Abstracts of the 59th Symposium of the International Society for Clinical Electrophysiology of Vision (ISCEV): Liverpool, 3–6 August, 2022

Abstract Editing Committee:
Scott E. Brodie, Paul Constable, Mary Johnson, Jonathan Lyons, Omar Mahroo, J. Jason McAnany, Anne Moskowitz

Foreword In this Special 2022 Symposium Issue of Documenta Ophthalmologica, we have compiled the meeting abstracts which reflect the depth and breadth of the international community dedicated to clinical electrophysiology of vision. The Abstract Editing Committee has made every effort to optimize the abstracts for clarity and readability—we aimed to respect the intended meaning of the original submissions and apologise for any inadvertent misinterpretation.

Oral session 1

O1 01 Predicting ERG group in ABCA4-retinopathy by machine learning and scoring of variant severity
Omar A. Mahroo1,2,3, Antonio Calcagni1,2, Sophie Glinton1,2, Watjana Lilaonitkul1,3, Nikolas Pontikos1,2, Gongyu Zhang1,2, Sandra Vermeirsch1,2, Gavin Arno1,2, Michel Michaelides1,2, Siegfried Wagner1,2, Pearse A Keane1,2, Andrew R. Webster1,2, Anthony G. Robson1,2
1Moorfields Eye Hospital, London, United Kingdom. 2University College London, London, United Kingdom. 3King’s College London, London, United Kingdom

Purpose ABCA4 (associated with Stargardt disease) is the gene most commonly implicated in monogenic inherited retinal disease. Full-field ERG findings are of relevance to visual prognosis but can be difficult to predict from genotype due to the existence of a very large number of allelic variants. This study examined data from a large genetically confirmed cohort of patients with ABCA4-retinopathy, with the following aims: (1) to report prevalence of different ERG groups in a large cohort; (2) to develop and evaluate a machine-learning model to classify ERGs; and (3) to develop objective ERG-based severity scores for the more frequent ABCA4 variants.

Methods ISCEV-standard full-field ERGs were recorded in 597 individuals with ABCA4-retinopathy and were classified into three functional phenotypes by expert analysis: isolated macular dysfunction (group 1; normal ERGs), macular dysfunction with additional generalised cone system dysfunction (group 2), or macular dysfunction with generalised cone and rod system dysfunction (group 3). Algorithms were developed for automatic selection of appropriate ERG traces and for automated identification and measurement of ERG parameters. A machine-learning pipeline was developed to predict ERG phenotypic group, and performance was evaluated by comparison with expert classification. Elastic-net regression was used to quantify severity of specific ABCA4 variants based on the effect on retinal function.

Results By expert classification, 57.6% of the cohort were in group 1, 7.4% in group 2, and 35.0% in group 3. Machine learning classification had an overall accuracy of 91.8% (SE 0.169), with 96.7%, 39.3% and 93.8% accuracy for groups 1, 2, and 3, respectively. If the cohort was re-classified into restricted (group 1) and generalised disease (groups 2 and 3 combined) phenotypes, the average hold-out group accuracy was 93.6% (SE 0.142). The regression model assigned ERG-based severity coefficients to the 42 most frequent variants in the cohort, where lower coefficients were associated with more severe disease. Known mild variants showed high coefficients, and known null variants exhibited low coefficients. Both dark-adapted and light-adapted ERG parameters predicted similar levels of severity (average r = 0.82).

Conclusion This study quantifies, by expert and automated methods, the prevalence of ERG-phenotype groups in a uniquely large single-centre cohort of ABCA4-retinopathy and provides proof of principle for applicability of machine learning to such ERG datasets. Novel regression-based analyses of ABCA4 variant severity appeared to be accurate for those variants whose severity is already known and may provide an objective classification for variants whose functional effect is not yet defined. Such scores could predict predisposition to severe disease, potentially identifying those most likely to benefit from early therapeutic intervention.

O1 02 ERG is specific for and correlates with severity of Pantothenate Kinase-Associated Neurodegeneration
Robert Spaul1,2, Audrey K. S. Soo1,2, Apostolos Papatheodorou1,2, Allison Gregory3, Penelope Hogarth3, Susan J. Hayflick3, Manju A. Kurian1,2, Dorothy A. Thompson1,2
1Molecular Neurosciences, Developmental Neurosciences, Zayed Centre for Research into Rare Disease in Children, UCL Great Ormond Street Institute of Child Health, UCL, London, United Kingdom. 2Department of Neurology, Great Ormond Street Hospital...
for Children, London, United Kingdom. 3Departments of Molecular & Medical Genetics and Neurology, Oregon Health & Science University, Portland, Oregon, USA. 4Tony Kriss Visual Electrophysiology Unit, Clinical and Academic Department of Ophthalmology, Great Ormond Hospital for Children, London, United Kingdom

**Purpose** Pantethenate kinase-associated neurodegeneration (PKAN) is a severe progressive neurodegenerative disorder caused by biallelic loss-of-function variants in PANK2. Affected children and young people develop debilitating dystonia, lose ambulation and speech, and are at risk of premature mortality. PKAN causes pigmented retinopathy with retinal degeneration which can be detected early in the disease with imaging and electrophysiology (Egan et al., Am J Ophthalmol:2005;140(2):267–274). PKAN can sometimes be difficult to diagnose due to rarity and the often non-specific clinical presentation, with similarities to many progressive movement disorders including other syndromes of neurodegeneration with brain iron accumulation (NBIA). We aimed to (1) assess the utility of ERG and VEP in diagnostic testing of children presenting with a suspected NBIA disorder; (2) assess progressive retinopathy in children and young people with PKAN.

**Methods** Records for children with a suspected/confirmed NBIA disorder investigated at a single tertiary centre were reviewed. The study was approved by the hospital research and development department (19NM23) which confirmed exemption from NHS-REC approval. ERG and VEP were recorded in awake children using established techniques (Thompson et al., Eye:2021;35:2438–2448).

**Results** 41 children with a suspected or confirmed NBIA disorder had visual electrophysiology testing over a 17-year period; 32/41 assessments were performed at a single institution. Median age at assessment was 7.2 years (range 1–17 years); 23 were female and 18 male. ERG was abnormal in 11/34; this included all ten patients with PKAN and one with Cockayne syndrome (ERCC8). The 23/34 patients with normal ERG had a non-PKAN NBIA disorder [11/23: 8 with PLA2G6-associated neurodegeneration (PLAN), 2 with mitochondrial membrane protein-associated neurodegeneration (MPAN), 1 with beta-propeller protein associated neurodegeneration (BPAN)], or other disorders with radiological suggestion of brain iron accumulation (MT-ND1, MT-ND6, and 1 each with KMT2B-dystonia, ATP1A3-related disorder, Waisman syndrome (RAB39B), DNAJC3-related neurodegeneration, optic pathygliaomia), or without (5 with non-diagnostic investigations including negative NBIA gene panels). By combining our PKAN cohort (10 patients) with published cohorts by Egan et al. (16 patients) and Jesus-Ribeiro et al. (7 patients; Br J Ophthalmol:2017;0:1–7), we observe that ERG changes are more severe in classical vs atypical PKAN, and that severity correlates with earlier disease onset (R = −0.542). Changes appear to suggest progression from cone, to rod, then generalised photoreceptor dysfunction. VEPs were available for 36/41, and 20/36 were abnormal; 36 abnormal in PKAN patients, all with severe ERG retinopathy. In one patient with compound heterozygous PANK2 variants of uncertain significance, specific ERG abnormalities combined with the clinical and MRI phenotype, were used to upgrade the assessment of variant pathogenicity.

**Conclusion** Visual electrophysiology testing of children with a suspected NBIA disorder confirms a clear dichotomy of photoreceptor disease in PKAN compared to retinal ganglion cell or retinal nerve fibre loss in others. This highly specific investigation finding can be used to aid diagnosis and genetic variant classification. In addition, ERG changes appear to be measurable and progressive, providing an opportunity for use in disease monitoring as a non-invasive, objective disease biomarker.

**O1 03 Vessel density and photopic negative response changes in glaucoma**

Zainab Alrikabi, Lorraine Cameron, Uma Shahani, Andrew Logan

Glasgow Caledonian University, Glasgow, United Kingdom

**Purpose** Glaucoma is an irreversible and potentially blinding condition that is estimated to affect over 80 million people worldwide (Tapply I, Broadway DC. Patient Prefer Adherence: 2021;15:1477–1489). The insidious nature of glaucoma can result in later presentation and poorer prognosis. Specifically, asymptomatic retinal changes often occur before functional damage to the visual field (VF). The primary purpose of this pilot study was to investigate the relationship between blood vessel density measured with optical coherence tomography angiography (OCT-A) at the level of the superficial capillary plexus (at optic nerve head and macula) and standard automated perimetry (SAP) indices commonly used to detect glaucoma. In addition, we compared one component of the ERG signal—specifically the photopic negative response (PhNR)—between patients with glaucoma and controls. ERG measures have the potential to add to our understanding of the effect of glaucomatous damage upon the retinal ganglion cells, as well as to provide a comprehensive measure of visual function, when used in conjunction with SAP (Beykin et al., Prog Retin Eye Res:2021;80:100875.).

**Methods** Participants were at least 50 years old and categorized as controls (no glaucoma or other eye disease), pre-perimetric glaucoma (defined as having signs of glaucomatous optic nerve head damage but no visual field loss), or confirmed glaucoma (with signs of both optic disc damage and visual field loss) and taking medication for the disease. Optic nerve head and macular retinal angiograms were captured using a swept-source OCT-A instrument (Topcon, DRI OCT Triton). Threshold SAP was performed using the Humphrey Visual Field Analyzer (HFA 24-2 SITA FAST) for each eye. Full-field ERG and PhNR were recorded using the handheld portable RETeval (LKC Technologies) by utilising the ISCEV photopic flash/tickler and PhNR Td protocol. A percentage of vessel area was calculated from OCT-A scans of the macula, circumpapillary zone and whole-image of the optic nerve head. Vessel density was calculated by ImageJ (image analysis software) as the proportion of white pixels on the binarised image [i.e., white/white + black]. Glaucomatous field loss was quantified in terms of mean deviation (dB) and pattern standard deviation (dB). Intracocular pressure (mmHg) was measured using the iCare tonometer.

**Results** Our data indicate that mean vessel density (%) is significantly reduced in both the pre-perimetric and perimeter glaucoma groups compared to controls. This reduced vessel density was evident in both the region of the macula and optic nerve head. Mean vessel density values were significantly different (p < 0.05) between all three groups at the circumpapillary zones. ERG results indicated that the amplitude of the PhNR was reduced in the glaucoma group, relative to the control and pre-perimetric groups.

**Conclusion** Using OCT-A, our results suggest that glaucoma is associated with reduced circumpapillary vessel density and a weaker PhNR. RETeval was a practical device for RGC function assessment and can be helpful for clinical work.
**O1 04 Bornholm eye disease; an overlooked diagnosis**

Dzenita Smajlhoedzic1,2, Timo W. F. Mulders3, Gerard de Wit1, Lonneke Haer-Wigman3, Carol H. Hoyn3, Ingeborg van den Born2, Jeroen B. Klevering3, Maria M. van Genderen1,5

1Bartiméus Diagnostic Center for Complex Visual Disorders, Zeist, Netherlands. 2The Eye Hospital, Rotterdam, Netherlands. 3Department of Ophthalmology Radboud UMC, Nijmegen, Netherlands. 4Department of Ophthalmology, Utrecht Medical Center, Utrecht, Netherlands.

**Purpose** Bornholm eye disease (BED) is an X-linked cone dysfunction caused by mutations in the L and M opsin genes. Clinical features of Bornholm include subnormal visual acuity (VA), myopia, red-green color vision deficiency, and variably reduced cone ERG. As 8% of the total male population have color vision deficiencies, and as high myopia is often associated with reduced visual acuity, it may be challenging for ophthalmologists to recognize BED. In order to aid accurate diagnosis, we describe the clinical findings and follow-up in BED patients.

**Methods** We identified 40 male patients, 29 children (age 3–14 years) and 11 adults (age 19–66 years), originating from 33 families with genetically confirmed mutations in opsin genes. Thirty-three patients had follow-up data. We reviewed the best corrected VA (BCVA), refractive error, fundus autofluorescence (FAF), optical coherence tomography (OCT), color vision, and full-field electroretinography (fERG).

**Results** Median follow-up time was 4.02 years (range 0.82–12.36 years). Median BCVA at the first visit in children and adults was 0.35 (range 0.10–0.80). In children, we found statistically significant improvement of VA, with a median BCVA of 0.5 (range 0.25–0.8). Seven adults had follow-up data available. Four patients demonstrated macular atrophy and decline in VA. Phenotypes were similar, consisting of moderate to high myopia, mean spherical error of −6.51 (95% CI −5.12 to −7.90) diopters, accompanied by a median cylindrical refractive error of −2.00 (range −7.50 to 0.00) diopters. fERG showed reduced cone but normal rod responses. On OCT, central retinal thickness was reduced (mean 230 μm, ranging from 184 to 288 μm, SD 27 μm).

**Conclusion** Children with BED cone dysfunction demonstrate, to some degree, visual development. The main reason for referral in children was myopia. Even at a young age they have moderate to high myopia, indicating that the greatest myopic shift occurs before diagnosis. While some adult patients demonstrate foveal atrophy as seen in cone dystrophy, other adult patients preserve sub-optimal visual acuity into older age. In a male patient with moderate to high myopia and moderately reduced VA but without fundus abnormalities, Bornholm eye disease should be suspected. Examinations to establish the diagnosis include color vision testing, fERG, and molecular analysis of the opsin genes.

**O1 05 GUCY2D-associated cone-rod dystrophy: identifying best correlates for natural history studies**

John R. Grigg1,2, Amanda J. Scopelliti2, Elizabeth H. Barnes3, Elisa E. Cornish1,2, Benjamin M. Nash4,5, Robyn V. Jamieson1,2

1Save Sight Institute, The University of Sydney, Sydney, Australia. 2Eye Genetics Research Unit, Sydney Children’s Hospitals Network, Save Sight Institute, Children’s Medical Research Institute, The University of Sydney, Sydney, Australia. 3NHMRC Clinical Trials Centre, University of Sydney, Sydney, Australia. 4Sydney Genome Diagnostics, Western Sydney Genetics Program, Sydney Children’s Hospitals Network, Sydney, Australia.

**Purpose** GUCY2D encodes the photoreceptor guanylate cyclase, a key phototransduction enzyme involved in the restoration of cGMP. The knockout mouse, which lacks the cGMP and the return to the dark state of the photoreceptor. We investigated visual functional measures including best corrected visual acuity (BCVA), full-field electroretinogram (ERG) and pattern electroretinogram (PERG) in GUCY2D-associated autosomal dominant cone-rod dystrophy (adCRD) patients and correlated them with fundus autofluorescence (FAF) and macular optical coherence tomography (OCT).

**Methods** A retrospective, observational cohort study was conducted on data from 16 patients with GUCY2D-associated adCRD. Assessments included central macular thickness (CMT) and length of disruption to the ellipsoid zone (EZ) via OCT, ERG parameters, BCVA (measured in logMAR letters), and FAF.

**Results** At first visit, with a mean age of 30 years (range 5–70 years), 12 patients had a BCVA below the medical standards for holding an Australian Driver’s licence (logMAR ≥ 0.3 in both eyes), including one who was legally blind (logMAR ≥ 1). Analysis over the observation period (mean = 7 years, range 0–17 years) demonstrated a deterioration of logMAR by 0.019 per year (95% CI 0.014–0.024, p < 0.0001), during which three patients crossed the threshold of legal blindness. This study also demonstrated a significant reduction in CMT of 1.4 μm per year (95% CI −1.95 to −0.95, p = 0.005) and lengthened disruption of the EZ by 42 μm per year (95% CI 34–51 μm, p < 0.0001). Similarly, cone system function as measured by ERG decreased with increasing age; b-wave amplitude of both the light-adapted 30 Hz flicker and fused flicker decreased by 0.83 μV (95% CI 1.42–0.15 μV, p = 0.005) and 0.21 μV (95% CI 0.38–0.04 μV, p = 0.02) per year, respectively. Reduction in CMT and increased EZ disruption on OCT were significantly associated with functional decline including decreased BCVA and cone system function on ERG. Eighty one percent (26/32) of eyes assessed demonstrated fundal hyperautofluorescence before their first assessment. The mean area of FAF at first measurement was 1.6 ± 1.5 mm², with a range of 0–7.4 mm². No association was found between FAF area and average logMAR BCVA (p = 0.087); however, a clear trend was illustrated graphically in which a patient with a larger area of hyperautofluorescence tended to have worse vision. Larger FAF area was significantly associated with reduced P50 (β = 0.15 μV per 1 mm²; 95% CI 0.06–0.24, p = 0.0008).

**Conclusion** We have described the natural long-term decline in vision and cone function associated with mutations in GUCY2D. We have also identified a set of functional and structural biomarkers that may be useful as outcome parameters for future therapeutic clinical trials.

**O1 06 The clinical and electrophysiological features of CRB1-associated retinal dystrophies**

Anthony G. Robson1,2, Malena Daich Varella1,2, Michalis Georgiou2,3, Shaheeni Khoda1,2, Kaoru Fujinami1,2,4, Yu Fujinami-Yokokawa1,5, Andrew R. Webster1,2, Michel Michaelides1,2

1Moorfields Eye Hospital, London, United Kingdom. 2UCL Institute of Ophthalmology, London, United Kingdom. 3Jones Eye Institute, Little Rock, USA. 4National Institute of Sensory Organs, National Hospital Organization Tokyo Medical Centre, Tokyo, Japan. 5Keio University, Tokyo, Japan.
Purpose Biallelic pathogenic variants in CRB1 are associated with a wide range of retinal phenotypes. This multicentre retrospective study presents the largest CRB1 cohort to date, with the aim of detailed clinical and electrophysiologically phenotyping, relevant to future interventional clinical trials.

Methods 111 patients (98 probands) with likely damaging CRB1 variants were ascertained. The clinical records, ophthalmic images and results of genetic testing were reviewed. ISCEV standard pattern and full-field ERG (PERG; ERG) were obtained in 29 subjects using corneal recording electrodes after mydriasis, and a further 9 (ages 2–8 years) underwent ERG testing according to an abbreviated ERG protocol using lower eyelid skin electrodes.

Results Eighty-one pathogenic CRB1 variants were detected including 24 which were novel. Based on the clinical and retinal imaging findings, 26% were diagnosed with retinitis pigmentosa (RP), 51% with early onset severe retinal dystrophy, and 23% with macular dystrophy (MD). Common fundus features included maculopathy (97%), nummular pigment (45%), preserved para-arteriolar RPE (26%), white/yellow dots (21%) and retinal telangiectasia (10%). PERG P50 was undetectable in 13 of 27 subjects and was subnormal in 13 others. Eight patients had undetectable ERGs consistent with the clinical diagnosis of LCA. The ERGs in others (8 patients with clinically suspected MD and 6 with RP) revealed a similar degree of rod and cone system involvement, with marginally greater rod than cone system dysfunction in 5 cases. Seven patients had MD both clinically and electrophysiologically (normal ERGs). Four of 9 of the youngest cases tested using an abbreviated ERG protocol had undetectable responses; detectable ERGs showed a similar degree of cone and rod system involvement (N = 3), dysfunction confined to the cone system (N = 1), or were normal but with an undetectable PERG (N = 1).

Conclusion This study describes the clinical and electrophysiologically findings in the largest CRB1-retinopathy cohort to date, further establishing phenotypic variability. The importance of ERG testing is highlighted, revealing a range of functional phenotypes of relevance to diagnosis, patient management, and future treatment strategies.

Oral Session 2

O2 01 Effect of test flash duration on the Photopic Negative Response (PhNR)

Suresh Viswanathan1, Behrad Garmarsi1, Ashwin Badrinath Pothiaadia-Irungovel1, Sarah Gleason1, Jeffrey Farmer2

1State University of New York, New York, USA. 2Diagnosys LLC, Lowell, USA

Purpose The Photopic Negative Response (PhNR) of the cone-mediated ERG is a slow potential with negative polarity that appears after the b-wave. The PhNR originates from the electrical activity of retinal ganglion cells (RGCs) and has clinical utility. The PhNR is typically recorded to a brief (<4 ms) test flash. We explored the effect of increasing the stimulus duration on the PhNR amplitude of normal subjects in an ongoing attempt to optimize the stimulus conditions for its clinical use.

Methods ERGs were recorded with DTL electrodes from normal subjects (N = 10) in the age range 23–53 years using the ColorBurst handheld Ganzfeld stimulator and hardware from Diagnosys (Lowell, MA). The stimuli consisted of red test flashes on constant blue background (8 phot cd s/m²). The test flashes were either brief stimuli (<4 ms duration) in the range of 0.00625–6.4 phot cd s/m² or longer duration stimuli (20–80 ms) in the range of 0.125–1500 cd/m². A new algorithm in the Espion software with objective sweep selection based on various noise and artifact identification criteria was used to average repeated responses at each test flash intensity. The PhNR amplitude of the averaged waveform was plotted as a function of test flash intensity and fitted with the standard Naka-Rushton equation. The saturated amplitude (Vmax), slope (n) and semisaturation constant (K) derived from the fits were analyzed. The Student t-test was performed to compare the fit parameters across different test flash durations with correction for multiple comparisons using the Holm’s method.

Results Vmax for the brief stimulus was 19 ± 5 microvolts and increased to 23 ± 2 microvolts for 20 ms stimuli (p = 0.036). Vmax for the 40–80 ms duration stimuli ranged between 25 and 27 microvolts and was significantly different from the 20 ms stimuli (p values 0.019–0.05). The semisaturation constant K was 69 cd/m² for the 20 ms stimuli and reduced to values in the range of 21–37 cd/m² for 40–80 ms duration stimuli (p values 0.01–0.04). The slopes of the functions were not significantly different for stimuli in the range of 20–80 ms duration.

Conclusion The maximal PhNR amplitude is larger for longer duration stimuli as reflected by an increase in the Vmax and sensitivity for stimuli in the range of 40–80 ms duration. These effects may reflect a more persistent inner-retinal response to light onset for longer duration stimuli with less interference from ERG signals at light offset that have positive polarity.

O2 02 Correlation between OP magnitude and area under the curve of the photopic negative response

Sara Safari1, Emanuel Boveri II1, Katherine Tsay1, Christopher Passaggia2, Jan Kremer3, Radosl Zzekovic4

1University of South Florida, Morsani College of Medicine, Tampa, USA. 2University of South Florida, Department of Medical Engineering, Tampa, USA. 3University Hospital Erlangen, Section for Retinal Physiology, Erlangen, Germany. 4University of South Florida, Department of Ophthalmology, Tampa, USA

Purpose A wealth of experimental evidence from the early 1960s to the present has shown a potential link between full-field ERG oscillatory potential (OP) activity and retinal ganglion cell (RGC) activity. However, a direct comparison between OP parameters and full-field ERG measures reflecting RGC activity [e.g. the photopic negative response (PhNR)], especially with clinical data, has not been reported. Therefore, the purpose of this study was to compare OP magnitude to PhNR parameters in a clinical data set.

Methods A retrospective chart review and data analysis of patients aged 18 and over undergoing routine ERG testing at USF Eye Institute (Tampa, FL) was conducted. The LA 3.0 ERG responses were recorded using DTL electrodes, white xenon flash (2.5 cd s/m²) on a white background (30 cd/m²) with a digitization rate of 3750 Hz and bandpass filtering range of 0.3–1500 Hz. For OP extraction, the signal was filtered using high-pass 4th order Butterworth filter with 58 Hz cut-off frequency. The root mean square (RMS) of the filtered signal was calculated to define the OP amplitude. The OP RMS values were compared by linear regression to the amplitude of the PhNR response, determined as PhNR1 amplitude (trough before i-wave; Ortiz et al. Doc Ophthalmol. 2020 140:115–128) and as area under the curve (AUC) from the peak of the b-wave to a range of times after it. Results The records of 55 patients/105 eyes (13 males, 42 females) were included. PhNR1 was determined reliably in 93.3% of the cases. AUC values were determined reliably in 100% of cases within a range from 9.07 to 14.93 ms (step 0.26 ms) after the b-wave peak. The PhNR1 showed reasonably good R² values with OP RMS: 0.8336 (right eyes), 0.8900 (left eyes) and 0.8555 (average right and left eyes). The PhNR AUC values showed even higher R² values with OP RMS: 0.8909–0.9043 (right eyes); 0.9426–0.9495 (left eyes) and
0.9227–0.9298 (average right and left eyes). These R2 values were higher compared to the values from OP RMS regression models with the a-wave amplitude (0.7215–0.7687) or the filtered b-wave amplitude (0.7333–0.7956). Of note, while the PhNR timing was 13.65 ± 2.2 ms (median 13.74 ms) after b-wave peak for right eyes, 14.19 ± 3.18 ms (median 13.60 ms) for left eyes, and 13.86 ± 2.29 ms (median 13.47 ms) for average right and left eyes, the optimal time for PhNR AUC was 12.27 ms for right eyes, 10.67 ms for left eyes and 10.40 ms for average right and left eyes.

**Conclusion** Our results add support to the notion that at least some RGC input could be contributing to the generation of photopic OPs in humans. Furthermore, PhNR AUC within the range of 11–12 ms after the b-wave peak is better correlated with OP RMS compared to PhNR amplitude or a- and b-wave amplitudes, and, therefore, it appears that it may be used as an alternative measure of RGC function in future studies.

**O2 03 The diagnostic accuracy of broadband versus chromatic photopic negative response stimuli**

Shaun Leo1,2, Magella M. Neveu1-2, Patrick Yu-Wai-Man1,2,3, Omar A. Mahroo1-2,4, Anthony G. Robson1,2

1 Moorfields Eye Hospital, London, United Kingdom. 2 Institute of Ophthalmology, University College London, London, United Kingdom. 3 Cambridge Centre for Brain Repair and MRC Mitochondrial Biology Unit, Department of Clinical Neurosciences, University of Cambridge, Cambridge, United Kingdom. 4 Department of Ophthalmology, King’s College London, London, United Kingdom

**Purpose** To determine the relative diagnostic value of the photopic negative response (PhNR) to red-blue (RB) and white-white (WW) stimuli for the detection of retinal ganglion cell (RGC) dysfunction in a heterogeneous clinical cohort.

