averaged.

For the present study, 50 children, aged 8-12years, were randomly selected from the ATOM2 study cohort to undergo full-field electroretinogram (ffERG) testing. The ffERGs were recorded 3 times; prior to commencing atropine (baseline), at the end of treatment (24months) and 8 months after treatment was stopped (32months). ERG recordings were performed after cycloplegic refraction using an extended ISCEV standard ffERG protocol. The children were dark-adapted for 20 minutes after which scotopic responses were recorded using flash stimuli ranging from 0.002 to 10 $cd.s.m^{-2}$ (with about 0.3 log unit increment). Children were then light-adapted for 10 minutes, and photopic responses were recorded with flash stimuli of 0.5 to 10 $cd.s.m^{-2}$, and 30 Hz flicker responses were recorded with a flash stimulus of 2.5$cd.s.m^{-2}$. Signals were acquired with an Espion (Diagnosys, LLC, Littleton, MA, USA) and DTL electrodes were used. Recordings were deemed to be of good quality if they had minimal noise, minimal eye movement artifacts and were reproducible for at least 3 trials. 35 children (70%) consented to undergo tests and 29 children (58%) had good quality responses on all 3 visits.

Analysis:

The response amplitudes and implicit times of the a- and b-waves were ascertained at each flash intensity level. The ISCEV ffERG responses at flash intensity levels of scotopic 0.01 cd.s.m^{-2} (rod response), scotopic 10 cd.s.m^{-2} (combined rod-cone response), photopic 2.5 cd.s.m^{-2} (cone response) and 30Hz flicker were selected for further analyses (Figure 1). For 26 subjects, data from the right eye were included in the analysis. In the remaining 3 subjects, recordings from the right eye were noisy or unreliable, and recordings from the left eyes were better; therefore, the latter were used. Naka-Rushton function was used to determine the values of Vmax and logK; Vmax being the maximum response recorded, and logK being the stimulus intensity where half the Vmax value is achieved. A least-squares minimization procedure was used to fit the Naka-Rushton curve to the lower limb of the intensity-response data because the second limb of the intensity-response obtained with brighter flashes are much more complex due to interactions between the photoreceptor, bipolar and Muller cell potentials [9]. Curve fitting was achieved using a computer spreadsheet (Excel; Microsoft) and all parameters (Vmax, logK and the slope of the function 'n') were free to vary.

Baseline information in this ffERG study was summarized in mean, standard deviation (SD) and range for continuous variables, and counts and percentages for categorical variables. For the children in the ffERG study, Fisher's exact test was used to test against difference in gender proportions among atropine groups, while analysis of variance (ANOVA) used for mean difference of age, AL and SE among groups, at baseline.

The ffERG parameters were summarized in mean and SD at baseline, 24 months and 32 months. 95% confidence interval (CI) of baseline ffERG parameters was reported based on t-distribution. The relationship at baseline between ERG parameter (ffERG amplitudes, ffERG implicit times, Vmax and logK) and AL or SE at baseline was explored using Pearson correlation coefficient. In order to examine the significance of the ffERG parameter changes, the parameter differences between baseline and 24 (or 32) months were used to test against

the null hypothesis of no difference by 1-sample t-test. Due to the exploratory purpose only, none of the tests was adjusted for multiplicity. For the parameters with significant changes, the multivariate regression analysis that contains atropine dose levels as the independent variables while controlling age, AL and change in AL was employed.

All the analyses were performed in statistical software SAS (version 9.2). All the tests were 2-sided and findings were considered significance if $p<0.05$.

Results:

Data presented in this paper were based on the 29 children (mean age 9.5+/-0.8years) who had complete, good quality and reliable ffERG responses at baseline, 24 and 32 months. Eight of these children had been randomized to the Atropine 0.01% group, while 12 and 9 children had been randomized to the Atropine 0.1% and 0.5% groups respectively (Table 1). There was no difference in age, gender and SE between groups. All children were of ethnic Chinese origin except for one child who was ethnic Indian.

<u>ERG responses and their relationship with axial length (AL) and spherical equivalent (SE) at baseline</u>

Figures 1 and 2 explore the relationship of ERG amplitudes and implicit times with AL at baseline when children were aged 8.1-10.9 years. Although there was a slight tendency towards a decreased in combined rod-cone b-wave amplitudes with increasing AL (Figure 2), this correlation was not significant based on the data ($r=-0.25$, degrees of freedom (dof) = 27, $p= 0.190$). There was also no evidence on any correlation between AL and any of the other ERG scotopic and photopic responses (Figure 2&3). Correlation between SE and the scotopic, photopic and 30Hz flicker amplitudes and implicit times were also not present.

Figure 4 shows the relationship of Vmax and logK with AL and SE. There was a weak correlation between logK and AL ($r=0.37$, dof = 27, $p=0.047$) and between logK and SE ($r=-0.42$, dof = 27, $p=0.025$). There was no

correlation between Vmax and AL (r=0.06, dof= 27, p=0.742) or between Vmax and SE (r=-0.03, dof = 27, p=0.876) (Figure 4).

