Published in final edited form as:

Doc Ophthalmol. 2020 October ; 141(2): 149–156. doi:10.1007/s10633-020-09760-5.

Long-term PERG monitoring of untreated and treated glaucoma suspects.

Phillip S. Gordon, Maja Kostic, Pedro F. Monsalve, Giacinto Triolo, Iuri Golubev, Gabriel Luna, Lori M. Ventura, William J. Feuer, Vittorio Porciatti

Bascom Palmer Eye Institute, University of Miami Miller School of Medicine, Miami, FL, USA

Abstract

Purpose: To investigate long-term structural and functional progression of untreated and treated glaucoma suspects (UGS, TGS)

Methods: Retrospective analysis of serial steady-state pattern electroretinogram (PERG), Mean Retinal Nerve Fiber Thickness (RNFLT), and Standard Automated Perimetry Mean Deviation (SAP-MD) in UGS (N=20) and TGS (N=18). Outcome measures were the rates of change (linear regression slopes) of PERG amplitude, PERG phase, mean RNFLT, and SAP-MD over 9.8 ± 1.3 years (15.6 ± 4.2 visits).

Results: The number of patients with significant ($P < 0.05$) progression slopes for PERG amplitude, PERG phase, RNFLT and SAP-MD, were respectively, UGS: 5, 0, 4, 2; TGS: 8, 2, 6, 5. In UGS, outcome measures were not correlated with each other. In TGS, both PERG amplitude and RNFLT were significantly ($P < 0.05$) correlated with SAP-MD ($R = 0.58$) while PERG amplitude and RNFLT were not correlated to each other ($R = 0.43$, $P = 0.064$). The rate of change of SAP-MD was predicted ($P < 0.05$) by a linear combination of RNFLT slope and PERG amplitude slope.

Conclusions: Results substantiate and extend previous results showing that steady-state PERG amplitude progressively decreased over time in a proportion of glaucoma suspects, with relatively steeper slope in TGS compared to UGS. RNFLT progression also had a steeper slope in TGS

Address for correspondence: Vittorio Porciatti D.Sc., Bascom Palmer Eye Institute, University of Miami Miller School of Medicine, Mc Knight Vision Research Center, 1638 NW 10th Ave., Room 101, Miami, FL, 33136, vporciatti@med.miami.edu, Tel: 305-326-6050; Fax: 305-482-5093.

Financial disclosure: None for all authors.

Conflict of interest

The authors declare that there is no conflict of interest regarding the publication of this article. The authors alone are responsible for the content and writing of the paper.

Compliance with ethical standards

Statement of human rights

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent

All individuals involved in the study were informed of the purpose of the study, and their informed consent was obtained. This study followed the tenets of the Declaration of Helsinki and was approved by the ethics committee of the institutional First Affiliated Hospital of Chongqing Medical University.

Statement on the welfare of animals

This article does not contain any studies with animals performed by any of the authors.

compared to UGS; however, progressions of PERG amplitude and RNFLT were not significantly correlated. Both PERG progression and RNFLT progression independently contribute to prediction of visual field progression.

Keywords

Retinal ganglion cell function; Pattern electroretinogram; Retinal Nerve Fiber Layer Thickness; glaucoma suspects

Introduction

The Pattern Electroretinogram (PERG) is a well-established, sensitive measure of retinal ganglion cell (RGC) function that is extensively used to detect early RGC dysfunction in optic nerve disorders [1]. A number of cross-sectional studies have shown that the PERG is early altered in glaucoma [2–6]. Longitudinal PERG assessment may provide indication of the magnitude of progression of disease and whether progression is altered with treatment. Longitudinal PERG studies in early glaucoma are scarce and limited to 5 years [7–9]. Bode et al, 2011 [10] monitored glaucoma suspects for about 10 years with PERG and visual field but did not provide information on associated structural changes as measured by Optical Coherence Tomography (OCT). Here we report the results of a retrospective study of two groups of patients --untreated and treated glaucoma suspects-- that were monitored over an average of 10 years with PERG, Visual Field, and OCT. Progressive PERG, Visual Field, and OCT changes are compared to investigate the association between structural and functional changes.

