Flash and Pattern ERG Findings in Schizophrenia and Their Relationships to Visual Function

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Purpose: In this ongoing study we are using flash and pattern electroretinography (fERG and pERG) to clarify the contributions of retinal signaling abnormalities to previously reported changes in contrast sensitivity, visual acuity, and contour integration in people with schizophrenia.

Methods: Data were collected on 24 patients and 25 age-matched healthy controls. fERG data were collected under both light- and dark-adapted conditions, using a range of flash intensities, backgrounds, and temporal frequencies. The primary fERG variables of interest were a-wave activity (reflecting photoreceptor response), b-wave activity (reflecting primarily bipolar cell activity) and the photopic negative response (PhNR) (reflecting ganglion cell activity). The primary pERG variables of interest were magnitude, magnitude D, and the magnitude D/magnitude ratio for low and high contrast stimuli.

Results: On photopic fERG tests, schizophrenia patients demonstrated significantly weaker photoreceptor response when a flash was presented against an unlit background (p<.05), and during a steady-state flicker test (p<.005). On scotopic tests, the ratio of response gain per unit of intensity increase was significantly weaker for patients than controls (group x condition interaction p=.001). In both light- and dark-adapted conditions, patients demonstrated weaker signaling of bipolar cells (p<.005). The schizophrenia group was also characterized by a weaker PhNR (p<.05). Multiple tests' a- and b-wave amplitudes were related to behavioral contrast sensitivity impairments in the schizophrenia group (p<.05 or .001), but not to visual acuity or contour integration. The groups did not differ significantly on pERG variables. For patients only, significant relationships were observed between poorer contour integration and reduced pERG amplitudes and longer latencies (all ps either <.05 or .001). For controls only, higher pERG values were related to better near and far visual acuity (ps <.05 or .1).

Conclusions: These data suggest that both reduced signaling of photoreceptor and bipolar cells, as well as attenuated response gain, are associated with schizophrenia. Both rod and cone responses appear to be affected, and these changes may be related to the contrast sensitivity reduction in this group. The issue of ganglion cell function in schizophrenia is less clear, but its relationships to contour integration warrant further study.

Commercial Relationships: Steven Silverstein, None; Docia Demmin, None; Roché Matthew, None; Quentin Davis, LKC Technologies, Inc. (E); Frank Taranto, Diopsys, Inc. (E); Aaina Menon, None.
The clinical standards for multifocal electroretinogram
Wendy W. Harrison
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Thirty subjects (age 27.1±3.5 years) with 20/20 vision and no retinal abnormalities were included. Subjects reported for two visits and were fully dilated to over 6 mm at both visits. At visit one a FFERG was recorded (VERIS 6.2) using our clinical protocol which includes an ISCEV standard flash sequence with an additional 10.0 log bright flash; each flash condition was repeated 4-6 times. Following the FFERG, an mfERG was recorded using a 4 minute m-sequence at near 100% contrast (VERIS FMSII). At visit two only the mfERG was recorded. A burian-ellen contact lens electrode filled with celluvisc was used for all recordings with a ground clip on the earlobe. The two mfERGs were compared for foveal and overall implicit time (IT) and amplitudes (amp). Paired t-tests were used to evaluate the data.

Results: There was a small but statistically significant difference in foveal amplitudes (p=0.004) wherein the amplitude was larger following the FFERG stimuli. When examining individuals this was true for 24 of the 30 subjects. The mean difference was 11.1 nV (100.9 nV vs 89.8nV). There was no difference in foveal IT (p=0.66). There was no difference in overall IT or amp when averaging the entire eye (p=0.27 amp and p=0.56 IT). Qualitative noise between the two recordings did not appear to differ.

Conclusions: The small difference in foveal amplitude is most likely the result of a small long term cone adaptation but further studies are needed here. While it is statistically significant, the small difference of 11 nV is unlikely to be clinically important. These results should help increase clinical confidence in mfERG results when recorded following a FFERG.