Changes in ffERG responses over 32 months follow up

The mean ffERG responses at baseline, 24 months and 32 months are presented in Table 2. The combined rod-cone a-waves were lower and more delayed at 32 months compared to baseline. It seems that cone response a- and b-waves amplitudes were smaller and implicit times longer at 24 and 32 months compared to baseline. Likewise, the 30Hz flicker responses were smaller at 24 and 32 months. Based on the data, there was, however, no evidence to show any change in the rod b-wave, combined rod-cone b-wave responses, or in Vmax and logK. The mean change in combined rod-cone a-wave, cone and 30Hz flicker responses are presented in Table 3.

Amplitude reductions equal to or greater than 20% occurred in 70% of subjects for the cone b-wave response, in 55% for the 30Hz flicker and 48% for the cone a-wave response; scotopic responses were affected in fewer children (Figure 5). Changes in implicit times were less marked. No change was noted in Vmax (t-statistic=-1.53, dof=28, p=0.137) or logK (t-statistic=0.13, dof=28, p=0.898) values over the 32 months period.

Effect of atropine dose, age, AL and change in AL on ffERG responses

Table 4 explores the contribution of atropine dose, age, AL and change in AL to the changes in combined rod-cone response and cone responses seen. Multivariate analysis looking at the each variable, while adjusting for other variables in the model, suggested that dose of atropine used, age of the child, and baseline axial length did not contribute to the observed ffERG changes. There was, however, a likely association between 30Hz flicker amplitude and AL change; with a reduction of 28.5μV in 30Hz flicker amplitude noted for every 1mm increase in AL over the first 24 months.

Discussion:

We found that, at baseline, the full-field ERG amplitudes and implicit times were not correlated with AL or SE in the myopic children. We did, however, find a positive relationship between retinal sensitivity (logK) and AL. Analysis of longitudinal data showed that cone and 30Hz flicker responses became more reduced and delayed during the 32 month study period. A smaller reduction in combined rod-cone a-wave amplitude and increase in implicit time was also seen. These ERG changes were not related to atropine dose, age of child and baseline AL. There was an inverse association between the change in 30Hz flicker amplitude and change in AL over the first 24 months of the study.

The lack of relationship between AL and ffERG parameters but an association between AL and logK in this study are contrary to those studies involving older subjects, which have reported a negative correlation between AL and ffERG amplitudes [1,3], and between AL and Vmax [2,3]. Chen et al (1992) postulated that there are two possible mechanisms for reduced responses; the retina may either be structurally stretched (and thus less sensitive resulting in an increase in logK) or functionally less responsive resulting in a reduction in Vmax [2]. In a study involving 15 persons, aged 15 to 38 years, with a range of refractive errors from +5D to -9.5D and AL from 21.1 to 27.4mm, they found that Vmax was reduced in eyes with larger AL but the logK remained unchanged, suggesting that there was an overall reduction in responsiveness rather than sensitivity. These findings were replicated by Westall et al (2001) in 60 subjects, aged 13 to 37, with myopia ranging from -0.75 to -14.5D and AL from 22.2 to 30.0mm; they noted strong correlations between AL and reductions in Vmax (R^2= 0.56) and cone b-wave amplitude (R^2=0.54), and weaker correlations between AL and rod response (R^2=0.33), rod-cone a-wave (R^2=0.32), rod-cone b-waves (R^2=0.35), 30Hz flicker responses (R^2=0.37) and summed oscillatory potentials (R^2=0.36). They did not find any correlation between AL and logK or implicit times [3].

The lack of correlation between Vmax and AL in children in our study suggests that the changes that occur in adults may not yet have occurred in children <12 years. Clinically, this suggests that myopic status may be less relevant when evaluating ffERG responses in young myopic children. This outcome is consistent with the finding from an earlier study by Luu et al (2006) which found no correlation between mfERG N1, P1 and N2 amplitudes and AL in 102 myopic children (aged 8-15years), but a negative correlation in 31 myopic adults (aged 20-37years) [6]. Alternatively, it could also be that the range of spherical equivalent in our subjects (-1.8 to -7.9D) may just be too narrow to demonstrate a strong effect. Compared to previous studies by Chen et al and Westall et al [2,3], there were no emmetropic or hyperopic children in this study for comparison, and the number of children in our study was also small.

However, we noted a small positive correlation between logK and AL at baseline which suggests that there may be some reduction in retinal sensitivity in young myopic children. As this relationship was not seen in older children and adult [2,3], it is possible that there may be an initial reduction in sensitivity (that could possibly be associated with the rapid growth of the eye) in the younger child which recovers or readapt itself with time.

