Light-Adapted Electroretinograms Obtained with a Portable Device in Patients with *ABCA4*-Retinopathy: Associations with Genotype

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Purpose

- Electroretinogram (ERG) parameters can be used to quantify severity in Stargardt disease (*ABCA4*-retinopathy) and provide prognostic information.
- Standard tests take up to an hour and often require a separate patient visit, sometimes to another hospital.
- Alternatively, a portable device (Figure 1) can be used to record light-adapted ERGs within minutes in the outpatient clinic.
- We sought to explore whether ERG parameters obtained with the device associate with severity of genotype.



Figure 1. Images of the portable ERG system

Methods

- Patients in a large inherited disease service with genetically confirmed *ABCA4*-retinopathy were recruited to undergo light-adapted ERG recordings with the portable device (RETeval system, LKC Technologies) and specialised skin electrodes (Sensor Strips, LKC).
- Stimuli delivered retinal illuminances equivalent to international standard LA3 and LA 30Hz stimuli.
- Parameters were averaged for both eyes where available.
- Variants were classified by severity according to a recent meta-analysis: Mild, Mild/Moderate, Moderate, Severe[1]
- Each patient was classified genotypically by the severity of the milder of the two alleles.
- Mean ERG amplitudes were compared across groups.

Results

- Fifty-five patients (29 females) were included: mean (SD) age, 51 (16) years.
- Numbers classified genotypically as mild, mild/moderate, moderate, and severe were 30, 9, 8, and 8 respectively.
- Figure 2 (right) shows example 30 Hz flicker ERG traces obtained with the device for participants from mild, moderate and severe groups.
- Figure 3 (below) displays means LA3 b-wave and 30 Hz flicker amplitudes by group.
- For both parameters, the mean value for the severe group differed significantly from each of the other groups ($p<0.05$).

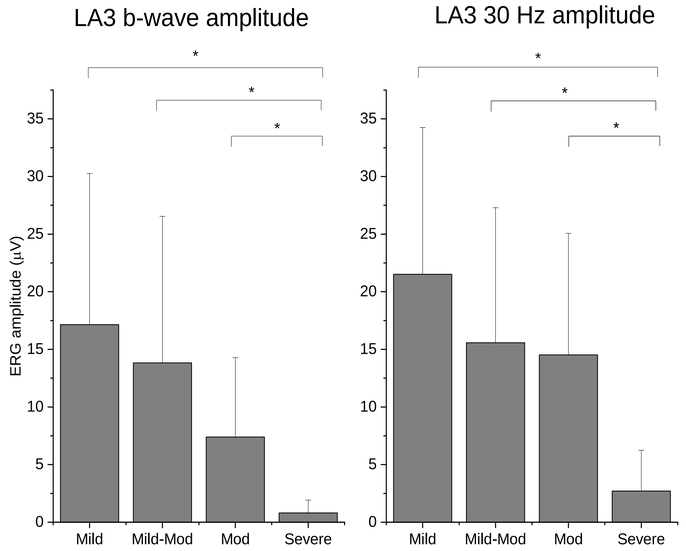
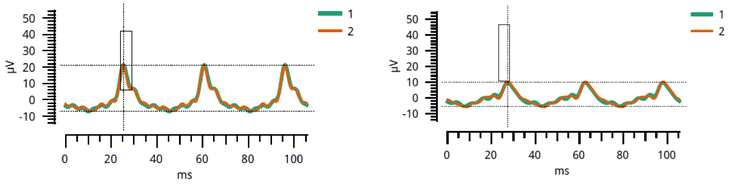
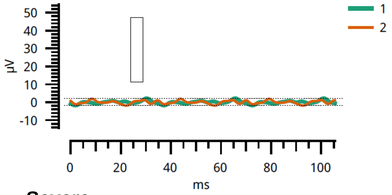


Figure 3. Mean ERG amplitudes by group. Error bars show standard deviations. Left panel shows LA3 b-wave amplitudes; right panel shows LA 30 Hz flicker ERG amplitudes. *Asterisk denotes significance ($p<0.05$).



Mild
c.5882G>A p.(Gly1961Glu) (Mild)
c.1317G>A p.(Trp439Ter) (Severe)

Moderate
c.4539+2028C>T (Moderate)
c.5461-10T>C (Severe)



Severe
c.1496G>A p.(Trp499Ter) Homozygous (Severe)

Figure 2. Examples of 30 Hz flicker ERG recordings obtained with the device from patients from different groups. In each case the green trace represents the averaged waveform from the first series of stimuli and the orange trace from the second series, demonstrating high intrasession repeatability. Genotypes are given; the patient is classified by the milder of the two variants.

Conclusions

- The findings suggest that the portable ERG recordings yield an assessment of retinal function that correlates with genotype.
- The test may help in predicting severity of as-yet unclassified variants, as well as giving a useful prediction of disease severity in patients who have not been able to undergo genetic testing.

Acknowledgements:
Wellcome Trust; Fight for Sight UK; Macular Society; NIHR Biomedical Research Centre at Moorfields Eye Hospital and the UCL Institute of Ophthalmology.
Views expressed are those of the authors and not the funding organisations.

References
1. Fujinami K *et al*. A longitudinal study of Stargardt disease: clinical and electrophysiologic assessment, progression, and genotype correlations. *Am J Ophthalmol*. 2013 Jun;155(6):1075-1088.e13.
2. Glinton SL *et al*. Phenotyping of ABCA4 Retinopathy by Machine Learning Analysis of Full-Field Electroretinography. *Transl Vis Sci Technol*. 2022 Sep 1;11(9):34.
3. Cornelis SS *et al*. Compendium of clinical variant classification for 2,247 unique ABCA4 variants to improve genetic medicine access for Stargardt disease. https://www.medrxiv.org/content/10.1101/2023.04.24.23288782v1

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