Methods

Subjects

Study subjects were part of a longitudinal cohort of patients tested at the Bascom Palmer Eye Institute in the period 2006-2018. Patients (N=38) were defined as glaucoma suspects (GS) at their initial visit based on detailed medical and ocular history, and a comprehensive eye examination[11]. According to Ventura et al, 2005 [11], Inclusion criteria were: refractive errors within -5 to +3 diopters, best corrected visual acuity (BCVA) 20/25 (Snellen), acceptable normal standard automated perimetry (SAP, Humphrey central 24-2 program) according to the Ocular Hypertension Treatment Study (OHTS) criteria [12] (reliability < 15% on all indices, normality > 5% on all global indices in two consecutive sessions 6 months apart), and glaucomatous optic disc appearance (vertical cup-to-disc ratio [VCDR] 0.5, VCDR asymmetry 0.2, localized thinning of the disc) or moderately increased IOP (>21 to <28 mm Hg). Exclusion criteria were the presence of ocular or systemic disease that may cause nonspecific PERG abnormality, such as age-related macular degeneration, diabetes, Parkinson's disease, and multiple sclerosis. Patients with previous intraocular surgery, except for uncomplicated cataract extraction, were excluded. None of the patients had cataract surgery during the study period. By the time initial PERG and OCT were recorded, a subgroup of patients (N=18) had started treatment. Initiation of therapy was weighted by the glaucoma specialist in concert with the individual patients taking into account a constellation of risk factors including optic disc cupping, corneal thickness, family

history, race, life expectancy, and psychosocial issues [8, 13]. The initial decision to treat was not based on PERG, OCT, or SAP measurements. Treatment consisted of either prostaglandin analogs (16/18) or beta-blockers (2/18), medications that are known not to cause changes in pupil size (American Academy of Ophthalmology Preferred Practice Pattern, Glaucoma Panel, Hoskins Center for Quality Eye Care, available in the public domain at www.aaopt.org/ppp) and impact PERG results [14]. The study followed the tenets of the Declaration of Helsinki and was approved by the Institutional Review Board of the University of Miami. Informed written consent was obtained from all subjects after the nature of the test and possible risks were explained in detail. PERG, OCT and SAP serial measurements over 9.8 ± 1.3 years (UGS, N= 15.4 ± 3.8 visits; TGS, N= 15.1 ± 5.8 visits) were obtained. A summary of baseline characteristics of patients is shown in Table 1. For PERG amplitude, RNFL thickness, SAP-MD and IOP, baseline values represent the average of the first three measurements in the longitudinal series (~one year).

PERG Recording

We used a recording paradigm optimized for glaucoma detection (PERGLA) incorporated in an instrument (Glaide, Luce Elettronica, Rome, Italy) whose details have been previously described [11, 15] and has been used in previous studies of our group [7–9]. In brief, steady-state PERGs were recorded simultaneously from both eyes by means of surface electrodes taped on the lower eyelids (reference ipsilateral temple) while subjects fixated from a distance of 30 cm the center of a CRT display (25° diameter circular field, 40 cd/m² mean luminance) displaying horizontal gratings (1.7 cy/deg, 98% contrast) reversing 16.28 times per second. Subjects were fitted with the appropriate lens correction to reach J1+ visual acuity; they did not receive dilating drops and were allowed to blink freely. Recording lasted approximately 3 minutes including a brief pause at half recording. Signal acquisition periods occasionally contaminated by blinks were automatically rejected. PERG waveforms were analyzed automatically in the frequency domain to isolate the frequency component at the contrast-reversal rate (16.28 Hz) and compute its zero-to-peak amplitude in μ V. The stimulus luminance/contrast did not change over the observation period as measured annually with a photometer (DR-2000-1; Gamma Scientific, San Diego, CA).

OCT Recording

Peripapillary mean RNFL thickness was evaluated using the fast RNFL program of the Stratus OCT (Carl Zeiss Meditec, Dublin, CA), and analyzed using software version 3.0 (Carl Zeiss Meditec). OCT measurements were included in the analysis if signal strength was 7 or higher. RNFL thickness was determined at 256 points of a circular scan (diameter 3.4 mm) centered around the center of the optic disc that was repeated 3 consecutive times. For each eye, RNFL scans were repeated 4 times at each visit and an average scan for mean RNFLT was calculated. As Stratus OCT was phased out in year 2014 and substituted with Cirrus OCT (Carl Zeiss Meditec), patients had initial measurements taken with Stratus-OCT (2003–2013) and final measurements (2014–2018) taken with Cirrus-OCT. Established conversion formulas for early glaucoma are available [16] to convert Cirrus-RNFLT to Stratus-RNFLT [Mean RNFLT (μ m): Cirrus = Stratus * 0.79 + 11.9].