Changes in ffERG responses occurred between baseline, 24 and 32 months. Care needs to be taken in interpreting p-values as although reduction/relationship appeared to be significant, it may happen by chance since the sample size in the present exploratory study may not be big enough to make our findings conclusive. Our findings, however, suggest that there was reduction and delay in the combined rod-cone a-wave and cone responses, as well as a reduction in the 30Hz flicker response over time. Presumably, these changes if progressive over time, particularly in more myopic persons, may eventually result in the ffERG changes noted in adult subjects. None of the children in this study had visible myopic fundal changes, but functional changes seen in ffERG could indicate that subtle myopic fundal changes may begin in childhood.

As there was no reduction in the b-wave amplitude of the rod response but there was a reduction in the a- and b-wave cone response, we believe that the reduction in combined rod-cone a-wave amplitude reflected alteration in the cone function only. These findings suggest that the cones may be affected earlier than the rods in myopia.

Also of interest was whether use of atropine played a role in the change in retina response. Atropine has been shown to be effective in controlling myopia progression in young children [9-13]. Atropine is a non-specific muscarinic antagonist and is believed to play a role in scleral fibroblast proliferation and modification [14,15]. In this Atropine Treatment of Myopia (ATOM2) study, where Atropine doses of 0.5%, 0.1% and 0.001% arms were utilized, mean increase myopia over 2 years in treated eyes were -0.30±0.60D, -0.38±0.60D and -0.49±0.63D and the average increase in axial lengths was 0.27±0.25, 0.28±0.27 and 0.41±0.31mm respectively [8]. If atropine did affect retinal function, then changes in response should manifest in a dose-related manner in the 24 months of treatment after which a reversal or stabilization of responses might be expected to occur. Multivariate regression analysis with appropriate control of potential confounders, however, showed that there was no significant dose-related atropine effect on ffERG scotopic and photopic responses (Table 3). These findings support those of an earlier ATOM1 study where no significant differences in mfERG first and second kennel amplitudes and implicit time were noted in the atropine 1% and placebo treated eyes over a 24months period [16].

The results from the multivariate regression analysis also suggest that most ffERG changes were not associated with age, axial lengths and change in axial lengths (Table 3). The only potentially significant association was an inverse association between changes in 30Hz flicker amplitudes and axial length. Studies suggest that bipolar cell activity play a role in the regulation of eye growth, and the corresponding modifications in the ON-OFF bipolar systems could interfere with eye growth and refractive compensation in animal models [17-22]. This

may explain why the 30Hz flicker, which is derived from the ON-OFF system, was more sensitive in detecting changes associated with myopia progression.

There were several weaknesses in this study. All children were on atropine and although one of the treatment groups received a very low atropine concentration, there was no control group for comparison. Normal variations in ffERG may also be quite wide. The number of subjects in this study was small, and it may thus lack the power to demonstrate significant level of differences. The follow up period was relatively short (32 months) thus we were unable to determine when the relationship between ERG amplitudes and myopia eventually become significant.

In summary, we found no associations between ffERG amplitudes and axial length in young myopic children less than 14 years of age. There was a association between logK and AL at baseline indicating that there may be a reduction in retina sensitivity in young myopic children that occurs prior to later amplitude reduction typically found in adults. The longitudinal data showed that the photopic ERG seem to be altered more than the scotopic ERG suggesting that the cone system is affected earlier than the rod system in myopia.

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Full-field electroretinogram findings in children in the Atropine Treatment of Myopia (ATOM2)

Table 1: Baseline parameters in children in whom ffERG were performed

Baseline	Total (n=29)	Subjects in different atropine groups			
		A0.01 (n=8)	A0.1 (n=12)	A0.5 (n=9)	P Value [1]
Age (years), mean (SD)	9.5 (0.8)	9.1 (0.7)	9.4 (0.9)	9.9 (0.8)	0.137
Range	8.1 to 10.9	8.3 to 10.2	8.1 to 10.6	8.3 to 10.9	
Male gender, n (%)	13 (44.8)	4 (50.0)	6 (50.0)	3 (33.3)	0.719
Spherical Equivalent (D), mean (SD)	-5.0 (1.6)	-5.5 (0.9)	-4.8 (1.9)	-4.7 (1.7)	0.582
Range	-7.9 to -1.8	-6.5 to -3.8	-7.9 to -1.8	-7.1 to -2.3	
Axial length (mm), mean (SD)	25.6 (1.0)	25.8 (0.8)	25.3(1.1)	25.6 (0.9)	0.528
Range	23.4 to 27.6	25.0 to 27.6	23.4 to 26.9	23.7 to 26.6	

P-value [1] is from Fisher's exact test for comparing gender among the atropine groups and is from ANOVA for comparing age, AL and SE.

