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Pattern Electroretinogram and Psychophysical Tests of Visual Function for Discriminating Between Healthy and Glaucoma Eyes

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Abstract

Purpose—To compare the diagnostic accuracy of the pattern electroretinogram (pattern ERG) to that of standard automated perimetry (SAP), short-wavelength automated perimetry (SWAP), and frequency-doubling technology (FDT) perimetry for discriminating between healthy and glaucomatous eyes.

Design—Cross-sectional study.

Methods—83 eyes of 42 healthy recruits and 92 eyes of 54 glaucoma patients (based on optic disc appearance) from the University of California, San Diego, Diagnostic Innovations in Glaucoma Study were tested with pattern ERG for glaucoma detection (PERGLA, Lace Elettronica, Pisa, Italy), SAP, SWAP, and FDT within 9 months. Receiver operating characteristic (ROC) curves were generated and compared for pattern ERG amplitude and SAP, SWAP and FDT mean deviation and pattern standard deviation (PSD). Sensitivities and specificities were compared and agreement among tests was described.

Results—The area under the ROC curve for pattern ERG amplitude was 0.744 (95% Confidence Interval = 0.670, 0.818). The ROC curve area was 0.786 (0.720, 0.853) for SAP PSD, 0.732 (0.659, 0.806) for SWAP PSD and 0.818 (0.758, 0.879) for FDT PSD. At 95% specificity, sensitivities of SAP and FDT PSD were significantly higher than that of pattern ERG amplitude; at 80% specificity, similar sensitivities were observed among tests. Agreement among tests was slight to moderate.

Conclusion—The diagnostic accuracy of the pattern ERG amplitude was similar to that of SAP and SWAP, but somewhat worse than that of FDT. Nevertheless, the pattern ERG may hold some advantage over psychophysical testing because of its largely objective nature.

Glaucoma is a neurodegenerative disease that results in optic nerve damage and characteristic visual field loss.¹ Although glaucoma is treatable, early detection is important because lowering intraocular pressure reduces the rate of glaucomatous progression. Psychophysical tests of visual function have been developed to detect early glaucomatous visual loss and standard automated perimetry (SAP) is the current clinical standard.² SAP is a relatively non-selective test in that all subtypes of retinal ganglion cells are sensitive to its stimulus.³ More recently, function-specific tests that target sub-populations of retinal ganglion cells preferentially, though not exclusively, have become available.⁴ These function-specific tests

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include short-wavelength automated perimetry (SWAP) and frequency-doubling technology (FDT) perimetry. SWAP presents a blue light on a yellow background to emphasize the response characteristics of the blue-yellow (koniocellular) pathway⁵⁻⁷ and FDT perimetry uses a rapidly reversing contrast grating to emphasize the response characteristics of the magnocellular pathway.^{8, 9}

The psychophysical tests of visual function described above are subjective in nature. Their results can be affected by fatigue, inattention to stimulus presentation and learning effects.¹⁰ Furthermore the decision criterion can vary from participant to participant. As an example, when testing with psychophysical tests, “trigger-happy” participants are more likely to respond to near-threshold targets than participants that adopt a more conservative decision strategy.¹¹ Electrophysiological tests of visual function have the advantage of being generally objective and unaffected by patient response. The pattern electroretinogram (pattern ERG) is an electrophysiological test that assesses the function of retinal ganglion cells by isolating the ganglion cell response using a reversing checkerboard or grating pattern that carries no change in average luminance over time. Recently, a pattern ERG measurement paradigm designed specifically for glaucoma detection (pattern ERG for glaucoma detection)¹² has been introduced that attempts to optimize stimulus (e.g., short test duration) and recording (e.g., use of skin electrodes) characteristics for ease of clinical use.

In the current study we compared the diagnostic accuracy of objective pattern ERG for glaucoma detection to that of the subjective SAP, SWAP and FDT tests for discriminating between healthy eyes and those with glaucomatous optic neuropathy.

METHODS

Participants

Eighty-three healthy eyes of 42 healthy recruits, and 92 eyes with glaucomatous appearing optic discs (i.e., glaucomatous optic neuropathy) of 54 glaucoma patients enrolled in the University of California, San Diego Diagnostic Innovations in Glaucoma Study were included in this study. All eyes were tested with pattern ERG, had good quality stereo-photography of the optic disc and reliable SAP, SWAP and FDT, within 9 months (eyes included were all Diagnostic Innovations in Glaucoma Study eyes meeting these criteria; no eyes were excluded for poor quality photography or unreliable visual function testing).

