EDITORIAL

Introduction to the special section on *Visual electrophysiology 2021: a coming of age*

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Eye (2021) 35:2339–2340; <https://doi.org/10.1038/s41433-021-01678-9>

In this special issue of *Eye*, we explore the changing applications of visual electrophysiology and their impact upon clinical ophthalmology. We sought clinical updates to outline the ways that visual electrophysiology findings can support everyday clinical decisions and contribute to evidence-based practice. The topics summarised by international experts show the value and limitations of electrophysiology tests across a wide range of rare and common conditions affecting adults and children. In this series, we also sought to highlight the increasing relevance of electrophysiology in multidisciplinary discussions of genetic findings.

Clinical visual electrophysiology tests provide objective measures of function and unique insight into the neurobiology of retinal and CNS diseases. The interpretation of these tests follow clear diagnostic logic paths, yet for too long these data have appeared daunting and overly technical. The International Society for Clinical Electrophysiology of Vision (ISCEV) is committed to making visual electrophysiology more accessible.

Members of ISCEV publish agreed standards and guidelines that specify test protocols. A patient should expect the same test results from any clinic across the world using an ISCEV standard test. Distinguishing normal from abnormal findings requires adequate reference data and ISCEV initiatives are pooling electrophysiological reference data to support new electrophysiology clinics and improve patient safety. Test standardisation also paves the way for artificial intelligence to provide an individual patient with a quantitative likelihood score for a condition. A convergence with advances in other techniques, such as ocular imaging, will enhance diagnostic accuracy, but will require careful consideration of the patients' perspective along with the technical and ethical dilemmas common to digital medicine [1].

Ruth Hamilton, President of ISCEV, provides an enlightened commentary about the history and future of clinical visual electrophysiology. She recognises the need to improve the patient experience by making test shorter for patients and notes the possibilities of more compact equipment to change future models of care delivery and bring diagnostic electrophysiology tests to patients in primary and secondary care.

Elisa Cornish, Anagha Vaze, Robyn Jamieson and John Grigg describe their experiences working in ophthalmic genetic clinics and provide a fresh practical guide to the role of electrophysiology in the genomic era. They set out how the flash electroretinogram functionally dissects the retina, before showing the synergy of structural imaging and electrophysiological function using common and uncommon clinical examples of outer retina, photoreceptor dysfunction. They reflect upon the evolving role of the ophthalmologist when genetic results are not clear cut and explain how ERG findings can improve diagnostic rates when assessing variants of unknown significance or stratifying patients to new treatments or clinical trials.

Xiaofan Jiang and Omar Mahroo continue the journey through the retina with a clinical update about the electronegative ERG. The meaning of this distinctive ERG phenotype is a frequent FRCOphth fellowship question. The authors of this review describe the nuances that allow further discrimination and take the reader from the physiology of the inner retina to a likelihood framework of conditions to guide diagnosis when an electronegative ERG is reported. As in the review of the outer retina by Cornish et al., Jiang and Mahroo explain the value of visual electrophysiology when they re-evaluate clinical phenotypes and determine which genetic variants are relevant.

The need for shorter and more accessible tests is most apparent for children, particularly those with neurodevelopmental or neurodegenerative conditions. Dorothy Thompson, Sian Handley, Robert Henderson, Oliver Marmoy and Paul Gissen use a shorter paediatric ERG method to elaborate the natural history of retinopathy in children with CLN2 Batten disease. Children with CLN2 disease now have enzyme replacement delivered intrathecally, but this doesn't treat the rapidly progressive and blinding retinopathy. The authors combined ERG and OCT data from patients treated for CLN2 in their clinic with other published studies to refine the likely therapeutic window for prospective intra-vitreous treatment of CLN2 associated retinopathy.

The combination of visual electrophysiology with ocular imaging and psychophysics is explored in a thought-provoking review of electrophysiology in glaucoma by Khaldoun Al-Nosairy, Michael Hoffmann and Michael Bach. They synthesise the findings of recent clinical and research studies combining OCT and OCTa imaging with different electrophysiology protocols. They specifically consider the dynamic range or floor effects of the various techniques in the quest for biomarkers at different stages of glaucoma disease progression.

The differential diagnosis of visual loss due to retinal ganglion cell and optic nerve disease can be challenging. Oliver Marmoy and Suresh Viswanathan review the sensitivity and timing of functional changes in electrophysiological features, including the visual Evoked Negative Response, combined with ocular imaging and visual field assessments across a wide range of optic nerve conditions, such as hereditary optic nerve disease, optic neuritis, optic nerve compression, papilloedema and concussive optic neuropathy in sports and military situations.

Visual field assessment is problematic for young children or patients with neurodevelopmental delay, but often needed. A practical clinical review by Sian Handley, Maja Šuštar and Manca Tekavčič Pompe explores the sensitivity of multichannel visual evoked potentials to detect possible visual field deficits in children. Using a range of clinical examples along the visual pathway they illustrate the role of electrophysiological assessment of the visual field in a range of conditions such as intracranial

tumours, premature birth and pre-epileptic surgery evaluations when radical disconnection or resection are planned.

In a review that encompasses all the electrophysiological tests, Emily O'Neill and Richard Smith review cases of clinically important toxicity and deficiency states where there is evidence that visual electrophysiological testing can assist the clinician. This concise update includes the relatively new diagnosis ARFID, (Avoidant Restrictive Food Intake Disorder), which appears to be an increasing cause of micronutrient deficiency particularly in children with autistic spectrum disorders.

This special visual electrophysiology section is a summary snapshot of the adaptable and evolving role of visual electrophysiology in ophthalmology clinical practice. Visual electrophysiology is a valuable clinical companion particularly in paediatric, neuro-ophthalmology and genetics clinics and an important partner at the interface of function and structure associations in clinical research.

In common with other diagnostic specialities, visual electrophysiology will need to be flexible and creative to deliver meaningful tests that are more accessible and easier for patients, but also clearer for clinicians and scientists from different disciplines to understand. Advances in automated AI analysis in visual electrophysiology will add its own story to the debate about digital medicine as will the changes in models of health economics needed to deliver care closer to the patient.

Rising to these challenges ISCEV is a point of reference and an open source of expert advice and opinion. Look out for the ISCEV symposium in the UK, Liverpool 2022 and for ISCEV's welcoming educational programme with opportunities to discuss clinical

cases in which electrophysiology has a role and sometimes provides unique insight. As this up-to-date review series highlights, clinical visual electrophysiology has an exciting and evolving role in future ophthalmological care.

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COMPETING INTERESTS

The author is an Eye editorial board member. No other conflicts declared.

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