**Methods** In this prospective, single-centre, paired diagnostic accuracy study, consenting adult NHS patients (aged 18 +) referred for routine electrophysiology were recruited consecutively at Moorfields Eye Hospital. Participants underwent additional PhNR testing on the same day including the ISCEV extended protocol (Frischman et al., Doc Ophthalmol:2018;136(3):207–211). PhNRs were recorded to a red flash (627 nm; 1.5 phot cd s m−2) on a blue (448 nm; 10 phot cd m−2) background (RB PhNR) and to the ISCEV-standard LA 3 white flash (3.0 cd s m−2) on a standard white (30.0 cd m−2) background (WW PhNR). PhNR amplitudes were measured from baseline to trough and compared against reference ranges from our clinical control population. Participants were categorised as having RGC pathology if they tested positive for at least two of the reference tests. The reference tests were the PERG, VEP, visual fields, optical coherence tomography (OCT) nerve fibre layer thickness, and OCT mean retinal ganglion cell layer volume. The diagnostic status of the participants was unknown at the recruitment stage and the author interpreting the PhNRs (SL) was masked to the results of the reference data.

**Results** Between March 2021 and February 2022, 245 consenting participants (median age, 52; range 18–95; female 58%) were enrolled. Of these, 45 were excluded due to residual/undetectable responses or low technical quality. The reference test battery identified 45 participants with RGC pathology. Sensitivity was estimated to be 53% (95% CI 33.4–73.3%) and 62% (95% CI 44.3–44.3%) for WW and RB PhNRs, respectively. The combined sensitivity of the two PhNR stimuli was 67% (95% CI 49.8–83.5%). Specificity was 80% (95% CI 73.0–87.0%) and 78% (95% CI 70.7–85.4%) for WW and RB PhNRs, respectively. The combined specificity of the two PhNR stimuli was 70% (95% CI 62.6–78.0%). The ratio of the true- and false-positive fractions was 1.17 (95% CI 0.80–1.43) and 0.91 (95% CI 0.88–1.04), respectively. McNemar’s test found no statistically significant difference between the sensitivity or specificity of the two PhNR stimuli ($p = 0.16$ and 0.56 for sensitivity and specificity, respectively).

**Conclusion** The findings highlight the diagnostic accuracy of PhNRs for the detection of retinal ganglion cell dysfunction in a heterogeneous clinical cohort. There was no statistically significant difference in sensitivity or specificity between the two PhNR methods, highlighting the potential clinical value of LA 3 ERGs in the evaluation of RGC function.

**Acknowledgements** Provisional findings from this study were submitted to Aston University as part of an MSc dissertation (SL).

**O2 04 Using dim blue flash stimuli to elicit predominantly rod-driven ERGs with minimal dark adaptation**

Katrina L. Prise1, Dorothy A. Thompson1,2, Oliver R. Marmoy1,2,3

1 Tony Kriss Visual Electrophysiology Unit, Clinical and Academic Department of Ophthalmology, Great Ormond Street Hospital for Children, London, United Kingdom. 2 UCL-GOS Institute for Child Health, University College London, London, United Kingdom. 3 Manchester Metropolitan University, Manchester, United Kingdom

**Purpose** A dim blue flash stimulates predominantly rod-driven retinal function in an alternative skin ERG protocol for children (Marmoy et al., Acta Ophthalmologica 2021;100(3):322–330). This study assessed the changes to the amplitude and peak times from scotopic blue flash skin ERGs with and without dark adaptation.

**Methods** Blue (460 nm) 4 ms flashes were delivered 3/s by a Diagnosys ColorFlash™ handheld LED stimulator held 30 cm from the participant. Skin ERGs were recorded without pupil mydriasis from adhesive skin electrodes placed below the lower eyelid referred to the outer canthus. Skin ERGs from healthy participants were recorded to two flash strengths, dim blue 1 cd s m−2 and blue 3 cd s m−2. Patients with CNNGA3—and CNGB3—associated achromatopsia were tested in the same sequence using the stronger 3 cd s m−2 blue flash. The test sequence recorded bilateral skin ERGs in light adapted conditions. After immediately extinguishing the room light, one eye was occluded with a double patch whilst the other eye was stimulated continuously at 3/s with the blue flashes and unilateral ERGs were recorded for up to 23 min. Up to 3 min in scotopic conditions, ERGs were recorded in 15 s epochs. After 3 min, these were recorded in 30 s epochs. After 10 min, the patch was removed, and ERGs were recorded bilaterally. The patch was reapplied for a further 10 min before a final bilateral ERG was recorded at 20 min DA.

**Results** Within 1 min of scotopic conditions, the blue flash b-wave peak-time increased from 30 ms to 55 ms and amplitude increased 3–5 × in healthy subjects. The serially recorded b-wave amplitudes and peak-times plateaued with low covariance (range 5–15%) to blue 3 cd s m−2 flashes over 23 min. Blue flash ERGs recorded in the first minutes are comparable (within 100–80%) to those from the occluded fellow eye that experienced strict DA. Patients with achromatopsia, who lack cone function, had non-detectable blue flash ERGs under light adapted conditions. Within 1 min of scotopic conditions, blue flashes produced detectable b-waves with covariance ~ 15% over 23 min. These data confirm that the b-wave amplitude increase observed immediately in scotopic conditions reflects primarily rod-system activity, with no significant difference observed between timing of the DA ERG amplitude rise in achromatopsia patients and healthy subjects.

**Conclusion** The scotopic blue flash stimulus is an effective rod stimulus within 1 min of lights off. Data from patients with achromatopsia confirm blue flash ERGs in scotopic conditions are predominantly rod-driven. The blue flash ERG amplitude and time to
peak quickly plateau with continuous 3/s, 4 ms duration, flashes, making the blue flash an effective alternative test of rod function with minimal dark adaptation and advantageous for paediatric ERG protocols.

O2 05 Use of a portable ERG system for ON–OFF ERGs in congenital stationary night blindness

Mahnoor Z. Malik1, Xiaofan Jiang1,2,3, Zihe Xu1, Isabelle Chow4, Christopher J. Hammond1,4, Andrew R. Webster1,2, Omar A. Mahroo1,2,3

1Institute of Ophthalmology, University College London, London, United Kingdom. 2Genetics Service, Moorfields Eye Hospital, London, United Kingdom. 3Section of Ophthalmology, King’s College London, St Thomas’ Hospital Campus, London, United Kingdom. 4Department of Ophthalmology, St Thomas’ Hospital, London, United Kingdom

Purpose To explore the use of a portable ERG testing and recording system to record ERG responses to long duration flashes (ON–OFF ERGs) in cases of genetically confirmed complete and incomplete congenital stationary night blindness (CSNB).

Methods The RETeval portable device (LKC Technologies, Gaithersburg, MD) was used to deliver long flash stimuli (250 cd/m²) to record the ERG responses, using either Sensor Strip (LKC Technologies) skin electrodes or conductive fibre electrodes. Responses were averaged from 100 to 200 flash presentations. Participants underwent recordings following mydriasis. Participants included healthy controls as well as patients with complete or incomplete CSNB. The shape of the waveform was analysed in this exploratory study.

Results Responses from 12 participants (6 healthy controls and 6 patients) were qualitatively analysed. In healthy controls, aged 21–34 years, clear a-waves and b-waves were seen in response to the sine wave (at 0°, 90°, 180°, and 270°) flash at 1, 5, 10, and 25 Hz temporal frequencies; (3) to the combined presentation of the flashes and the sine wave. The flashes were presented at 8 different phases during the sine wave; 0° and 325° in 45° steps (luminance of the sine wave at 0°, 90°, 180°, and 270°; 50, 100, 50 and 0 cd/m², respectively). The responses to the sine wave were subtracted from the responses to the combined flash plus sine-wave stimuli to obtain the flash ERGs at different phases. In a second experiment, the responses to 5 ms flashes of various strengths (between 0.12 and 29.8 cd s/m²) varied in 9 steps while doubling the strength at each step were recorded on a 1 Hz sinusoidally modulating (50 cd/m² mean luminance; 100% contrast) background at phases 0°, 90°, 180° and 270°.

Results In the first experiment, all responses were photopic for the 270° conditions where the sine wave stimulus was 0 cd/m². The flash response amplitudes strongly depended on the phase of the flash relative to the sine wave. With a 1 Hz sine wave, the response was substantially larger (factor 3 or more larger a- and b-waves) for the flash at 270° phase compared to the flash ERG on a steady background. The response to the flash was minimal around 90°. The responses to the flash at 0° and 180° were comparable to the flash ERG on a steady background. The effects of background modulation on the flash ERG decreased with increasing frequency of the sine wave. Furthermore, the phase of maximal response shifted towards higher phases with increasing frequency, indicating a delay in processing. The amplitudes of the components as a function of flash strength and sine wave frequency could be modelled using the Weber fraction of the flash plus a saturation and a delay. The second experiment showed that this effect was present at all flash strengths for the a-wave and up to 1.9 cd s/m² for the b-wave. For flashes stronger than 1.9 cd s/m², the b-wave amplitude decreased again (due to the photopic hill effect). Beyond the photopic hill, the b-waves were not modulated by the sine wave.

Conclusion Weber fraction of the flashes is an adequate quantification of stimulus strength to describe the amplitudes of the flash ERGs, but saturation and delays should be included in a description of the mechanism underlying the ERG response. The proposed technique can be useful to enhance the flash ERG responses and to increase signal to noise ratio in a clinical environment.

O2 07 Slope between the positive and negative ERG waves in patients with open-angle glaucoma

Maja Sustar Habjan, Barbara Cvenkel

Department of Ophthalmology, University Medical Centre Ljubljana, Ljubljana, Slovenia

Purpose Recently, a new feature has been identified in the waveform morphology of the pattern electroretinogram (PERG). In patients with severe optic neuropathy associated with dysfunction of retinal ganglion cells, the slope of the top of P50 toward N95 is not as steep as in normal subjects. In such manner, the N95 slope can be used as an additional biomarker of ganglion cell disease. The aim of this study was to identify if the N95 slope is a sensitive parameter of ganglion cell dysfunction also in patients with open-angle glaucoma. Additionally, waveform morphology of the photopic ERG was studied to identify if the slope between the b-wave and the photopic negative response (PhNR slope) is affected in a similar manner.

Methods The PERG and photopic ERG from 28 eyes of 16 patients with open-angle glaucoma (8 females and 8 males; aged 55–84; mean age, 69.3 years) were retrospectively analyzed, along with 41 eyes of 21

O2 06 The effect of sinusoidally modulating backgrounds on flash electroretinograms

Jan Kremers, Avinash J. Ahir, Cord Huchzermeyer

University Hospital Erlangen, Erlangen, Germany

Purpose To study how the information about a background is processed and influences the flash ERG.
age-matched control subjects (15 females and 6 males; aged 58–71 years; mean age, 65.0 years). PERGs were recorded using a 0.8° checkerboard pattern on a 21.6° x 27.8° screen. Photopic ERGs were elicited with 2.5 cd s/m² monochromatic red (635 nm) stimuli on a blue, 10 cd/m² background. The ERG signal between the top of the positive wave (P50 and b-wave) towards the negative wave (N95 and PhNR) was described by a linear regression, y = a + bx, in which the parameter b indicated the steepness of the N95 and PhNR slope. Results were compared between both groups with two sample t-tests, sensitivity and specificity were evaluated with receiver-operating characteristic curve (ROC), and correlations were evaluated by Pearson coefficients.

Results The patients with open-angle glaucoma exhibited a significant reduction of the PhNR amplitude (8.3 ± 5.7 versus 25.6 ± 8.0 μV in controls, p < 0.001, 68% decrease), N95 amplitude (3.9 ± 1.3 versus 6.8 ± 1.7 μV, p < 0.001, 43% decrease) and P50 amplitude (3.1 ± 1.0 vs. 5.1 ± 1.6 μV, p < 0.001, 39% decrease). The N95 slope was significantly less steep in glaucoma patients (−0.081 ± 0.035 vs. −0.169 ± 0.049 in controls, p < 0.001, 52% decrease), while the PhNR slope was not affected (−4.14 ± 1.96 vs. −4.42 ± 1.24, p = NS, 7% decrease). The PhNR and the N95 slope appeared to be the most sensitive parameters, with the largest area enclosed by the receiver-operating characteristic curve (AUC: 0.96 and 0.94, respectively), while the sensitivity of the PhNR slope was indicated the steepness of the N95 and PhNR amplitude. Results were the focus of the present study. ERG peak times were averaged for the first and second visits, respectively. For the cohort as a whole, peak times at the second visit were significantly longer than those measured at the first visit (p = 0.048, paired t-test). Twenty-two participants (58%) showed a peak time that was ≥0.5 ms longer at the second visit; for 6 participants (16%), the peak time was ≥0.5 ms shorter at the second visit; for 10 participants, peak time differences between visits were within 0.5 ms. The mean change in peak time for the cohort was an increase of 0.11 ms per year. The coefficient of correlation between yearly change in peak time and participant age (averaged between the two visits) was 0.57 (p = 0.0002).

Conclusions In this longitudinal study, light-adapted flicker ERG peak times increased on average by 0.6 ms after a mean period of 5.2 years. There was a moderately strong and significant positive correlation between change in peak time and participant age, indicating that peak time does not change at a constant rate with age, but older individuals experience a faster increase. Thus, linear adjustments for age may not be appropriate.

O3 02 Exploring longitudinal changes in flicker ERG peak times with age in an adult cohort

Xiaofan Jiang1,2, Diana Kozareva1, Isabelle Chow2, Andrew R. Webster1,3, Pirro G. Hysi2, Christopher J. Hammond2, Omar A. Mahrou1,2,3

1UCL Institute of Ophthalmology, London, United Kingdom. 2Departments of Ophthalmology and Department of Twin Research and Genetic Epidemiology, King’s College London, St Thomas’ Hospital Campus, London, United Kingdom. 3Retinal Service, Moorfields Eye Hospital, London, United Kingdom

Purpose Several cross-sectional studies have shown a correlation between standard light-adapted flicker ERG peak times and age, whereby peak times are longer in older individuals. In this study we sought to explore the effect of age longitudinally within the same individuals.

Methods The TwinsUK cohort comprises adult twins who have volunteered to participate in research studies based at St Thomas’ Hospital in London. Over 1500 individuals underwent photopic 28.3 Hz flicker ERG recordings (RETeval system with Sensor Strip skin electrodes, LKC technologies, Gaithersburg, MD). Stimuli were delivered through undilated pupils, but the device measured pupil diameter and adjusted stimulus strength accordingly to provide retinal illumination (85 Td s white flicker stimulus; 850 Td white background) equivalent to the international standard LA 30 Hz. A subset of participants underwent recordings on two occasions, and these were the focus of the present study. ERG peak times were averaged from both eyes. The difference of peak times between two visits was calculated and its correlation with age was explored.

Results Thirty-eight participants were included in this longitudinal study; 76% were female. The mean (SD) age at first visit was 53.2 (16.0) years (ranging from 25 to 80 years), and the mean (SD) duration between visits was 5.2 (0.5) years (ranging from 4.2 to 6.2 years). Mean (SD) peak time was 25.6 (1.1) ms and 26.2 (1.5) ms for the first and second visits, respectively. For the cohort as a whole, peak times at the second visit were significantly longer than those measured at the first visit (p = 0.048, paired t-test). Twenty-two participants (58%) showed a peak time that was ≥0.5 ms longer at the second visit; for 6 participants (16%), the peak time was ≥0.5 ms shorter at the second visit; for 10 participants, peak time differences between visits were within 0.5 ms. The mean change in peak time for the cohort was an increase of 0.11 ms per year. The coefficient of correlation between yearly change in peak time and participant age (averaged between the two visits) was 0.57 (p = 0.0002).

Conclusions In this longitudinal study, light-adapted flicker ERG peak times increased on average by 0.6 ms after a mean period of 5.2 years. There was a moderately strong and significant positive correlation between change in peak time and participant age, indicating that peak time does not change at a constant rate with age, but older individuals experience a faster increase. Thus, linear adjustments for age may not be appropriate.
Purpose The ISCEV ERG standard stipulates “at least 20 min” of dark-adaptation before recording dark-adapted (DA) ERGs, a recommendation based on studies using strong pre-adapting bleaches. The 2022 update proposes a non-standard abbreviated protocol with 10 min dark adaptation. Studies on healthy individuals have shown no effect of shorter dark adaptation (10 vs 20 min) on the DA3 ERG, whereas the DA0.01 ERG is reduced by 10–17% with no effect on peak times. The current study, interrupted by COVID-19, has tested 74 patients of a projected cohort of 200+, powered to show noninferiority (maximum of 5% difference in abnormal classification) of DA0.01 ERGs after 10 (DA0.01,01) vs 20 (DA0.01,01) mins of dark adaptation.

Methods Eligible patients were adults attending routine electrodagnostic appointments that included full-field dilated DA ERGs using gold foil electrodes. Ten min into the 20 min dark adaptation period, additional DA0.01 and DA3 ERGs were recorded. Normal/abnormal classification for the DA0.01 b-wave amplitude was the primary outcome measure. Normality cutoff after 20 min was determined using local reference data; for ERGs recorded after 10 min, these limits were scaled using healthy adult factors. Patients were scored as concordant (10 and 20 min ERGs both normal or both abnormal) or discordant (differing classifications between 10 and 20 min of dark adaptation). Only right eye data are considered. ClinicalTrials.gov registration NCT03275441.

Results Seventy-four (52 female) patients aged 17–76 (median 50) years participated, with a diverse range of indications for testing. DA0.01,01 ERG b-waves were smaller (68%: 127 vs 187 μV, \( p < 0.0001 \)) and marginally slower (85 vs 88 ms, \( p = 0.02 \)) than DA0.01,01 ERGs. DA0.3 ERG a-waves were smaller (90%: 198 vs 220 μV, \( p < 0.0001 \)) but not meaningfully slower (22.0 vs 22.5 ms, \( p = 0.001 \)) than DA3 ERG a-waves. DA0.3 ERG b-waves were smaller (94%: 369 vs 394 μV, \( p < 0.0001 \)) and marginally slower (47 vs 49 ms, \( p < 0.0001 \)) than DA3 ERG b-waves. Seventy patients had concordant findings. The four with discordant findings had abnormal ERGs after 10 min, but normal after 20 min (4/74 subjects, 5.4%, 90% confidence interval (CI) 2.1–13%). DA0.01 ERGs were always abnormal in patients whose DA3 a- and b-wave amplitudes were abnormally small. Peak times were normal under all conditions except extinguished ERGs.

Conclusions Shortening dark adaptation to 10 min and modifying reference data accordingly resulted in low discordance of DA0.01 ERG classification. Noninferiority of a 10 min DA duration has not (yet) been established, as the upper limit of the confidence interval of the observed difference exceeds the pre-specified maximum difference of 5%. Recruitment is planned to continue to meet the calculated sample size of 262 subjects. If shorter dark adaptation is not inferior, ERG testing could be simplified, saving patient and clinic time and resources. It remains possible, but not within the design scope of this study, that shorter dark-adaptation is more diagnostically accurate, utilizing the slower dark adaptation of a diseased rod system. The greater effect (smaller, slower ERGs) of shortening dark adaptation in this mixed patient cohort than in non-diseased cohorts is preliminary evidence for this effect.

O3 04 Age-related changes in ERG parameters in companion dogs

Frey M. Mowat1,2, Wojciech K. Panek3, Gilad Fefer2, Alejandra Mondino Vero2, Hans D. Westermeyer4, Margaret E. Gruen2, Natasha J. Olby2

1University of Wisconsin-Madison, Madison, USA. 2North Carolina State University, Raleigh, USA

Purpose The purpose of this study was to determine the association between age and full-field ERG measures in companion (pet) dogs, an important translational model species for human retinal and neurologic aging.

Methods We recruited adult companion dogs with no significant ophthalmic abnormalities for an ISCEV-like dog ERG protocol evaluating unilateral dark- and light-adapted retinal responses following mydriasis. We performed multivariate regression analysis to evaluate the effects of age, breed, sex, body weight, and use of anxiolytic medication on ERG peak times and amplitudes.

Results Median age was 139.7 months (\( n = 45 \), 29 purebred dogs from 18 breeds, range 74–188.7 months). Age was negatively associated with ERG amplitudes (\( p \) value range 0.0008–0.65), whereas there was minimal positive association between age and ERG peak time (\( p \) value range 0.03–0.90). Administration of anxiolytic medication was negatively associated with ERG amplitudes (\( p \) value range 0.004–0.22).

Conclusions Aging in companion dogs is associated with a decline in both rod- and cone-mediated full-field ERG amplitudes. Statistical or methodological consideration of anxiolytic medication use should be made when conducting ERG studies in dogs.

Acknowledgements Funded by NIH grants K08EY028628 and P30EY016665, an Unrestricted Grant from Research to Prevent Blindness Inc. to the UW-Madison Department of Ophthalmology and Visual Sciences, and the Dr. Kady M. Gjessing and Rhanna M. Davidson Distinguished Chair in Gerontology.

O3 05 Reference data for flash VEP

Quentin Davis1, Emilii Albert2, Konstantin Kotliar2

1LKC Technologies, Inc., Gaithersburg, USA. 2Aachen University of Applied Sciences, Aachen, Germany

Purpose To collect reference data for flash VEP.

Methods Reference data for flash VEP were obtained from 100 subjects (58 female, age range 17–68) having normal vision. Reference subjects had visual acuity better than or equal to 20/25. Through an interview process, subjects having the following conditions were excluded: cardiovascular disease, diabetes, multiple sclerosis, epilepsy, migraine, Parkinson’s, other neurologic diseases, glaucoma, macular degeneration, retinitis pigmentosa, optic neuritis, achromatopsia, cataract, and endocrine orbitopathy. Measurements were recorded at the Aachen University College of Applied Sciences as a bachelor’s thesis project in optometry. The flash VEP was measured using the RETeval device with a gold cup electrode at Oz, ear clip for ground, and reference on the forehead. Patients were not dilated. The stimulus was 64 flashes of 24 Td s white light delivered at 1 Hz to one eye at a time. P2 was defined as the peak closest to 120 ms; N1 was the first trough with a time larger than 25 ms. P1, N2, N3, and P3 were then added as appropriate. The maximum of P1, P2, P3 minus the minimum of N1, N2, N3 was defined as the peak-to-peak VEP amplitude.

Results The pupil diameter was 3.4 mm ± 0.95 mm (mean ± standard deviation). The cursor method produced unimodal frequency distributions for cursor times, although P1 and N2 were not present in about 27% of waveforms. P2 time had a median value of 116 ms, with a 95% reference interval (RI) of 73–151 ms, with no dependence on age (\( p = 0.1 \)) or pupil diameter (\( p = 0.8 \)). The peak-to-peak VEP amplitude had a median of 17.5 μV, with a RI of 9.2 μV to 31.4 μV. There was no dependence on age (\( p = 0.1 \)) or pupil diameter (\( p = 0.9 \)).

Conclusions Reference data aid clinicians in determining whether or not a patient’s result is consistent with normal visual function. The cursor algorithm was selected to produce unimodal distributions under the assumption that doing so would make each cursor more...
closely associated with an activity in the brain. The preferred amplitude metric was peak-to-peak VEP amplitude because its RI is far from 0 μV and therefore is expected to be useful for distinguishing between subjects with normal vision and those with limited light perception. The stimulus for the flash VEP can be delivered without artificial dilation while compensating for pupil size (Troland stimulation) or with dilation (candela or luminance stimulation). Here, Troland stimulation was used and there was no residual dependence on pupil size. Based on the measured pupil diameters, if the stimulus instead was 3 cd s/m², the ± 1 standard deviation in pupil diameter would equate to a retinal illumination range of 14 Td s to 45 Td s. We do not have any data to support whether this range of retinal illumination would or would not materially contribute to the variability in the flash VEP obtained with luminance stimulation. The primary limitation in this study is the age range because we did not record from young children.

O3 06 Paediatric PERGs: a modified protocol and indirect reference data
Ruth Hamilton1,2, Bruce Hudson3, Martin Shaw3
1Royal Hospital for Children, Glasgow, United Kingdom. 2University of Glasgow, Glasgow, United Kingdom. 3Department of Clinical Physics and Bioengineering, Glasgow, United Kingdom

Purpose Younger children may not be able to comply with ISCEV Standard pattern ERGs (PERGs), particularly the requirement for corneal-contacting active electrodes. Furthermore, it is challenging to obtain accurate direct reference data, i.e. prospective sampling of > 120 healthy subjects per partition. An alternative to this gold standard is indirect reference data, which uses mathematical procedures to extract a ‘health-related’ sub-population from patient data. Here we describe a modified PERG protocol suitable for children from around 4–5 years old and reference intervals.

Methods Paediatric patients who had their PERG recorded between September 2016 and February 2022 were identified from the clinical service database. The PERG protocol (Espion E2 system) followed the ISCEV Standard, with the following adaptations to aid paediatric compliance: skin electrodes; large field size (48 by 34 degrees), slower reversal rate, more averaging (500 sweeps/trials). Recordings were binocular if the child had no strabismic deviations wearing their glasses, or serial and monocular in case of a deviation. P50 and N95 amplitudes and peak times were retrieved from the patient’s electronic record. The N95:P50 amplitude was calculated. Only PERGs from a first visit were included. If a PERG was deemed to be absent, amplitudes were given arbitrary non-zero values (0.1 μV) and no peak time was noted. Data were treated per eye rather than per patient. N95 amplitude was considered the parameter with most clinical significance and used for inclusion/exclusion of eyes; an eye excluded due to its N95 value had all other parameters also excluded. Separation of the data into ‘health-related’ and ‘disease-related’ sub-populations was assessed using a mixed Gaussian model. Reference limits of the health-related sub-population were constructed (Med-Calc® v20.0134) with one-sided limits for amplitudes (small but not large amplitudes associated with pathology) and two-sided limits for peak-times (both too early and too late associated with pathology).