In addition to the testing described above, each study participant underwent a comprehensive ophthalmologic evaluation including review of medical history, best-corrected visual acuity testing, slit-lamp biomicroscopy, intraocular pressure (IOP) measurement with Goldmann applanation tonometry, gonioscopy, and dilated slit lamp fundus examination with a 78 diopter lens. To be included in the study, participants had to have a best-corrected acuity better than or equal to 20/40 at study entry, spherical refraction within $\pm 5.0D$ and cylinder correction within $\pm 3.0D$, and open angles on gonioscopy. Eyes with coexisting retinal disease, uveitis, or non-glaucomatous optic neuropathy were excluded.

Eyes were classified as healthy or having glaucomatous optic neuropathy based on subjective clinical assessment of stereoscopic optic disc photographs. Simultaneous stereophotographs were obtained after maximal pupil dilation using Topcon camera (TRC-SS; Topcon Instrument Corp of America, Paramus, NJ). Each photograph was assessed by two experienced graders using a stereoscopic viewer (Asahi Pentax StereoViewer II; Asahi Optical Co, Tokyo, Japan) and a standard fluorescent light-box. Each grader was masked to the participants' identity, clinical diagnoses, results from the other grader, and other test results. When the two graders disagreed, a third experienced grader adjudicated. The classification of glaucomatous optic neuropathy was based on neuroretinal rim-thinning, notching, excavation, or nerve fiber layer

thinning (focal or diffuse) characteristic of glaucoma. Neither intraocular pressure (IOP) nor results from perimetric testing were considered when classifying eyes as glaucomatous optic neuropathy. Healthy eyes required healthy appearing optic discs and no history of increased IOP 22 mm Hg OU, regardless of perimetric testing results.

The average age (95% CI) of healthy individuals was 63.6 (61.4, 65.8) years and the average age of patients was 70.4 (68.2, 72.5) years [$p(t) < 0.02$]. Fifty-five (66%) healthy individuals and 53 (57%) patients were female [$p(\chi^2) = 0.24$]. IOP at the time of pattern ERG recording was similar in healthy and glaucomatous optic neuropathy eyes [14.99 (14.13, 15.84) mmHg and 14.21 (13.39, 15.02) mmHg, respectively; $p(t) = 0.19$].

Pattern Electoretinogram Testing

A commercially available modification of the Glaid (Lace Elettronica, Pisa, Italy, software version 2.1.14) electrophysiology instrument, called PERGLA was used to measure the pattern ERG response.^{12, 13} The pattern ERG for glaucoma detection stimulus is a black and white (contrast 98%, mean luminance 40 cd/m²), horizontal square wave grating (1.6 c/deg), counter-phasing at 8.14 Hz, presented on a computer monitor (14.1 cm diameter circular field). At a viewing distance of 30 cm, the display subtends 25 deg centered on the fovea (assuming fixation towards a prominent central fixation circle). Responses from both eyes are measured simultaneously. Electrical signals from silver-chloride skin electrodes (9 mm adhered with conductive cream and tape) (both lower eyelids active, both temples referenced, forehead ground) are fed into a two-channel differential amplifier, amplified (100,000 fold), filtered (1–30 Hz) and then digitized with 12-bit resolution at 4,169 Hz. Before testing, the electrode impedance is monitored automatically and an on-screen indicator signals acceptable impedance (≤ 5 k Ω). Additionally, an on-screen oscilloscope displays background noise.