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Full-field ERG measurements of the photopic negative response recorded under four different conditions in a clinical setting

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Purpose: Accurate and precise measurement of the full-field ERG photopic negative response (PhNR) could be very useful as an estimate of the retinal ganglion cell function in various ophthalmic diseases. The purpose of this work was to evaluate and compare PhNR parameters recorded under four different conditions in a clinical setting.

Methods: A retrospective analysis of the PhNR records of patients undergoing routine clinical full-field ERG testing at USF (Tampa, FL) was conducted. All records had to have recordable PhNR response under four different conditions: red flash on a white background of 30 cd/m2 (Condition #1); red flash on a dim blue background of 1.9 cd/m2 (Condition #2); red flash on a bright blue background of 28 cd/m2 and a stimulation rate of 1 Hz (Condition #3) and red flash on a bright blue background and a stimulation rate of 2.8 Hz (Condition #4). The intensity of the red flash was kept at 5.35 cd.s/m2 for all conditions. The PhNR was measured at two locations on the ERG trace: before the i-wave (PhNR#1) and after the i-wave (PhNR#2).

Results: The records of 29 patients satisfied the criteria; one patient’s records contained significant artifacts; of the remaining 28 patients, 10 were males (50.4 +/- 20.4 yrs.) and 18 were females (45.9 +/- 20.5 yrs.). Statistical analysis demonstrated that there was no difference in PhNR#1 amplitude between the four conditions. However, Condition #1 and Condition #2 showed larger PhNR#2 amplitude compared to Condition #4 (p<0.05). Correlations between PhNR#1 and PhNR#2 amplitudes were high (0.84, 0.73, 0.71, 0.89). PhNR amplitudes were more correlated with the amplitudes of the corresponding a-waves (range 0.12 to 0.63) compared to the amplitudes of the b-waves (range 0.002 to 0.24) for every condition. Eye movement artifacts were relatively infrequent and interfered more with the PhNR#2 (6.8%) vs. PhNR#1 (4.1%) responses. In two patients, reliable PhNR responses could not be recorded in Condition #4 and the magnitude of eye movement artifacts were more pronounced in that condition.

Conclusions: Some conditions were more favorable for acquiring a reliable PhNR response compared to others. The implications for introducing PhNR into the clinical ERG standard are discussed.

Commercial Relationships: Erin G. Sieck; Robert Enzenauer, None; Michelle Pedler, None; Radouil T. Tzekov, None; Gonzalo Ortiz, None; Connor Hyde, None

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Presentation Time: 3:45 PM–5:30 PM

Effect of Induced Refractive Error on Electroretinograms

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Purpose: Prior studies have noted decreased amplitudes in myopic patients compared to age related controls in electroretinograms (ERGs). However, these studies did not account for any retinal degeneration commonly associated with myopia. In refractive error, there is an optical defocus of light that we hypothesized would decrease recorded amplitudes in the absence of retinal pathology.

Methods: Ten otherwise healthy rabbits were selected for our study. Refractive error was induced by placing Proclear Cooper Vision™ contact lenses with powers of -10D, +10D, -20D and +20D. Control ERGs were performed with no contact lenses first. The rabbits were then randomized into receiving varied strengths of contact lenses and ERGs were repeated. Six rabbits received +10 or -10D and four received +20D or -20D as a higher impact on ERGs with increasing refractive error was anticipated. ERGs were performed by standard protocol, with 20 minutes of dark adaption prior to scotopic testing. A total of three ERGs were performed per rabbit per eye.

Results: Step 1 of the ERG was analyzed for the dark adapted scotopic response as rods predominate in rabbit retinas. Comparing control ERGs to ERGs preformed with contact lenses, there was a statistically significant decrease in amplitudes using the two tailed paired t-test in 3 of the 4 groups of induced refractive errors. There was no difference of implicit times in both induced myopia or hyperopia. The greatest reduction in amplitude occurred with +20D induced myopia (n=4), with p=0.021 (95% CI 5.5 to 54.5). Induced myopia with +10D (n=6) noted significant decrease in amplitude, p=0.049 (95% CI 0.14 to 27.36). Lastly, induced hyperopia with -20D lens (n=4) also was found to significantly decrease amplitude, p=0.048 (95% CI 0.11 to 19.9). Induced hyperopia with -10D lens (n=6) was found to cause no statistically significant change, p=0.82.