Results Data were available for 329 patients’ first episodes, comprising 656 eyes. Age range was 4.6–17.5 years. Data from 525 eyes were classified as health-related after further exclusion of any eyes whose fellow eye was classified as disease-related. The P50 amplitude lower limit was 2.0 μV (90% CI 1.9–2.1), the P50 peak time lower limit was 42 ms (90% CI 42–42 ms) and the upper limit was 53 ms (90% CI 52–54 ms). The N95 amplitude lower limit was 2.9 μV (90% CI 2.7–3.0), the N95 peak time lower limit was 81 ms (90% CI 79–82) and the upper limit was 125 ms (120–129 ms). The N95:P50 amplitude ratio lower limit was 1.01 (90% CI 1.0–1.04). Conclusions These data suggest that young children can comply with a modified PERG protocol, giving spatial retinal data in combination with the full-field ERG with the added benefit of understanding ganglion cell function. P50 should be at least 2.0 μV and lie between 42 and 53 ms. N95 should be at least 2.9 μV and lie between 81 and 125 ms. The reference data here may be applicable for use in other centres after following validation/transference procedures.

Oral Session 4
O4 01 Of mice and men: Retinal horizontal cell ERGs and their clinical applications
Mary A. Johnson1, Yamato Maeda2, James C. DeMar3, Gilbert Xue4, Taro Chaya5, Mineo Kondo6, Ryotaro Tutsumi7, Venkatasivasai S. Sajja8, Peethambaran Arun9, Andrew B. Batuure3, Takahisa Furukawa6
1University of Maryland, Baltimore, Baltimore, MD, USA. 2Osaka University, Osaka, Japan. 3Walter Reed Army Institute of Research, Silver Spring, MD, USA. 4Mie University, Tsu, Japan. 5Wakayama University, Wakayama, Japan

Purpose We previously have described an ERG protocol, based on rod inhibition of cone function (see Frumkes & Eysteinsson, Vis. Neuroscience:1988;1:263–273), that reflects retinal horizontal cell (HC) function. Herein, we describe validation of the protocol in an HC-deficient knock-out mouse, we demonstrate preferential HC loss in an animal model of mild, repetitive blast overpressure, and we describe results of HC testing in patients having a variety of diagnoses.

Methods The ERG protocol consists of taking the ratio of b-wave amplitudes obtained by flashing a bright light (0.5 log cd s/m²) on a dim background (1 cd/m²) to flashing a light of the same luminance (0.50 log cd s/m²) onto a bright background (30 cd/m²). Traumatic brain injury (TBI) was induced in rats by exposing them to mild blast overpressure (6 psi), one exposure per day for 14 days, using the Advanced Blast Simulator. The Advanced Blast Simulator produces high-fidelity Friedlander waveforms with a very sharp rise (microseconds), short duration (< 3–5 ms), a true negative phase, and dampened reflective waves. Animals were euthanized 28 days after blast onset, and immunohistochemistry was performed using anti-calbindin antibodies to stain HC and Prox-1 to counterstain HC and bipolar cells. Horizontal cell-deficient (dHC) knock-out mice were generated as described in Chaya et al., Sci Rep;2017;7:5540–5554. The protocol used in patients involved inserting 1 extra flash into the basic ISCEV recommendations.

Results Standard ERG protocols and immunohistochemistry indicated that retinal photoreceptors and bipolar cells were functioning normally in dHC mice (median maximum b-wave amplitudes was 606 μV for controls, 625 μV for dHC, p = 0.459), but rod-cone inhibition as measured by the HC ERG protocol was significantly reduced (p = 0.005; n = 8 control and 10 KO mice). The distribution of ratios of ERG b-wave amplitudes was significantly higher (i.e., less rod-cone inhibition) in animals exposed to full-body blasts (p < 0.0001; n = 18 control and 22 blasted rats), with little overlap between data distributions. Humans showed the same ratio ranges as did rats, but had larger ERG a-waves. Patients with TBI, with rod dystrophies, or who were taking vigabatrin showed elevated ratios (reduced HC function), unlike patients with a variety of other conditions including cone dystrophy, Stargardt disease, MERRF, concomitant rod-cone dystrophy, chronic open angle glaucoma, and other optic neuropathies.
Conclusions Rod-cone inhibition, as modulated by horizontal cells, can be measured by ERGs. Experimental mild, repetitive TBI produces a reduction in horizontal cell numbers, dendritic connections, and rod-cone inhibition. The same changes are seen in patients with TBI, horizontal cell dysfunction due to vigabatrin, and rod dystrophies.

O4 02 Diurnal rodent models for the study of cone pathophysiology

Alexander Günter, Regine Mühlfriedel, Soumaya Belhadj, Mathias Seeliger

Division of Ocular Neurodegeneration, Institute for Ophthalmic Research, UKT, University of Tübingen, Tübingen, Germany

Purpose Cone photoreceptors typically provide high-acuity, color vision. Their highest densities are present in the macula in humans and in the visual streak region in many day-active animals. Often, the vasculature is also "deviated" to avoid vascular shadowing of vision in these regions. Due to the many genetically engineered homologous defects, mice are currently the most popular animal model to study retinal diseases and the associated pathophysiology. However, due to their nocturnal lifestyle, the demands on murine vision are very different from those of diurnal animals, and so their retina has a minimal visual streak region, if at all. Here, we present functional data of a diurnal rodent model (Mongolian gerbil, Meriones unguiculatus), whose cone system is much more similar to the human situation due to its lifestyle, and thus may be used as an alternative rodent model to study cone physiology and pathophysiology.

Methods Full-field ERG was performed, including a dark-adapted single flash series ranging from 1 mcd s/m² to 30 cd s/m², followed by a light-adapted single flash series ranging from 10 mcd s/m² to 30 mcd s/m² on a rod-saturating 30 mcd s/m² background. Additionally, a dark-adapted 3 cd s/m² and a light-adapted 10 cd s/m² flicker series ranging from 0.5 to 30 Hz were recorded. The ERG results from adult Mongolian gerbils were compared with those from 2-month old C57BL/6 mice. Immunohistochemistry (lectin, S- and M-opsin staining) was performed on frozen dorsal–ventral retinal cross-sections from Mongolian gerbils. SLO/OCT in vivo imaging data were also obtained.

Results Rod system responses in the dark-adapted ERG were comparable between Mongolian gerbils and C57BL/6 mice. In contrast, the cone system-related responses of the Mongolian gerbils were both larger and shorter. This led to much larger flicker ERG amplitudes and an increased flicker fusion frequency of up to about 60 Hz, in comparison to 20–30 Hz in mice. Further, the immunohistochemical analysis of the Mongolian gerbil retina, particularly the visual streak region located dorsal to the optic nerve, revealed elongated cones with no co-expression of S- and M-opsins. In contrast to mice, no gradient of opsins between the dorsal and ventral retina was found, a further aspect in which Meriones are more similar to humans than mice.

Conclusions While the murine retina shares many characteristics with the human counterpart, the nocturnal lifestyle has led to a functional organization that is not ideal for research on the cone system. If genetic defects are not the main focus of research, diurnal rodents that have a specialized retinal region (visual streak) are better suited in this regard. Due to its much better cone ERG performance, the Mongolian gerbil may thus be a superior model to investigate the physiology of the cone system and potential functional changes.

Acknowledgements BMFB grant TargetRD 16GW0268.

O4 03 Effect of flicker-induced retinal stimulation on full-field electoretinography in mice

Milan Rai1,2, Yamuna Devi Lakshmanan3, Henry Ho-lung Chan1,3,4

1School of Optometry, The Hong Kong Polytechnic University, Hong Kong, China. 2Laboratory of Experimental Optometry (Neuroscience), School of Optometry, The Hong Kong Polytechnic University, Hong Kong, China. 3Centre for Eye and Vision Research (CEVR), 17W Hong Kong Science Park, Hong Kong, China. 4Research Centre for SHARP Vision (RCSV), The Hong Kong Polytechnic University, Hong Kong, China

Purpose Flickering light stimulation has been found to increase retinal blood flow in response to increased metabolic demands of retinal neurons, but the effect of flickering light exposure on full-field electoretinography (ffERG) remains unclear. The purpose of this study was to investigate electrical activity of the retina by ffERG following flickering light stimulation in mice.

Methods Four experimental groups of C57BL/6 J mice (age 8–10 weeks) were used. Three groups (n = 6 per group) were stimulated under 3 levels of flickering light with 2 intensity levels; one group was used as a control (n = 6). After overnight dark adaptation (> 12 h), anesthetized mice were light adapted at 1 cd/m² for 10 min. Baseline ffERG was recorded, which was followed by a 60 s washout period to eliminate the aftereffect of light flashes. After the washout period, the three experimental groups were stimulated with either 8-Hz, 12-Hz, or 16-Hz flickering light of 0.1 cd s/m² for 160 s. This was immediately followed by ffERG recording, which was followed by a resting period of 300 s. After the resting period, another set of pre- and post-flicker ffERG was recorded following similar procedures, except that the flickering light intensity was doubled (0.2 cd s/m²). ffERG was recorded following similar procedures in the control group without flickering light stimulation.

Results At 0.1 cd s/m², 12-Hz flickering light was found to induce the greatest percentage increase in b-wave amplitude, compared to 8 Hz and 16 Hz flickering light (8 Hz: 5.81% ± 1.31%, p < 0.05; 12 Hz: 8.48% ± 2.29%, p < 0.01; 16 Hz: 7.63% ± 3.11%, p < 0.05). At 0.2 cd s/m², the greatest percentage increases in b-wave amplitude were found after 8 Hz flickering light stimulation, compared to 12 Hz and 16 Hz flickering light (8 Hz: 7.51% ± 1.86%, p < 0.05; 12 Hz: 4.31% ± 1.73%, p < 0.05; 16 Hz: 1.07% ± 2.69%, p > 0.05). However, none of the flickering lights had a significant effect on the b-wave implicit time, a-wave amplitude, or a-wave implicit time. There were no significant changes in ERG responses at different time points in the control group.

Conclusions Our findings suggest that retinal stimulation by flickering light enhances the ERG responses originating from the middle retinal layer, primarily from bipolar cells, but does not have a significant effect on responses originating from the photoreceptor cells. Different flickering light frequencies and light intensities would have different effects on retino-electrical activity, which may be associated with flicker-induced hyperemia.

O4 04 ERG responses to flashes presented upon sinewave modulation in mice

Anneka Joachimsthaler1,2, Nina Stallwitz1,2, Jan Kremers1

1University Hospital, Eye Clinic, Erlangen, Germany. 2Friedrich-Alexander University, Animal Physiology, Erlangen, Germany

Purpose To investigate how the flash ERG in mice depends on the time of the flash relative to a sinusoidal luminance modulation,
thirty achieving insight about the retinal mechanisms that influence the origins of the flash ERG.

**Methods** We recorded ERG responses to 5 ms flashes upon 1 Hz sinewave stimuli in 5 wild type (Opn1lw WT, C57Bl/6 J background) mice (12–14 weeks old, both sexes) while varying the flash time relative to the sinewave (0°, 32°, 93°, 149°, 180°, 213°, 270°, and 323°). The measurements were performed at two mean luminance (ML) levels with a fixed ratio between sinewave ML and pulse strength (mesopic: sinewave ML 1 cd/m², flash strength 0.4 cd s/m²; photopic: sinewave ML 25 cd/m², flash strength 10 cd s/m²). In addition, we recorded responses to the 1 Hz sinusoidal luminance modulation only (ML 1 and 25 cd/m²), and to the flashes upon a steady background of the same ML as the sinewaves. Also, noise recording to the steady backgrounds in the absence of a flash were performed.

**Results** The b-wave amplitude of the flash response did not change with the position of the pulse upon the sinewave. However, at mesopic conditions, we found that the b-wave displayed a double-peak at flash positions between 0° and 213°. At photopic conditions, the double-peak was less pronounced and was found only for flash positions between 0° and 149°. For both luminance conditions, the second peak started as a small shoulder upon the descending part of the b-wave, which became more pronounced and was most distinct at a 93° pulse position. We also subtracted the flash response upon a steady background from the responses to combined stimuli to get flash-corrected responses to the underlying 1 Hz sinusoidal luminance modulation. At photopic conditions, the flash-corrected responses also changed shape due to the presence of the additional flash. While the response to a single 1 Hz sinewave is defined by a slow negative wave followed by a positive going, wide double-peak, the flash-corrected responses lacked the negative wave and the positive peak was less defined and strongly dependent on the position of the pulse.

**Conclusion** Our results show a complex interaction between flash and sinewave responses in mice. The responses to both flash and sinusoidal luminance modulation depend strongly on the position of the pulse upon the sinewave stimulus. This was true for mesopic and photopic luminance conditions. In contrast, the photopic responses to the sinewaves are not influenced by the flashes in human observers (see Kremers et al., this meeting). The ERG responses to the flashes in mice were less strongly influenced by the sinewave than in humans. Possibly, mechanisms that lead to an ERG response are much slower in the mouse.

**Acknowledgements** AJ, NS and JK planned the experiments; AJ & NS generated the stimuli and analyzed the data; NS performed recordings; AJ & JK interpreted the data.

**O4 05 Calpain as a biomarker for retinal degeneration due to phosphodiesterase 6 (PDE6) deficiency**

Soumaya Belhadj1, Regine Mühfriedel1, Alexander Günter1, Stylianos Michaelsakis2, Martin Bieß2, Francois Paquet-Durand3, Mathias Seeliger1

1Division of Ocular Neurodegeneration, Centre for Ophthalmology, Institute for Ophthalmic Research, Tübingen, Germany. 2Center for Integrated Protein Science Munich CiPSM and Department of Pharmacy—Center for Drug Research, Ludwig-Maximilians-Universität München, Munich, Germany. 3Cell Death Mechanisms Group, Centre for Ophthalmology, Institute for Ophthalmic Research, Tübingen, Germany

**Purpose** Loss of PDE6 function, which results in a massive increase in cyclic guanosine monophosphate (cGMP) in rod photoreceptors, is a cause of retinitis pigmentosa (RP). We have previously shown that cyclic nucleotide gated (CNG) channels in the rod outer segment are essential mediators for cGMP-based degeneration (Paquet-Durand et al., Hum Mol Genet 2011;20:941–7). Recent evidence suggests that calpain imaging may be used as a biomarker for PDE6-related retinal degeneration in vivo. Here, we present evidence that the activity of the calpain-2 isofrom in the living retina is related to cell death and may be used for non-invasive follow-up with in vivo imaging (SLO/ OCT) to accompany the functional (ERG) biomarkers during the course of disease.

**Methods** rd1 and rd10 PDE6A-deficient mice, their degeneration-protected rd1/Cngb1 and rd10/Cngb1 double mutant counterparts, and corresponding wild-type (wt) mice were evaluated in vivo with ERG and in vitro via a histological work-up. Full-field ERG was performed, including a dark-adapted single flash (1 mcd s/m² to 30 cd s/m²) and flicker (3 cd s/m², 0.5–30 Hz) series, followed by a light-adapted single flash (10 mcd s/m² to 30 mcd s/m²) and flicker (10 cd s/m², 0.5–30 Hz) series on a rod-saturating 30 mcd s/m² background. To detect calpain activity in the living retina, we tested the capacity of the calpain-specific substrate t-BOC-Leu-Met-CMAC in organotypic retinal explant cultures derived from wild-type mice, as well as from rd1 and RhoP23H+/− RD-mutant mice. These results were compared to TUNEL staining as markers for cell death. SLO/OCT in vivo imaging data were also obtained.

**Results** We have established the functional aspects of retinal degeneration in both PDE6A and PDE6B-related mouse models of RP and their corresponding double mutant lines protected from degeneration by an additional loss of Cngb1 function. While these data suggest that cGMP by itself is not the key for retinal degeneration, we were looking at calpain as a potential biomarker that was possibly more closely related to cell death. We found that calpain-2 activity may indeed be used for such a purpose, and that its activation appears to be a relatively short-lived event that occurs only towards the end of the cell-death process.

**Conclusions** The detailed pathomechanism in cGMP-related RP is still not fully resolved. High intracellular cGMP levels trigger the degeneration via CNG channels but do not directly cause cell death, so that a total absence of CNG channels protects from apoptosis in rd1 and rd10 models. A potential biomarker that is more closely related to cell death is calpain. We developed an assay to visualize calpain activity, shown to be related to TUNEL staining for cell death, in living retina. Our results build the basis for further work to integrate calpain activity detection as a novel in vivo biomarker into the functional and morphological follow-up of PDE6-related animal models.

**Acknowledgements** BMBF grant TargetRD 16GW0268.

**O4 06 Retinal dysfunction in the rd10 mouse: a comparison of the pupillary light reflex and ERG**

Jason C. Park, Oksana Persidina, Tara Nguyen, Xincheng Yao, J. Jason McAnany

Department of Ophthalmology and Visual Science, University of Illinois at Chicago, Chicago, USA

**Purpose** To study the pupillary light reflex and ERG in the rd10 mouse model of retinitis pigmentosa. (RP) is characterized by severe retinal degeneration that results in attenuated or extinguished ERGs, often by postnatal day 60 (P60). In humans with photoreceptor degeneration, the response of the pupil to flashes of light, the pupillary light reflex (PLR), can persist in the absence of a measurable ERG. The purpose of this study was to record and compare the PLR and ERG in rd10 mice over time.

**Methods** rd10 mice were tested at P21 (n = 7), P28 (n = 7), P35 (n = 4), and P42 (n = 4). For comparison, wild type (WT) mice were tested at P21 (n = 2). Prior to testing, mice were dark adapted for 2 h and the PLR was measured using short-wavelength (“blue”) 10 and
1000 cd/m² stimuli. The maximum pupil constriction (MPC) elicited by the 10 cd/m² stimulus was recorded. The post-inhibition pupil response (PIPR) elicited by the 1000 cd/m² stimulus was defined as the median pupil diameter 6–8 s after stimulus offset. The MPC is thought to reflect photoreceptor input into intrinsically photosensitive retinal ganglion cells (ipRGCs) and the PIPR is thought to reflect the activation of melanopsin within the ipRGCs. Dark-adapted ERGs were recorded in response to a 3.0 cd s/m² flash (DA 3) and light-adapted ERGs were recorded in response to a 10 cd s/m² flash presented against a rod suppressing background (LA 10).

**Results** At P21, the rd10 MPC was reduced by 28% and the PIPR was reduced by 19% compared to WT. The MPC decreased from P21 to P35, but remained measurable in 3 out of 4 mice at P42. The PIPR was approximately constant from P21 to P42 in all but one mouse. The DA 3 ERG was markedly attenuated at P21 compared to WT; the a-wave was reduced by 80% and the b-wave was reduced by 68%. The LA 10 b-wave was reduced by 38% at P21 compared to WT. All ERGs were extinguished by P42.

**Conclusion** The time-course of abnormality differed for the MPC, PIPR, and ERG in rd10 mice. The ERG is affected early and severely, becoming extinguished by P42. In contrast, the MPC was measurable in most mice at P42, suggesting that residual photoreceptor function may persist for longer than implied by ERG measurements. The PIPR was only modestly reduced and nearly independent of age, indicating retained ipRGC function until at least P42 in rd10 mice.

**Acknowledgements** This research was supported by National Institutes of Health research grant P30EY001792 and an unrestricted departmental grant from Research to Prevent Blindness.

### Oral Session 5

**O5 01 Albinism on the outside but not on the inside: The remarkable phenotypic variability of OCA4**

**Maria M. van Genderen,1,2 Charlotte C. Kruijt,3 Ralph J. Florijn,4 Gerard C. de Wit1**

1Bartiméus Diagnostic Center for Complex Visual Disorders, Zeist, Netherlands. 2University Medical Center Utrecht, Utrecht, Netherlands. 3Leiden University Medical Center, Leiden, Netherlands. 4Amsterdam University Medical Center, Amsterdam, Netherlands

**Purpose** Oculocutaneous albinism type 4 (OCA4) is a relatively rare cause of albinism. We investigated the phenotype of a patient cohort with OCA4.

**Methods** Medical records of 11 patients from 9 families with two disease causing variants in the SLC45A2 gene were reviewed. Data were collected on pigmentation (skin, hair, eyes), visual acuity, nystagmus, foveal hypoplasia, and chiasmal misrouting. Foveal hypoplasia was assessed by optical coherence tomography and graded according to the method of Thomas et al. (Ophthalmology:2011;118:1653–1660). Iris translucency and fundus hypopigmentation were graded according to Kruijt et al. (Ophthalmology:2018;125:1953–1960). Misrouting was assessed by multichannel VEP, using pattern onset VEP in adults and children > 6 yrs and flash VEP in younger children. We calculated the chiasm coefficient (cc) by correlation of the hemispherical signal differences when stimulating each eye. The cc can take a value from –1 to +1; –1 indicates complete asymmetry and +1 complete symmetry.

**Results** All 11 OCA4 patients had severely reduced pigmentation of hair and skin, iris translucency grade 3–4, and fundus hypopigmentation. Eight patients had poor visual acuity, nystagmus, and severe foveal hypoplasia (grade 3–4). They all had misrouting, with cc values from –0.48 to –0.99. In contrast, three patients had normal visual acuity, no nystagmus, normal fovea, and normal routing (cc values +0.75 to +1.0).

**Conclusion** We describe 11 patients with OCA4 who all showed hypopigmentation of skin and hair, iris translucency, and fundus hypopigmentation. However, patients were either severely affected with regard to visual acuity, foveal hypoplasia, and misrouting, or visually not affected at all. The three OCA4 patients with normal visual development are proof that the relationship between pigmentation defect and ocular deficits in albinism is more complicated than previously thought.

**Acknowledgements** The authors thank Herman Talsma for performing VEP recordings and help with obtaining the images.

**O5 02 Pattern-reversal VEPs are degraded in patients with albinism and different types of nystagmus**

**Herman Talsma,1 Ashita Mohile1, Frank Hoeben1, Charlotte Kruijt1,2, Maria van Genderen1**

1Bartiméus, Diagnostic Centre for Complex Visual Disorders, Zeist, Netherlands. 2Leiden University Medical Center, Leiden, Netherlands

**Purpose** To distinguish different nystagmus parameters and their influence on the pattern-reversal VEP (prVEP) in a group of Dutch patients with albinism.

**Methods** Clinical, genetic, and electrophysiologic data were collected from 522 Dutch patients with albinism (Kruijt et al. Ophthalmology:2018;125:1953–1960). In a subgroup of 60 patients, nystagmus was recorded with a Tobii 60XL eyetracker. Nystagmus characteristics including waveform shape, amplitude, and frequency were determined. Twelve waveforms (Dell’osso & Daroff. Doc. Ophthalmol:1975;309,155–182) were clustered into jerk (J), pendular (P), and mixed (M) waveform types. Waveform types were then correlated with the binocular prVEP characteristics (P100 amplitude and latency for a 60° check size).

**Results** 39% of the 60 albinism patients exhibited J-type nystagmus, 30% P-type, and 31% J + P type. P-type nystagmus amplitudes were significantly higher than J-type nystagmus amplitudes. Also, nystagmus amplitude was inversely correlated with the amplitude of the prVEP. This resulted in P-type nystagmus being associated with the lowest prVEP amplitudes. P-type nystagmus was found to occur most frequently in the low VEP range of 0–2.7 µV. No correlation was found between VEP latency and nystagmus characteristics. A negative correlation was also found between nystagmus amplitude and visual acuity (log MAR). As expected, patients with poor visual acuity mainly exhibited P-type nystagmus.

**Conclusion** This study gives information on how the VEP response is degraded for various types of nystagmus, with their characteristic amplitude, frequency, and shape. We found that prVEP amplitude, but not latency, is affected in different nystagmus types. For future clinical purposes, we created a new VEP pattern reversal stimulus that is connected to an eye tracker, triggers the reversal stimulus, and is synchronized to the patient’s nystagmus.

**O5 03 VSX2 variants are responsible for bipolar cell dysfunction with distinct lens alterations**

**Vasily M. Smirnov,1,2 Matthieu Robert1,4 Christel Condroyer1, Jean-Michel Rozet3, José Sahel6, Isabelle Perrault5, Isabelle Audo1,7, Christina Zeitz4**

1Sorbonne Université, INSERM, CNRS, Institut de la Vision, Paris, France. 2Université de Lille, Faculté de Médecine, Lille, France. 3Ophthalmology Department, Hôpital Universitaire Necker-Enfants Malades, Paris, France. 4Borelli Centre, UMR 9010, CNRS-SSA-ENS
Purpose: Congenital stationary night blindness (CSNB) is a group of genetically and clinically heterogeneous retinal disorders, usually manifesting with infantile nyctagmus, reduced visual acuity, variable degree of myopia and poor visual behavior in dim light. The diagnosis is done on the basis of full-field electroretinogram (ffERG) features. Most of the patients are characterized by an electronegative Schubert-Bornschein-type of ffERG, showing either a signal transmission defect from photoreceptor to all bipolar cells (incomplete (ic)CSNB) or selectively affecting rod and cone ON-bipolar cells (complete (c)CSNB). The goal of this study was to identify the gene defect in a family with non-syndromic CSNB with peculiar characteristics.

Methods: Three patients from two unrelated families have been clinically and genetically explored by state-of-the-art methods.

Results: Patients had infantile nyctagmus, low stable visual acuity, myopia and night blindness. Two older patients had bilateral lens luxation and underwent lens extraction. All patients presented atrophic peripheral chorioretinal changes. The ffERG revealed an electronegative Schubert-Bornschein appearance, but combining characteristics of incomplete and complete CSNB, affecting rod and cone ON- and OFF-bipolar cells. Whole exome and Sanger sequencing identified in each index case a novel homozygous variant (respectively c.595C>T p.(Arg199Cys) and c.696C>T p.(Pro233Leu)) in VSX2, co-segregating with the phenotype in available family members.

Conclusions: Variants in VSX2 can lead to different phenotypes, either defects of early ocular development (anophthalmia, microphthalmia and coloboma) or peculiar CSNB with lens luxation and chorioretinal changes, described herein. VSX2 is a major regulator of early ocular development and is highly expressed in bipolar cells in adult retina. Further studies are needed to understand the pathogenic mechanisms associated with variants in VSX2 leading to two distinct phenotypes.