The pattern ERG for glaucoma detection software obtains each waveform by averaging 600 artifact-free time-periods (i.e., sweeps) of 122.8 msec each, synchronized with the contrast alternation of the stimulus grating. Two independent response blocks of 330 sweeps each are recorded and separated by a user-defined inter-stimulus interval. For each block, the first 30 sweeps are rejected from the average to eliminate onset effects from the steady-state recording. Sweeps containing spurious signals attributable to blinks and eye movements are rejected over a threshold voltage of ± 25 μ V. Resulting steady-state pattern ERGs take the form of near-sine waves that are Fourier transformed to isolate the harmonic component at the contrast reversal rate (16.28 reversals per second). In addition, a noise response is obtained by multiplying alternate sweeps by 1 and -1 before averaging. The noise response also is Fourier transformed at the contrast reversal rate to allow calculation of SNR. Previous studies indicate that repeatability of pattern ERG for glaucoma detection measurements is excellent.^{12, 14–16}

The same operator (AT) tested all participants. Test time was approximately 4 minutes per test, although preparation and electrode placement added approximately 5 minutes per examination. All eyes were refracted, appropriate corrections for viewing distance were made and near acuity was Jaeger acuity of 1 or better for all participants.^{13, 17} Participants were asked to fixate on a small circle in the center of the display screen and the operator monitored fixation subjectively.

Psychophysical Testing

All tests assessed the central 48 degrees (52 test points) of the visual field and required fixation by the patient (monitored by instrument software). Adequate refraction was provided for each device and the pupils had a diameter of at least 3 millimeters. The pupils were dilated when this requirement was not met. All tests were reliable, defined as false positives $\leq 15\%$, fixation

losses and false negatives $\leq 33\%$ with no observable testing artifacts. The order of testing was randomized across participants.

Standard Automated Perimetry—Each participant was tested using the 24-2 program on the Humphrey Field Analyzer II, using the Swedish Interactive Thresholding Algorithm (SITA)¹⁸ version 4.1 (Carl Zeiss Meditec Inc, Dublin, California). The target used in this achromatic test is a 0.43° flash of white light presented on a 10 cd/m^2 background for 200 milliseconds (msec). This instrument and its operation have been described in great detail previously.¹⁹

Short-Wavelength Automated Perimetry—Each participant was tested using the 24-2 program with SITA¹⁸ (version 4.1). SWAP targets the short-wavelength sensitive cones and pathway with a bluish (440-nm wavelength) narrow-band target of 1.8° presented for 200 msec on a bright (100 cd/m^2) yellow background.⁶ The details of this test have been described elsewhere.⁵

Frequency-Doubling Technology—Each participant was tested using FDT with the Humphrey Matrix (i.e., 24-2) FDT Visual Field Instrument (Carl Zeiss Meditec, Dublin, CA) with Welch–Allyn technology (Skaneateles Falls, NY) and the Zippy Estimation by Sequential Testing (ZEST) thresholding algorithm.²⁰ FDT measures the contrast necessary to detect vertical grating targets that undergo counter-phase flicker. Each target subtends 5° of visual angle, has a spatial frequency of 0.5 cyc/deg and counter phases with a temporal frequency of 18Hz. The test is based on the frequency-doubling illusion and is sensitive to glaucomatous visual field loss. The details of the test have been described elsewhere.⁹

Analyses

Student's t-tests were used to compare continuous measures of pattern ERG amplitude and SAP, SWAP and FDT mean deviation (MD) and pattern standard deviation (PSD) between healthy and glaucomatous optic neuropathy eyes. Differences with $P \leq 0.05$ were considered statistically significant. For each visual function test, we generated receiver operating characteristic (ROC) curves for discriminating between healthy and glaucomatous optic neuropathy eyes. The relative diagnostic accuracies of pattern ERG and the psychophysical tests were assessed by comparing areas under the ROC curves. Statistically significant differences between areas under the ROC curves were determined using the method of De Long et al.²¹

Using the ROC curve of each test, we derived abnormality cut-offs at moderate (approximately 80%) and high (approximately 95%) specificities for all parameters. The ROC-derived abnormality cut-offs associated with the set specificities of 80% and 95% were applied to classify each test as normal or abnormal to determine sensitivity. Sensitivities at each specificity cut-off were compared among parameters using McNemar's test.

The level of agreement at the 80% and 95% specificity cut-offs among the tests (pattern ERG amplitude, SAP PSD, SWAP PSD, FDT PSD) also were assessed using the kappa (κ) statistic.²² Kappa values range from zero to one, with values between 0.00 and 0.20 indicating slight agreement, 0.21 and 0.40 indicating fair agreement, 0.41 and 0.60 indicating moderate agreement, 0.61 and 0.80 indicating substantial agreement, and 0.81 and 1.00 indicating almost perfect agreement.