Data analysis

For all analyses, PERG and OCT data were corrected for physiological age-related changes using pre-established norms in cross-sectional studies of our group using identical PERG and OCT instruments. Namely, age-predicted PERG amplitude was calculated as previously described [15] from data obtained in a cohort of 114 normal subjects [11] using the equation $[\text{Log (Amp)} = 0.583 - 0.357 \times \text{Log (Age)}]$. Linear regression of age-predicted amplitudes in the age range of present study patients resulted in the equation $[\text{Amp} = 1.2246 - 0.0057 \times \text{Age}]$. Age-predicted PERG phase [11] was derived by the equation $[\text{Phase} = 1.99 - 0.0027 \times \text{Age}]$. Age-predicted mean RNFLT was derived from data obtained in a cohort of 425 normal subjects using the equation $[\text{Mean RNFLT} = 115.86 - 0.24 \times \text{Age}]$ [17]. For each patient, rates of change over time (linear regression slopes) for PERG amplitude/phase, mean RNFLT, and MD were estimated. In order to compare significance of slopes for different measures on a similar scale, individual linear regression slopes for PERG amplitude/phase, RNFLT, and SAP-MD were divided by corresponding standard errors (SE) of regression and expressed as t-values. This is analogous to evaluating meaningful SNRs >2 . T-values have a counterpart in P-values [18]. However, t-values were preferred to P-values as the latter do not distinguish between negative and positive slopes. We checked that all t-values < -2 had a P-value < 0.05 . As the results were similar in the two eyes, only the results of the right eye are reported.

Results

Figure 1 summarizes the changes of age-corrected PERG amplitude, PERG phase, mean RNFLT and SAP-MD over time for all study participants. Different subjects are identified by different color of symbols and corresponding linear regression lines and 95% confidence boundaries of regression. It can be noted that in the majority of subjects, regression slopes were close to horizontal for all outcome measures. In some subjects, however, regression slopes appeared more negative, in particular in the treated group compared to the untreated group. Mean age-corrected mean progression slopes for different measures in UGS and TGS patients are summarized in Table 2. In UGS, the mean slope was significantly different from zero (negative) for PERG amplitude and SAP-MD. In TGS, the mean slope was significantly negative for PERG amplitude, RNFLT and SAP-MD. PERG phase and mean RNFLT has significantly steeper slopes in TGS, compared to UGS.

In order to compare slopes for different measures on a normalized scale, age-corrected regression slopes of individual in patients were divided by corresponding standard errors of regression and expressed as t-values. A t-value smaller than -2 is equivalent to a statistical significance of $P < 0.05$ with the present sample size. Figure 2 summarizes t-values for different measures in untreated and treated GS patients. It can be noted that the majority of t-values were higher than -2 , meaning that regression slopes were not significant. In some patients, however, t-values were < -2 ($P < 0.05$). For all measures, the number of significantly negative slopes was higher in the treated group compared to the untreated group.

A pertinent question was whether progression slopes for different measures were correlated. Figure 3 and Table 3 summarize pairwise correlation analysis. In untreated patients, all correlations coefficients (Pearson's) were modest (ranged between $R = -0.011$ and $R = 0.36$)

and none of them was significant. In treated patients, correlations were moderate to strong between PERG amplitude slope and SAP-MD slope ($R=0.58$, $P=0.009$) and between RNFLT slope and SAP-MD slope ($R=0.64$, $P=0.0031$). The correlation between PERG amplitude slope and RNFLT slope was not significant ($R=0.43$, $P=0.064$). A multiple regression analysis on all patients using SAP-MD slope as dependent variable and PERG amplitude/phase and RNFLT as predictor variables, showed that SAP-MD slope could be predicted by a linear combination of PERG amplitude slope ($P=0.0068$) and RNFLT slope ($P=0.0071$). PERG phase slope did not significantly contribute to the regression ($P=0.2$). The prediction expression was, $[MD\text{-slope (dB/Y)} = -0.46 + 0.26 \times \text{Amp-slope } (\mu\text{V/Y}) + 0.3057 \text{ RNFLT-slope } (\mu\text{m/Y})]$.

The association between t-values for different measures in individual patients is summarized in Figure 4. It can be noted that the association between significant negative slopes for different measures in individual patients was poor. Significant progression slopes of all 4 measures were concurrent in only one treated patient (#30). PERG amplitude, RNFLT and MD slopes were concurrently altered in 1 untreated patient (#11) and one treated patient (#29); PERG amplitude and MD slopes were concurrently altered in 1 treated patient (#31); RNFLT and MD slopes were concurrently altered in 1 treated patient (#36). In all other patients only one measure was altered.