Conclusions: ERGs remain a mainstay in visual prognosis. Based on our small study, both induced hyperopia and myopia decrease recorded amplitudes as predicted. It appears that there may be a relationship between decreasing amplitudes and increasing power of refractive error. Consequently, knowledge of high refractive errors would be important in considering abnormal ERG results.

Commercial Relationships: Erin G. Sieck; Robert Enzenauer, None; Michelle Pedler, None; Radouil T. Tzekov, None

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The late foveal response component in slow flash multifocal electroretinogram: A parametric study


Purpose: To investigate the characteristics of the late foveal response component (lfrc, Kariman et al. 2016) that presents only on the fovea on the first slice of the second-order kernel (K2.1) in multifocal electroretinograms (mfERGs) obtained with a slow base rate.

Methods: mfERGs with 103 hexagonal stimulus elements were recorded under a base rate of 18.75 Hz and a net recording time of 3 min 38 seconds using bipolar contact lens electrodes from four healthy subjects. The intensity of the stimulus (Ist) was changed parametrically, i.e., 0.16, 0.33, 0.67, 1.33, 2.67, 5.33, 10.67 c/ds/m2. Responses on the centermost 7 hexagons (with a diameter of 3.0–4.1°) were summed into a foveal mfERG.

Results: At Istim 0.33 c/ds/m2, measurable lfrc on K2.1 of foveal mfERGs was recorded initially from all subjects. The amplitude (0.5 ± 0.1 microV) was between the start (37.7 ± 5.5 ms) and the end (62.3 ± 1.3 ms) peaks. Istim 5.33 c/ds/m2 maximized lfrc (2.1 ± 0.4 microV between 43.7 ± 2.0 ms and 55.2 ± 3.0 ms). At the highest Istim 10.67 c/ds/m2, lfrc was reduced keeping the peak times unchanged (1.7 ± 0.6 microV between 43.5 ± 0.8 ms and 55.0 ± 5.3 ms).

Conclusions: Although the lfrc obtained with a 18.75 Hz base-rate differed in form from the lfrc with a 75 Hz base-rate, the timing of the potential change around at 50 ms was common. Dim flashes evoked the lfrc with an early start peak and a late end peak. At high Istim values, the behavior of lfrc was nonmonotonic, saturated with 5.33 c/ds/m2 and then decreased with 10.67 c/ds/m2.

Commercial Relationships: Yoshiaki Shimada, None

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Electrophysiological Characterization of Macular Telangectasia Type 2 (MacTel)
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Purpose: To investigate the electrophysiological features of Macular Telangectasia type 2 (MacTel) and their relationship to structure as determined by optical coherence tomography (OCT) imaging.

Methods: Retrospective observational study of patients enrolled in the MacTel Natural History Observation Study who had electrophysiological study as part of their diagnostic work-up. Forty-two eyes from 21 patients were analysed. All patients had full-field (ERG) and pattern (PERG) electroretinography with a subset of patients (n=13) additionally having multifocal electroretinography (mFERG). Multiple linear regression modelling assessed the relationship between size of the ellipsoid zone break on en-face OCT imaging to the mFERG central hexagon response amplitude.

Results: Full-field ERG was normal in all 42 eyes. Eleven eyes (26%) had subnormal PERG P50 amplitudes. Twenty of 26 eyes (77%) had reduced central or paracentral stimulus response on mFERG. There was a significant correlation between ellipsoid zone break size and both the P1 amplitude (Correlation coefficient B = -1.4, p = 0.002, overall model R² = 0.46) and P1:N1 ratio (B = -0.7, p = 0.002, R² = 0.45) of the central hexagon on mFERG.

Conclusions: The electrophysiological findings are consistent with the central localized involvement of MacTel type 2 demonstrated by OCT imaging and known from histological examination. There is a relationship between ellipsoid zone break size and mFERG reduction. The reduced P1:N1 ratio is in keeping with an inner retinal dysfunction. The mFERG is more sensitive than the PERG in demonstrating the highly localised dysfunction present in MacTel.