RESULTS

Table 1 compares pattern ERG for glaucoma detection amplitude and SAP, SWAP, and FDT MD and PSD between healthy and glaucomatous optic neuropathy eyes. Significant differences

(all $p(t) \leq 0.04$) were found for all parameters between groups. Pattern ERG amplitude was decreased by approximately 31% in glaucomatous optic neuropathy eyes compared to healthy eyes, SAP threshold (most appropriate perimetry analog for pattern ERG amplitude) was decreased by approximately 9%, SWAP threshold was decreased by approximately 11%, and FDT threshold was decreased by approximately 18%.

Table 2 shows the areas under the ROC curves obtained for each parameter from each test, the 95% confidence interval (CI) associated with each area under ROC curve and the sensitivities at set specificities of approximately 80% and 95%. We compared pattern ERG amplitude to SAP, SWAP and FDT tests based on the abnormality cut-offs obtained for PSD only. Two reasons prompted this decision: 1) the ROC-derived PSD was the best parameter (that with the highest area under the ROC curve) for all three tests and 2) PSD performs better at distinguishing between normal and glaucoma subjects than MD, although MD may be better for determining progression.²³ Figure 1 shows the ROC curves for pattern ERG amplitude and SAP, SWAP and FDT using PSD. The area under the ROC curve for FDT PSD (0.818) was significantly greater than that obtained for pattern ERG amplitude (0.744; $p = 0.04$). No statistically significant differences were observed between pattern ERG ROC curve area and those of SAP PSD (0.786; $p = 0.17$) and SWAP PSD (0.732; $p = 0.41$).

At 95% specificity, 18/92 (19.6%) of glaucomatous optic neuropathy eyes had an abnormal pattern ERG amplitude, 33 (35.9%) had an abnormal SAP PSD, 27 (29.3%) had an abnormal SWAP PSD and 42 (45.7%) had an abnormal FDT PSD. McNemar's tests showed that the sensitivities of SAP ($p = 0.02$) and FDT ($p = 0.0002$) were significantly greater than that of pattern ERG. No significant difference was found between the sensitivities of SWAP and pattern ERG ($p = 0.05$). At 80% specificity, McNemar's test showed no significant difference between the sensitivities of pattern ERG and those of SAP ($p = 0.20$), SWAP ($p = 0.90$) and FDT ($p = 0.23$).

At 95% specificity, there was slight agreement between pattern ERG amplitude and SAP PSD (76% agreement, $\kappa = 0.14$, CI = 0.00, 0.31) and between pattern ERG amplitude and FDT PSD (74% agreement, $\kappa = 0.19$, CI = 0.03, 0.34), while the agreement between pattern ERG and SWAP PSD was fair (82% agreement, $\kappa = 0.30$, CI = 0.12, 0.49). Agreement among SAP, SWAP and FDT PSD was substantial for all pairs (Table 3). At 80% specificity, slight agreement was found between pattern ERG amplitude and SWAP PSD, while pattern ERG amplitude showed fair agreement with SAP and FDT PSD. There was fair to moderate agreement among the psychophysical tests.

A Venn diagram showing the number of glaucomatous optic neuropathy eyes with abnormal results on each test at 95% specificity for amplitude (pattern ERG) and for PSD (SAP, SWAP and FDT) is presented in Figure 2. Thirty-eight of the 92 glaucomatous optic neuropathy eyes (41%) had normal results on all four tests, while 7 glaucomatous optic neuropathy eyes (8%) had abnormal results on all tests. Some glaucomatous optic neuropathy eyes had abnormal test results uniquely on SAP ($n=3$, 3%), FDT ($n=9$, 10%) and pattern ERG ($n=7$, 8%). A similar diagram is shown for 80% specificity (Figure 3).

DISCUSSION

Previous studies have shown a significant reduction in pattern ERG amplitude in glaucoma (and ocular hypertensive, OHT) eyes when compared to healthy eyes (see Trick for review²⁴) using both steady-state and transient stimuli with some evidence that the steady-state response is more sensitive to glaucomatous changes.^{25, 26} Consistent with these studies, our results showed significantly reduced pattern ERG in glaucomatous eyes compared to healthy eyes. While previous studies have shown that pattern ERG is able to distinguish

between healthy and glaucomatous eyes, the present study compares its diagnostic accuracy to that of the most commonly used psychophysical tests of visual function in the same population.