Discussion

This study shows that in both untreated and treated glaucoma suspects the age-corrected PERG amplitude significantly decreased over 10 years on average. The mean rate of PERG amplitude decline in UGS ($-0.012 \mu\text{V/Y}$) was in the range ($-0.007 \mu\text{V/Y}$ to $-0.0418 \mu\text{V/Y}$) of that previously reported in UGS using similar instrumentation on a shorter observation time [8]. The mean rate of PERG amplitude decline in TGS ($-0.020 \mu\text{V/Y}$) was not significantly different from that of UGS. It is possible that progressive loss of RGC was alleviated by IOP-lowering treatment as previously shown [8]. The progression rate of age-corrected RNFLT in UGS was not different from zero. In TGS, the mean progression rate of RNFLT ($-0.66 \mu\text{m/Y}$) was significant and comparable to the progression rate ($-0.61 \mu\text{m/Y}$) reported for preperimetric glaucoma patients [19] using similar OCT technology.

Over the follow-up period, based on the statistical significance of SAP-MD slope, 2/20 (10%) UGS patients converted to glaucoma, whereas 5/18 (28%) converted in the TGS subgroup. The increased rate of conversion to glaucoma in TGS patients compared to UGS was associated with increased number of patients with significant progression of PERG amplitude/phase and RNFLT in TGS compared to UGS. The frequency of patients with significant progression of PERG amplitude was similar to the frequency of RNFLT progression (13/38: 34% vs. 10/38: 26%). In UGS patients, no correlation was found between all outcome measures. In TGS, both PERG amplitude slope and RNFLT slope were significantly correlated to SAP-MD slope, but PERG amplitude slope and RNFLT slope were not significantly correlated to each other. A multiple regression analysis showed that both PERG amplitude slope and RNFLT slope independently contributed to prediction of SAP-MD slope. This implies that the combined assessment of PERG amplitude and RNFLT may improve prediction of SAP-MD progression.

In general, significant progressions of PERG amplitude/phase, RNFLT and SAP-MD rarely coincided in the same patients. This may not be surprising, considering that these tests reflect, at least in part, different functional, structural, and topographical aspects, and may become abnormal at different times over the course of the disease [7, 10].

Thus, each test may contribute unique information to better understanding, monitoring, and treatment of glaucoma. Interestingly, all measures were altered in greater number in TGS patients compared to UGS. This was consistent with the subjective perception of increased risk at baseline from the glaucoma specialist who prescribed treatment in these patients based on a constellation of real and potential risk factors [8, 13].

This study has some limitations. The control group for PERG and OCT progression was based on pre-established cross-sectional data. A longitudinal control group would have been ideal, although this is very difficult to obtain in a long-term study. It seems unlikely that age-correction based on a longitudinal normal cohort control would have substantially changed the present results. Patients had initial RNFLT measurements taken with Stratus-OCT and final measurements taken with Cirrus-OCT. While Cirrus-RNFLTs were converted to Stratus-RNFLTs using an established formula [16], we cannot exclude that Cirrus to Stratus conversion may have altered RNFL slopes. Our analysis was limited to global indices (mean RNFL thickness, PERG amplitude, SAP-MD) as the PERG response originates from the entire posterior pole. New generation OCT instruments that assess multiple retinal layers and topographical areas [20], coupled with new PERG protocols that detect local RGC function [21–23] may offer distinct longitudinal structure-function relationships and help identifying regions of highest vulnerability in glaucoma.

In conclusion, results substantiate and extend previous results showing that PERG amplitude progressively decreases over time in glaucoma suspects, more frequently so in patients deemed at higher risk of developing the disease and treated with IOP-lowering drops. PERG progression and RNFLT progression independently contribute to prediction of visual field progression.

Acknowledgements

This work was supported by NIH-NEI RO1 EY014957, NIH center grant P30-EY014801, and by unrestricted grant to Bascom Palmer Eye Institute from Research to Prevent Blindness, Inc.