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Comparison of ERG responses obtained using a portable device and a conventional recording system

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Purpose: In pediatric centers, full-field electroretinography (ffERG) may be performed under anesthesia because of age or behavioral issues. The RETevalTM (LKC Technologies, Inc.) is a portable ERG device that uses skin electrodes and does not require pupil dilation. The aim of this study is to compare RETeval results to results obtained with a conventional ERG device (e2 and ColorDome; Diagynos LLC).

Methods: Full-field ERGs were recorded from 12 healthy dark-adapted adult volunteers (median age 22.5, range 20-39 years) using both recording systems. For the RETeval, pupils were undilated; a strip electrode array containing an active, a reference and a ground electrode was placed on the skin overlying the inferior orbital rim; and responses were recorded to the five standard ISCEV stimulus conditions. For the e2, one pupil was dilated; a bipolar Burian-Allen contact electrode was placed on the cornea and a ground electrode over the mastoid; and responses were recorded to series of scotopic flashes (dark adapted, -5 log range, blue) and photopic flashes (white background, ~2.4 log range, red). The ISCEV stimuli were included in these stimulus series. Amplitude and implicit time of the a- and b-waves were measured.

Results: Across the five ISCEV conditions, RETeval amplitudes were approximately 15% that of e2, and the average coefficient of variation was approximately 1.6 times larger for the RETeval amplitude data [mean (SD) 0.348 (0.041)] than for the e2 amplitude data [mean (SD) 0.222 (0.037)]. For the ISCEV scotopic conditions, a-wave and b-wave amplitude [Spearman’s rho; a-wave R=0.46, p<0.05; b-wave R=0.57, p<0.05] and implicit time [a-wave R=0.69, p<0.01; b-wave R=0.81, p<0.01] recorded by the RETeval correlated to e2 a-wave and b-wave amplitude and implicit time. Photopic and 30 Hz flicker measures obtained by the RETeval did not correlate to e2 measures.

Conclusions: While correlation was demonstrated, caution should be exercised translating results from one device to another. The high coefficient of variation indicates that larger sample sizes are needed to achieve similar statistical power. High variability may be a consequence of using a skin electrode. In a previous study, we found that the coefficient of variation for skin electrodes was 0.32 compared to 0.19 for Burian-Allen contact electrodes for subjects tested with dilated pupils and the conventional ERG.

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Modeling the pattern electroretinogram in patients with primary open-angle glaucoma
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Purpose: Previous work from our lab and others indicates that the pattern electroretinogram (PERG) may be modeled from responses generated by the flash electroretinogram (FERG) using appropriate stimulus patterns. Since patients with primary open-angle glaucoma (POAG) typically exhibit normal FERG responses, but reduced PERG responses, the present work sought to validate this PERG model by testing it in a sample of glaucoma patients.

Methods: Both transient (2.0 Hz) and steady-state (SS, 7.5 Hz) PERG and FERG responses were collected from a group of patients with diagnoses of severe POAG (N = 15, mean age = 71.6±2.41 years) and age-similar controls (N = 12, mean age = 61.00±3.52 years). The height and width of each stimulus subtended 14.3° ×14.3°. To create the PERG simulation, long-duration increment and decrement FERG responses were additively combined and then subjected to a series of modeling parameters that manipulated the amplitudes and phases of the individual responses to the increment and decrement flashes. Amplitudes were measured from both the actual PERG responses and the simulations for both the control group and the patient group.

Results: For PERG recordings, amplitude of the transient P50 component was found to be statistically equal between the control group and the POAG group. However, N95 amplitude was reduced in the POAG group relative to the control group (M = 1.198 vs. 2.201; t(25) = 2.522, p = 0.018), and this same pattern was found
for SS amplitudes of the POAG group relative to the control group (M = 0.573 vs. 0.347, t(25) = 2.621, p = 0.015). Using the modeling parameters that provided the best fit for each individual, the same pattern was found with the P50 showing no significant amplitude difference between the POAG and control group, but both N95 and SS amplitudes being reduced in the group with POAG relative to the controls (N95: M = 1.385 vs. 2.205, t(25) = 2.722, p = 0.012; SS: M = 0.322 vs. 0.438, t(25) = 2.372, p = 0.026). This suggests that both N95 and SS PERG responses can be successfully modeled using long-duration FERG responses.