Table 2: FfERG response amplitude and implicit time in 29 myopic children using DTL electrodes at baseline, and at 24 and 32 months

	Baseline		24months		32months	
	Mean (SD)	95% CI	Mean (SD)	P-value[1]	Mean (SD)	P-value[2]
Rod response						
- B wave amplitude (μV)	212.7(46.3)	195.1-230.3	202.2(55.3)	0.356	195.7(58.1)	0.091
- B wave implicit time (ms)	95.6(6.7)	93.1-98.2	94.7(7.2)	0.560	95.3(7.6)	0.839
Combined rod-cone response						
- A wave amplitude μV)	215.7(40.4)	200.3-231.0	205.7(31.7)	0.274	193.9(35.0)	0.007
- A wave implicit time (ms)	14.4(0.8)	14.1-14.7	14.9(0.9)	0.024	15.1(1.1)	0.014
- B wave amplitude (μV)	292.3(50.8)	273.0-311.7	282.8(45.8)	0.338	277.8(76.7)	0.172
- B wave implicit time (ms)	49.8(4.1)	48.3-51.4	50.8(4.4)	0.261	50.6(4.6)	0.604
- b/a ratio	1.4(0.2)	1.3-1.5	1.4(0.2)	0.900	1.4(0.2)	0.506
VMax (μV)	260.6(55.7)	239.4-281.8	249.7(59.4)	0.328	246.8(68.2)	0.137
logK	-2.7(0.2)	-2.8--2.6	-2.7(0.2)	0.789	-2.7(0.2)	0.898
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Cone response						
- A wave amplitude (μV)	28.2(6.9)	25.6-30.9	24.0(6.3)	0.008	22.8(5.7)	0.003
- A wave implicit time (ms)	14.3(0.9)	13.9-14.6	15.0(1.3)	0.017	15.3(1.0)	<0.001
- B wave amplitude (μV)	94.5(25.3)	84.9-104.1	79.5(20.0)	0.004	70.9(19.1)	<0.001
- B wave implicit time (ms)	28.7(0.7)	28.4-28.9	30.0(1.0)	<0.001	30.2(1.1)	<0.001
- b/a ratio	3.5(1.0)	3.1-3.9	3.4(0.8)	0.615	3.2(0.7)	0.197
30Hz flicker response						
- amplitude (μV)	58.2(15.3)	52.4-64.0	52.9(16.3)	0.028	44.6(13.9)	<0.001
- implicit time (ms)	26.9(1.6)	26.3-27.5	27.0(1.2)	0.830	27.4(1.7)	0.161

P-value [1] is from 1-sample t-test against the null hypothesis of no difference by using the changes between 24 months and baseline.

P-value [2] is from 1-sample t-test against the null hypothesis of no difference by using the changes between 32 months and baseline.

The rod responses were tested under scotopic conditions using a 0.01 cd.s.m-2 stimulus. The combined rod-cone responses were tested under scotopic using a 10 cd.s.m-2 stimulus. The cone responses and 30Hz flicker responses were tested under photopic condutions using a 2.5cd.s.m-2 stimulus.

Table 3: Mean change in amplitudes and implicit times in the responses which showed significant differences between baseline and 24 and 32 months in Table 2 (i.e. combined rod-cone a-wave, cone and 30Hz flicker responses).

	Change between baseline and 24 months			Change between baseline and 32months		
	Mean	95% CI	P-value [1]	Mean	95% CI	P-value [1]
Mixed rod-cone response						
- A wave amplitude (μV)	-	-	-	18.8	5.5 - 32.1	0.007
- A wave implicit time (ms)	-	-	-	0.7	0.2 – 1.2	0.014
Cone response						
- A wave amplitude (μV	4.2	1.2 – 7.3	0.008	5.5	2.1- 8.9	0.003
- A wave implicit time (ms)	0.7	0.1 – 1.3	0.017	1.1	0.5 – 1.6	<0.001
- B wave amplitude (μV)	15.0	5.3 - 24.7	0.004	23.6	16.4 - 30.7	<0.001
- B wave implicit time (ms)	1.3	1.0 – 1.7	<0.001	1.5	1.1 – 1.9	<0.001
30Hz flicker response						
- Amplitude (μV)	5.3	1.6 – 10.1	0.028	13.7	8.4-18.9	<0.001

P-value [1] is from 1-sample t-test.

Table 4: Multivariate regression analysis for the effect of atropine dose, age, axial length and change in axial length on ERG responses, adjusted for each other and for atropine dose.

