Reversal Rate Dependence and Nasal-Temporal Field Differences in High Luminance Peripheral Pattern Electroretinogram (ppPERG) Responses in Healthy Human eyes

S Patangay 1, Z Derafshi 1, JCPark 2, E Ghabhari 2, T Vajaranant 2, JJ McAnany 2, JR Hetling 1,2
1 Department of Bioengineering, University of Illinois at Chicago
2 Department of Ophthalmology and Visual Sciences, University of Illinois at Chicago

Abstract Number: 5765

Contact: JHetti1@uic.edu

I. Introduction

• Ganglion cell (GC) dysfunction due to glaucoma typically begins in the mid-periphery. The pattern ERG (pPERG) evokes a response dominated by GC's, and is a sensitive measure of GC dysfunction associated with glaucoma.

• The conventional pPERG stimulus subtends approximately 4.5 degrees of visual angle. A pattern stimulus that probes the red- and far-peripheral retina may be advantageous for detecting early stage glaucoma.

• The conventional pPERG stimulus is technology limited to 100 ph s^-1. A pattern stimulus course that delivers higher luminance may elicit larger amplitude responses, potentially decreasing test time to reach acceptable SNR.

• Here we recorded pattern ERG responses elicited from the red- and far-peripheral retina, using a three-dimensional high-luminance stimulus source.

• These peripheral pattern ERG (ppPERG) responses were characterized with respect to reversal rate and field subtended in healthy eyes. In addition, ppPERG responses were compared to conventional pPERG in a small group of glaucoma patients.

II. Methods

A. Pattern stimulus was delivered to the peripheral retina as a hexagonal spiral. Field subtended (30°–40° field angle) in all directions. Unless otherwise stated, mean ON luminance was 1070 photopic candelas per square meter (cd/m^2) for the nasal field, 15 degrees of visual angle. A pattern stimulus that probes the red- and far-peripheral retina may be advantageous for detecting early stage glaucoma.

B. Responses recorded with DTL, normal electrodes, reference and ground on ipsilateral temple and neck, respectively.

C. ppPERG responses were amplified 30,000x, passed 3-1000 Hz, and digitized at 5 kHz. Responses were recorded in 5-second epochs until at least 200 “clean” pattern reversals were recorded.

ppPERG response waveform analysis. Waveforms were recorded from six normally-sighted subjects, and five glaucoma patients. Panel A. Typical ppPERG response waveform (p=1.500 Hz) exhibits high- and low-frequency components; these were isolated prior to evaluation of each response for amplitude and implicit times. Panel B. Isolated low-frequency components (5.57 Hz). Amplitude of the early positive component (P) was measured from baseline; amplitude of the late negative component (N) was measured from P. Panel C. Isolated high-frequency components (58-1000 Hz). F2 was measured from baseline to peak; F1 and F2 are measured from the preceding trough to peak. For all components, peak and trough amplitudes were evaluated as the maximum or minimum values within standard time windows defined by the average response across the normally-sighted subjects.

Participants. Normally-sighted subjects had no history of eye disease, normal visual acuity, RNFL thickness within normal limits, and refractive error that ranged from -3 to +0.25 diopters. Patients with primary open-angle glaucoma had acuity better than 20/40, no media opacity, no prior glaucoma surgery, and HIV mean deviation ranged from -3.80 to -7.02.

III. Results – Healthy Eyes

Dependence of ppERG responses on reversal rate. Panel A. Average temporal ppPERG response waveforms (n=6) at 3, 6, 4.6 and 9.2 reversals per second (RPS). Panel B. Isolated low-frequency components. Panel C. Isolated high-frequency components. Panel D. Amplitude of each response component (P, N, F1, F2, F3) at each reversal rate. Panel E. Implicit time of each response component at each reversal rate. Error bars in D and E plot ± one SD.

On average, with increasing reversal rate, amplitude of P increased (3.3 μV, p<0.05) and decreased (1.0 μV RMS, r=0.02). The differences in amplitudes were statistically significant with 5.2-9.2 and 6.0-9.81 stimulus responses were significant for P (R=0.02), and nearly so for F2 (R=0.06). The high-frequency components were nearly constant for all reversal rates.

ppERG responses from nasal and temporal fields. Panel A. Average ppERG response waveforms (n=6) elicited by a dot check pattern presented to the nasal or temporal field. Stimulus pattern subtended 22°-23° of visual angle; this was achieved by moving the subject away from the stimulus source to a point where the visual edge of the pattern was no longer observed by the bridge of the nose. Panel B. Isolated low-frequency components. Panel C. Isolated high-frequency components. Panel D. Amplitude of each response component (P, N, F1, F2, F3) evaluated for each field subtended. Error bars in D and E plot ± one SD.

The mean amplitudes of both P and N were larger in the temporal field, but not significantly (p=0.07, 0.17, respectively). The high-frequency component amplitudes were nearly constant in both fields. The difference in amplitudes may be due to the nasal-temporal asymmetry in ganglion cell density (Caruso and Allen, 1990).

Cluster analysis comparing ppPERG and ppERG responses in glaucoma. Each subject (n=6) and patient (n=5) response was plotted in an dimensional feature space, where n=4 for ppERG (amplitude and implicit time of N1 and P1; ps) and n=4 for ppPERG (amplitude and implicit time of P1 and N1, ps). The distance of each patient/subject from the healthy mean was calculated (leave-one-out cross validation for normally-sighted subjects). Panel A. Histogram plotting ppERG results. Panel B. Histogram plotting ppERG results.

Correlation of functional test results with RNFL thickness. Euclidean distance from the healthy eye mean in the feature space plotted against retinal nerve fiber layer (RNFL) thickness. RNFL was converted to percent of normal for each participant’s age group. Panel A. Results for P1, slope of best fit line = -0.039 μV. Panel B. Results for pPERG, slope of best fit line = -0.26 μV.

IV. Results – Glaucomatous Eyes

V. Summary

• Test and re-test repeatability was high. Inter-subject variability of high-luminance ppPERG responses are comparable to conventional (SCEV standard) pPERG responses (CV = 18 and 11 for ppPERG and pPERG, respectively [Otto and Bach, 1997]).

• On average, the ppPERG response component N decreased more rapidly (5.0 μV RMS) with reversal rate than N1 in conventional pPERG (0.6 μV RMS) for normal subjects from 2-7 RPS, reported by Bentinger and Schuurmans (1995).

• High frequency ppPERG response components were relatively insensitive to reversal rate over the range investigated.

• The ppPERG P and N components were slightly (not significantly) larger in the temporal field (nasal retina), which may reflect the known nasal-temporal asymmetry in ganglion cell density (Caruso and Allen, 1990).

• Cluster analysis of the small glaucoma population studied here suggests significantly higher sensitivity of ppPERG responses to glaucomatous damage compared to conventional pPERG.

Acknowledgments

We thank the local vascular surgeons and Prevent Blindness Illinois for technical assistance. We thank Steven Lee for his help with data collection. We are grateful to the Center for Research on Vision and Aging for their support of this research.