Supplementary material

Cone dysfunction in *ARR3*-mutation-associated early-onset high myopia: an electrophysiological study

Table S1. Primer names and the exons of *ARR3* amplified by PCR

Primer name	Sequence	Spanned exons
Arr3_ex2Fw	TGGTATGCTGGAGTGGGGTG	2, 3, 4, 5
Arr3_ex2Rev	ACTCATCGGGTTACCTGTCTG	2, 3, 4, 5
Arr3_ex6Fw	ACCACCAAGCCAGGCTAATAC	6, 7
Arr3_ex6Rev	CCCACTGTTCCTCTTCCCTG	6, 7
Arr3_ex8Fw	TCTTTGCCCTTGTCCCTTTACA	8, 9
Arr3_ex8Rev	GCCTGCCCAAGTAGGAAATC	8, 9
Arr3_ex10Fw	GGCAATAGCGCTAAGGAAGC	10, 11
Arr3_ex10Rev	GATGGGACTCCTGGGGGTAA	10, 11
Arr3_ex12Fw	CCCACCAGAACTAATTTCTCCC	12
Arr3_ex12Rev2	TGGTCCCACAGGCATTATTGAG	12
Arr3_ex13Fw	AGGGTGTGGTGATAGGAATGC	13, 14
Arr3_ex13Rev	CCCTCAGACCCTCCAGAATCA	13, 14
Arr3_ex15Fw	AACTAAGGGAGGGAGGTTCAG	15, 16
Arr3_ex15Rev	CACCCCAAGGAAGCATTTTCA	15, 16
Arr3_ex17Fw	AAAAAGAGTGGACACGGAGGA	17
Arr3_ex17Rev2	CCAGGAAGAGGAAATAGGCAAGAG	17

ERG results

Description of the ERG waveforms based on Figure 1 of the manuscript

LA flash responses displayed an initial negative component (a-wave) in which the peak amplitude was at about 12 ms after the flash onset followed by a larger positive component (b-wave) at about 28 ms peak amplitude. LA ERG a-wave and b-wave are known to originate in cones / hyperpolarizing-bipolar cells and cone-to-bipolar cell synapses, respectively [1,2]. LA flicker ERG

displayed 30 Hz sine-like responses representing cone-driven activation of cone-to-bipolar cell synapses [3]. DA ERG to weak flashes elicited a rod-dominated response with only a positive component (b-wave) peaking at about 85 ms. This component represents the activation of rod-to-On (depolarizing) bipolar cell synapses. The DA ERG to standard flash elicited a response containing a-wave, at around 15 ms, and b-wave, at around 48 ms. The a-wave represents photoreceptors' and bipolar cells' activation and the b-wave is mainly originated at the On-bipolar cells [2,4]. The oscillatory potentials (OPs) were isolated from ERG signals obtained with the standard flashes using a band-pass filter of 75 to 300 Hz. They are thought to originate at the amacrine cells through feedback interactions taking place in the inner retina [5]. Table S2 shows mean ± standard deviation of ERG results.

Light-adapted and dark-adapted peak times

Peak times were comparable among the groups for the three LA components: a-wave ($F_{(2,47)}$ = 2.107, p = 0.133), b-wave ($F_{(2,47)}$ = 1.225, p = 0.303) and flicker ($F_{(2,47)}$ = 0.274, p = 0.762). They were also comparable among the groups for the three DA components: b-wave weak flash ($F_{(2,47)}$ = 0.423, p = 0.657), a-wave standard flash ($F_{(2,47)}$ = 0.331, p = 0.720) and b-wave standard flash ($F_{(2,47)}$ = 0.884, p = 0.420).

Dark-adapted oscillatory potentials

DA OP amplitudes were statistically comparable among the groups either comparing the sum of the OP amplitudes ($F_{(2, 47)}$ = 0.657, p = 0.523) or comparing individual DA OP amplitudes (OP2: $F_{(2, 47)}$ = 1,456, p = 0.243; OP3: $F_{(2, 47)}$ = 0.915, p = 0.407 and OP4: $F_{(2, 47)}$ = 0.674, p = 0.515). Similarly, no differences in peak time were observed (OP2: $F_{(2, 47)}$ = 0.011, p = 0.989; OP3: $F_{(2, 47)}$

= 0.273, p = 0.762 and OP4: $F_{(2, 47)}$ = 0.175, p = 0.840). Means and standard deviations as well as p-values of OP amplitude and peak time comparison can be found in supplemental material (Table S2).

Table S2. ERG results (mean ± standard deviation)

ERG mean ± SD	E-CTRL (N = 20 eyes)	M-CTRL (N = 14 eyes)	MYP-26 (N = 14 eyes)
LA FLASH 3.0			
a-wave time	11.91 ± 1.08	12.48 ± 1.03	12.71 ± 1.45
a-wave amplitude	6.04 ± 1.56	6.51 ± 2.69	4.18 ± 1.40
b-wave time	27.77 ± 1.31	28.24 ± 0.86	28.30 ± 1.02
b-wave amplitude	30.47 ± 5.63	31.49 ± 11.01	20.51 ± 5.02
LA FLICKER 3.0			
implicit time	24.65 ± 0.92	24.74 ± 0.86	24.48 ± 1.05
amplitude	30.47 ± 5.66	31.49 ± 11.04	20.51 ± 5.05
DA FLASH 0.01			
b-wave time	86.25 ± 12.02	84.64 ± 9.88	88.71 ± 12.95
b-wave amplitude	39.68 ± 11.61	46.98 ± 18.15	38.66 ± 9.16
DA FLASH 3.0			
a-wave time	14.80 ± 2.33	15.32 ± 2.11	14.83 ± 1.04
a-wave amplitude	45.63 ± 13.00	39.55 ± 12.28	36.93 ± 10.40
b-wave time	47.68 ± 6.07	48.73 ± 5.25	46.13 ± 2.91
b-wave amplitude	75.68 ± 28.46	77.17 ± 21.10	64.17 ± 11.17
DA OP2			
implicit time	24.27 ± 2.19	23.78 ± 3.24	23.81 ± 2.81
amplitude	19.00 ± 20.43	13.03 ± 9.08	13.87 ± 4.56
DA OP3			
implicit time	31.21 ± 2.38	30.37 ± 3.57	31.54 ± 3.94
amplitude	11.99 ± 10.42	12.28 ± 5.91	9.05 ± 4.36
DA OP4			
implicit time	39.28 ± 2.91	38.13 ± 3.77	39.17 ± 4.26
amplitude	7.94 ± 8.96	6.58 ± 3.70	6.62 ± 3.12

REFERENCES

1. Bush RA, Sieving PA. A proximal retinal component in the primate photopic ERG a-wave. Invest Ophthalmol Vis Sci. 1994;35:635–45.

2. Frishman LJ. Origins of the electroretinogram. Principles and practice of clinical electrophysiology of vision. 2nd ed. MIT Press, Cambridge; 2006. p. 139–83.

3. Robson AG, Frishman LJ, Grigg J, Hamilton R, Jeffrey BG, Kondo M, et al. ISCEV Standard for full-field clinical electroretinography (2022 update). Doc Ophthalmol. 2022;144:165–77.

4. Robson JG, Frishman LJ. The rod-driven a-wave of the dark-adapted mammalian electroretinogram. Prog Retin Eye Res. 2014;0:1–22.

5. Wachtmeister L, Dowling JE. The oscillatory potentials of the mudpuppy retina. Invest Ophthalmol Vis Sci. 1978;17:1176–88.