Conclusions: Both the N95 and steady-state amplitudes from simulations could be adequately modeled in POAG patients and age-similar controls. Further studies with larger sample sizes will be required to address the predictive validity of PERG modeling as a tool for tracking disease progression in clinical populations.

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Presentation Time: 3:45 PM–5:30 PM

Evaluation of a soft, disposable, conformal ERG lens electrode prototype vs. Burian-Allen lens and DTL fiber electrodes

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Purpose: The Burian-Allen (B-A) contact lens electrode and the DTL fiber electrode (invented in 1954 and 1979, respectively) are the most frequently used electrodes in the US for recording the electroretinogram (ERG), but each present challenges with regard to convenience, safety and/or signal quality. A new design for an ERG electrode (RM) that overcomes many of the limitations of the B-A and DTL electrodes was developed (Fig. 1A-C) and compared to the older designs for signal quality, comfort and ease of use.

Methods: A soft silicone electrode substrate was designed to closely conform to the anterior surface of the eye and position a ring-shaped electrode outside the margin of a diluted pupil. The electrode is recessed within a channel and makes electrical contact via the tear film. The substrate extends beneath the eyelids for stability, and is shaped to prevent blinking. The three electrode styles were compared using full-field flash stimuli in a dark-adapted healthy subject. Responses were evaluated for pre-stimulus noise, a- and b-wave amplitudes, and repeated-measure variability.

Results: Mean a-wave amplitudes (+/-1 SD) were significantly larger with the RM electrode (198+/-13 uV) compared to the B-A electrode (92+/-3 uV) and the DTL electrode (145+/+-13 uV); similar results were obtained for b-wave amplitudes. The B-A reference electrode picks up a measurable ERG signal, which is then subtracted from the signal recorded at the corneal electrode by differential amplifiers. A-wave amplitudes for repeated stimuli were most consistent with the B-A electrode, and least consistent with the DTL electrode (standard deviation as % of mean: 4% for B-A, 7% for RM, 9% for DTL). Both DTL and B-A electrodes had significant baseline drift (+/-200 uV) compared to the RM design (+/-50 uV). The RM design was more comfortable and less imposing during installation than the B-A but comparable to the DTL.

Conclusions: The greater signal to noise ratio and lower baseline drift observed with the RM electrode design is attributed to the increased stability on the eye, optimum corneal contact and reference electrode location. These advantages are obtained in a soft, disposable design, increasing patient comfort and safety.
Routine Testing of Visual Evoked Potential Asymmetry in Pediatric Patients with Albinism
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Purpose: Visual evoked potential (VEP) asymmetry in which a preponderance of nasal and temporal retina afferents project to the contralateral hemisphere after full-field monocular stimulation is considered to be specific to albinism. In this study, we examined whether a commercially available VEP testing unit, under ordinary clinical conditions, could evaluate VEP asymmetry in pediatric patients with albinism.

Methods: Monocular transient pattern onset/offset VEP testing was performed using a UTAS Visual Diagnostic Test System manufactured by LKC Technologies Inc.® (MD, USA). The stimuli were presented on a 19-inch Acer LCD monitor. Three scalp electrodes were positioned with reference to bony landmarks and in proportion to the size of the head, according to the International 10/20 system. The center electrode was placed at Oz and the lateral electrodes placed at O1 and O2 (about 3 cm away on both sides of Oz). Only VEP results obtained from the lateral electrodes were analyzed.

Results: Between January 2016 and November 2016, 16 albino children of various types from OCA 1-4 (63% male; age range: 0.25-14.2 yo, with mean age of 5.07 yo) were recruited. The VEP results in 11 children (69%) were irreproducible in both right (OD) and left (OS) eyes recorded at both O1 and O2. In the remaining 5 children (31%), reproducible VEP results were found in only one eye at one of the lateral electrodes, or in only one eye at both lateral electrodes, making determination of laterality impossible in this cohort.