O5 04 Electrically evoked responses in severe retinitis pigmentosa

Yu Fujinami-Yokokawa1,2,3, Yasutaka Suzuki1, Hisatetu Tachimori4, Hiroaki Miyata2, Jeffrey Farmer5, Kei Shinoda6, Kazushige Tsunoda7, Yozo Miyake8, Kaoru Fujinami1,3,9

1Laboratory of Visual Physiology, Division of Vision Research, National Institute of Sensory Organs, National Hospital Organization Tokyo Medical Center, Tokyo, Japan. 2Department of Health Policy and Management, Keio University School of Medicine, Tokyo, Japan. 3UCL Institute of Ophthalmology, London, United Kingdom. 4Endowed Course for Health System Innovation, Keio University School of Medicine, Tokyo, Japan. 5Diagnosys LLC, MA, USA. 6Department of Ophthalmology, Saitama Medical University Faculty of Medicine, Saitama, Japan. 7Division of Vision Research, National Institute of Sensory Organs, National Hospital Organization Tokyo Medical Center, Tokyo, Japan. 8Next Vision, Kobe Eye Center, Kobe, Japan. 9Moorfields Eye Hospital, London, United Kingdom

Purpose Electrically evoked response (EER) elicited by transcorneal electrical stimulation (TES) is an objective method to evaluate the visual pathway (Potts, 1968–1970; Miyake, 1980–1984; Takei, 1989–1993). This study aims to validate EER to predict the efficacy of advanced therapies for diseases with severe photoreceptor damage. The technical studies and preliminary data were presented at the ISCEV 2019/2020 annual symposia. We herein describe EERs in patients with severe retinitis pigmentosa (RP) and compare the data with healthy subjects.

Methods Sixteen eyes of eight patients with a clinical diagnosis of RP were enrolled. EERs were recorded after 20 min dark adaptation) using DTL-Pz stimulation, Oz-Pz potential recording at current intensities of 0.5 mA, 1 mA, 1.5 mA, and 2 mA. Two ground electrodes were used: one for the stimulation and one for the recording channels. All tests were conducted with an Espion Profile electrophysiology system (Diagnosys LLC, MA, USA). The presence of EER responses for each component and each stimulus condition was evaluated by two investigators (YFY, KF). A positive peak was defined as a peak with an amplitude > 0.8 µV (Takei 1988). The sum of EER amplitudes [30–90 ms (P1), 90–150 ms (P2), and 150–210 ms (P3)] was calculated. Ten eyes of five healthy participants were also enrolled. The sum of EER amplitudes in RP patients was compared to that of the healthy subjects.

Results The median age of disease onset and age at examination of eight patients were 18.0 (range 5–42) years and 54.5 (38–67) years, respectively. The median visual acuity was, 2.0 (0.2–2.8) logMar in each eye. The full-field ERG responses were undetectable. The presence of positive peaks for 0.5 mA, 1.0 mA, 1.5 mA, and 2.0 mA components was identified in 43.8%, 62.5%, 87.5%, and 81.3%, respectively, in the eight RP patients. The median value of the sum of EER amplitudes in the eight RP patients was 1.75 (range 0.56–4.86). The presence of positive peaks for 0.5 mA, 1.0 mA, 1.5 mA, 2.0 mA components was identified in 80.0%, 100%, 100% and 100% in the five healthy subjects. The median value of the sum of EER amplitudes in five healthy subjects was 3.61 (range 1.38–16.48). A statistically significant difference in terms of the sum of EER amplitudes was revealed between the RP patients and the healthy subjects.

Conclusion The presence of positive responses in EERs was frequently (> 80%) identified in eight severe RP patients. The sum of EER amplitudes, significantly reduced in the RP patients, can be used as a parameter to evaluate the visual pathway even when ERGs are undetectable. These findings imply that EERs derived predominantly from residual retinal ganglion cells in RP patients can help in objectively assessing the residual function in patients with severe photoreceptor damage. Further studies such as comparing EER values with the other clinical parameters would be helpful to delineate the usefulness and applications of EERs.

O5 05 Genome-wide association study (GWAS) meta-analysis of flicker ERG peak times recorded in > 1000 adult twins

Zihe Xu1, Xiaofan Jiang2, Christopher J. Hammond, Omar A. Mahrou1,3, Pirro G. Hysi1

1King’s College London, London, United Kingdom. 2University College London, London, United Kingdom. 3University of Cambridge, London, United Kingdom

Purpose Whilst rare pathogenic variants in certain genes are known to have severe effects on visual function, little is known about the effects of common genetic variants on retinal electrophysiology in the healthy population. We sought to explore the latter by means of genome-wide association studies (GWAS) of cone-driven flicker ERG data from a large healthy cohort.

Methods As part of wider studies, adult participants from the TwinsUK cohort were recruited to undergo flicker ERG recordings. Those participants for whom genetic data were available were included in the present study. This included the following groups: 185 participants who had undergone standard light-adapted 30 Hz flicker ERG recording using conductive fibre electrodes following mydriasis.
with myopia risk supports the notion that retinal signalling might be
regulated. The highlighting of some genes that have been associated
that common variants in genes associated with rare disease might
small sample size in GWAS terms. However, a number of interesting
loci attained genome-wide significance, likely owing to the relatively
times in 1242 subjects represents the first GWAS of ERG data. No

genes (encoding one of the subunits of the cyclic nucleotide gated channel in cone photoreceptor outer seg-
ments; rare pathogenic variants in this gene give rise to
achromatopsia) as well as genes that have been implicated in myopia
(PCCA, GJD2), and the GJD2 gene which encodes connexin-36 and
which forms retinal gap junctions, enabling electrical coupling
between retinal neurons.

Results This exploratory meta-analysis of flicker ERG peak
values in 1242 subjects represents the first GWAS of ERG data. No
loci attained genome-wide significance, likely owing to the relatively
small sample size in GWAS terms. However, a number of interesting
genes emerged amongst the top hits. The CNGB3 association suggests
that common variants in genes associated with rare disease might
underlie some of the normal variation in retinal function in the pop-
ulation. The highlighting of some genes that have been associated
with myopia risk supports the notion that retinal signalling might be
important in myopia development.

Oral Session 6
O6 01 FrACT—automated assessment of behavioural acuity
not only for visual electrophysiology
Michael Bach
University Eye Center, Freiburg, Germany

Purpose Knowing the visual acuity during electrophysiological
assessment, in particular at the stimulus distance, is mandatory for
appropriate interpretation of the findings. To help with this, I have
developed and continually modernised the “Freiburg Visual Acuity
(and Contrast) Test” (FrACT, [https://michaelbach.de/fract/]) over
37 years.

Methods FrACT is a visual test battery in the form of a free computer
programme. It uses psychometric methodology, maximum likelihood
fitting, and anti-aliasing to provide automated, self-paced assessment
of visual acuity, contrast sensitivity, and Vernier acuity. The pro-
gression of optotypes is based on a Bayesian approach. Each outcome
can be adorned with a bootstrap-based confidence interval.

Results The latest version “FrACT10” is based on Javascript frame-
works and runs on all computer platforms, including tablets;
smartphones are usually too small. FrACT can cover an ultra-wide
range from hand movement/finger counting [https://michaelbach.de/
saci/acity.html] to better than −0.3 logMAR. The 95% test–retest
limit of agreement is ≈ ± 0.15 logMAR. For infants, we found
testability to rise with age (unsurprisingly), reaching near 100% at
6 years of age. FrACT has been verified by independent laboratories;
the code for FrACT10 is open-source [https://github.com/michael
bach/FrACT10]. The presentation will focus on the psychophysics of
visual acuity testing and also cover integration into the electrophys-
iology clinic, including solutions for close ranges and automatic
transfer of results to the clinic/hospital documentation environment.

Conclusion FrACT has proved invaluable to us in routine daily
assessment of patients.

O6 02 Effect of nystagmus on VEP-based objective visual acuity
estimates
Michael B. Hoffmann1, Elizabeth V. Quanz1, Juliane Reupisch1,
Francie H. Kramer1, Michael Bach2,3, Sven P. Heinrich2,3,
Khaldoon O. Al-Nosairy1
1Department of Ophthalmology, University Magdeburg, Magdeburg,
Germany. 2Eye Center, Medical Center—University of Freiburg,
Freiburg, Germany. 3Faculty of Medicine, University of Freiburg,
Freiburg, Germany

Purpose In order to determine the effect of nystagmus on objective
visual acuity (VA) estimates, we compared subjective and objective
(VEP) VA estimates in participants with nystagmus.

Methods After ophthalmological examination, 20 participants with
nystagmus of different origin (albinism, idiopathic, acquired) were
recruited for this study. A group of healthy controls with best cor-
rected visual acuity (BCVA) ≥ 0 [logMAR] were included for
comparison. Estimates of BCVA for each eye were determined using
the subjective Freiburg visual acuity test (FrACT; VA_subj) and
objective VEP-acuity (VA_obj) testing [1]. Visual acuity VEP testing
(with EP2000 program) followed the respective ISCEV protocol [2].
Eyes of each participant were stratified into eyes with higher (N_high)
or lower (N_low) nystagmus using the degree of fixation loss esti-
mated with the Nidek microperimeter (MP1, Nidek Instruments).
VA_subj and VA_obj of either group were compared separately for
the eye N_high and N_low via paired t-tests. We also tested whether
the difference between VA_subj and VA_obj correlated with the
degree of fixation loss determined by Pearson correlation (r).

Results In N_high of the nystagmus group, VA_obj was better than
VA_subj [mean ± SE of VA_obj vs VA_subj: 0.18 ± 0.06 vs.
0.30 ± 0.06, p = 0.017], while there was no significant difference
between VA_obj and VA_subj—neither for N_low [0.21 ± 0.05 vs
0.24 ± 0.05, p = 0.61] nor for healthy controls [− 0.01 ± 0.05 vs
− 0.04 ± 0.09, p = 0.54]. Further, we found in N_high of the nys-
tagmus group a significant correlation of the difference of VA_obj
and VA_subj and the degree of nystagmus in N_high (r = 0.52,
p = 0.022). In both nystagmus groups, there was a significant corre-
lation between the estimates of VA_obj vs VA_subj (N_high [N_low]
r = 0.70 [0.60], p < 0.001 [0.005].

Conclusions We report a VA overestimation for VEP-based objective
VA measures in participants with nystagmus which depended on the
magnitude of the fixation instability. The higher the degree of nys-
tagmus, the more significant the influence on objective and subjective
VA difference. Overall, the difference was about 1 line.

[1] Bach et al. (2008) Visual evoked potential-based acuity assess-
ment in normal vision, artificially degraded vision, and in patients. Br
J Ophthalmol 92:396–403.

[2] Hamilton et al. (2021) ISCEV extended protocol for VEP methods
of estimation of visual acuity. Docum Ophthalmol 142:17–24.
O6 03 ISCERG: the first symposium of electroretinography
Scott Brodie1, Richard Smith2
1NYU Langone, New York, USA. 2BriSCEV, Liverpool, United Kingdom

Introduction The International Society for Clinical Electroretinography (“ISCERG”) was founded in 1958. The first Symposium met in Stockholm in June, 1961. I recently happened upon the program volume from this meeting, which provides a valuable perspective on the progress in our field over the last six decades. [The name of the society was changed to the International Society for Clinical Electrophysiology of Vision (“ISCEV”) in 1975.]

Methods I have reviewed the program volume and offer related historical perspectives for discussion.

Results The meeting was divided into two parts: presentations of the reports of standardization study groups over two days, followed by one day of free papers. Seventeen attendees participated in the “Standardization Symposium,” joined by an additional twenty-four participants for the general meeting. All but three were from Europe—there was one participant from the United States, one from Lebanon, and one from Japan.

The volume opens with a detailed description of the ERG facilities and procedures at the Karolinska Institute in Stockholm. The stimulus was an incandescent bulb driven by a capacitor discharge; intensity was adjusted by varying the distance from bulb to subject. Only scotopic single flash responses were obtained. Normal B-wave amplitudes ranges were 340 ± 8 µV for men aged 19–50 years, 390 ± 14 µV for women, with 10% reductions for older patients. Five reports were presented by the standardization study groups. Their suggestions were summarized in 12 Recommendations endorsed by the ISCERG Board. These included using a range of stimulus intensities, with emphasis on reporting B-wave amplitudes; using dilated pupils when possible, using a wide-angle stimulus (“at least 60°”), as uniform as possible [Ganzfeld stimulation first appears in the literature in 1975]; modulation of stimulus strength by means of neutral-density filters; endorsement of Karpe, Henkes, or Burian-Allen contact glass electrodes as standards; subjects to avoid bright illumination and undergo pre-adaptation in the dark prior to testing, with further research suggested as to the recommended duration of dark adaptation; and suggestions for calibration of recording devices.

Seventeen free papers were presented. Topics included ERG oscillatory potentials, with examples of loss of OPs in glaucoma, central retinal artery occlusion (with electrophoretic waveform), achromatopsia, Behçet’s disease, diabetic retinopathy, diffuse uveitis, and siderosis bulbi; “re-adaptation” of ERG amplitudes after exposure to bright light; ERGs in response to red flash stimuli; integration of responses to rapidly repeating flashes; ERGs in isolated frog retinas; ERGs after extirpation of retinal ganglion cells by optic nerve crush; ERGs in achromats; novel designs for ERG recording electrodes; ERG “glare testing”; ERG testing in retinal vein occlusion; ERGs in retinitis pigmentosa; lack of ERG changes in solar retinopathy; and ERG monitoring for chloroquine retinal toxicity.

Conclusions While significant progress in ERG methodology has occurred over the past six decades, many of the themes addressed at the First Symposium remain important areas of ongoing research. ERG standardization has continually evolved: the first comprehensive ERG standards were published in 1989; revisions were adopted in 2015 and 2022.

O6 04 The early days of visual electrophysiology and the foundation of ISCERG/ISCEV
Sven Erik G. Nilsson
Dept. of Ophthalmology, Linköping, Sweden

Purpose To describe the earliest steps in visual electrophysiology and to remind us of the foundation of ISCERG/ISCEV.

Methods Literature research and personal sources.

Results Electrophysiology. The Swedish physiologist F. Holmgren was the first to show an electrical response to light from the eye (frog) in 1865. Then Einthoven and Jolly were able to record a full ERG from the frog eye, using a string galvanometer in 1908. This recording showed an amazing quality, showing an a-, a b-, and c-wave. The first response from a human eye was published by Kahn and Löwenstein in 1924. It was recorded under very difficult conditions and could not be repeated. The Finnish-Swedish physiologist R. Granit (The Karolinska Institute) went further with a component analysis of the cat ERG—a high quality work, published in 1933. He received the Nobel Prize together with Hartline and Wald in 1966. In 1941, L. Riggs (USA) introduced the contact lens electrode for ERG, which allowed much more stable recordings. Independently (this was during the war), and based on Granit’s work, G. Karpe (The Karolinska Institute) developed a similar method, also with contact lens electrodes, for stable and reproducible clinical recordings of the human ERG, published in 1945. This method was widely used thereafter. Some of my own contributions will also be mentioned, such as the first direct current (DC) recordings from the human eye: the c-wave of the ERG (1974) and the slow oscillations of the standing potential (the “EOG” potentials) in 1975. Also, for the first time, the effects of ethyl alcohol on the human c-wave, very similar to the response to light (1975), were shown. An impressive further development of visual electrophysiology has taken place throughout the years.

ISCERG/ISCEV. Our Society started as ISCERG, since at that time, the ERG was the only response recorded. When other responses were added (such as EOG and VEP), the name was changed to ISCEV. The first Board of officers included Karpe, President; Franceschetti and François, Vice Presidents; Henkes, Secretary General; Burian, Secretary Western Hemisphere; and Straub, Treasurer. An Advisory Board was also set up: Granit, Riggs, and van der Tweel (The Netherlands). The first Symposium was held in Stockholm in 1961 with G. Karpe as organizer. The main theme was Standardization of the ERG. The Society had 160 members. In 1962, Nakajima (Japan) joined the Board as Secretary Far East and Jacobson (USA) as Editor of the Newsletter. The next 10 symposia after Stockholm were held in Rotterdam (1963), Chicago, Hakone, Ghent, Efurt, Istanbul (my first time as a speaker), Pisa, Brighton, Los Angeles, and Bad Nauheim (1973). Karpe was President until 1973 and H. Henkes from 1973 to 1983. Then I, Sven Erik Nilsson, Linköping University, Sweden, was elected to be the third President until Eberhart Zrenner, Tübingen, Germany, took over. Some photos from the early days will be shown. Conclusions Visual electrophysiology has progressed enormously since the early days, and the ISCEV Society is healthy and vivid after 60 years of action.

Oral Session 7
O7 01 Digital Light Processing laser projectors work as visual display units in visual electrophysiology
Oliver R. Marmoy1,2, Dorothy A. Thompson1,2
1Tony Kriss Visual Electrophysiology Unit, Clinical and Academic Department of Ophthalmology, Great Ormond Street Hospital, London, United Kingdom. 2UCL-GOS Institute for Child Health, London, United Kingdom. 3Manchester Metropolitan University, Manchester, United Kingdom

Purpose To assess the properties of Digital Light Processing (DLP) projector technology as a potential alternative to obsolete visual
display units (VDU) for pattern testing in visual electrophysiology. We investigated the photometric, spectral, spatial, and temporal properties of DLP projectors and compared these to existing VDUs. We also assessed physiological agreement between pattern ERGs and VEPs from DLP projector stimulation against those currently established within our service.

**Methods** Two ultra-short throw laser DLP projectors were assessed (HiSense model 100L5FTUK and Viewsonic model LS831WU). Photometric measurements were made to identify luminance and contrast profiles of the stimuli alongside temporal characteristics of commonly used pattern stimuli. Spectral measurements of white checks were made. Spatial characteristics were assessed in terms of element and field sizes. A small group of healthy participants had PERGs and PVEPs assessed on existing VDUs within the service (Plasma screen, Pioneer Electronics Corp., model PDP422XME) and repeated on the Viewsonic LS831WU which was photometrically, temporally and spatially matched to the existing VDUs.

**Results** The HiSense laser DLP projector demonstrated a detrimental input lag jitter making temporal synchronisation to time-locked electrophoretic responses/epochs unpredictable. The Viewsonic laser DLP did not have this issue so was used for all subsequent analyses. This projector is capable of high luminance levels for white-checks (0–587.5 cd m\(^{-2}\)) without reducing Michelson contrast below 93%, although black-checks increased from 1.4–22.2 cd m\(^{-2}\) with increasing luminance. The optimal luminance range to maintain black-checks below 10 cd mm\(^{-2}\) was 76–152 cd m\(^{-2}\). The temporal profile of square wave reversing checks was fast with rise times of < 8 ms and fall times of < 8 ms, without mean luminance change. Spectral properties of white checks showed a large irradiance spike at 457 nm alongside a smaller, broad profile between 480 and 700 nm with peaks at 535 nm and 597 nm. We found the warm-up time was fast for DLP projectors, achieving 99% of maximal luminance within 2 min. This is faster than published data for CRT and LCD monitor warm-up times. PERG and VEP component amplitude and peak-times to ISCEV standard check widths showed high agreement between devices for the same subject. We observed some larger and earlier P100 for smaller check width PVEPs using the DLP projector. As both VDUs were photometrically and temporally matched, this likely reflects faster rise times or improved resolution of DLP projectors relative to our existing systems leading to improving edge contrast.

**Conclusions** Laser DLP projectors are a suitable replacement VDU for pattern testing in visual electrophysiology. It is evident that some devices may succumb to input lag jitter similar to organic light-emitting diode (OLED) monitors. Laser DLP projectors are capable of high luminance and high contrast and can achieve large field sizes which is of particular benefit for paediatric practice. Ultra-short throw ratios also hold the benefit that they do not demand large laboratory space requirements to achieve large field sizes.

**O7 02** A scoping review of current practice in full-field stimulus threshold (FST) testing

Linda F. Shi\(^{1,2}\), Dorothy A. Thompson\(^{1,3}\), Amanda Hall\(^{2}\)

\(^{1}\)Tony Kriss Visual Electrophysiology Unit, Clinical and Academic Department of Ophthalmology, Great Ormond Street Hospital for Children NHS Foundation Trust, London, United Kingdom. \(^{2}\)College of Health and Life Sciences, Aston University, Birmingham, United Kingdom. \(^{3}\)UCL-GOS Institute for Child Health, London, United Kingdom

**Purpose** Full-field stimulus threshold (FST) testing is a psychophysical measure of whole-field retinal light sensitivity, useful for assessing visual function in patients with inherited retinal disease in whom the ERG may be severely affected or undetectable. Deliverable using ganzfeld or perimeter hardware available in most visual science settings, it is an increasingly adopted clinical trial endpoint with growing potential as a supplementary clinical measure of retinal sensitivity. While research trials may specify their own FST protocols, there is as yet no formal standardised guidance for FST testing. This scoping review explored the current variability in the conduct and reporting of the FST, with the aim of identifying gaps in research and discussing further research considerations.

**Methods** A comprehensive electronic search and review of the literature was carried out according to Preferred Reporting Items for Systematic Reviews and Meta-analysis Extension for Scoping Reviews (PRISMA-ScR) framework. Data regarding source details, participant characteristics, test methodology, stimulus parameters, and reporting of outcomes were extracted, evaluated, and synthesised using both quantitative and qualitative methods.

**Results** Data from 72 sources had sufficient reporting of FST testing. These highlighted inconsistencies in the units of reporting, such that nearly a third of studies reporting in decibels (dB) did not specify the 0 dB reference in relation to the absolute luminance units (cd s m\(^{-2}\) or cd m\(^{-2}\)). There was considerable variation and lack of reporting in test parameters including stimulus spectral wavelength, flash duration (4 ms vs 200 ms), pupillary dilation, testing strategy (single-choice vs dual-choice), and duration of dark adaptation. Moreover, there is an unmet need for paediatric-specific considerations: despite indication for greater therapeutic potential for earlier treatment in inherited retinal disease, FST testing of preschool-age children (aged ≤ 5 years) was only achieved by one group. There are no current strategies to optimise testing or test analysis for patients who are younger or have learning needs who find prolonged psychophysical testing challenging.

**Conclusion** Moving forward, stakeholders may wish to conduct further evidence synthesis, empirical research, or structured panel consultation to establish coherent guidance on FST test methodology. They might also choose to consider context-dependent protocol modifications, the establishment of a core set of minimum reporting requirements, and further discuss criteria for clinical significance. In parallel, the development of guidance for quality assurance and calibration and generation of reference data appropriate to context and age will further strengthen reliability and rigour of measurement as FST testing becomes more widely adopted across research and clinical settings.

**Acknowledgements** All research at Great Ormond Street Hospital NHS Foundation Trust and UCL Great Ormond Street Institute of Child Health is made possible by the NIHR Great Ormond Street Hospital Biomedical Research Centre. The views expressed are those of the author(s) and not necessarily those of the NHS, the NIHR, or the Department of Health.

**O7 03** Dark-adapted full-field stimulus threshold in severely affected patients with retinitis pigmentosa

Kaoru Fujinami\(^{1,2}\), Yu Fujinami-Yokokawa\(^{1,4,5}\), Yasutaka Suzuki\(^{1}\), Jeffrey Farmer\(^{6}\), Kazushige Tsunoda\(^{7}\)

\(^{1}\)Laboratory of Visual Physiology, Division of Vision Research, National Institute of Sensory Organs, National Hospital Organization Tokyo Medical Center, Tokyo, Japan. \(^{2}\)Department of Genetics, UCL Institute of Ophthalmology, London, United Kingdom. \(^{3}\)Department of Genetics, UCL Institute of Ophthalmology, London, United Kingdom. \(^{4}\)Department of Genetics, UCL Institute of Ophthalmology, London, United Kingdom. \(^{5}\)Moorfields Eye Hospital, London, United Kingdom. \(^{6}\)Department of Genetics, UCL Institute of Ophthalmology, London, United Kingdom. \(^{7}\)Department of Health Policy and Management, Keio University School of Medicine, Tokyo, Japan. \(^{8}\)Diagnosys LLC, MA, USA. \(^{9}\)Division of Vision Research, National Institute of Sensory Organs, National Hospital Organization Tokyo Medical Center, Tokyo, Japan.
**Purpose**: Full-field stimulus threshold (FST) measures the sensitivity of the visual field by testing for the lowest luminance flash that elicits a visual sensation perceived by the subject. FST is essential in assessing visual function, especially in patients with severe visual impairment. We describe the distribution of luminance thresholds in subjects with retinitis pigmentosa (RP), aiming to establish a deep phenotyping system for therapeutic trials.

**Methods**: RP cases showing severe visual acuity decline (counting finger or worse) were enrolled. Comprehensive ophthalmological examinations were performed, including full-field electroretinograms (fERGs) recorded according to the ISCEV standard. Full-field color stimuli were generated by the Diagnosys Profile Ganzfeld ColorDome (Diagnosys, LLC, MA, USA) that utilizes narrow-band LEDs of 448 nm (blue), 530 nm (green), and 627 nm (red). FST was performed based on the published method (Klein & Birch, Doc Ophthalmol 2009;119:217–224). The colour FST was performed after 40 min of dark adaptation: (i) blue, (ii) red, and (iii) white stimulus. For this study, a 0-decibel (dB) reference point was chosen, which was 0.1 cd s m⁻². The FST data obtained in RP patients were compared with those of seven healthy subjects (median age 29, range 23–45 years) with no ocular disease.

**Results**: The median age of onset/examination of 28 eyes from 14 RP cases was 9.0 (range 0–40)/64.0 (36–75) years, respectively. The median visual acuity of 28 eyes was 2.7(range 1.98–3.00) logMAR. The full-field ERGs were undetectable both in dark-adapted and light-adapted conditions in all 14 RP cases. The median value of thresholds for blue/red/white FST was 7.06 (range −33.1 to 21.8)/10.00(− 6.5 to 18.9)/9.37(− 25.5 to 24.7) dB, respectively, in the 14 RP cases. The median value of thresholds for blue/red/white FST was −59.9/−35.8/−54.0 dB, respectively, in the seven healthy subjects. FST revealed a significantly different range of thresholds for each colour stimulus between severe RP and healthy subjects.