	Atropine 0.1% vs 0.01%		Atropine 0.5% vs 0.01%		Age (year)		Axial length (mm)		Change in axial length (mm)	
	Coeff. Est.	P value	Coeff. Est.	P value	Coeff. Est.	P value	Coeff. Est.	P value	Coeff. Est.	P value
Change between 0 & 24m										
Combine rod-cone response										
- A amplitude (μV)	-3.13	0.899	-22.60	0.405	-12.90	0.349	3.10	0.771	2.25	0.963
- A implicit time (ms)	-0.08	0.877	0.70	0.225	-0.58	0.053	-0.23	0.307	-0.83	0.419
Cone response										
- A amplitude (μV)	-0.47	0.904	7.77	0.076	-2.84	0.193	-0.94	0.575	-9.16	0.235
- A implicit time (ms)	0.02	0.980	0.63	0.476	-0.29	0.511	0.04	0.902	-1.91	0.235
- B amplitude (μV)	8.67	0.513	7.84	0.587	-4.22	0.564	-2.87	0.614	-24.40	0.350
- B implicit time (ms)	0.01	0.991	-0.28	0.623	0.19	0.503	0.13	0.566	-0.34	0.738
30Hz flicker response										
- Amplitude (μV)	-10.98	0.057	-5.13	0.398	0.12	0.969	2.56	0.287	-28.5	0.014
Between 24 & 32m										
Combined rod-cone response										
- A amplitude (μV)	-18.40	0.501	-13.70	0.641	19.78	0.174	-9.89	0.357	132.10	0.230
- A implicit time (ms)	0.49	0.516	-0.08	0.921	-0.06	0.872	0.32	0.286	-0.73	0.806
Cone response										
- A amplitude (μV)	-6.06	0.127	-5.41	0.197	-1.74	0.387	0.53	0.727	10.49	0.498
- A implicit time (ms)	0.74	0.299	0.38	0.613	-0.03	0.942	0.28	0.308	0.42	0.880
- B amplitude (μV)	-13.10	0.266	-10.60	0.396	-2.04	0.734	0.86	0.849	24.89	0.591
- B implicit time (ms)	-0.06	0.909	-0.08	0.886	0.47	0.084	-0.13	0.519	0.58	0.774
30Hz flicker respons										
- Amplitude (μV)	-5.03	0.557	-7.64	0.404	-1.32	0.763	-2.84	0.395	-9.21	0.786

Note: P-value is obtained through the regression model that controls age, axial length and change in axial length, and compares 0.1% and 0.5% atropine groups with 0.01% atropine group. Legend: Coeff. Est.: coefficient estimate

Figure 1: Full-field ERG recording of the rod, combined rod-cone, cone and 30Hz flicker responses