The diagnostic accuracy of pattern ERG amplitude (area under the ROC curve = 0.744) was statistically similar to that of SAP PSD (see also Bowd et al., using an overlapping data set²⁷) and SWAP PSD (areas under the ROC curves = 0.786 and 0.732, respectively). However, pattern ERG has the possible advantage of being a largely objective test in which participants are not required to actively respond to the visual stimulus that is presented (although fixation on the test stimulus is required, similar to psychophysical tests). In this respect, pattern ERG (and other electrophysiological tests, such as multi-focal visual evoked potential testing^{28, 29}) may be more useful than psychophysical procedures, particularly in participants that have difficulty producing reliable results on psychophysical tests.

The diagnostic accuracy of pattern ERG was somewhat worse than that of FDT (area under the ROC curve = 0.818). This is not surprising because previous studies have shown that FDT has better diagnostic accuracy than both SAP and SWAP.³⁰ However, another study³¹ comparing pattern ERG amplitude, FDT MD and SWAP MD in SAP-normal fellow eyes of eyes with repeatable SAP defects (n = 36), and healthy eyes (n = 36) reported a slightly higher area under the ROC curve for transient pattern ERG amplitude (area under the ROC curve = 0.78) than for FDT MD (area under the ROC curve = 0.72). This finding likely was attributable, in part, to the use of a previous generation FDT (C-20 version) that tests only the central 40 deg of the visual field (C-20 results might be more fairly compared to pattern ERG than 24-2 results, but this version of FDT technology is obsolete). The area under the ROC curve for SWAP in the described study was 0.82.

Pattern ERG is a central vision test (assesses vision out to 12.5° from fixation) and glaucomatous defects of the visual field usually first manifest peripherally. As a result, it is possible that a significant proportion of our early glaucoma patients had primarily local peripheral defects undetectable by pattern ERG but detectable by perimetry, in particular FDT. Theoretically FDT might be more sensitive to peripheral defects because of the distribution of magnocellular cells (primarily) that it tests.³² While FDT may be better at detecting early glaucoma than pattern ERG, no studies to date have reported its ability to monitor glaucomatous progression. The ability of a specific method to detect visual field progression is dependent on minimal variability of repeat measurements in healthy and/or stable eyes and a sufficient dynamic range. Previous studies indicate that pattern ERG for glaucoma detection measurements of amplitude are highly reproducible,^{12, 14–16} suggesting promise for its ability for change detection, however the dynamic range of pattern ERG might not be ideal¹⁴ compared to FDT.³³

Pattern ERG amplitude is negatively correlated with IOP and age in healthy eyes.¹² Many eyes in the current study were treated using IOP lowering medication and induced decreases in IOP may result in concomitant increases in pattern ERG amplitude. This effect may have decreased somewhat the diagnostic accuracy of the pattern ERG in the current study. On the other hand, the significant difference in age observed between healthy recruits and patients may have increased its diagnostic accuracy. A *post-hoc* assessment of the association between age and pattern ERG amplitude revealed that a difference in age of approximately one decade results in a decrease in pattern ERG amplitude of approximately 10%. For SAP, SWAP and FDT, both MD and PSD are age adjusted so age differences likely did not have a similar effect on these tests. However, the diagnostic accuracy of these tests may have been increased by the exclusion of tests that did not meet our reliability criteria based on software provided reliability indices. Although the pattern ERG for glaucoma detection paradigm removes noise from

recordings and requires acceptable electrode impedance, it currently does not have algorithms to assure test reliability.

At high specificity (95%) the sensitivity obtained for pattern ERG amplitude was significantly lower than that obtained for SAP and FDT PSD and was similar to that of SWAP PSD. Because glaucoma is a slowly progressing disease, high specificity levels are desirable to avoid false positive diagnoses. This is because detection one or two visits earlier may be unlikely to improve the long-term prognosis for glaucoma suspect eyes. However, seven glaucomatous eyes were uniquely identified by pattern ERG, suggesting that electrophysiological and psychophysical tests may provide complementary information. Alternately, these eyes could represent false positive results.