**Conclusions**: The distribution of luminance thresholds was demonstrated in 14 severe RP cases, which was significantly higher than that of healthy subjects. Quantitative assessment for patients with severe visual impairment was available with FST, in keeping with previous reports (Roman AJ et al., Prog Retin Eye Res 2021;87:101000; Klein and Birch, Doc Ophthalmol 2009). Further data from additional affected and unaffected participants are required to validate the clinical investigation in patients with severe visual impairment.

**Acknowledgements**: Kaoru Fujinami is supported by grants from Grant-in-Aid for Young Scientists (A) of the Ministry of Education, Culture, Sports, Science and Technology, Japan (16H06269); grants from Grant-in-Aid for Scientists to support international collaborative studies of the Ministry of Education, Culture, Sports, Science and Technology, Japan (16KK01930002); grants from National Hospital Organization Network Research Fund, Japan (H30-NHO-Sensory Organs-03); grants from Foundation Fighting Blindness Alan Laites Career Development Peogram (CF-CL-0416-0696-UCL), USA; grants from Health Labour Sciences Research Grant, The Ministry of Health Labour and Welfare, Japan (201711107A); and grants from Great Britain Sasakawa Foundation Butterfield Awards, UK.

**O7 04 Small area flexible U. Waterloo electrodes using nanoparticle chains for recording electroretinograms**

**Vivek Maheshwari, Daphne L. McCulloch, Hua Fan, Saikiran Khamgaonkar**

University of Waterloo, Waterloo, Canada

**Purpose**: New material strategies can contribute to the development of flexible skin electrodes that incorporate a high contact area within a limited physical size while maintaining a high signal-to-noise ratio. Such electrodes facilitate recording electroretinograms and other physiological signals with greater comfort, especially in situations where space is limited, such as monitoring of infants. The flexibility of electrodes allows for conformal contact with skin leading to low contact impedance. Nanostructured materials are an avenue to generate small surface area materials with high electrical conductivity. Here we present electroretinograms recorded with flexible electrodes made using a colloidal nanostructured material. The synthesis and fabrication process ensures low cost of the electrodes while maintaining high performance.

**Methods**: A nanostructured material was prepared by a self-assembly process using gold or platinum nanoparticles. The final material has a continuous branched chain morphology, with length of microns while being confined to nanometer scale in other dimensions. These colloid chains are then fabricated into circular electrodes on a flexible substrate. The electrodes have a porous three-dimensional structure with high conductivity. The developed electrodes were then configured with contact surface areas of 7 mm² to be used with the RETeval device for recording of electroretinograms. For comparison, LKC sensor strip electrodes were used as the commercial benchmark.

**Results**: Standard light-adapted 3.0 ERG and 30 Hz flicker ERGs were recorded with natural pupils with real-time adjustment of retinal illumination using LKC RETeval Device. The fabricated U.Waterloo electrodes have 1/10 the contact areas of LKC sensor strip electrodes. Clear recording of the ERG signal with comparable pattern were obtained with both electrodes. Amplitudes of the a- and b-waves of the light-adapted single flash ERG and the peak-to-peak amplitude of the flicker ERGs are higher (by ~30%) with the U.Waterloo electrode compared with those recorded with the commercial electrode. The impedance of the electrodes is also reported to characterize their ability to record the ERG signals. Further, cost analysis of the U.Waterloo electrodes is presented to assess their commercial feasibility.

**Conclusions**: The ability to measure ERG with high signal amplitude using an electrode made with nanostructured material is presented. Despite its 10 times lower surface area, the high signal values are due to two key advantages: 1. The novel electrode material being a 3-D nanostructure leads to higher contact area than a planar metal film. 2. The flexible nature of the material and the electrode leads to better contact with the skin surface. Combined with the ease of synthesis and fabrication, such electrodes can further improve the patient comfort and measurement of ERG signals.

**Oral Session 8**

**O8 01 Evidence of the role of the full-field ERG in staging diabetic retinopathy: A literature review**

**Mitchell G. Brigell**

Biotech Consultant, Belmont, MA, USA

**Purpose**: Provide evidence of the role of the full-field ERG in revision of a staging system for diabetic retinopathy (DR).

**Methods**: A search of PubMed was performed of journal articles in English using the terms “diabetes” and “electroretinogram” on 10 October 2021. 440 studies involving human subjects were identified. Results were pruned if the method was not a full-field flash, if the subjects did not have diabetes, if the study was not related to DR severity, if no ERG data were reported, or if the study did not include human subjects. 279 studies involving non-human species were identified. Results were pruned if the study was published more than 5 years prior to the search, the model was not of DR, no ERG data were reported, or the paper was purely methodological.

**Results**: 107 human studies met the criteria. 39 of the studies were longitudinal or prognostic, 62 were cross-sectional, and 6 were...
reviews. The b-wave was measured in 38, OPs in 50, flicker in 27, and 5 measured other parameters. Implicit time (IT) measurements were shown to have low coefficients of variation and to have prognostic value. 91 non-human studies met criteria. The vast majority measured b-wave amplitude. The effect of an intervention was assessed using the ERG in 76% of studies.

**Conclusion** The literature on ERG OPs, photopic flicker IT, and photopic B-wave IT provide Level 1B evidence (one or more validation studies with consistent results) of prognostic value in patients with DR.

**O8 02 Rod activation and deactivation in early-stage diabetic eye disease.**

J. Jason McAnany, Jason C. Park

Department of Ophthalmology and Visual Sciences, University of Illinois at Chicago, Chicago, IL, USA

**Purpose** Accumulating evidence indicates that diabetes can affect photoreceptor function, but the nature and extent of abnormalities in the rod photoreceptor remain incompletely understood. The purpose of this study was to measure dark-adapted flash ERGs to infer the characteristics of the activation and deactivation phases of rod phototransduction in diabetics who have mild or no clinically-apparent retinopathy.

**Methods** Fifteen non-diabetic controls and 30 type-2 diabetics participated. Fifteen of the diabetic subjects had no clinically-apparent diabetic retinopathy (NDR) and 15 had mild non-proliferative diabetic retinopathy (MDR). To measure rod activation, dark-adapted single flash ERGs were recorded for a series of stimulus retinal illuminances (3.7–4.9 log scot td-s) using conventional techniques. The a-waves of the responses were fit with a delayed Gaussian model to derive \( R_{amp3} \) (maximum amplitude of the massed photoreceptor response) and \( S \) (phototransduction sensitivity). To measure rod deactivation, a paired flash paradigm was used in which a-waves were measured for two flashes (both 2.9 log scot td-s) separated by an interstimulus interval (ISI) of 0.125–16 s; the ISI needed for the a-wave amplitude of the second flash to recover to 50% of the first flash (t50) was determined.

**Results** Analysis of variance indicated that both diabetic groups had significant log \( S \) reductions compared to the controls (\( p < 0.001 \)). \( S \) was reduced by approximately 33% and 46% for the NDR and MDR subjects, respectively. In contrast, \( R_{amp3} \) did not differ significantly for either diabetic group compared to the controls (\( p = 0.08 \)). Likewise, \( t_{50} \) did not differ significantly for either diabetic group compared to the controls (\( p = 0.25 \)). Log \( S \) or log \( R_{amp3} \) for any subject group (all \( p > 0.10 \)).

**Conclusions** Only the activation phase of the rod photoreceptor was abnormal in this sample of diabetic subjects who had minimal or no clinically-apparent retinopathy. Reduced sensitivity of the activation phase could be attributed to factors including reduced quantum absorption, hypoxia, and/or downregulation of rod protein expression. The normal deactivation kinetics suggests that circulating rod current is normal and that molecules necessary for both activation and inactivation are not likely responsible for rod abnormalities. These findings begin to constrain possible explanations for abnormal rod function in early diabetic retinal disease.

**O8 03 Screening for diabetic retinopathy with a handheld ERG device performed by an advanced practice nurse**

Marine Krug, Jenny Fontaine, Céline Lukas-Croisier, Brigitte Delemer, Carl Arndt

Reims University Hospital, Reims, France

**Purpose** Report of the preliminary results for diabetic retinopathy screening (DR) with electoretinography (ERG) performed by an advanced practice nurse.

**Methods** A descriptive, quantitative, prospective and monocentric study from January to April 2022 was carried out in a diabetes day hospital. A portable device (RetEval) was used to record ERGs by an advanced practice nurse trained in visual electrophysiology. Skin electrodes were used; pupils were undilated. The following data were collected: age, gender, ophthalmological history, duration of diabetes, date of the previous ophthalmological examination, Hb Alc, BP, current medical treatments, and diabetic retinopathy (DR) score (algorithm, abnormal if > 23.05).

**Results** Thirty five patients were included, 14 of whom were being treated for hypertension. The last retinal screening had been performed 2–3 years previously, the mean duration of diabetes was 12.5 (range 1–33) years, mean Hb Alc was 8.2 (6.3–13). No DR was detectable on the retinal imagery except in 1 of 3 patients who had an abnormal DR score. In addition, 19 patients had at least one borderline or abnormal amplitude or implicit time parameter.

**Conclusions** In our preliminary series, compared with retinal imaging, the sensitivity of DR detection was 100%, with a specificity of 33%. In a recent series of 172 patients, the sensitivity was 81% and the specificity 82% compared to conventional imaging. This set-up for DR screening based on use of a handheld ERG device appears to be reliable when performed by an advanced practice nurse.

**O8 04 Clinical and electrophysiological findings in patients with post-COVID-19-related retinal complications**

D. Marwa, A. Tabl, Tarek S. Esawy, Mohamed A. Awwad, Taher K., Ahmed A. Tabl

Benha University, Benha, Egypt

**Background** The clinical spectrum of coronavirus disease (COVID-19), due to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection, may be pretty broad, including ocular symptoms.

**Purpose** This study aimed to illustrate the clinical and electrophysiological features in a series of patients with post-COVID-19-related retinal manifestations.

**Methods** This is an observational study of 39 patients who developed retinal manifestations following COVID-19 infection. The subjects were recruited from the retina clinic in Benha University Hospital from April 2021–October 2021 during the second COVID-19 outbreak in Egypt. COVID-19 infection was confirmed in all patients using a nasopharyngeal swab (tested positive for SARS-CoV-2 by PCR testing), followed by detection of serum IgG antibodies against SARS-CoV-2. All participants underwent complete clinical ophthalmological examination, fluorescein angiography (FA), optical coherence tomography (OCT), and electrophysiological assessment, including ERG, VEP and mfERG.

**Results** 25 males (64%) and 14 females (36%) with ages ranging from 15 to 55 years were included in this study. BCVA ranged from 6/9 to perception of light. Using FA and OCT, we established diagnoses of unilateral central retinal vein occlusion (CRVO), without any prior history or risk factors for thromboembolism, in 11 (28%) patients, branch retinal vein occlusion (BRVO) in 9 (23%) patients, optic neuritis (ON) in 5 (13%) patients, central serous chorioretinopathy (CSR) in 4 (10%) patients, chorioretinitis in 3 (8%) patients, central retinal artery occlusion (CRAO) in 2 (5%) patients, papillovasculitis in 2 (5%) patients, para-central acute middle maculopathy (PAMM) in 2 (5%) patients, and acute macular neuroretinopathy (AMN) in 1 (3%) patient. Electrophysiological findings were as follows: In CRVO, the amplitude of the b-wave was...
decreased relative to the a-wave; the b/a ratio was reduced to less than or equal to 60% of that of the fellow normal eye. ERG findings were correlated with a relative afferent pupillary defect (RAPD) and retinal thickness. Unilateral electronegative ERG was seen in eyes with CRAO. In eyes with BRVO, the plotted waveform tracings, 2D, and 3D displays of the mfERG showed that the response densities derived from the affected retina area were reduced. The five responses of ERG were significantly reduced in eyes with chorioretinitis. In eyes with ON, the flash and pattern VEP showed considerably delayed implicit time and moderately reduced amplitude at every spatial frequency. In eyes with CSR, the mfERG showed that the response densities derived from the fovea were significantly reduced, that from parafovea were moderately reduced, and other areas of the retina were normal. Flash and pattern ERG were normal in eyes with PAMM and AMN, while the mfERG showed areas of reduced function corresponding to areas of visual field defects.

Conclusions Our study demonstrated various retinal and optic nerve manifestations related to COVID-19 infection. Electrophysiological tests may represent a fundamental tool in the early diagnosis and follow-up evaluations of these patients.

Acknowledgements The authors report no conflicts of interest in this work.

O8 05 High-quality control measures allow detection of three-year changes in a placebo group of a randomized double-blind international multicenter safety study

Eberhart Zrenner1, Graham E. Holder2, Ulrich Schiefer3, John M Wild4
1University of Tuebingen, Tuebingen, Germany. 2Moorfields Eye Hospital, London, United Kingdom. 3University of Applied Sciences, Aalen, Germany. 4Cardiff University, Cardiff, United Kingdom

Purpose We have previously illustrated the benefit of identical equipment, stringent on-site instruction and training, continuous control measures and validation methods to ensure high quality data in multi-center trials for each of the 5 ISCEV standard-ERGs, D15 color vision test (CV), static automated perimetry (SAP) and semi-automated kinetic perimetry (SKP). These findings were derived from a three-year multicenter, international, prospective, double blind, randomized placebo-controlled safety study in patients with chronic stable angina pectoris (EudraCT No. 2006-005475-17) conducted at 11 international ophthalmic centers (Zrenner et al., TVST:2020;9:38). Here we present evidence that such measures allow detection of significant deteriorations in such tests of visual function in a placebo-treated control group within three years, attributable to ageing.

Methods Changes in visual function (BCVA, ERG, CV, SAP, SKP) between baseline and month 36 were analyzed by means of a two-tailed Wilcoxon signed-rank test, based on the Hodges and Lehman corrections and high-pass filtering. The post-hoc, non-causal filters provided by a beta-test version of the Diagnosys Espion3 software. Useful signal extraction procedures included linear baseline correction factors for age-related changes in visual function as suggested here may be useful in future trials to determine whether an observed deterioration in visual functions is related to intervention or to ageing.

Acknowledgements The authors express their gratitude to Servier (France) for access to the baseline and 36 month data of the trial and for professional statistical support. Special thanks are due to the investigators at the ophthalmological study sites, Drs. S. Andreasson, V. Balazs, E. Chelva, J. Cheng, P. Cunha-Vaz, T. P. Kenna, Kivela¨, B. Leroy, L. Ribeiro, G. Schlottmann, and A. Vingrys.

Oral Session 9

O9 01 Separation of ERG waveforms in infants from unsteady baselines using high-pass filters

Scott Brodie1, Karen Holopigian2
1NYU Langone Health, New York, USA. 2Novartis Institutes for BioMedical Research, East Hanover, NJ, USA

Purpose: To demonstrate the use of high-pass filters to extract useful ERG waveforms contaminated by unsteady baselines in recordings from awake infants.

Methods: ERGs were recorded from awake infants held in a parent’s arms according to ISCEV standards with the exception of use of a hand-held stroboscopic flash stimulator (DiagnosysLLC ColorFlash) in lieu of a ganzfeld stimulator. Recordings were obtained with ERG-IVT contact lens electrodes modified with a pressure-fit cylindrical stent to facilitate electrode placement and prevent lid closure, referenced to a 3 M Red Dot adhesive skin electrode placed on the forehead. Data were acquired using the DiagnosysLLC Espion3 electrodeagnostic system. Amplifier bandwidth cutoff settings conformed to the ISCEV standard of 0.3 Hz and 300 Hz. The sampling frequency was 1 kHz. In many cases, it was necessary to disable waveform-triggered artifact rejection in order to record any waveforms at all. In cases where unsteady baselines (often extreme) precluded ready interpretation and measurement of ERG waveforms, the ERGs were post-processed using post-hoc filtering options provided by a beta-test version of the Diagnosys Espion3 software. Useful signal extraction procedures included linear baseline correction and high-pass filtering, typically with a cutoff frequency of 5 Hz, or rarely, 10 Hz. Waveforms were further clarified by signal averaging.

Results: Recordings from awake, frequently squirming infants are frequently contaminated by baseline excursions of 100s of µV, often dwarfing the superimposed ERG waveforms, due to motion artifacts and variable galvanic effects. Though large in amplitude, these baseline variations are typically confined to frequencies below 5 Hz, or at worst, 10 Hz, and can be readily suppressed by linear baseline corrections and high-pass filtering. The post-hoc, non-causal filters cause little or no latency shift of waveform peaks and reduce waveform amplitudes (with little power below these band-pass cutoffs) by

Conclusions Statistically significant deteriorations in visual functions were detected over a period of three years in a multi-centric placebo group with chronic stable angina pectoris. As chronic stable angina pectoris, per se, is not known to affect visual function, it is reasonable to assume that the physiological ageing process was the predominant factor underpinning the distributions of changes in the current study (Zrenner et al., TVST:2022;11(1):2). The novel finding of statistically significant changes over 36 months in a longitudinal multicenter trial also underlines the importance of a robust methodology incorporating identical and standardized techniques, central reader evaluation, and stringent quality control of the data acquisition. Longitudinal correction factors for age-related changes in visual function as described here may be useful in future trials to determine whether an observed deterioration in visual functions is related to intervention or to ageing.
O9 02 Indications for the use of multichannel VEPs in children without nystagmus
Joanne Cowe1,2, Oliver R. Marmoy1,3,4, Sian E. Handle1,3, Lisa Tucker1,3, Dorothy A. Thompson1,3
1Great Ormond Street Hospital for Children NHS Foundation Trust, London, United Kingdom. 2University Hospitals of Leicester NHS Trust, Leicester, United Kingdom. 3UCL Great Ormond Street Institute for Child Health, London, United Kingdom. 4Manchester Metropolitan University, Manchester, United Kingdom

Purpose In paediatric practice, multichannel VEPs are typically used to assess chiasmal misrouting associated with albimism in children with nystagmus. We sought to explore the indications and benefits of multichannel VEPs in children without nystagmus.

Methods During 2020, a single centre retrospective case note review was carried out of children who had multichannel pattern VEP recordings to an ISCEV large check (50° check width), presented in both a full 30 degree field and vertical 0–15 degree hemi-fields. Children presenting with nystagmus were excluded. Full-field pattern reversal VEPs (ffVEP) were recorded according to ISCEV VEP standards, from electrodes positioned at O1 and O2, in addition to Oz, referred to mf. The ffPVEP P100 amplitude and peak time at Oz were compared to reference range limits. The percentage difference between O1 and O2 was measured at the same peak time as P100 at Oz. The ipsilateral positive peak (ip100) hemi-field amplitude was compared to the contra-lateral occipital response to assess its trans-occipital distribution.

Results The findings of sixty three children with complete full and hemi-field PVEP data (median age 10.5 years, range 4.4–16.9 years) clustered into two main groups. Group 1: 7/63 (11%) children had ‘abnormal’ ffPVEPs at Oz from one or both eyes. This included 3 bilateral and 4 unilateral cases (10/14 eyes). Hemi-field VEPs showed involvement of the fellow eye in the 3 apparent unilateral cases. These children were investigated for reduced vision [3/7: 2 bilateral, 1 with a family history of optic neuropathy, 1 unilateral with pale disc], 2 glioma, 2 craniohypophisy, Group 2: The remaining 56 children had ‘normal’ ffPVEPs at Oz with P100 within reference ranges: a) 12/56 (21%) produced normal ffPVEP P100 at Oz, but had abnormal hemi-field PVEPs. These children were referred to investigate reduced vision [5/12: 2 glioma, 1 craniohypophisy, 1 epilepsy presurgical evaluation, 1 papilloedema, 2 foveal hypoplasia. b) 33/56 (59%) showed an asymmetric trans-occipital distribution of the ffPVEP, but the summed distribution of each hemi-field explained the full-field distribution. These children were referred with reduced vision [12/33 [including non-specific visual loss, possible visual field abnormalities, colour vision disturbance and/or headache], 3 epilepsy pre-surgical evaluation, 2 glioma, 1 hearing loss, 1 optic neuritis, 1 dizziness, 1 retinosischisis, 6 papilloedema/disc drusen, 6 craniosynostosis], c) 10/56 (18%) produced symmetrically distributed ffPVEPs and normal hemi-field PVEPs. These children were referred with reduced vision [4/10: 4 craniosynostosis, 2 papilloedema.] d) 1/56 case of craniosynostosis had very atypical skewed hemi-field and ffVEPs all maximal on the right occiput.

Conclusions Paediatric practice benefits from multichannel VEPs to investigate reduced vision and to identify or exclude visual loss associated with chiasmal or visual pathway turnouts or conditions associated with raised ICP or cortical malformations, epilepsy, or stroke. In this series, 21% of children with normal midline ffVEPs would not have had vision loss identified without a multichannel VEP.

O9 03 SsVEP in children with poor visual behavior: additional considerations to improve test compliance
Lucia Ambrosio1,2, Ronald M. Hansen2, Anna Maria Baglieri2, Anne B. Fulton1, Jeffrey D. Farmer2, James D. Akula2
1University of Naples Federico II, Naples, Italy. 2Boston Children’s Hospital, Boston, MA, USA. 3Diagnosys, LLC, Lowell, MA, USA

Purpose Visual evoked potential (VEP) acuity tests make estimations of acuity in preverbal and nonverbal patients with visual impairment feasible, yet the interpretation of VEP acuity and the relationship to the more commonly measured behavioral preferential looking (PL) acuity test remain incompletely understood. Indeed, the degree of (dis)agreement between behavioral and VEP acuity may contain useful information about the origins of visual impairment. Accordingly, this study compares Teller Acuity Card (TAC; Stereo Optical Company, Chicago IL USA) and stepwise sweep VEP acuity estimates on a commercially available system (ssVEP; Espion E3, Diagnosys, LLC, Lowell MA USA) in children with different causes of visual impairment. In addition, procedural options to improve test compliance in young children with disabilities are explored.

Methods Binocular best-corrected acuity (BCVA) was measured in 32 subjects (23 with cerebral visual impairment, CVI; 9 with other ocular disorders) aged 0.6–15 (median 2) years at test, using both TAC PL and ssVEP procedures (see Bach & Farmer, Doc Ophthalmol, 2019) and was compared to BCVA in 4 healthy controls. Acurities, so obtained, were expressed in logMAR and plotted against the normal limits of binocular acuity for age. Differences among the three groups were evaluated by analysis of variance. The relationship of acuity to the delta between PL and ssVEP measures of BCVA was investigated. In 20 subjects, an additional analysis of ssVEP extrapolated from Oz channel alone compared to Laplace (3 channels) was undertaken. Also, recordings collected with 40 sweeps/steps protocol were divided into 2 recordings of 20 sweeps/steps protocol and the two “runs” compared.

Results All subjects had measurable PL and ssVEP acuities. In nearly all subjects, both PL and ssVEP acuities were below normal for age. PL BCVA spanned 2.08–0.00 logMAR (Snellen 20/2400-20/20) and ssVEP acuinity spanned 1.03–0.17 logMAR (Snellen 20/215-20/29), with a strong correlation (r = 0.79) between the two measures. However, ssVEP tended to exceed PL acuity, especially in the subjects with the lowest BCVA. That is, 3 of the 4 healthy controls but only 4 of 9 ocular disorder subjects and a mere 2 of 23 CVI subjects had better PL than ssVEP acuity. Furthermore, the delta between PL and ssVEP was more than twice as large in subjects with CVI as in those with other ocular conditions (p < 0.05). We extrapolated comparable ssVEP acuities using the shorter protocol (20 sweeps/steps) placing 3-channels, Oz-O1-O2, with the longer protocol (40 sweeps/steps) using simply Oz.

Conclusions Acuity by ssVEP exceeds the estimation of acuity by PL in patients with visual dysfunction, particularly CVI. This discrepancy might result from differences in the stimuli, including the stimulated retinal locations. That said, larger discrepancies in acuity measured using both PL and ssVEP may imply cerebral involvement. To improve test subject compliance, it may be advisable to reduce the time of recording, keeping the Laplace montage.
Poster Session 1

P1 01 Effect of nutraceutical supplementation on redox status and mfERG on retinitis pigmentosa patients

Emilio González-García, Lorena Oliva-González, David Salom, David Hervas, Natalia Mejía-Chiqui, Mar Melero, Sheyla Velasco, Bianca T. Muresan, Isabel Campillo, Natalia Mejía-Chiqui, María del Castillión, Regina Rodrigo, Marta Pavlak, Anna Gotz-Więckowska, Patrycja Pijanka, Anna Chmielarz-Czarnocinska

Department of Ophthalmology, Poznan University of Medical Sciences, Poznan, Poland

Purpose: The aim of the study was to analyse the role of FVEP in the assessment of infants without eye contact.

Methods: The study included children aged 6 weeks to 12 months who were examined in the Paediatric Ophthalmology Outpatient Clinic in the Department of Ophthalmology of Poznan University of Medical Sciences between June 2014 and November 2019 due to absence of eye contact or visual responses. The patients underwent full ophthalmological examination and FVEP performed according to the ISCEV standards with a hand-held stimulator (Retiport System, Babylight, Roland Consult, Germany). The first and the last FVEP performed were used for the analysis. The relationship between the result of the first FVEP and visual function on the last visit and between the improvement in the FVEP result (between the first and last FVEP) and visual function on the last visit were evaluated.

Results: Forty-two patients were included in the study. The mean age at first visit was 5.2 months. FVEP were performed in 36 patients (at least twice in 21 patients). The mean age at the first FVEP was 9 months and at the last FVEP was 28 months. On the last visit, 21 patients (50%) presented with eye contact and visual responses were present in 35 children (83%). A statistically significant correlation was found between the improvement in the FVEP result between the first and last examination and visual reactions on the last visit. No statistically significant correlation was found between the result of the first FVEP and visual reactions or visual contact on the last visit.

Conclusions: We were not able to prove that the result of the first FVEP can help predict final visual reactions. However, FVEP may be helpful in monitoring changes in the visual function of patients. Lack of eye contact on the first visit cannot forejudge the potential visual outcome.