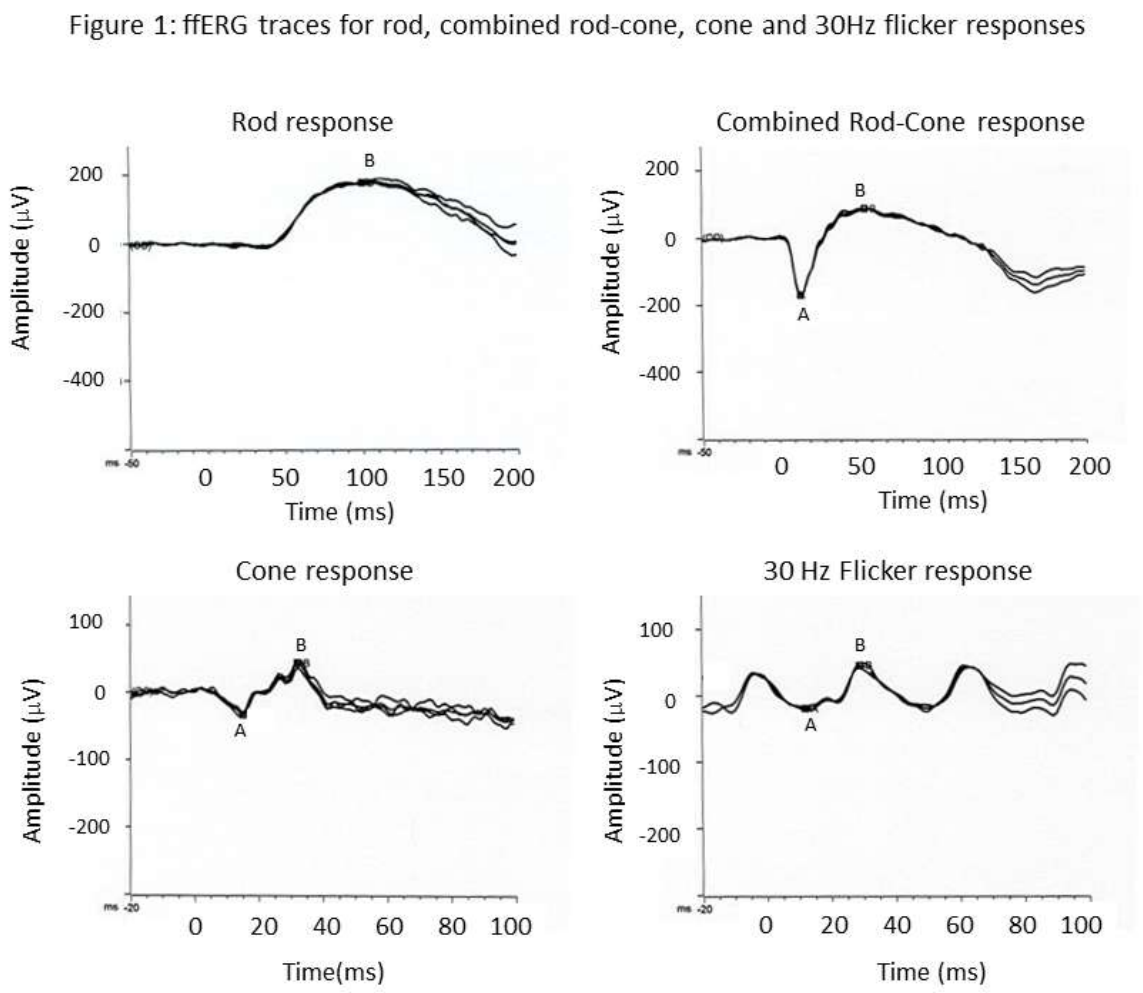
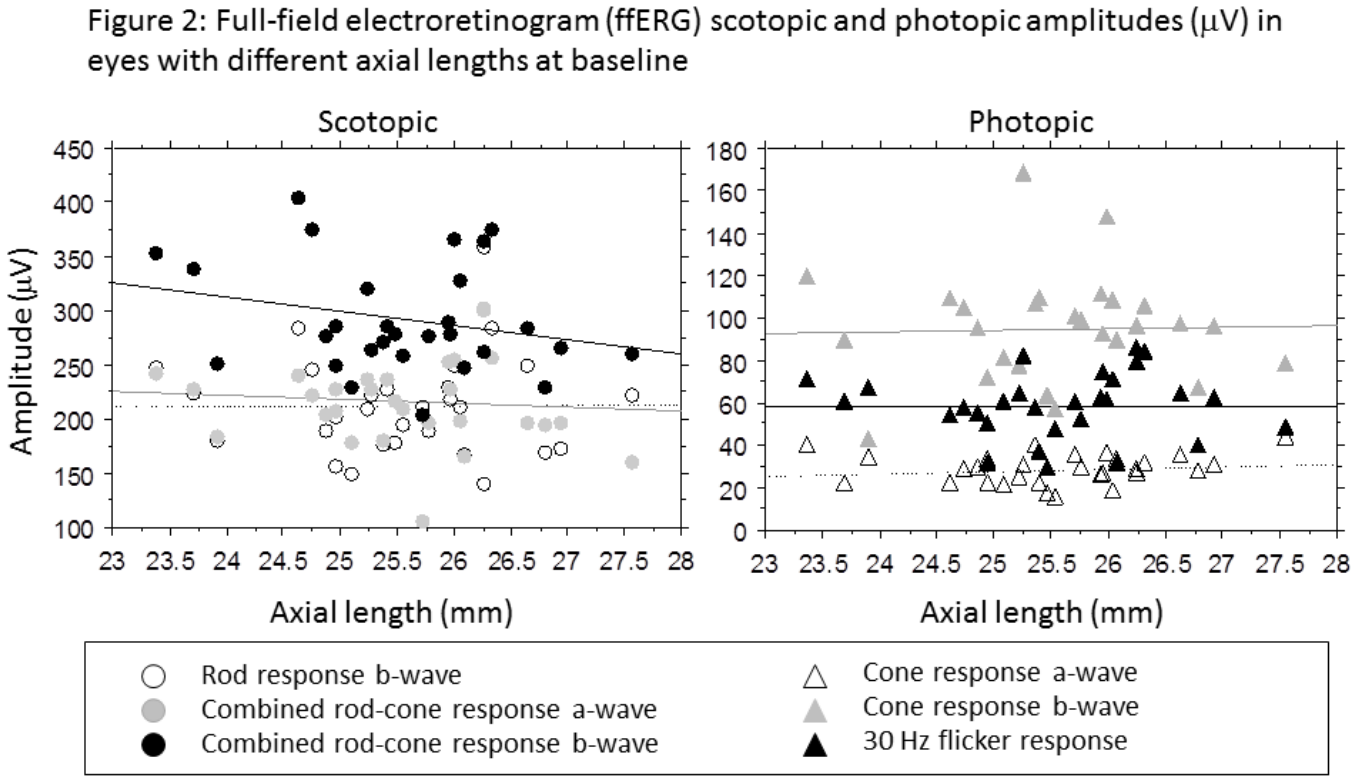


Figure 2: Full-field electroretinogram (ffERG) scotopic and photopic amplitudes (μV) in eyes with different axial lengths at baseline



Note: Dotted line represents regression line of empty circles and triangles. Grey line represents regression line of grey-filled symbols. Black line represents regression line of black-filled symbols.