Agreement among tests was best when comparing psychophysical tests to other psychophysical tests. This finding may be attributable in part to pattern ERG amplitude being a massed ganglion cell response from the whole retina.^{34–37} The psychophysical tests of visual function used in this study evaluate thresholds at many discrete locations. This difference in testing strategy (massed response versus discrete locations) may account for the marginal agreement between pattern ERG and each of the psychophysical tests. Furthermore, the psychophysical tests evaluate areas beyond those of the maximal eccentricity allowed by pattern ERG (as described above).

The lack of a truly independent gold standard for glaucoma is a limitation common to all glaucoma detection studies and this limitation may have affected our reported diagnostic accuracy and agreement among tests. To minimize classification bias, we did not use a measure of visual function to classify our participants into study groups, and instead required that patients show evidence of glaucomatous optic neuropathy on stereophotographs. It is possible that some glaucomatous optic neuropathy eyes were misclassified using this subjective technique. Another limitation of this study is that we did not require confirmation of test results. Without confirmation, previous studies have shown that sensitivities may be inflated due to the presence of false positive results.³⁸ Finally, we acknowledge that this study had insufficient statistical power (i.e., < 0.8039) to prove pattern ERG less accurate than SAP PSD and more accurate than SWAP PSD (areas under the ROC curves were 0.744, 0.786, and 0.732, respectively). The number of participants in the current study was chosen to approximate the 100 eyes in each group needed to attain a power of approximately 90% for detecting an area under the ROC curve difference of 0.05 with a two-tailed $\alpha = 0.05$. However, because we included both eyes of many individuals, and because results from both eyes likely are correlated somewhat, the power of the current study to detect an area under the ROC curve difference of 0.05 likely was decreased. Given a larger sample, it is possible that significant differences among the diagnostic accuracies of pattern ERG amplitude, SAP PSD and SWAP PSD would be observed.

Overall, our results suggest that pattern ERG amplitude using the pattern ERG for glaucoma detection paradigm is significantly different between healthy eyes and early glaucoma eyes, and the diagnostic accuracy of pattern ERG amplitude likely is similar to that of SAP and SWAP and somewhat worse than FDT. Pattern ERG (and other electrophysiological techniques) has the advantage of being a mainly objective visual function test and may be useful for patients who are unable to perform reliably on psychophysical tests.

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Figure 1.

Areas under the receiver operating characteristic (ROC) curves for discriminating between healthy and patient eyes for pattern electroretinogram (ERG) for glaucoma detection amplitude and standard automated perimetry (SAP), short-wavelength automated perimetry (SWAP) and frequency doubling technology perimetry (FDT) mean deviation (MD) and pattern standard deviation (PSD). The area under the ROC curve for pattern ERG for glaucoma detection amplitude (0.744) is significantly smaller than that of FDT PSD (0.818). The area under the ROC curve for SWAP MD (0.570) is significantly smaller than that of all other parameters.

Figure 2.

Venn diagram showing the number of glaucomatous optic neuropathy eyes with abnormal results at the 95% specificity cut-off for pattern electroretinogram (ERG) for glaucoma detection amplitude, standard automated perimetry (SAP) pattern standard deviation (PSD), short-wavelength automated perimetry (SWAP) PSD, and frequency-doubling technology perimetry (FDT) PSD. 38 glaucomatous optic neuropathy eyes were classified as within normal limits by all four tests.

Figure 3.

Venn diagram showing the number of glaucomatous optic neuropathy eyes with abnormal results at the 80% specificity cut-off for pattern electroretinogram (ERG) for glaucoma detection amplitude, standard automated perimetry (SAP) pattern standard deviation (PSD), short-wavelength automated perimetry (SWAP) PSD, and frequency doubling technology perimetry (FDT) PSD. 14 glaucomatous optic neuropathy eyes were classified as within normal limits by all four tests.

Table 1

Pattern ERG for glaucoma detection amplitude and SAP, SWAP, and FDT mean deviation (MD) and pattern standard deviation (PSD) between healthy and glaucomatous optic neuropathy eyes are compared. Significant differences were found between groups for all parameters, although significance was marginal for SWAP MD.