P1 03 A novel approach to analyse white noise ERGs in mice

Nina Stallwitz, Anneka Joachmsthaler, Jan Kremers

1University Hospital, Erlangen, Germany. 2Friedrich-Alexander Universität, Erlangen-Nürnberg, Germany

Purpose: To analyse correlations between white noise ERGs (wnERGs) recorded to luminance modulating and single opsin isolating temporal white noise (TWN) stimuli.
Methods Mice were dark adapted overnight and all further handling was done under dim red light. Using mice that express a long-wavelength sensitive L-Opsin instead of the murine M-Opsin enables the isolation of single opsin-driven ERGs by combining the TWN stimulus with the silent substitution method (52% rod-contrast, 48% L-cone contrast, 77% S-cone contrast). Recordings of the anesthetized animals were performed at different mean luminances (ML), and each recording was performed twice. TWN stimuli (containing all frequencies up to 20 Hz with equal amplitudes and random phases) were luminance modulation (100% contrast white light) and shown at MLs ranging from −0.7 to 1.1 log cd/m². In addition, opsin isolating stimuli were employed at MLs between −0.8 and 1.0 log cd/m². The reproducibility of the wnERGs was quantified using a correlation coefficient. The ERG potentials at identical instances during the repeated measurements at one ML and condition were plotted against each other. The correlation coefficient of the linear regression through the data was extracted (r² repr). Correlation coefficients vary between 1, meaning complete accordance of both results, and 0, indicating no similarities at all. To investigate whether the change in appearance of the wnERGs depend on ML, another correlation coefficient was used (r² ML). To receive r² ML, the two repeated recordings at each ML were averaged and the averaged wnERG of each ML was either plotted against the wnERG obtained at the lowest ML (for rod isolating and luminance stimuli) or highest ML (for cone isolating and luminance stimuli). The linear regression through the data gave the correlation coefficient r² ML to quantify the correlations between responses at different MLs.

Results For luminance stimuli, r² repr values decreased with increasing ML up to −0.1 log cd/m² ML, above which r² repr increased with increasing ML and reached a plateau for MLs higher than 0.5 log cd/m². The r² repr values for S-cone-driven wnERGs initially decreased up to a ML of −0.2 log cd/m² and then increased. The r² repr values for L-cone-driven ERGs continuously increased with increasing ML. R² ML values for luminance modulation decreased with increasing ML when the responses were plotted against those obtained at the lowest ML, whereas they increased when plotted against the responses obtained at the highest ML. For L- and S-cone-driven ERGs, r² ML values increased with increasing ML, whereas r² ML values decreased with increasing ML for rod-driven wnERGs.

Conclusions Differences between the characteristics of the r² values between rods and cones point at fundamental differences of the dynamics of the ERG origins. Luminance ERGs originate in rods at all MLs and in cones at high MLs. Responses at intermediate MLs are generally weak.

Acknowledgements Section for Retinal Physiology, University Hospital Erlangen. Animal Physiology, FAU Erlangen-Nürnberg.

P1 05 The annual carbon footprint of a visual electrodiagnostic service
Joanne Cowe, Julie Kempton
University Hospitals of Leicester NHS Trust, Leicester, United Kingdom

Purpose To combat global heating, the National Health Service (NHS) in England has committed to ‘net-zero’ by 2040 with an ambition to reduce the NHS carbon footprint by 80% by 2028–2032 [NHS England and NHS Improvement (2020), Delivering a ‘Net Zero’ National Health Service, Publication approval reference: PAR133]. Greenhouse gases are emitted at all stages of the electrodiagnostic process from procurement, activity (patient testing), production of goods/services (e.g. patient reports), and from waste. A carbon footprinting methodology for an electrodiagnostic service is described. An estimate of the annual carbon equivalent footprint of our service is presented for the calendar year 2021.

Methods The carbon dioxide equivalent emissions were calculated for energy use, water use, procurement, waste, and travel (staff business travel, commuter travel, and patient travel). UK Government GHG Conversion Factors for Company Reporting were used to find the carbon dioxide equivalent emissions for staff commuter travel, hotel stays for business travel, and for water use. The carbon dioxide emission for patient travel and business travel was estimated using the carbon calculator from the Centre for Sustainable Healthcare (“Carbon footprint calculator for (avoided) patient travel”). Departmental spend in various procurement categories was converted using weighting factors provided by the Greener NHS team (https://www.england.nhs.uk/greener NHS/). The Royal Mail Letter Carbon Calculator was used to calculate emissions from the postal service. Emissions from energy use were calculated as a proportional fraction of the building’s total carbon emissions stated on the Display Energy Certificate (DEC). Consumable waste was converted using GHG emissions factors from a waste stream study (Rizan C. et al., Cleaner Production, 2021; 286:a125446).

Results The total estimated 2021 carbon footprint for our electrodiagnostic service was 24.95 tonnes CO₂e. Some emissions such as those from use of personal protective equipment and office waste could not be quantified making this a lower bound for our service. The results from each category were: energy: 15.43 tonnes CO₂e (62%); travel: 7.61 tonnes CO₂e (30%); procurement: 1.90 tonnes CO₂e (8%); waste: 0.01 tonnes CO₂e (0%); and water: 0.01 tonnes CO₂e (0%). The primary contributors to the carbon footprint, together accounting for 92% of the total, were therefore energy use followed by patient and staff travel. Visual electrodiagnostics carried out 237 patient appointments in 2021. The average carbon footprint per patient is therefore 105 kg CO₂e which could allow for more meaningful comparison between larger and smaller test centres.

Conclusions The NHS produced an estimated 6.1 MtCO₂e in 2020 (NHS England and NHS Improvement (2020), Delivering a ‘Net Zero’ National Health Service, Publication approval reference: PAR133). To reduce this to net zero it is clear that every part of the NHS will need to contribute, including its suppliers. The results encourage us to make more efficient use of energy in our area. We could consider the use of satellite clinics to bring testing closer to patients. We can also promote more sustainable forms of transport for our staff and in our patient communications such as sign posting to public transport.

P1 07 The effect of fixation location on full-field ERG waveforms
David T Murray, Julie Kempton, Joanne Cowe
Medical Physics Department, University Hospitals of Leicester NHS Trust, Leicester, United Kingdom

Purpose When performing a full-field ERG, patients are requested to look at the central fixation spot within a Ganzfeld dome. Some patients find this difficult and either consistently look elsewhere in the dome or vary their gaze position during the test. This study analyses the clinical impact of fixating at alternative locations.

Methods ERG recordings were performed on 14 eyes using our light-adapted 3.0 ISCEV protocol (but without dilation), with DTL electrodes placed at the junction where the lower eyelid meets the sclera/cornea. Eleven different gaze locations were used within the Ganzfeld: central, 3 eccentricities in both nasal and temporal directions, and 2 eccentricities in both superior and inferior directions. Volunteer were asked to keep their head facing forwards and only move their eye to the various
positions. A- and b-wave amplitudes and peak times were analysed to assess the clinical impact of gaze position.

**Results** Data from one subject (both eyes) were excluded, as both a- and b-wave amplitude and peak time measures were outside our reference ranges for the standard central fixation. While this is a small study including only 12 eyes, the results indicate that the amplitude is more susceptible to changes in the gaze position than peak time, with a-wave and b-wave amplitudes being markedly affected. An overall amplitude increase is seen when looking superiorly, i.e. above the central fixation light, whilst looking to either extreme side or downwards causes a reduction in the amplitude. A mean b-wave amplitude reduction of 38% was seen in a fully downwards position, while a partial downwards gaze caused a mean reduction of 22%, relative to the standard central fixation position. Conversely, an increase of 46% was seen on the a-wave amplitude and an increase of 10% on b-wave amplitude while looking in the full up position. The maximum deviation from the peak time measured in the central position was smaller, with a mean delay of 8% on the a-wave and 3% on the b-wave, both when eyes were looking in the full down position.

**Conclusions** The central fixation point should always be used during testing. Patients should be monitored for compliance during testing using an IR camera, with any notable deviations recorded. A variance in fixation direction could push a result in or out of a reference range(s), potentially impacting report conclusion. This highlights the need for repeatability, consistency, and the importance of monitoring compliance, not only in patient testing but also in the collection of the normative data with which patient data will be compared.

**P1 09 Morphological and electrofunctional evaluation of ganglion cells in pre-perimetric glaucoma**

Viviana D’Alterio¹, Gennaro Ambrosio¹, Ciro Costagliola¹, Lucia Ambrosio¹,2

¹Eye Clinic Department of Neuroscience, Reproductive and Odontostomatological Sciences, University of Naples Federico II, Naples, Italy. ²Department of Public Health, University of Naples Federico II, Naples, Italy

**Purpose** PERG testing was used to assess functional changes of retinal ganglion cells after decrease of intraocular pressure in patients with early stage (pre-perimetric) glaucoma. This study showed that an early and reversible window of time may exist, during which retinal ganglion cell dysfunction (prior to axonal loss) is clinically associated with normal optic nerve parameters by spectral-domain optical coherence tomography (SD-OCT).

**Methods** Twenty-eight patients (56 eyes) with pre-perimetric glaucoma were studied retrospectively between January and December 2019. Per-Gla, GLAID, Ingenesi, Italy) at baseline and after 12 months of treatment. Patients’ intraocular pressure had been measured with the Goldmann tonometer every 2 months. The thickness of the ganglion cell complex (GCC) and retinal nerve fiber layer were measured using RTVue SD-OCT imaging. Focal loss volume (FLV) and overall loss volume (GLV) were calculated and collected at baseline.

**Results** During follow-up, good compliance to the treatment was noted. Decrease of ocular pressure was documented in the treated patients. PERG was recorded for all patients at baseline and after 12 months of treatment. PERG response amplitudes (µV) were compared with the normative values available with GLAID software. A statistically significant effect between the treated (pre-treatment

Conclusions Reducing intraocular pressure in patients with suspected (pre-perimetric) glaucoma results in functional recovery of retinal ganglion cells that are still in a transitional stage and that retain the normal structure of GCC.

**P1 11 Investigating the relationship between visual electrophysiology results, phenotype and genotype of patients assessed at an ocular-genetics service**

Clodagh Duffy1,2, Sarah Francis1,2, David F. Gilmour1, Daniela T. Pilz1,2, Sinead M. Walker1,2

¹Glasgow Centre for Ophthalmic Research, Gartnavel General Hospital, Glasgow, United Kingdom. ²Medical Devices Unit, Glasgow, United Kingdom. ³West of Scotland Genetics Service, Queen Elizabeth University Hospital, Glasgow, United Kingdom

**Purpose** A monthly joint ophthalmic and genetics multidisciplinary team (MDT) clinic has been operational at Glasgow Centre for Ophthalmic Research (GCOR) for almost 10 years. Most patients have visual electrophysiology (EP) testing and ophthalmic imaging performed prior to attending the clinic and virtually all have genetic testing conducted following their clinic attendance, typically using the Manchester Retinal Degeneration Panel. An audit was performed to investigate the relationship between visual electrophysiology results, phenotype and genotype of patients who attended the clinic in 2019.

**Methods** Ophthalmology, visual electrophysiology and genetics records were examined from all patients. The audit aimed to determine what proportion of patients:

1. Had a positive genetics panel outcome.
2. Had visual EP results that were in alignment with their phenotype.
3. Had visual EP results that were in alignment with their genotype.

**Results** 54 patients attended the clinic in 2019, 8 were discounted from the audit for various reasons including pending genetics results. 42 of these 46 patients from the sample group underwent genetic testing. 28 (66.7%) of these patients had a positive genetics panel outcome, 9 (21.4%) had a negative genetics panel outcome, and 5 (11.9%) were borderline. Of these borderline results, 2 (4.8%) detected a mutation of uncertain significance, and 3 (7.1%) identified only a single gene mutation where two would have been documented to be pathogenic. 44 patients (95.7%) had EP results that aligned with their phenotype. Of the 28 patients who had a positive genetics panel outcome, 25 (89.3%) had EP results that were in alignment with their phenotype.

**Conclusions** The 66.7% (n = 42) of patients in the sample group who received genetic testing and had a pathogenic mutation identified was similar to the results of an audit performed in 2017, in which 69.2% (n = 32) of patients had a positive Manchester Retinal Degeneration Panel outcome. The vast majority of patients (95.7%) had EP results that were in alignment with their phenotype, which indicates that visual EP is an accurate way to confirm a patient’s phenotype. The visual EP results were also highly aligned with the patient’s genetics outcome, with 89.3% of patients having visual EP results that were in keeping with their genotype. The audit confirmed that visual electrophysiology is a valuable tool to confirm that patients referred to the MDT have phenotypes resulting from pathology that is in keeping with genetic conditions and helps to ensure that only appropriate patients are referred for genetic testing.
P1 13 Flicker ERG in preterm infants
Aylin Taner1, James V. M. Hanson1, Caroline Weber2, Dirk Bassler2, Daphne L. McCulloch3, Christina Gerth-Kahlert1
1Department of Ophthalmology, University Hospital Zurich and University of Zurich, Zurich, Switzerland. 2Newborn Research, Department of Neonatology, University Hospital Zurich and University of Zurich, Zurich, Switzerland. 3School of Optometry and Vision Science, University of Waterloo, Waterloo, Canada

Purpose Infants born prematurity are at risk of developing retinopathy of prematurity (ROP) which has been associated with abnormalities in conventional ERGs. We have reported non-invasive flicker ERGs in term infants; the aim of this study was to measure and analyze non-invasive flicker ERGs of preterm and very preterm infants. The long-term goal of the study is to evaluate the utility of flicker ERG as a diagnostic tool to assess children at risk for ROP.

Methods Flicker ERGs of moderate preterm (gestational age (GA) 34 0/7 to 36 6/7 weeks, group A) and extremely and very preterm (GA ≤ 31 weeks, group B) infants were recorded at the University Hospital Zurich. Uniocular measurements were performed within the first week of life (group A) and between 34 and 37th week postmenstrual age (PMA) (group B) while infants were asleep. Flicker stimuli were presented through closed eyelids at 28.3 Hz, with stimulus levels of 3, 6, 12, 30, and 50 cd s/m², using the portable RETeval® device and disposible skin electrodes. Two measurements per stimulus level were recorded and averaged after checking for reproducibility. Primary endpoints were peak time (ms) and amplitude (μV) for each stimulus. Statistical analysis was performed in SPSS®.

Results Data of 59 infants were analysed (group A: 40, group B: 19 including 1/19 with ROP stage 1, zone II at the time of testing). With increasing stimulus levels, flicker ERGs were more often reproducible, with the highest reproducibility at 30 cd s/m² (52/59 infants). Amplitudes increased with stronger flicker (Kruskal–Wallis-H Test, p < 0.001), while peak times did not differ significantly between stimulus levels. As not all data were normally distributed, comparison between groups A and B was made using the Mann–Whitney-U Test. Significantly higher amplitudes at stimulus levels 12 and 50 cd s/m² (exact Mann–Whitney-U-Test: Z = 2.037, p = 0.042 and Z = −3.788, p ≤ 0.001, respectively) were evident in group B. Cohen’s effect size is medium at 12 cd s/m² (0.30) and large at 50 cd s/m² (0.55). No inter-group differences in peak times were detected.

Conclusions Feasibility of collecting flicker ERG data in the majority of preterm infants was confirmed in this study. Although the groups were comparable in terms of PMA at the time of data collection, extremely and very preterm infants seem to have higher amplitudes in two stimulus levels than moderate preterm infants. However, no difference was found between the two groups for the lower stimulus levels nor for the peak times. The difference detected could indicate acceleration of retinal development following birth, triggered by visual stimulation. Data collection in Group B is ongoing.

P1 15 Unusual OCT findings in a patient with CABP4-associated retinopathy
Jit Kai Tan1,2, Omar Mahroo3,4
1GKT School of Medical Education, London, United Kingdom. 2UCL Institute of Ophthalmology, London, United Kingdom. 3Guy’s and St Thomas’ NHS Foundation Trust, London, United Kingdom. 4Moorfields Eye Hospital NHS Foundation Trust, London, United Kingdom

Purpose Bi-allelic variants in CABP4 are associated with congenital cone-rod synaptic disorder, also known as incomplete congenital stationary night blindness (iCSNB). Patients show characteristic electroretinogram (ERG) abnormalities, and fundus findings are typically reported as normal. We describe clinical findings in a patient, who demonstrated an unusual macular optical coherence tomography (OCT) phenotype, not previously reported.

Methods The patient was assessed clinically and also underwent spectral domain OCT imaging (Spectralis, Heidelberg Engineering, Heidelberg, Germany) and international standard full-field ERG testing (Diagnosys Colordrome, Diagnosys UK, Cambridgeshire, UK) with conductive fibre electrodes placed in the lower conjunctival fornices. Genetic testing was performed via whole genome sequencing. Frequency of likely pathogenic variants found were assessed in the online Genomes Aggregation Database (gnomAD).

Results The patient was a 60 year old Caucasian woman. She reported lifelong non-progressive visual impairment since birth and a preference for dim lighting, for which she wore dark tinted contact lenses. She had a history of multiple squint surgeries, nystagmus, fibromyalgia, sleep apnoea, and arthritis. Clinical fundus examination was largely unremarkable. OCT imaging revealed a hypo-reflective zone under an elevated fovea in both eyes. ERG testing showed an electronegative dark-adapted ERG, with severely abnormal light-adapted responses consistent with iCSNB. Whole genome sequencing revealed that the patient was homozygous for a novel variant in CABP4 (a premature stop at codon position 111); this variant was absent from the gnomAD database. No other variants were found that could explain the patient’s phenotype.

Conclusions The OCT findings of foveal elevation and an underlying hyporeflective zone are novel in this condition. Whilst the patient’s clinical history was similar to that seen in achromatopsia and other cone dysfunction syndromes, the ERG findings pointed to iCSNB, which is associated with CACNA1F and CABP4. As CACNA1F is X-linked, and our patient was female, CABP4 was likely and was confirmed on genetic testing. Although the variant was novel, the highly specific ERG phenotype made this the likely cause. The patient saw better in dim light, confirming that “night blindness” is a misnomer in CABP4-associated disease. Our case highlights the value of ERG testing in discriminating between causes of cone dysfunction and also extends the range of phenotypes and genotypes reported in this disorder.

P1 17 How onset VEP can help in neurosurgical decision-making in infants.
Eszter Mikó- Baráth1,2, Valéria Gaál3, János Rado1,2, Gábor Jando1,2
1Institute of Physiology, Medical School, University of Pécs, Pécs, Hungary. 2Centre for Neuroscience, University of Pécs, Pécs, Hungary. 3Department of Ophthalmology, Medical School, University of Pécs, Pécs, Hungary

Purpose To follow up on an infant with nystagmus and lack of visual attention, having a space-occupying lesion in the posterior cranial fossa proven by Magnetic Resonance Tomography (MRT). Here we demonstrate how the 14 months-long regular VEP testing supported the neurosurgical decision making.

Methods The patient was observed between 4 and 19 months of age. Regular orthoptic examination and checkerboard onset-VEP were performed to 120-7 check sizes five times in accord with the ISCEV standard. VEPs were evaluated manually and by using T2circ statistics, focusing on the presence of stimulus-related responses. The peak times of C1 and C2, comparison of monocular records, and occurrence of responses for the smaller check sizes were monitored. MRT was carried out under anaesthesia at 4 and 12 months of age.
Results: At 4 months of age, a continuous large-amplitude, slow-wave horizontal nystagmus, a sluggish pupillary reaction, and lack of fixation and following light target suggested severely impaired visual function or even blindness in the otherwise healthy boy. Ophthalmoscopy revealed a healthy disc and fundus, and cycloplegic retinoscopy was normal for age at each examination. The first MRT revealed a cystic space-occupying lesion (9 × 10 × 12 mm) compressing the right optic tract and displacing the hypothalamus. These findings suggested an arachnoid cyst and posed the necessity of neurosurgical intervention, which would have been a complicated and risky operation. Onset VEP results suggested the presence of pattern recognition in both eyes at 4 months. Next, a gradual improvement in the wave morphology indicated the development of fairly good visual function. The surgery was postponed and the careful follow-up was continued. At 1 year of age, a significant regression (3 × 5 mm) of the cerebral inhomogeneity was observed in the repeated MRT. No compression of the chiasmatic region and normal myelination of the optic tract could be seen. At the age of 16 months, responses to the smallest check sizes appeared.

Conclusions: Arachnoid cysts are quite common, mostly asymptomatic and harmless findings among infants. In some rare cases, their surgical removal may be necessary when causing severe compression to major brain structures. When the morphological alteration does not accompany functional impairment, surgery can be postponed. In this infant, the careful follow-up by using onset-VEP guided the clinical decision-making. The nystagmus is still present at a slower frequency and it might be associated with hemianopia. The overall visual function of the toddler seems to be satisfying.

P1 19 Comparison of mfERG recordings with DTL and gold cup skin electrodes

Khaldoon O. Al-Nosairy, Theresa Eckermann, Michael B. Hoffmann

Otto-von-Guericke, Magdeburg, Germany

Purpose: (i) To compare mfERG recordings between DTL and gold cup skin electrodes in healthy young and old adults and (ii) to test the sensitivity of both electrodes to age-related changes in the responses.

Methods: Twenty participants aged 20–27 years (‘young’) and 20 participants aged 60–75 (‘old’) with a visual acuity of ≤ 0 (log-MAR) were included. The mfERG recordings were acquired using a 61-field stimulus spanning 5 eccentricities, using the VERIS Science 6.4.9d13, and complied with the ISCEV standard [1]. The mfERG responses were recorded simultaneously using DTL and skin electrodes placed along the lower lid and 5 mm below the lid margin. The outcome measures were the comparison and correlations of P1 amplitudes, peak times, and signal-to-noise ratios (SNRs) of the mfERG between electrodes and age groups. Furthermore, each electrode’s performance in discriminating responses between the age-groups was tested using area under curve (AUC) of receiver operating characteristic.

Results: Both electrodes recorded the typical waveform of mfERG recordings. The skin electrode, however, resulted in significantly (p < 0.001) smaller P1 amplitudes (DTL young [old]: 841.8 ± 182.13 nV [643.18 ± 170.46 nV], gold cup young [old]: 232.57 ± 68.68 nV [189.53 ± 42.87 nV]), shorter peak times (DTL young [old]: 33.2 ± 1.12 ms [35.29 ± 1.61 ms], gold cup young [old]: 33.58 ± 1.14 ms [33.79 ± 1.49 ms]), and smaller SNRs (log DTL young [old]: 0.79 ± 0.13 [0.71 ± 0.15], log gold cup young [old]: 0.37 ± 0.15 [0.34 ± 0.13]) compared to DTL electrodes. Nevertheless, all mfERG components showed strong significant correlation (r ≥ 0.25, p < 0.001) between both electrodes for all eccentricities. Both electrodes allowed for the identification of age-related P1 changes, i.e., P1 amplitude reduction and peak time delay in the older group. There was a trend to higher AUC for the DTL electrode (e.g., averaged P1 amplitude AUC DTL [gold cup] = 0.78 ± 0.07 [0.69 ± 0.09]) to delineate these differences between age groups which, however, failed to reach statistical significance (e.g., p = 0.219 for averaged P1 amplitude).

Conclusions: Both electrode types allow successful mfERG recordings. However, in compliant patients, the use of the DTL electrode appears preferable due to the larger amplitudes, higher SNR, and its better reflection of physiological changes, i.e., age effects. Nevertheless, skin electrodes appear a viable alternative for mfERG recordings. This might be of importance in patients who might not tolerate corneal electrodes such as children and disabled patients.

[1] Hoffmann MB, Bach M, Kondo M, Li S, Walker S, Holoogian K, Viswanathan S, RobsonAG (2021) ISCEV standard for clinical multifocal electoretinography (mfERG) (2021 update) Documenta Ophthalmologica 142:5–16.

P1 21 Visual electrophysiology phenotype in children with BBS1 mutation causing Bardet-Biedl Syndrome (BBS)

Ajeeta Patel1, Elizabeth Forsythe2, Sian E. Handley1,2, Robert Henderson2,3, William Moore3, Oliver R. Marmoy1,2, Dorothy A. Thompson1,2

1Tony Kris Vis Visual Electrophysiology Unit, Great Ormond Street Hospital for Children, London, United Kingdom. 2UCL Great Ormond Street Institute of Child Health, University College London, London, United Kingdom. 3Clinical and Academic Department of Ophthalmology, Great Ormond Street Hospital for Children, London, United Kingdom

Purpose: To elaborate on the natural history of retinal phenotype in children with BBS1 mutations in anticipation of forthcoming gene therapy.

Methods: A retrospective case note review of children with confirmed BBS1 mutation who underwent visual electrodagnostic testing (EDT) at a single specialist centre, Great Ormond Street Hospital (GOSH), UK, from May 2009 to January 2020 was carried out. Genotype, age, medical history, skin ERG, and pattern reversal VEP (prVEP) data were collated. Specifically, prVEP P100 amplitudes and peak times produced by 98% contrast black and white checks presented in a 30° field with check widths 100’, 50’ and 25’ were documented alongside flash ERG a- and b-wave amplitudes and peak times produced to a published alternative GOSH-ERG protocol. These data were compared to laboratory reference ranges.

Results: Of 28 patients with pathogenic variants in BBS1, 16 had Met390Arg homozygous variants and 10 were compound heterozygous with one Met390Arg. Two unrelated children were homozygous for truncating mutation of p.Asp145Glyfs*21. Age of BBS diagnosis ranged from 1 month to 9 years for the Met390Arg homozygotes, with 3/16 investigated for BBS having retinopathy as a primary presenting feature (mean age 8.3 years). BBS investigation was later for compound heterozygotes (1–14 years) and 7/10 had established retinal dysfunction at diagnosis (mean age 8.7 years). Age at first EDT was comparable for Met390Arg homozygotes (range 0.1–13.4 years, median 8.2 years) and compound heterozygotes (0.9–15.1 years, median 7 years). Children with compound heterozygous mutations had more severe retinal dysfunction compared to Met390Arg homozygotes of similar age. Flash ERGs were absent to all stimuli from 9/10 compound heterozygotes at a mean age of 7 years, with the youngest aged 3 years. In contrast only 3/16 of the Met390Arg homozygotes had absent ERGs, mean age 9 years, youngest 8 years. Met390Arg homozygotes with measurable flash ERG showed an array of retinal function: normal responses (n = 6),
rod-cone dysfunction (n = 5), and cone-rod dysfunction (n = 2). With increasing age progression of retinal dysfunction correlated strongest with a decrease in rod b-wave amplitude, seconded by increasing cone b-wave peak time. The two children with homozygous p.Aspl450G-lyfs*21 mutations had no detectable skin ERGs at EDT presentation (aged 11 and 16 years) with some pattern VEP evidence of central field preservation. Spearman’s rank correlation coefficient showed a positive association within Met390Arg compound heterozygotes for increased P100 peak time with increasing age to 100’, 50’, and 25’ check widths (rs 0.87, rs 0.73 and rs 0.75, respectively). This was less apparent for Met390Arg homozygotes (rs 0.38 for 100’ check width), with time to peak for the 50’ and 25’ checks within reference range up to and including the eldest patient aged 17 years.