Conclusions: VEP asymmetry can only be determined using reproducible recordings in both eyes. Our current routine clinical VEP testing using a pattern onset/offset with the commercially available LKC UTAS Visual Diagnostic Test System paired with an LCD monitor is insufficient to determine asymmetry in a mixed clinical population of patients with albinism. This could be due to the difficulty for LCD displays to maintain the mean luminance during the transition from checkerboard pattern to diffuse blank screen in a pattern onset/offset presentation.
To characterize the changes of flash visual evoked potential (fVEP) in patients with early-sickie-cell retinopathy according to hemoglobin type.  

**Methods:** In this pilot study, we included patients with non-proliferative sickle-cell retinopathy, with bilateral preserved visual acuity (>20/25), between November 2014 to April 2016. All patient underwent a ffERG, according to the ISCEV standards. Six eyes of healthy patients were used as control group. Scotopic ERG responses for the successive spatial frequencies were 119.11ms (95% CI:112.06 to126.16), 116.88ms (95% CI:112.22 to 121.48) and 125.37ms (95% CI:123.03 to 127.71) for the three spatial frequencies. 

**Results:** For fVEP in OU stimulation, the wave amplitude of 0-N1 were significantly decreased at 8wks post exposure (vs. the baseline p=0.027), There were no significant differences in P1-N1 and N1-P2. In OD stimulation, the wave amplitudes of 0-N1, P1-N1 and N1-P2 were significantly decreased at 8wks post exposure (vs. the baselines p=0.012, 0.046 and 0.009). In OS stimulation, there were no significant changes of wave amplitudes being observed. For fVEP latencies in OD stimulation, there were only significant differences in P1-N1 at 72h, 1w and 2wks post exposure (vs. the baseline p=0.019, 0.026 and 0.006). There were no significant differences of the latencies in OS or OU stimulations. fERG b-wave amplitudes in OD were significantly decreased at 72h and 2wks post exposure (vs. the baseline p=0.024 and 0.013). There were no significant differences of b-wave amplitude in OS, and a-wave amplitudes in both OD and OS. There were no significant changes of fERG latencies in OD and OS in both a-wave and b-wave. 

**Conclusions:** The single blast exposure resulted in abnormal wave amplitudes and latencies in fVEP and fERG in rats. The head accelerations may cause blast related TBI and responsible for such changes. The morphological studies in visual neurons will be useful to elucidate the mechanisms of such visual dysfunction.

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**Presentation Time:** 3:45 PM–5:30 PM

**Visual Evoked Potential as a Clinical Tool with Regard to mTBI**

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**Purpose:** Can biasing the magnocellular pathways with pattern reversing checkerboard stimulus using successive spatial frequencies while simultaneously measuring the Visual Evoked Potential latency be an indicator of the neural impulse. If the VEP is an indicator, then it can determine dysfunction of the retina neural network represented by the loss of synchronization or the successive differing spatial frequencies resulting from mTBI when compared to normal patients. Will visual therapy remedy the cognitive and related motor disorders, resulting in a synchronized VEP.

**Methods:** Fiftysix normal controls ranging in age from 13 to 67 year-old, fortyone mTBI patients ranging in age from 13 to 67 year-old, were tested with Diopays NOVA Vision Testing System’s VEP ad hoc module to measure their electrophysiological visual function’s responsen to successively presented with 16x16, 32x32 and 64x64 checkerboard stimuli at a 15% Michelson contrast level. Twentoy mTBI patients received treatment and had VEPs obtained post treatment. The latencies of the normal controls were compared to the latencies of the mTBI patients pre and post treatment. The Pearson’s coefficient was calculated for the pre and post treatment population at the three spatial frequencies.