Figure 3: Full-field electroretinogram (ffERG) scotopic and photopic implicit times (ms) in eyes with different axial lengths at baseline

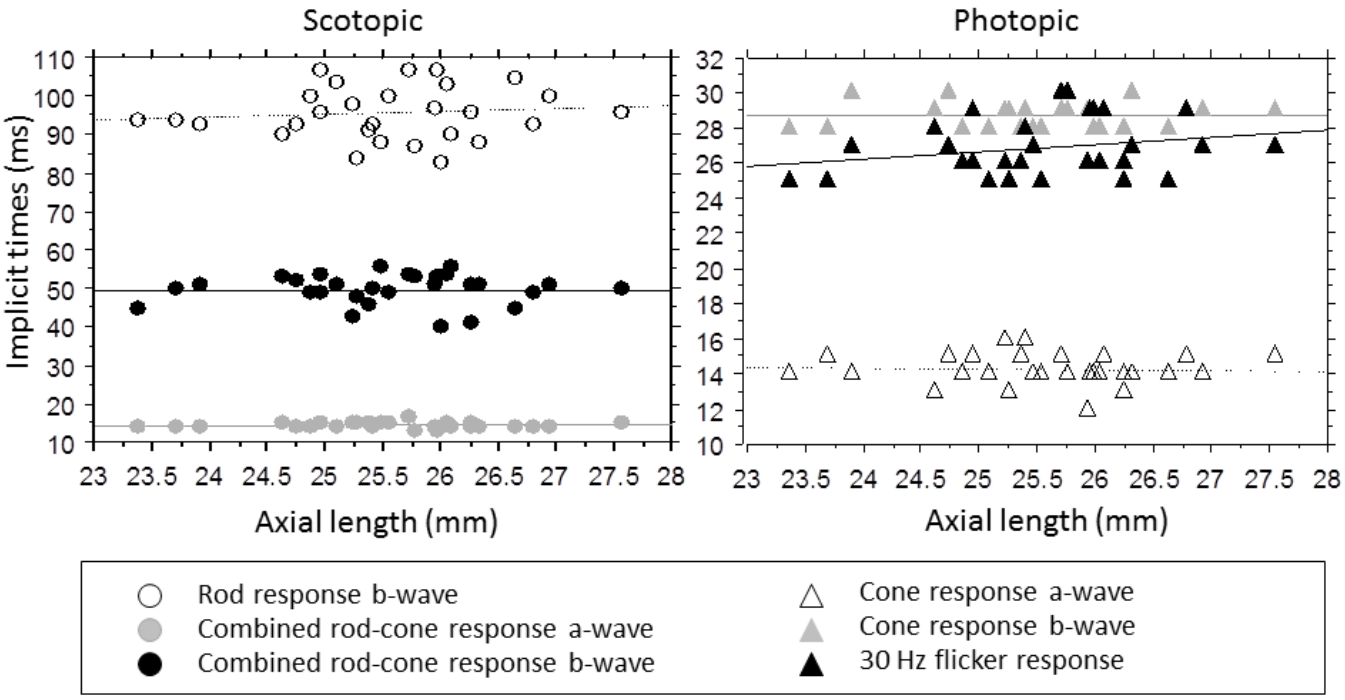


Figure 4: Vmax and logK as a function of axial length at baseline (solid line: regression line. dotted lines: 95% confidence intervals)

Figure 4: Vmax and log K as a function of axial length at baseline (solid line: regression line and dotted lines: 95% confidence intervals).