Conclusions Most children with Met390Arg homozygous mutations undergo BBS1 associated retinopathy later compared to compound heterozygotes but may be younger when referred for BBS investigation due to other presenting features. Retinal change is most likely to manifest after age 5 years in these children as rod-cone dysfunction as is often cited, but can present as cone-rod dysfunction, with the likelihood for preservation of central macular function in the first two decades of life.

P1 23 Electroretinographic evaluation with skin electrodes in eyes with intraocular lymphoma
Jun Makita, Yuji Yoshikawa, Tomoyuki Kumagai, Yuro Igawa, Shunichiro Takano, Takeshi Katsumoto, Takluel Shoji, Masayuki Shibuya, Kei Shinoda
Department of Ophthalmology, Saitama Medical University, Iruma-Gun, Japan

Purpose To evaluate retinal function in eyes with intraocular lymphoma using skin electrodes.

Methods The ERG components in 11 eyes of 11 cases (male 4, female 7) aged between 38 and 88 years (mean ± SD, 69.4 ± 11.5) diagnosed with intraocular lymphoma from December 1, 2016, to May 30, 2022 at Saitama Medical University Hospital were reviewed.

Results Visual acuity ranged from hand movement to logMAR 1.2 (median 0.2). Cell cytology for the vitreous specimen showed class II in 2 eyes, class III in 6 eyes, class IV in 2 eyes, and class V in 1 eye. Immunoglobulin heavy chain (IgH) gene rearrangement was positive in 3 eyes. The severe attenuation of the ERG waveform amplitudes was found in 6 of 11 eyes (54.5%) in the dark adapted (DA) 0.01 b-wave, in 45.5% in the DA 3.0 a-wave, in 36.4% of the DA 3.0 b-wave, in 36.4% of the light-adapted (LA) 3.0 a-wave, in 18.2% of the LA 3.0 b-wave, and in 36.4% of the 30 Hz flicker response. No eyes showed negative shape (b/a ratio < 1.0) in DA 3.0 ERG. The DA 0.01 ERG was likely to be predominantly impaired. In the DA 3.0 and LA 3.0 ERGs, the a-wave tended to be equally or more severely altered compared to the b-wave.

Conclusions The ERG shows various changes in eyes with intraocular lymphoma which may suggest relatively severe dysfunction in the outer retinal layer.

P1 25 Phenotypical variation with age in CERKL gene-related retinitis pigmentosa in a single family
Deepika C. Parameswarappa
LV Prasad Eye Institute, Hyderabad, India

Purpose To describe the phenotype and genotype correlation of CERKL (Ceramide kinase-like protein) gene mutation-related autosomal recessive retinitis pigmentosa in four members of the same family.

Methods Four patients with autosomal recessive retinitis pigmentosa (RP) from a single family were examined. The retinal phenotypical features were correlated with CERKL gene variant changes within the family.

Results The family consisted of two sisters (39-year-old and 42-year-old) affected with autosomal recessive RP and their two male children (10-year-old son of the 39-year-old mother and 12-year-old son of the 42-year-old mother) affected with autosomal recessive RP. The children were born out of non-consanguineous marriage. The genotype confirmation was performed in the whole blood sample by targeted next-generation sequencing using Illumina chemistry. All the four affected members showed recessive (homozygous) frameshift deletion at exon 7 of CERKL. All four of them had central vision problems in childhood. The best-corrected visual acuity of the male children was 20/30 to 20/80 and both mothers were able to perceive only hand movements at the time of examination. The common phenotypical features in the affected sons at the younger age were minimal optic disc pallor, minimal arteriolar attenuation, early loss of macular photoreceptors, visual field showing central scotomas, and a severely affected near extinguished full-field electroretinogram. There were no pigmentary or chorioretinal atrophic changes in the retina noted in the children. The common phenotypical features in the affected mothers in the later part of life were prominent vascular attenuation, optic disc pallor, total macular atrophy, peripheral bony spicule pigmentation, peripheral scalloped chorioretinal atrophic patches, and an extinguished full-field electroretinogram.

Conclusions CERKL gene-related RP shows a wide spectrum of phenotypical changes in various age groups. The phenotypical features vary from early macular involvement and no typical retinal pigmentary abnormalities like RP in the first decade of life to severe macular atrophy and typical retinitis pigmentosa changes in the later part of life. The above family highlights the evolving phenotypical characteristics of CERKL gene-related RP over different age groups. The knowledge of changing phenotypes due to CERKL gene from early to later part of life helps in the appropriate diagnosis during younger age and provides guidance for future prognosis.

P1 27 Full field electroretinogram in ocular siderosis
Deepika C. Parameswarappa
LV Prasad Eye Institute, Hyderabad, India

Purpose To describe the full-field electroretinogram findings in 15 eyes of ocular siderosis from a tertiary eye care centre.

Methods Fifteen eyes of ocular siderosis were included in the study. The full-field electroretinogram (ffERG) was performed with the Metrovision system as per standard ISCEV protocol. The study was conducted at a tertiary referral eye care centre and was approved by the institutional review board. ffERG responses were analysed as isolated rod specific, mixed rod-cone, oscillatory potentials (OPs), single flash cone, and cone flicker responses.

Results All 15 eyes had an abnormal ffERG. 53% (8/15) of the eyes had severely affected ERG with extinguished rod specific, mixed rod-cone, OPs, and single flash cone responses. All 8 eyes with severely affected ERG had affected cone flicker responses as well. Of the 15 eyes, isolated rod-specific ERG responses were extinguished in 60% (9/15) and were subnormal in 33% (5/15). The mixed rod-cone ERG responses were extinguished in 53% (8/15) and were subnormal in 40% (6/15). The OPs responses were extinguished in 60% (9/15) of the eyes and were subnormal in 20% (3/15) of the eyes. The single flash cone ERG responses were extinguished in 53% (8/15) and were subnormal in 40% (6/15). Most of the eyes (12/15, 80%) had affected
Purpose: Anisah Kalam1, Anne L. Georgiou1, Magella M. Neveu1,2, Louis Philippe Dormegnie1, Sophie Gruchociak2, Carl F. Arndt1

P1 29 Evidence of both optic nerve and inner retinal dysfunction in patients with neuromyelitis optica
Anisah Kalam1, Anne L. Georgiou1, Magella M. Neveu1,2, Antonio Calcagni1,2, Neringa Jurkute1,2, Anthony G. Robson1,2
1 Moorfields Eye Hospital, London, United Kingdom. 2 UCL Institute of Ophthalmology, London, United Kingdom

Purpose: Neuromyelitis optica (NMO; Devic’s Disease) is a demyelinating autoimmune disorder, associated with serum auto-antibodies to aquaporin-4 (AQP4). AQP4 is an astrocyte water channel protein; thus, AQP4-antibodies lead to an autoimmune inflammatory process targeting optic nerves and spinal cord astrocytes. This study describes the electrophysiological findings in 4 NMO cases.

Methods: Four patients with AQP4 auto-antibodies and clinical signs of NMO and were ascertained. All underwent ISCEV-standard pattern reversal and flash VEP (PVEP, FVEP) and pattern and full-field ERG (PERG; ERG) testing. Two patients had comprehensive serial assessments over a 5-year period.

Results: Baseline PVEPs were abnormal in 3 subjects, with peak time delay in 4 eyes and moderate to severe amplitude attenuation in 3 eyes. In one patient, the baseline PVEPs were within the reference range bilaterally. Flash VEPs were abnormal without delay in 3 of 8 eyes. The PERG N95:P50 ratio was reduced in all subjects with an abnormal PVEP and there was additional shortening of P50 peak time in 2 of these cases. Full-field ERGs revealed DA 0.01 peak times that were delayed (N = 4 eyes), of borderline timing (n = 2 eyes), or within the reference range (2 eyes of 1 patient). The DA 10 ERG b-wave peak times showed borderline delay (95th percentile) in 2 eyes of 1 patient and a significant delay in 4 eyes of 2 other patients, including those of the waveforms resembling an electronegative ERG bilaterally. At five years follow-up, one patient with severely abnormal PVEPs at baseline showed partial recovery bilaterally but developed asymmetrical PERG delays (by 7 ms and 37 ms); another patient, who at baseline had unilateral PVEP delay (by 22 ms), N95:P50 ratio reduction, and bilaterally abnormal DA0.01 and DA10 ERG b-waves showed response stability.

Conclusions: A range of PVEP and PERG abnormalities were seen in patients with NMO, including evidence suggesting demyelination or evolving optic nerve conduction delay, with or without evidence of retinal ganglion cell involvement. Additional subtle to marked inner retinal dysfunction may be a common feature in NMO patients, but further studies are required to investigate the cause and better understand the pathogenesis and possible effect of AQP4 auto-antibodies on retinal function.

P1 31 Macular function after pneumatic vitreolysis
Louis Philippe Dormegnie1, Sophie Gruchociak2, Carl F. Arndt1
1 Reims University Hospital, Reims, France. 2 Pole Ophtalmologique de Champagne, Bezannes, France

Purpose: Recently gas injections have been reported in symptomatic vitreomacular traction (VMT). The consequences of pneumatic posterior vitreous detachment (PVD) on macular function have never been evaluated. We assessed the mFERG changes in patients undergoing pneumatic vitreolysis with perfluoropropane (C3F8) for symptomatic VMT.

Methods: The charts of patients undergoing 0.3 ml C3F8 gas injection for symptomatic VMT between January 1, 2021 and December 31, 2021 were examined in this study. The following parameters were noted before and 3 months after gas injection: best-corrected visual acuity, maximal horizontal vitreomacular adhesion, maximal foveal thickness (MFT) as determined with spectral domain optical coherence tomography, and mFERG parameters (N1, P1 amplitudes and implicit times).

Results: 45 eyes of 41 patients with symptomatic VMT had been treated in the predefined time frame. In five eyes, the mFERG had been recorded before and 3 months after gas injection. At 3 months, a significant change of MFT (p = 0.008) was observed. In the mFERG, no statistically significant changes in N1/P1 parameters (amplitude, implicit time) were found.

Conclusions: After pneumatic posterior vitreous detachment, despite improved thickness parameters on OCT, no significant electrophysiological changes were found. The mFERG recordings in a larger group of gas injected patients is necessary to confirm the stability of macular function after pneumatic PVD.
Vitamin A deficiency can be due to both congenital and acquired causes. It is common and to be expected in diseases with intestinal malabsorption, but in other causes of acquired deficiency, it is not present until the clinical manifestations are manifest. Night blindness or nystagmus in these cases is the first symptom to be noticed and may lead to the initial suspicion of retinal dystrophies. Therefore, an ophthalmological examination and the use of electrophysiological tests such as the electroretinogram are essential for the correct differential diagnosis.

Clinical case
We present the case of a 51-year-old male patient who came to the ophthalmology department for progressive visual impairment. Examination revealed cortic and nuclear cataracts in both eyes with discrete drusen outside the macular area and slight thinning of the neuroepithelium on macular optical coherence tomography (OCT). He underwent cataract surgery in both eyes with persistent low visual acuity. He also reported nystagmus and xerophthalmia. We performed ERGs, which showed severe loss of amplitude, predominantly scotopic responses (rods practically abolished); we were unable to assess alteration of the b/a ratio of the mixed response due to their low amplitudes. Given the findings, the patient was screened for any neoplasia due to suspicion of cancer associated retinopathy (CAR) and a vitamin A determination was requested. No tumours were found in the complementary tests, but vitamin A values of less than 0.02 mg/L were found. Treatment was started with Auzina A® at a severe deficiency rate, 2 capsules (100,000 IU of vitamin A) per day for 3 days, followed by 1 capsule (50,000 IU of vitamin A) per day for 2 weeks. In three weeks, the patient showed a clear improvement with 20/20 visual acuity and improvement of epiphora. ERGs at one month were within normal limits.

Conclusions
In clear cases of vitamin A deficiency due to malabsorption, such as in intestinal inflammatory disease or surgeries involving resection of the digestive tract, night blindness and xerophthalmia due to vitamin A deficiency may occur. In other cases, such as the one presented here, the visual deficit is not initially correlated with the patient’s nutritional deficit. Without other ophthalmological signs to justify it, retinal function tests such as the ERG give the necessary information to confirm the patient’s diagnosis. In cases of night blindness, vitamin A testing should be considered, especially if there is malabsorption or suspected nutritional deficiency. The ERG is a very useful tool for both diagnosis and follow-up, given that the changes are completely reversible following treatment with vitamin A.

P2 04 Range of clinical and electrophysiological phenotypes in GNB3- and GNB5-related retinopathies
Anupreet Tumber1, Heather MacDonald2, Regan Klatt2, Elise Heon1, Ajoy Vincent1
1Department of Ophthalmology and Vision Sciences, The Hospital for Sick Children, University of Toronto, Toronto, ON, Canada. 2Genetics and Genome Biology (GGB) Program, The Hospital for Sick Children Research Institute, Toronto, ON, Canada

Purpose
To describe the range of electrophysiology findings for GNB3- and GNB5-related disorders.

Methods
Two families with GNB3-related disease (4 affected; cases I-IV) and two families with GNB5-related disease (2 affected; cases V-VI) underwent ophthalmic examination including optical coherence tomography (OCT) and full-field ERG. Systemic features were obtained from chart review. ERG testing included the ISCEV recommended standard steps as well as extended and individualized testing protocols. For all patients, extended ERG testing consisted of a series of white flashes ranging in intensity from 0.006 to 30 cd m⁻² and red flash stimuli for the dark adapted (DA) ERGs and photopic On-Off responses for the light adapted (LA) ERG. Additionally, testing protocols consisted of an extended photopic stimulus–response series to white flashes ranging from 3.0 to 394 cd m⁻² for GNB3 patients. For GNB5, testing consisted of incremental inter-stimulus-intervals up to 60 s for DA 3.0, 10.0, and 30.0 ERGs and LA 30 Hz ERG durations ranging from 0.5 to 6 s.

Results
GNB3: One patient was asymptomatic (case I) whilst the others had childhood nystagmus, with late onset photophobia. Best-corrected visual acuity was 20/30 or better in all cases. Dilated fundus exams and OCTs were normal in all cases. Electrophysiologically, all GNB3 patients presented with normal rod photoreceptor function with moderate to severe rod ON-bipolar cell dysfunction and variably reduced cone sensitivity with partial or severe defects in cone ON-bipolar cell function. There were no systemic features in any subjects. GNB5: Both patients had varying levels of intellectual disability, global developmental delay, hypotonia, and sleep apnea. Case VI also had epilepsy, sick sinus syndrome, sinus bradycardia, escape beats, and poor feeding. The ophthalmic phenotype for case V included nystagmus and mild optic disc pallor, while case VI had progressive myopia with a myopic fundus appearance (tilted disc, peripapillary atrophy, tessellated fundus). OCTs for both patients were within normal limits. Electrophysiological findings of GNB5 were more varied. Case V had ERG findings that showed retinal signalling defects featuring bradyopsia and rod ON-bipolar dysfunction, while case VI demonstrated only a cone phototransduction recovery deficit with normal rod system function.

Conclusions
GNB3 and GNB5-related disease is variable, presenting with a range of unique ERG findings. In addition to a standard ophthalmic examination, ISCEV standard and extended or individualized ERG testing can discern the array of functional defects in such rare genetic disorders.

P2 06 Electroretinography in patients with moderate to severe multiple sclerosis
James V. M. Hanson, Sara Single, Veronika Kana, Christina Gerth-Kahleri
University Hospital Zurich, Zurich, Switzerland

Purpose
Although the effects of multiple sclerosis (MS) on the afferent visual system are often considered to be confined to the optic nerve and inner retinal ganglion cells, a number of studies over recent years have described abnormalities of the full-field electroretinogram (ERG) which are consistent with outer retinal dysfunction. To date, such studies have examined only patients with early or mild MS. Outer retinal function in patients with moderate to severe MS, in which neurodegenerative rather than inflammatory disease activity is more pronounced, remains unknown. We present here an interim analysis of the results of our ongoing study.

Methods
Patients with MS and Expanded Disability Status Scale score (EDSS) ≥ 3.0 were recruited from the neurology clinic at our hospital. Subjects underwent subjective refraction, measurement of best-corrected high- and low-contrast visual acuity (HCVA; LCVA), optical coherence tomography (OCT), and full-field ERG according to ISCEV standards. Generalised estimating equation (GEE) models accounting for age and sex were used to estimate the differences in ERG parameters between subjects and pre-existing clinical normative data. ERG amplitudes, peak times, and dark- and light-adapted (DA; LA) 3.0 b/a wave amplitude ratios were analysed. For this interim analysis, only ERG data was included in the GEE. P-values were
corrected according to the method described by Pipper et al. (Journ Roy Stat Soc, 2012; Series C 61:315–326). P-values < 0.01, > 0.01 < 0.05, and > 0.05 < 0.10 were considered strong, good, and mild evidence, respectively, of an effect of MS on the relevant parameter.

Results ERG data from 41 MS patients (38 medically treated; 25 with relapsing–remitting MS, 10 with secondary progressive MS, 6 with primary progressive MS; median EDSS 4.0; median disease duration 12 years 4 months; 77 eyes) and 46 normative subjects (79 eyes) of comparable age were compared in the GEE models. MS patients showed significantly delayed DA 3.0 a-wave and b-wave peak times compared to controls (estimated differences of 0.63 ms and 2.49 ms, corrected p-values < 0.001 and 0.008, respectively). No effects of MS on other ERG peak times or any ERG amplitudes or ratios were observed.

Conclusions Our interim results provide strong evidence for delayed DA 3.0 a- and b-waves in patients with moderate to severe MS, although the absolute differences are small and of uncertain clinical significance. The results are qualitatively slightly different from our previously published study of patients with early or mild MS (median EDSS 1.0; Hanson et al., IOVS, 2018;59:549–560), when we recorded evidence of significant delays to a larger number of ERG parameters as well as less conclusive effects on some ERG amplitudes. The different results may be due to an increased proportion of patients with confirmed progressive disease activity and/or effects of the different medical treatments in the present study. Final analyses will explore the influence of MS subtype and treatment status on ERG parameters in patients with MS.

P2 08 Atypical cases of enhanced S-cone syndrome (ESCS)?
Anne L. Georgiou1, Magella M. Neveu1,2, Antonio Calcagni1,2, Andrew Webster1,2, Anthony G. Rosson1,2
1Electrophysiology Department, Moorfields Eye Hospital, London, United Kingdom. 2Institute of Ophthalmology, University College London, London, United Kingdom

Purpose Enhanced S-cone syndrome (ESCS) is a rare autosomal recessive retinal dystrophy typically caused by variants of NR2E3. There is overexpression of S-cone opsin and reduced expression of L- and M-cone opsins and typically an absence of rod function, causing pathognomonic abnormalities in ISCEV standard ERGs. In addition, S-cone ERGs are often of abnormally high amplitude and are larger than LA 3 ERGs. This study describes four patients with unusual combinations of clinical and ERG findings that either overlap with or resemble those seen in typical cases of ESCS.

Methods Four patients were ascertained in the Department of Electrophysiology at Moorfields Eye Hospital, either with clinical or ERG features suggestive of ESCS, including two cases that had undergone genetic analysis. Fundus photographs, fundus autofluorescence (FAF), and optical coherence tomography (OCT) were reviewed. All patients underwent ISCEV-standard full-field and pattern ERG (ERG; PERG) testing and additional S-cone ERGs, using gold foil electrodes.

Results A 34-year-old patient had subretinal scarring and patchy loci of increased and decreased FAF. The ISCEV ERGs showed a pathognomonic pattern of abnormality; DA 10 and LA 3 ERGs had a low b:a ratio, and S-cone ERGs were of significantly high amplitude but with an unusual electronegative waveform. Genetic testing revealed novel pathogenic variants in NR2E3. A 27-year-old patient had typical nummular pigment, but FAF revealed concentric areas of increased and decreased signal; there was relative preservation of rod-dominated ERGs and LA 30 Hz ERGs were larger than the LA 3 ERG a-waves; the S-cone ERG was of significantly high amplitude (genetically unsolved). A 14-year-old girl showed typical yellow-white dots at the posterior pole, manifest as foci of increased FAF in the vicinity of the vascular arcades; the LA and S-cone ERGs were typical of ESCS, but there was relative preservation of rod-dominated responses (genetically unsolved). The oldest patient (57 years) had typical fundus and FAF features of ESCS but undetectable ERGs under all stimulus conditions. Genetic testing revealed known pathogenic variants in NR2E3. The youngest patient had a normal OCT but showed PERG P50 delay without amplitude reduction; the PERG in the remaining three cases was undetectable, with OCT evidence of macular schisis in one patient and extensive outer retinal changes with localised sub-foveal preservation in the other two.

Conclusions The phenotypic spectrum of ESCS ranges from undetectable DA and LA ERGs to unusually preserved DA ERGs in association with pathognomonic LA ERG characteristics. ISCEV ERGs consistent with ESCS can occur in NRL-related disease, but with unusual S-cone ERGs and atypical fundus features. Enlarged S-cone ERGs can occur without the standard pathognomonic LA ERG features. Macular dysfunction can occur in the absence of OCT abnormality.

P2 10 Comparison of signal-to-noise ratios for ERGs recorded with contact lens and skin electrodes
Stephanie Choi1, Karen Holopigian2, Vivienne Greenstein1, Scott E. Brodie1
1NYU Langone Health, New York, USA. 2Novartis Institutes for Biomedical Research, East Hanover, NJ, USA

Purpose Prior research has shown there to be high correlation between corneal contact lens (CL) and skin electrode amplitudes and that skin electrode amplitudes are about one-third the amplitude of contact lens electrodes. We aimed to measure the signal-to-noise ratio (SNR) using both methods for ERG recording.

Methods Twenty subjects referred for full-field ERG for multiple clinical indications had ERGs (obtained according to ISCEV standards) recorded simultaneously from both eyes with ERG-jet corneal CL electrodes and LKC Technologies Sensor Strip adhesive skin electrodes using multi-channel instrumentation (Diagnosys LLC, Espion3). Only photopic single-flash ERG responses were analyzed in this study. Photopic b-wave amplitude was used as the measure of signal strength. Baseline noise was calculated as the standard deviation of the waveform signal between 100 and 300 ms after the flash stimulus. The SNR was compared between corneal CL and skin electrodes using one-sided t-test with significance level of 0.05.

Results The CL electrode amplitude was 2.7 times the magnitude of the corresponding skin electrode amplitude. Absolute noise level with skin electrodes was slightly less than the noise level for CL electrodes (5.7 μV vs 7.1 μV, p = 0.035). The SNR using the CL electrode was significantly greater than with skin electrodes (22.8 vs 8.7, p < 0.001); the SNR using CL electrodes was 2.6 times greater than the SNR using skin electrodes.

Conclusions Both the amplitude and the signal-to-noise ratio are nearly three times greater using corneal CL electrodes as compared to skin electrodes.

Acknowledgements Sensor Strip adhesive skin electrodes for this study were provided by LKC Technologies, Inc., Gaithersburg, MD.

P2 12 Utility of electrodiagnostic testing following suboptimal outcome post amblyopia management
Ruth Hamilton1,2, Emily Robertson1, Eoghlan Millar1
1Electrophysiology Department, Moorfields Eye Hospital, London, United Kingdom. 2Institute of Ophthalmology, University College London, London, United Kingdom

Purpose Enhanced S-cone syndrome (ESCS) is a rare autosomal recessive retinal dystrophy typically caused by variants of NR2E3. There is overexpression of S-cone opsin and reduced expression of L- and M-cone opsins and typically an absence of rod function, causing pathognomonic abnormalities in ISCEV standard ERGs. In addition, S-cone ERGs are often of abnormally high amplitude and are larger than LA 3 ERGs. This study describes four patients with unusual combinations of clinical and ERG findings that either overlap with or resemble those seen in typical cases of ESCS.

Methods Four patients were ascertained in the Department of Electrophysiology at Moorfields Eye Hospital, either with clinical or ERG features suggestive of ESCS, including two cases that had undergone genetic analysis. Fundus photographs, fundus autofluorescence (FAF), and optical coherence tomography (OCT) were reviewed. All patients underwent ISCEV-standard full-field and pattern ERG (ERG; PERG) testing and additional S-cone ERGs, using gold foil electrodes.

Results A 34-year-old patient had subretinal scarring and patchy loci of increased and decreased FAF. The ISCEV ERGs showed a pathognomonic pattern of abnormality; DA 10 and LA 3 ERGs had a low b:a ratio, and S-cone ERGs were of significantly high amplitude but with an unusual electronegative waveform. Genetic testing revealed novel pathogenic variants in NR2E3. A 27-year-old patient had typical nummular pigment, but FAF revealed concentric areas of increased and decreased signal; there was relative preservation of rod-dominated ERGs and LA 30 Hz ERGs were larger than the LA 3 ERG a-waves; the S-cone ERG was of significantly high amplitude (genetically unsolved). A 14-year-old girl showed typical yellow-white dots at the posterior pole, manifest as foci of increased FAF in the vicinity of the vascular arcades; the LA and S-cone ERGs were typical of ESCS, but there was relative preservation of rod-dominated responses (genetically unsolved). The oldest patient (57 years) had typical fundus and FAF features of ESCS but undetectable ERGs under all stimulus conditions. Genetic testing revealed known pathogenic variants in NR2E3. The youngest patient had a normal OCT but showed PERG P50 delay without amplitude reduction; the PERG in the remaining three cases was undetectable, with OCT evidence of macular schisis in one patient and extensive outer retinal changes with localised sub-foveal preservation in the other two.