References

1. Bach M, et al., ISCEV standard for clinical pattern electroretinography (PERG): 2012 update. *Doc Ophthalmol*, 2013 126(1): p. 1–7. [PubMed: 23073702]
2. Bach M and Hoffmann MB, Update on the pattern electroretinogram in glaucoma. *Optom Vis Sci*, 2008 85(6): p. 386–395. [PubMed: 18521020]
3. Bach M and Poloschek CM, Electrophysiology and glaucoma: current status and future challenges. *Cell Tissue Res*, 2013 353(2): p. 287–296. [PubMed: 23525754]
4. Bach M and Ramharter-Sereinig A, Pattern electroretinogram to detect glaucoma: comparing the PERGLA and the PERG Ratio protocols. *Doc Ophthalmol*, 2013 127(3): p. 227–238. [PubMed: 24126828]
5. Ventura LM and Porciatti V, Pattern electroretinogram in glaucoma. *Curr Opin Ophthalmol*, 2006 17(2): p. 196–202. [PubMed: 16552256]

6. Wilsey LJ and Fortune B, Electoretinography in glaucoma diagnosis. *Curr Opin Ophthalmol*, 2016 27(2): p. 118–124. [PubMed: 26720775]
7. Banitt MR, et al., Progressive loss of retinal ganglion cell function precedes structural loss by several years in glaucoma suspects. *Invest Ophthalmol Vis Sci*, 2013 54(3): p. 2346–2352. [PubMed: 23412088]
8. Ventura LM, Feuer WJ, and Porciatti V, Progressive loss of retinal ganglion cell function is hindered with IOP-lowering treatment in early glaucoma. *Invest Ophthalmol Vis Sci*, 2012 53(2): p. 659–663. [PubMed: 22247462]
9. Ventura LM, et al., Pattern electroretinogram progression in glaucoma suspects. *J Glaucoma*, 2013 22(3): p. 219–225. [PubMed: 22071557]
10. Bode SF, Jehle T, and Bach M, Pattern electroretinogram in glaucoma suspects: new findings from a longitudinal study. *Invest Ophthalmol Vis Sci*, 2011 52(7): p. 4300–4306. [PubMed: 21372021]
11. Ventura LM, et al., Pattern electroretinogram abnormality and glaucoma. *Ophthalmology*, 2005 112(1): p. 10–19. [PubMed: 15629814]
12. Gordon MO and Kass MA, The Ocular Hypertension Treatment Study: design and baseline description of the participants. *Arch Ophthalmol*, 1999 117(5): p. 573–583. [PubMed: 10326953]
13. Walker RS and Pilts-Seymour JR, When to treat glaucoma, in *Ophthalmology*, Yanoff M and Ducker JS, Editors. 2009, Mosby, Elsevier: London, UK p. 1211–1215.
14. Porciatti V, et al., The effects of aging on the pattern electroretinogram and visual evoked potential in humans. *Vision Res*, 1992 32(7): p. 1199–1209. [PubMed: 1455694]
15. Porciatti V and Ventura LM, Normative data for a user-friendly paradigm for pattern electroretinogram recording. *Ophthalmology*, 2004 111(1): p. 161–168. [PubMed: 14711729]
16. Knight OJ, et al., Comparison of retinal nerve fiber layer measurements using time domain and spectral domain optical coherent tomography. *Ophthalmology*, 2009 116(7): p. 1271–1277. [PubMed: 19395086]
17. Feuer WJ, et al., Topographic differences in the age-related changes in the retinal nerve fiber layer of normal eyes measured by Stratus optical coherence tomography. *J Glaucoma*, 2011 20(3): p. 133–138. [PubMed: 20577113]
18. Draper NR and Smith H, *Applied linear regression analysis*. 2nd ed. 1981, New York: Wiley & Sons.
19. Na JH, et al., Rates and patterns of macular and circumpapillary retinal nerve fiber layer thinning in preperimetric and perimetric glaucomatous eyes. *J Glaucoma*, 2015 24(4): p. 278–285. [PubMed: 24633086]
20. Chen TC, et al., Spectral-Domain OCT: Helping the Clinician Diagnose Glaucoma: A Report by the American Academy of Ophthalmology. *Ophthalmology*, 2018 125(11): p. 1817–1827. [PubMed: 30322450]
21. Salgarello T, et al., Pattern Electroretinogram Detects Localized Glaucoma Defects. *Transl Vis Sci Technol*, 2018 7(5): p. 6.
22. Kreuz AC, et al., Macular and Multifocal PERG and FD-OCT in Preperimetric and Hemifield Loss Glaucoma. *J Glaucoma*, 2018 27(2): p. 121–132. [PubMed: 29329137]
23. Bach M, Cuno AK, and Hoffmann MB, Retinal conduction speed analysis reveals different origins of the P50 and N95 components of the (multifocal) pattern electroretinogram. *Exp Eye Res*, 2018 169: p. 48–53. [PubMed: 29374551]

Figure 1.