**Results:** The VEP’s P100 latency is an indicator of the neural impulse. Normal controls average P100 latencies was 102.40ms (95% CI:99.96 to104.70), 112.45ms (95% CI:110.34 to114.55) and 125.37ms (95% CI:123.03 to 127.71) for the successive spatial frequencies. This upward slope is interpreted as synchronization of the retina’s neural network. The mTBI patients showed a loss of synchronization. The VEP responses for the successive spatial frequencies were 119.11ms (95% CI:112.06 to126.16), 116.88ms (95% CI:112.22 to 121.48) and 120.70ms (95% CI:117.52 to 123.88). Post treatment VEP latencies of successive stimulus are: 107.36ms (95% CI:102.83 to 111.90), 114.45ms (95% CI:110.42 to 118.49) and 125.92ms.
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each stimulus permutation. VEP amplitudes from each participant were averaged for each stimulus type and data from trichromatic participants were analyzed using repeated-measures ANOVA for linear trends.

**Results:** One participant was missing 2x2-grating data at the O1 recording site and was excluded from these analyses (O1 N=4, O2 N=5). Typical waveform features (P1, N1, P2) were consistent across participants. At O1, a quadratic analysis produced large effect sizes, which we interpreted given our sample size limitations: VEP amplitudes decreased with lower spatial frequencies, then increased with higher spatial frequencies for P1 and N1 values ($\eta^2=0.40$ for P1; $p=0.05$; $\eta^2=0.38$ for N1). The opposite was true for P2 values ($\eta^2=0.25$, $p=0.04$ for P2). At O2, large effect sizes were present for a linear trend (also non-significant): VEP at P1 and P2 increased in amplitude with increasing spatial frequency ($\eta^2=0.63$ for P1; $p=0.001$; $\eta^2=0.33$ for P2); no trend was evident at N1. No pairwise amplitude comparisons were statistically significant, although large O1 N1, O2 P1, and O2 N1 $\eta^2$ values implied differences with a larger N.

**Conclusions:** The cortical responses to luminance contrast masked by chromatic noise were reliable among the subjects and this pilot study suggests VEP sensitivity to the combined impact of luminance and color on the visual system. Future work should expand on statistical trends observed here to confirm reliability of the VEP’s sensitivity to these measures.

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**Presentation Time:** 3:45 PM – 5:30 PM
**Relative genetic and environmental contributions to variations in electroretinogram responses quantified in a twin study**
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**Purpose:** To estimate heritability of parameters of human retinal electrophysiology in a classic twin study, and explore changes with age.

**Methods:** Adult monozygotic (MZ) and dizygotic (DZ) twin pairs were recruited from the TwinsUK cohort. Electroretinogram (ERG) responses were recorded using conductive fibre electrodes in response to stimuli incorporating standards set by the International Society for the Clinical Electrophysiology of Vision (ISCEV). ISCEV parameters were extracted, and, in addition, photopic negative response (PhNR, originating from retinal ganglion cells) and i-wave components were extracted from responses to the photopic single flash. Parameter values were averaged from both eyes. Mean values were calculated for the cohort. Coefficients of correlations with age were calculated (using one twin from each pair). Coefficients of intra-pair correlation were calculated for MZ and DZ twins. Age-adjusted heritability estimates were derived using structural equation modelling.

**Results:** Responses were recorded from 210 participants (59 MZ and 46 DZ twin pairs). 93% were female. Mean (SD) age was 62.4 (11.4) years. In general, age correlated negatively with response amplitudes, and positively with implicit times. Correlations were statistically significant ($p<0.05$) and moderate or strong (coefficient $>0.35$) for the following parameters: scotopic standard and bright flash a-wave implicit times; photopic 30 Hz flicker and single flash b-wave implicit times; PhNR and i-wave implicit times. Intra-pair correlations were higher for MZ than DZ twins, suggesting important genetic influences. Age-adjusted estimates of heritability were significant for all parameters (except scotopic dim flash b-wave implicit time), ranging from 0.34 to 0.85. Highest estimates were for photopic single flash a-wave and b-wave amplitudes (0.84 and 0.85 respectively).

**Conclusions:** Most parameters showed significant heritability, indicating genetic factors are important, determining up to 85% of the variance in some cone system response parameters. Parameters relating to retinal ganglion cell function were also heritable, and showed increasing delay with age. Scotopic responses tended to show lower heritability (possibly relating to greater rod system susceptibility to environmental factors).

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