Conclusions The phenotypic spectrum of ESCS ranges from undetectable DA and LA ERGs to unusually preserved DA ERGs in association with pathognomonic LA ERG characteristics. ISCEV ERGs consistent with ESCS can occur in NRL-related disease, but with unusual S-cone ERGs and atypical fundus features. Enlarged S-cone ERGs can occur without the standard pathognomonic LA ERG features. Macular dysfunction can occur in the absence of OCT abnormality.
Association of psychophysical rod/cone flicker thresholds therapy but otherwise normal ophthalmic findings. Compliance or transition to different acuity test types. EDT is not relatively insensitive to the blur experienced in amblyopia dystrophies, or acquired forms of cortico-visual pathway dysfunction. The normal EDT findings in most of these children suggests that the EDT is useful for those who have retina, macula, or optic nerve pathology as it is sensitive to pathology in these areas. EDT is relatively insensitive to the blur experienced in amblyopia which typically causes marked abnormalities in letter acuity tasks. The normal EDT findings in most of these children suggests that the cause of sub-optimal acuity post-treatment relates to poor treatment compliance or transition to different acuity test types. EDT is not indicated for children with sub-optimal compliance with amblyopia therapy but otherwise normal ophthalmic findings.

P2 14 Association of psychophysical rod/cone flicker thresholds with full-field ERG parameters

Amithavikram R, Hathibelagal1,2, Diwaakar Karthikeyan1,2, Subhadra Jalali3,4, Brijesh Takkar3,5, Deepika Parameswarappa3

1Brien Holden Institute of Optometry and Vision Sciences, L V Prasad Eye Institute, Hyderabad, India. 2Prof. Brien Holden Eye Research Centre, L V Prasad Eye Institute, Hyderabad, India. 3Srinath Kanuri Santhamma Centre for Vitreoretinal diseases, Anant Bajaj Retina Institute, L V Prasad Eye Institute, Hyderabad, India. 4Jasti V Ramanamma Children’s Eye Care Centre, L V Prasad Eye Institute, Hyderabad, India. 5Indian Health Outcomes, Public Health, and Economics Research (IHOPe) Centre, L V Prasad Eye Institute, Hyderabad, India

Purpose Cone and rod-enhanced stimuli can be created by selectively choosing specific spatiotemporal properties such as duration, temporal frequency, luminance, chromaticity, and size of the target (Hathibelagal et al., Plos One:2020;15(7), e0232784). These stimuli detect rod-specific and cone-specific defects in patients with inherited retinal diseases (Hathibelagal et al., Ophthalmic Physiol Opt:2021;41(4): 874–884). However, the relationship between rod/-cone flicker modulation thresholds (FMT) and full-field rod/cone ERG parameters remains unexplored. This study aims to explore whether there is an association between objective and subjective photoreceptor-specific measurements.

Methods Twelve individuals (10 male, 2 female), mean age 27.5 ± 16.8 years, with a diagnosis of an inherited retinal disease (cone-dominated disease, n = 6; rod-dominated disease, n = 6), confirmed by history, fundus appearance, and ERG findings participated in the study. The inclusion criteria were age ≥ 10 years and visual acuity of at least 20/160 in the better eye, with no history of any other ocular pathology. Written informed consent was obtained from all the patients before they participated in the study. Full-field ERG was performed as per the ISCEV protocol (20 min of dark adaptation and 10 min of light adaptation) and then cone and rod-specific flicker modulation thresholds (FMT) were measured at five different locations (central, superotemporal, superonasal, inferotemporal, and inferonasal) in the central 5° of the visual field using a 2-down 1-up adaptive staircase procedure. Patients used a numeric keypad to provide their responses.

Results There was significant correlation of photopic flicker b-wave amplitudes and photopic flicker b/a ratio of the amplitudes with central cone FMTs (Pearson correlation; r = −0.71, p = 0.02 [n = 10; 2 instances, where the ERG waveform was not measurable] and r = 0.80; p = 0.03 [n = 7; 5 unmeasurable], respectively), whereas there was no significant association of distance visual acuity with flicker b-wave amplitudes (r = 0.43; p = 0.16) and also with cone FMT (r = −0.26; p = 0.41). However, none of the scotopic ERG parameters was significantly correlated with rod/cone FMT.

Conclusions Although full-field ERG provides a global response, there seems to be an association between photopic flicker ERG amplitudes and flicker thresholds, which indicates that flicker sensitivity increases with an increase in the ERG amplitudes. These results will help in a better understanding of pathogenesis, which can lead to better management of patients with inherited retinal diseases.
amplitude, PhNR/b-wave amplitude ratio, and PhNR implicit time improved significantly after surgery ($p = 0.008$, 0.002, and 0.039, respectively). The a-wave and b-wave amplitudes showed no significant difference between pre- and post-operative recordings. The a-wave and b-wave implicit time improved significantly after surgery ($p = 0.027$ and 0.004, respectively).

**Conclusions** Even in the early postoperative period (within several days of surgery), various retinal functions improved following filtration surgery.

**Acknowledgments** The authors thanks members of Saitama Medical University Ophthalmology Department.

**P2 18 Peak times and amplitudes of 16 and 32 Td s flicker ERGs in over 400 adult twins**

Tsz Lun Ernest Wong¹, Xiaofan Jiang¹,², Isabelle Chow¹, Andrew R. Webster², Pirro G. Hysli¹, Christopher J. Hammond¹, Omar A. Mahroo¹,²

¹Section of Ophthalmology, King’s College London, St Thomas’ Hospital Campus, London, United Kingdom. ²NIHR Biomedical Research Centre at Moorfields Eye Hospital and the University College London Institute of Ophthalmology, London, United Kingdom

**Purpose** Whilst the international standard full-field flicker ERG assesses light-adapted cone system function, other protocols are sometimes used that deliver ~ 30 Hz flicker stimuli without an adapting background. A portable ERG system (RETeval, LKC Technologies, Gaithersburg, MD) delivers 16 and 32 Td s stimuli as part of a protocol aiming to screen for diabetic retinopathy. In the present study, we analysed such recordings from a cohort of healthy adult twins, exploring correlations with age and heritability.

**Methods** Participants (adult twins recruited from the TwinsUK cohort) underwent recordings with natural pupils using the RETeval device. The RETeval monitors pupil size and adjusts stimulus strength accordingly to deliver a fixed retinal illumination of 16 or 32 Td s. Responses were recorded with Sensor Strip skin electrodes (LKC Technologies). Response peak times and amplitudes were recorded. Correlation with participant age was calculated for each parameter as well as coefficients of intrapair correlation in monozygotic (MZ) and dizygotic (DZ) twins. Where available, parameters were averaged from both eyes.

**Results** 440 adult twins (90% female) aged between 21 and 90 were included in this study. Median age was 70. Results of 88 complete MZ pairs and 55 complete DZ pairs were available for intra-pair analysis. Mean (SD) peak times from 16 and 32Td s ERGs were 29.4 (2.1) ms and 28.3 (2.0) ms, respectively. Mean (SD) amplitudes were 20.4 (7.0) and 24.0 (8.0) microvolts, respectively. For peak times, Spearman correlation coefficients with age were 0.50 and 0.48 ($p < 0.001$), respectively. For amplitudes, coefficients were $-0.27$ and $-0.32$ ($p < 0.001$), respectively. Intrapair correlation in peak times was statistically significant for MZ and DZ pairs for both stimuli ($p < 0.001$). For 16 Td s, correlation coefficients were 0.80 and 0.45 for MZ and DZ pairs, respectively. For 32 Td s, coefficients were 0.69 and 0.61 for MZ and DZ pairs, respectively. Similarly, intrapair correlation for amplitudes was statistically significant for MZ and DZ pairs for both stimuli. For 16 Td s, correlation coefficients were 0.73 ($p < 0.001$) and 0.31 ($p = 0.023$) for MZ and DZ pairs, respectively. For 32 Td s, correlation coefficients were 0.72 ($p < 0.001$) and 0.36 ($p < 0.023$) for MZ and DZ pairs, respectively.

**Conclusions** As is the case for standard light-adapted flicker ERGs, we found significant correlations with age: older participants had longer peak times and smaller amplitudes, with stronger correlations seen for peak times than amplitudes in this study. As the RETeval device adjusts for pupil diameter, age-related changes in pupil size would not be expected to play a role. For most parameters, intrapair correlation coefficients were much higher in MZ than in DZ pairs, indicating that genetic factors make a significant contribution to the variance in these parameters in healthy individuals.

**P2 20 Assessment of macular side effects of fingolimod used in treatment of MS patients by mfERG and OCT**

Randa H. A. Abdelgawad, Abdelrahman G. Salman, Thanaa H. Mohamed, Hala K. H. Elshahed, Dina A. Zamzam

Ain Shams University, Cairo, Egypt

**Background** Multiple sclerosis (MS) is an inflammatory demyelinating disease affecting the CNS. Multiple factors may be implicated in its development: immunological factors, vitamin D deficiency, vitamin B12 deficiency, or infection by EBV or HHV6. MS has many ocular manifestations, including optic neuritis, diplopia, nystagmus, and ophthalmoplegia. Fingolimod is the first approved oral drug for Relapsing Remitting Multiple Sclerosis (RRMS). Macular edema is a reported ocular side effect of fingolimod, developing after 3 to 4 months of treatment; it is dose-dependent and reversible.

**Purpose** The objectives of our study were to screen macular side effects of fingolimod used for treatment of RRMS patients with no previous ophthalmic complaints before starting the treatment, to assess the structural changes using spectral domain optical coherence tomography (SD-OCT), and to correlate these structural changes with the alterations in visual function (visual acuity assessment and electrophysiological studies).

**Methods** Thirty eyes of fifteen patients, who were about to begin fingolimod treatment were included in this prospective one arm clinical trial study. Patients were recruited from the MS unit, neurology department, Ain Shams University. We performed full ophthalmological examination and SD-OCT macular scan for all patients before starting treatment with fingolimod. We repeated SD-OCT and the ophthalmological examination with electrophysiological studies after 4 months of fingolimod treatment.

**Results** We found that there was non-significant reduction in the mean best corrected visual acuity after treatment. IOP measurements were not changed after treatment. Despite the changes in visual acuity, fingolimod associated macular edema did not develop. Among the 15 patients (30 eyes), 14 eyes showed slightly increased macular thickness (MT), 5 eyes had stable MT, and 11 eyes had slightly decreased MT. Regarding electrophysiological tests performed in the follow up, there was reduction in P1 amplitude in mfERG in ring 1 in 15 eyes, without development of macular edema (ME).

**Conclusion** Fingolimod is an immunomodulator drug used for treatment of RRMS. Fingolimod-associated macular edema is a known complication with low incidence. Patients on fingolimod should have baseline and ophthalmic examination and SD-OCT of the macula to detect macular edema; these studies should be repeated after 3 to 4 months of treatment. In our study, we found that after 4 months of fingolimod treatment, there were changes of retinal function in some patients before macular edema development. Functional alterations may be suspected to develop before macular edema. Further studies are needed to support our results. We are working on another study with larger sample size, longer follow up, and baseline mfERG recordings prior to treatment.
P2 22 Hilbert Transform Analysis of the rodent scotopic ERG reveals distinct oscillatory potential bursts
Anna Polosa1,2, Mercedes Gauthier1,3, Jean-Marc Lina1,4, Pierre Lachapelle1
1Department of Ophthalmology & Neurology-Neurosurgery, Research Institute of the McGill University Health Centre/Montreal Children’s Hospital, Montreal, Canada. 2Département d’ophthalmologie, Hôpital Maïonneuve-Rosemont, CIUSSS de l’Est-de-l’Île-de-Montréal, Montreal, Canada. 3Département de Génie Électrique, École de Technologie Supérieure, Montreal, Canada. 4Centre de Recherches Mathématiques, Montreal, Canada

Purpose To compare ERG oscillatory potential (OP) data obtained using the traditional time domain (TD; peak time and amplitude measurements) with the time–frequency domain Hilbert Transform Analysis (HTA) which transforms the TD OP signal into an analytical signal (i.e., a signal composed of real and imaginary parts).

Methods Pigmented mice (C57BL/6, n = 8) scotopic ERGs (intensity: −6.3 to 0.9 log cd s m−2) were recorded following 12 h of dark adaptation. To isolate the OP signal, ERGs were first filtered (zero-phase FIR filter; order: 150) and subdivided in 3 successive bandpass domains of 25 Hz (65–90 Hz; 90–115 Hz; 115–140 Hz). The HTA was then applied on each of the 3 narrowband OP signals, and a time varying envelope was obtained from which amplitude, time, and phase information was retrieved. To isolate the OP burst segment in each envelope, a threshold (at 97.5% critical value) was set. The total duration of the OP burst and the mean peak time difference (PTD) between frequency band envelopes were also measured.

Results TD and HTA revealed no significant differences between the duration of the OP burst signal (p = 0.503) and its amplitude (measured with SOPs and AUC, respectively). Results revealed that the highest number of OPs (10.7 ± 1.9) and the longest burst duration (103.51 ± 16.43 ms) occurred between intensities of −3.9 log cd s m−2 (i.e., retinal sensitivity) and −2.7 log cd s m−2 (rodVmax). Interestingly, at these dim intensities, HTA analysis revealed that the OP burst was composed of two major and distinct peaks per envelope (i.e., an early- and a late-onset OP burst) and PTD values were largest (38.2 ± 11.7 ms). With brighter flashes, the two OP bursts were progressively merged into a single peak per envelope and significantly decreased PTD values (3.5 ± 0.8 ms; p < 0.05).

Conclusions Our results show that, compared to TD analysis of the ERG, HTA provides additional information on the synchronicity of the signal in the time–frequency domain. The relationship between the duration of the OP burst and its synchronicity peak (i.e., PTD) suggests that longer bursts are more disorganized in their frequency composition, which could explain the increase in the number of OPs observed at these dim intensities. Of note, these changes in the dynamic of the OP burst (i.e., duration, synchronicity, number of OPs, split into early and late OP bursts, etc.) occur at intensities between retinal sensitivity and rodVmax, which could suggest the involvement of a pure rod retinal pathway, a concept that needs to be further investigated.

P2 24 Photometric comparison of the LED-based ColorFlash(TM) versus xenon flashlubes (Grass and SLE)
Oliver R. Marmoy1,2, Vikki A. McBain3, Bruce Hudson5, Dorothy A. Thompson1,2, Ruth Hamilton2
1Tony Kriss Visual Electrophysiology Unit, Clinical and Academic Department of Ophthalmology, Great Ormond Street Hospital for Children, London, United Kingdom. 2UCL-GOS Institute for Child Health, University College London, London, United Kingdom. 3Manchester Metropolitan University, Manchester, United Kingdom. 4Ophthalmology Department, Aberdeen Royal Infirmary, Aberdeen, United Kingdom. 5Department of Clinical Physics and Bioengineering, Royal Hospital for Children, NHS Greater Glasgow and Clyde, Glasgow, United Kingdom

Purpose Handheld flash stimulators are useful for paediatric visual electrophysiology and for some adult testing. Until recently, available stimulators were xenon flashtube-based stimulators, such as the Grass photic stimulator mounted in a handheld device, typically held at 30 cm from the subject. These devices are no longer manufactured. Our aim was to compare photometric properties of xenon flashlubes with a new commercially available LED-based flash stimulator, the ColorFlash(TM).

Methods Three different UK centres undertook similar photometric measurements: Great Ormond Street Hospital, London, Royal Hospital for Children, Glasgow (GOSH), and Aberdeen Royal Infirmary, Aberdeen (ARI). Photometric methods were unplanned but are compared in retrospect. An LT1700 photometer was used at all centres, with R barrel (RHCG + ARI) or SED033 barrel (GOSH) and Y filter (RHCG + ARI) or 21526 filter (GOSH). Each center performed photometric recording of xenon-based flash tubes followed by ColorFlash measurements (white 6500 k; GOSH also measured to ‘ALL’ and red/blue chromatic flashes) to a 4 ms flash at a range of time-integrated luminance levels to find photometric matches. GOSH: Measurements performed at 30 cm using 2 Hz (sets of three, repeated several times) flashes from two xenon flashlubes (PS33) with marbled diffusing plates at settings GR1-GR16. RHCG: Measurement performed at 20 cm using 1 Hz (sets of 10, repeated several times) from a xenon flashlube (Grass PS22 +) with opaque diffusing plate, at setting 4 (used clinically). ARI: As above (RHGC), at 2 Hz and from xenon flashlube (SLE CPS-20) setting 3 (used clinically).

Results GOSH: Xenon flashlube (Grass PS33) flash strength for GR4 intensity was 184–227.7 cd s m−2, with other GR1-GR16 flash strengths ranging from 78.46–1522.6 cd s m−2, respectively. ColorFlash nominal flash strengths were varied from 1–1462 cd s m−2, and measured flash strengths could photometrically match to all Grass flash intensities (within 0.01 log units), except GR16 as only 1400 cd s m−2 could be achieved with the white (ALL) ColorFlash setting. RHCG: Xenon flashlube (Grass PS22 +) mean flash strength was 42.8 cd s m−2. Colorflash nominal flash strengths were varied from 0.1 to 760 cd s m−2, and measured flash strengths were 0.08–737 cd s m−2. A photometric match to the Grass stimulus was achieved with a nominal ColorFlash value of 48, which measured 41.5 cd s m−2 (within 0.01 log units). ARI: Xenon flashlube (SLE CPS-20) mean flash strength was 4.7 cd s m−2. ColorFlash nominal flash strengths were varied from 3 to 6 cd s m−2, and measured flash strengths were 3–5.08 cd s m−2. A photometric match to the SLE stimulus was achieved with a nominal ColorFlash value of 5.5 which measured 4.6 cd s m−2 (within 0.01 log units).

Discussion We find that the ColorFlash stimulator is capable of photometric matching a range of currently used xenon-based flashlubes. This finding is important for considering repeated measurements of patients between devices. Two centers (GOSH + RHCG) have found preliminary flash ERGs in healthy adults were perceived as brighter and ERGs larger than xenon-based ERGs, despite photometric matching. We suspect this may be due to the longer stimulus duration of LED-based stimuli increasing time-integrated luminance. This highlights the need for local reference data for these LED devices as some ERG responses may be larger than Xenon-based counterparts.
P2 26 The occurrence of crossed asymmetry in children with albinism attending an Irish paediatric hospital

John C. Maguire1, Gillian O’Mullane2
1Children’s Health Ireland at Crumlin, Dublin, Ireland. 2Children’s Health Ireland at Temple Street, Dublin, Ireland

Purpose The occurrence of crossed asymmetry in children with albinism is documented at a rate of 80%.1 It was our aim to determine the occurrence of crossed asymmetry in children with albinism attending tertiary paediatric ophthalmology services in Ireland.

Methods We conducted a retrospective database and chart review of children assessed in both centres over a 7-year period. In order to identify patients diagnosed with albinism, a database search using the following keywords was used: albinism, nystagmus, foveal hypoplasia, blonde, pale fundus, iris trans-illumination, and hypopigmentation. After patients were identified, our outcome measure was the presence of pathway misrouting as determined by VEP.

Results In total, we found 33 patients with a diagnosis of albinism based on one or more clinical features of the condition who had undergone electrodiagnostic testing. VEP data from these patients was examined and re-analysed post hoc to look for evidence of pathway misrouting. Evidence of crossed asymmetry was present in 29 (88%) of the 33 patients. The degree of misrouting varied on a spectrum from subtle to extreme. A positive correlation between the degree of amplitude asymmetry and the albinism score of each patient was observed.

Conclusions This study reflects an occurrence rate consistent with international data. The VEP is a highly sensitive indicator of optic nerve misrouting and thus an important tool in the diagnosis of albinism, and this is applicable to the Irish paediatric population.

Charlotte C. Kruijt, et al., Invest Ophthalmol Vis Sci, 2019;60(12):3963–3969.

P2 28 Visual function in late-onset retinal degeneration

Stephanie Quinn, Andrew Browning, James Blake, Clare Warriner

Newcastle upon Tyne Hospitals NHS Foundation Trust, Newcastle upon Tyne, United Kingdom

Purpose Late-onset retinal degeneration (L-ORD) is an autosomal-dominant inherited retinal dystrophy which typically starts in the 4th-6th decade of life. Patients initially present with night vision problems as rod function deteriorates. As the disease progresses, there is additional cone photoreceptor involvement and neovascular changes, causing loss of visual field and acuity (VA). Loss of VA in L-ORD, as in other retinal dystrophies, occurs late into disease progression, often postdating loss of macular function. Despite this, standard VA is used clinically to monitor disease progression and assess visual function. More sensitive and detailed measures of visual function are available but are often time consuming and expensive. Different psychophysical measures of visual function have been shown to be more sensitive at assessing retinal function earlier in disease but are still not used routinely. This work aims to assess the relationship between psychophysical measures of retinal function including VA, low luminance VA (LLVA), and contrast sensitivity (CS), with detailed quantitative measures of visual function with the full-field ERG (ffERG) and pattern ERG (PERG).

Methods A total of 26 patients with genetically confirmed L-ORD (Ser163Arg mutation) were included, with ages ranging from 37 to 80 years. Participants underwent ffERG and PERG assessment in line with ISCEV standards. VA and LLVA were undertaken with a standard ETDRS letters chart at 4 m, either with best corrected vision or with a + 2 log neutral density filter. Low luminance deficit (LLD) was calculated by subtracting LLVA from VA. CS was measured using a Pelli-Robson letter chart.

Results Generalised cone retinal function measured with the light-adapted 3.0 cd s/m² single flash (LA3) and macular function measured with the PERG P50 component was abnormal in 77% and 74% of patients, respectively. Within these abnormal groups, VA was only abnormal in 40% and 41% of patients, respectively, whilst both LLVA and CS were abnormal in 75% and 82% of patients in LA3 and P50 measurements, respectively. Isolated rod function measured with the dark-adapted 0.01 cd s/m² (DA0.01) was abnormal in 88% of patients, whilst VA was only classed as abnormal in 39% of these patients; LLVA and CS were classed as abnormal in 70%. The LLD was raised in 54% of patients, indicative of presence of disease processes, within this group, 94% and 79% demonstrate abnormal DA0.01 and LA3.

Conclusions The data support the use of LLVA and CS as psychophysical measures of central retinal function to monitor disease. In this cohort of L-ORD patients, abnormal macular, rod and cone retinal function is seen in greater proportion in groups of reduced LLVA and CS than in reduced VA alone. The additional measurement of LLD represents a supplementary measure that we propose may be raised in cases of normal VA with abnormal quantitative visual function measurements prior to the onset of symptoms measured with standard psychophysical measures used clinically, therefore representing a prognostic indicator. Future data collection will investigate the prognostic utility of this measurement.

P2 30 Focal chorioretinal changes in children with mucopolysaccharidosis

Linda F. Shi1,2, Dorothy A. Thompson1,2, Oliver R. Marmory1,3,4
1Tony Kriss Visual Electrophysiology Unit, Clinical and Academic Department of Ophthalmology, Great Ormond Street Hospital for Children NHS Foundation Trust, London, United Kingdom. 2College of Health and Life Sciences, Aston University, Birmingham, United Kingdom. 3UCL-GOS Institute for Child Health, London, United Kingdom. 4Manchester Metropolitan University, Manchester, United Kingdom

Purpose In mucopolysaccharidosis (MPS), widespread glycosaminoglycan deposition may affect the cornea, trabecular meshwork, sclera, retina, and optic nerve. Early multimodal assessment with VEP, ERG, and retinal imaging can be crucial for diagnosis, monitoring, and visual preservation. We report imaging and visual electrophysiological features of six paediatric patients where we have observed an atypical and distinctive chorioretinal presentation involving peripapillary fundal findings corresponding to changes in the choroid.

Methods A case note review was performed for six patients with MPS showing chorioretinal changes on both ultra-widefield retinal imaging (Optos, Optomap) and spectral domain optical coherence tomography (SD-OCT, Spectralis®, Heidelberg Engineering). Visual electrophysiology data was available for all patients, with VEP and ERG recorded according to local GOSH protocol described previously (Marmory et al., Acta Ophthalmol.2022;100(3):322–330).

Results The six patients included MPS type I-S (n = 1), MPS type II (n = 2), and MPS type VI (n = 3). Median age of MPS diagnosis was age 2 years (range 9 months–4 years). Age at baseline ocular imaging ranged from 8–13 years, with imaging follow-up duration ranging from 7 months to 4.4 years. All six patients had distinctive hypopigmented areas often in an annular distribution around the optic disc. SD-OCT revealed focal choroidal compression with local steepening of the choroid-scleral junction at these areas. Three
patients (MPS I and II) additionally had a thickened external limiting membrane (ELM) with subfoveal hyperreflectivity which in two cases corresponded to a foveal hyperfluorescent spot on fundus autofluorescence (FAF). One MPS II patient had ERG evidence of severe inner and outer retinal dysfunction affecting rods more than cones, with progressive midperipheral hypoFAF changes. The other MPS II patient also had inner retinal dysfunction predominantly affecting the rod system and clinical reports of nyctalopia. Two further patients (MPS I and MPS VI) had milder selective attenuation of b/a wave ratio for the scotopic maximal flash stimulus. Rod-cone retinal dysfunction has been reported in MPS types I, II, and III while electronegative ERG has been previously reported in MPS types I, II, and V.

**Conclusion** Our data further corroborates sparse literature reports of this uncommon fundus presentation in patients with MPS types I, II, and VI. The chorioretinal changes may reflect scleral GAG deposition, though they appear non-progressive on shorter term follow-up. Despite marked choroidal thinning, it is yet unclear whether patients exhibit direct functional sequelae. Additionally, we show foveal ELM thickening on SD-OCT corresponding to foveal hyperFAF in some of these cases. This may occur independently or colocalise with the chorioretinal changes and could suggest GAG deposition within the central retina. These features warrant further investigation to better understand the implications for inner retinal function.

**Acknowledgements** All research at Great Ormond Street Hospital NHS Foundation Trust and UCL Great Ormond Street Institute of Child Health is made possible by the NIHR Great Ormond Street Hospital Biomedical Research Centre. The views expressed are those of the author(s) and not necessarily those of the NHS, the NIHR or the Department of Health.

**Publisher’s Note** Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.