PERG amplitude, PERG phase, Mean Retinal Nerve Fiber Layer Thickness (RNFLT) and Standard Automated perimetry Mean Deviation (SAP MD) as a function of age for the right eyes of untreated (N=20) and treated (N=18) glaucoma suspects. Different subjects are identified by different color of symbols and corresponding linear regression lines and 95% confidence boundaries of regressions. PERG amplitude, PERG phase, and mean RNFLT have been corrected for physiological age-related changes.

Figure 2. t-values of linear regression slopes for PERG amplitude (Amplitude), PERG phase (Phase), Mean Retinal Nerve Fiber Layer Thickness (RNFLT) and Standard Automated perimetry Mean Deviation (MD) in untreated (N=20) and treated glaucoma suspects (N=18) over an average observation period of 9.8 years, t-values were calculated as [(patient slope – normal control slope) ÷ patient slope standard error]. A t-value of < -2 is equivalent to a significance level of P<0.05. Blue symbols identify untreated glaucoma suspects. Red symbols identify treated glaucoma suspects. The uniform pink area identifies t-values <-2 (P<0.05).

Figure 3.

Scatterplot matrix of pairwise Pearson's correlations between outcome measures for the right eyes of untreated (N=20) and treated (N=18) glaucoma suspects. All panels display the regression line and 95% level confidence curves for the fitted regression line.

Figure 4.

Association between significantly negative progression slopes (t-value < -2) for PERG amplitude (Amp), PERG phase (Phase), Mean Retinal Nerve Fiber Layer Thickness (RNFLT) and Standard Automated perimetry Mean Deviation (MD) in individual untreated and treated glaucoma suspects. Note that slopes of all 4 measures were concurrently altered in only one treated patient (#30).

Table 1.

Baseline characteristics of patients

	UGS, N=20		TGS, N=18		
	Mean	SD	Mean	SD	P
Age (years)	55.5	8.57	60.3	12.7	0.184
Follow up (years)	9.97	1.65	9.68	1.63	0.59
Mean IOP (mm Hg)	15.1	1.96	15.9	3.01	0.361
MD (dB)	-0.70	0.91	-1.50	1.41	0.051
PSD	1.68	0.409	2.13	1.28	0.168
VCDR	0.53	0.12	0.53	0.16	0.997
PERG Amplitude (μ V)	0.71	0.23	0.71	0.27	0.958
RNFLT Mean (μ m)	103	10.0	98.8	9.42	0.108

UGS: untreated glaucoma suspects; TGS: treated Glaucoma suspects; IOP: intraocular pressure; MD: Humphrey automated perimetry program 24-2; PSD: Pattern standard deviation; VCDR: vertical cup to disk ratio; PERG: pattern electroretinogram; RNFLT: retinal nerve fiber layer thickness

Table 2.

Mean rate of change for PERG, OCT and SAP in glaucoma suspects patients

	Untreated glaucoma suspects			Treated glaucoma suspects		
Measure	Slope	+95% CI	−95% CI	Slope	+95% CI	−95% CI
Amp ($\mu\text{V}/\text{Y}$)	−0.012	−0.0024	−0.022	−0.020	−0.0065	−0.035
Pha (π rad/Y)	0.0043	0.0086	−0.0001	−0.0025	0.0029	−0.079
RNFLT ($\mu\text{m}/\text{Y}$)	−0.060	0.49	−0.37	−0.66	−0.13	−1.18
MD (dB/Y)	−0.071	−0.015	−0.13	−0.22	−0.044	−0.40

Amp: PERG amplitude; Pha: PERG phase; RNFLT: mean retinal nerve layer thickness; MD: standard automated perimetry mean deviation. Rates of change emphasized in bold are significant ($P<0.05$)

Table 3.

Pairwise correlations among outcome measures

Untreated	Amp	Phase	RNFLT	MD
Amp	1			
Phase	0.018397	1		
RNFLT	0.02298	-0.01162	1	
MD	0.275528	0.365262	0.134171	1
Treated	Amp	Phase	RNFLT	MD
Amp	1			
Phase	0.137308	1		
RNFLT	0.431994	0.065453	1	
MD	0.579699	0.153639	0.641574	1

AMP: PERG amplitude; Phase: PERG phase; RNFLT: mean retinal nerve fiber layer thickness; MD: Standard automated perimetry mean deviation. Numbers represent Pearson's correlation coefficients. Correlations emphasized in bold identify significant correlations ($P < 0.05$)