	GON Mean (95% CI)	Healthy Eyes Mean (95% CI)	ANOVA P=
SAP			
MD (dB)	-2.53 (-3.06, -2.01)	-0.12 (-0.67, 0.43)	<0.0001
PSD (dB)	3.73 (3.22, 4.23)	1.67 (1.14, 2.21)	<0.0001
SWAP			
MD (dB)	-5.55 (-6.34, -4.76)	-4.32 (-5.16, -3.49)	0.04
PSD (dB)	4.55 (4.15, 4.95)	2.92 (2.49, 3.34)	<0.0001
FDT			
MD (dB)	-3.80 (-4.55, -3.05)	0.15 (-0.64, 0.94)	<0.0001
PSD (dB)	4.50 (4.18, 4.83)	2.78 (2.44, 3.12)	<0.0001
Pattern ERG			
Amplitude (μ V)	0.53 (0.48, 0.59)	0.77 (0.72, 0.83)	<0.0001

SAP: standard automated perimetry, SWAP: short-wavelength automated perimetry, FDT: frequency-doubling technology perimetry, Pattern ERG: pattern electroretinogram for glaucoma detection, GON: glaucomatous optic neuropathy, CI: confidence interval, ANOVA: analysis of variance, dB: decibels, μ V: microvolts

Table 2

Areas under the receiver operating characteristic (ROC) curve and associated 95% confidence intervals (CI) are presented for pattern ERG, SAP, SWAP and FDT parameters. The sensitivities obtained for each parameter at approximately 80% and 95% specificities, and the criteria used to reach those specificities, also are presented.

	AUC	95% CI	Specificity/ Sensitivity (%)	Criteria for 80% Specificity	Specificity/ Sensitivity (%)	Criteria for 95% Specificity
SAP						
MD (dB)	0.786	0.719, 0.853	81/65	-0.89	95/41	-1.92
PSD (dB)	0.786	0.720, 0.853	80/62	1.82	95/35	2.81
SWAP						
MD (dB)	0.570	0.485, 0.656	80/33	-7.36	95/19	-9.22
PSD (dB)	0.732	0.659, 0.806	81/53	3.50	95/31	4.73
FDT						
MD (dB)	0.789	0.722, 0.856	80/64	-1.70	95/29	-5.29
PSD (dB)	0.818	0.758, 0.879	80/61	3.19	95/46	3.86
Pattern ERG						
Amplitude (μV)	0.744	0.670, 0.818	80/52	0.52	95/19	0.32

SAP: standard automated perimetry, SWAP: short-wavelength automated perimetry, FDT: frequency-doubling technology perimetry, Pattern ERG: pattern electroretinogram for glaucoma detection, CI: confidence interval, dB: decibels, μV: microvolts

Table 3

Pairwise agreement between pattern ERG for glaucoma detection amplitude, SAP pattern standard deviation (PSD), SWAP PSD, and FDT PSD using the kappa statistic is presented along with the proportion and strength of agreement.

	κ	95% CI	Proportion Agreement	Strength of Agreement
80% Specificity				
Pattern ERG and SAP	0.26	0.12, 0.41	0.65	Fair
Pattern ERG and SWAP	0.18	0.03, 0.33	0.62	Slight
Pattern ERG and FDT	0.32	0.18, 0.46	0.67	Fair
SAP and SWAP	0.46	0.33, 0.60	0.74	Moderate
SAP and FDT	0.45	0.32, 0.58	0.73	Moderate
SWAP and FDT	0.38	0.24, 0.52	0.70	Fair
95% Specificity				
Pattern ERG and SAP	0.14	0.00, 0.31	0.76	Slight
Pattern ERG and SWAP	0.30	0.12, 0.49	0.82	Fair
Pattern ERG and FDT	0.19	0.03, 0.34	0.74	Slight
SAP and SWAP	0.672	0.532, 0.812	0.90	Substantial
SAP and FDT	0.651	0.519, 0.784	0.87	Substantial
SWAP and FDT	0.608	0.468, 0.747	0.86	Substantial

SAP: standard automated perimetry, SWAP: short-wavelength automated perimetry, FDT: frequency-doubling technology perimetry, Pattern ERG: pattern electroretinogram for glaucoma detection, CI: confidence interval, κ : kappa