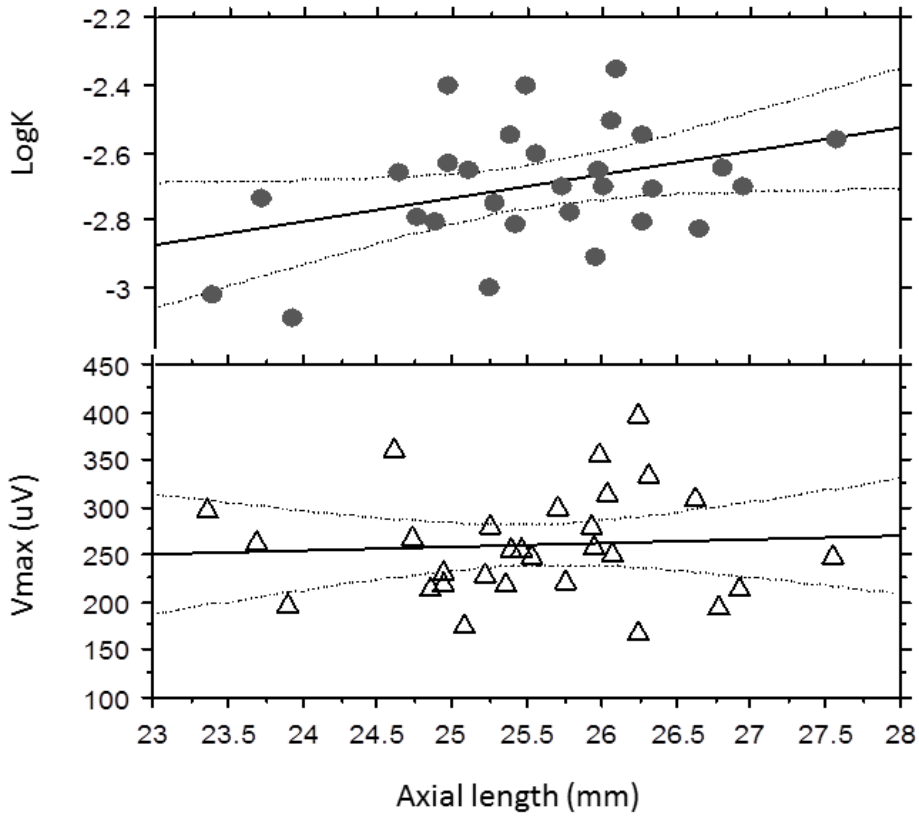
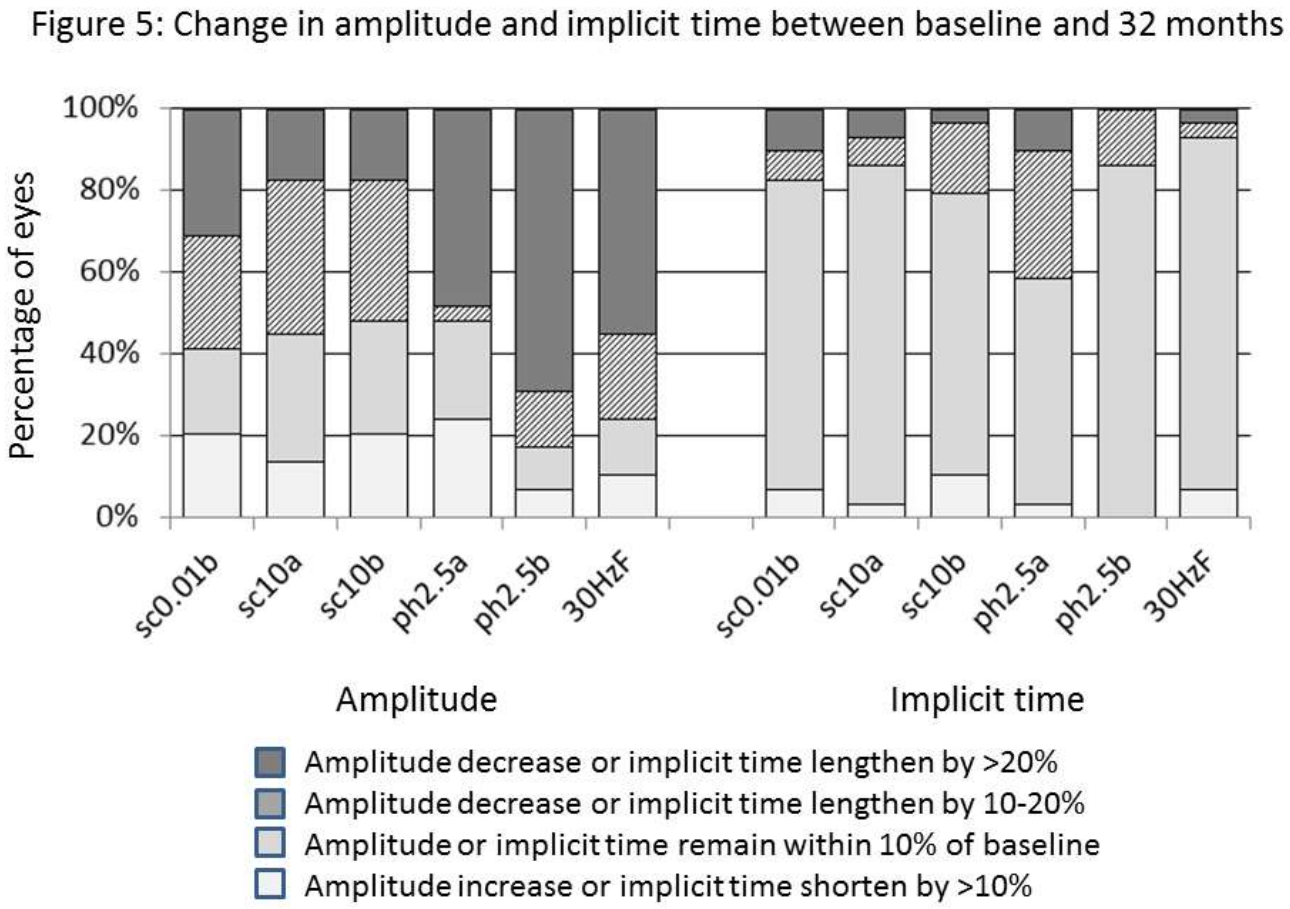


Figure 5: Change in amplitude and implicit times between baseline and 32 months



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