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Head-down posture in glaucoma suspects induces changes in IOP, systemic pressure and PERG that predict future loss of optic nerve tissue

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Abstract

Purpose—To obtain pilot data on posture-induced changes of IOP, systemic pressure and pattern electroretinogram (PERG) predictive of future optic nerve tissue loss glaucoma suspects (GS).

Methods—Mean peripapillary retinal fiber layer thickness (RNFLT) was measured with OCT two times/year in 28 GS aged 58 ± 8.9 years over 5.0 ± 0.73 years. All patients had a baseline PERG, IOP and brachial blood pressure measurements in the seated and – 10 degrees head-down-body-tilt position (HDT). Outcome measures were seated/HDT PERG amplitude and phase, IOP, mean arterial blood pressure (MAP), and estimated ocular perfusion pressure (OPP). An additional group of 11 similarly-aged controls (SAC) aged 56.9 ± 13 years was tested for comparison.

Results—While all GS had initial RNFLT in the normal range, 9/28 of them developed significant ($P < 0.05$) loss of mean RNFLT (thinners, T) over the follow-up period as opposed to 19/28 who did not (non-thinners, NT). Significant ($P < 0.05$) differences between SAC, NT and T were found in PERG amplitude, PERG phase, MAP, IOP, and OPP. A nominal logistic regression using baseline PERG and hemodynamic variables was able to distinguish T from NT with an AUROC of 0.89 (SE 0.07).

Conclusions—Baseline PERG, IOP, and systemic blood pressure, together with their changes upon HDT, may have predictive value for future loss of optic nerve tissue in GS. This study supports the rationale for a full-scale clinical trial to identify patients at high-risk of development of glaucoma.

Keywords

retinal nerve layer thickness; retinal ganglion cell function; pattern electroretinogram; glaucoma; progression; posture; systemic blood pressure

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Introduction

A central yet unresolved issue in open angle glaucoma (OAG) is determining, in individual subjects, the onset of the disease. This may be defined as the stage at which retinal ganglion cells (RGCs) become susceptible to a stressful environment and dysfunctional.¹ Thus, identifying RGC dysfunction before manifest glaucoma would represent the ideal time window for initiating therapeutic strategies to prevent cell death and visual loss.

Risk assessment² in patients with suspicion of glaucoma may provide an evidence-based rationale for timely treatment to prevent development of the disease. Risk assessment may be potentiated by the use of provocative tests.³⁻⁶ It is well known that head-down posture results in changes of the intraocular and systemic pressures that may be associated with a variety of ocular manifestations and visual loss whose severity depends on the angle of tilt and the duration of head-down posture.⁷⁻¹² Even a temporary head-down posture with small angle of tilt may induce reversible loss of neurophysiological function in normal subjects at both the retinal and cortical level.^{13, 14} Ventura et al, 2003¹⁵ using a head-down body tilt of minus 10 degrees below supine orientation for 8 minutes, reported reversible Pattern Electroretinogram (PERG) losses in a subpopulation of glaucoma suspects that was associated with IOP and systemic pressure elevation.¹⁵ Thus, temporary, moderate head-down posture can be potentially used as provocative test to identify glaucoma suspects (GS) that may develop glaucoma earlier than those less susceptible to the procedure. Here we show in a population of GS, longitudinally monitored with OCT over an average of 5 years, that baseline PERG and systemic/ocular pressures, together with their changes upon head-down posture, may predict future loss of nerve retinal fiber layer (RNFL) thickness.

Methods

Subjects

Study subjects were 28 GS (mean age 58 ± 8.9 years at baseline) that were part of a longitudinal cohort of 107 patients monitored two times per year over at least 4 years (mean 5.0 ± 0.73 years) with PERG and OCT.¹⁶ The present subgroup of 28 patients represented all GS who also received one PERG, IOP and hemodynamic assessment in the seated and HDT posture during the first year of the follow-up.¹⁵ An additional group of 11 similarly-aged healthy controls (SAC, mean age 56.9 ± 13 years, difference with study subjects, $P=0.3$) originating from a previous study¹⁵ was used to compare PERG, IOP, and hemodynamic parameters upon HDT with the study group.

Study patients were enrolled as glaucoma suspects at their initial visit based on detailed medical and ocular history, and a comprehensive eye examination as described previously.¹⁷ Subjects met the following inclusion criteria: refractive errors within -5 to $+3$ diopters, best corrected visual acuity (BCVA) 20/20 (Snellen), normal standard automated perimetry (SAP) according to the Ocular Hypertension Treatment Study (OHTS) criteria¹⁸ (reliability $< 33\%$ 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, splinter disc hemorrhages) or IOP > 21 mm Hg. At least one eye meeting the inclusion criteria qualified a patient as GS,

although none of the study patients had elevated IOP. For all subjects, exclusion criteria were age-related macular degeneration, high myopia (>5 diopters), uveitis, diabetes, Parkinson's disease, multiple sclerosis, and the presence of any other ocular or systemic disease that may cause nonspecific PERG abnormalities. Patients with history of previous intraocular surgery were also excluded. None of the patients had history of, or took medications for, systemic hypertension/peripheral vascular disease/cardiac disease. Baseline characteristics of patients are summarized in Table 1.

Enrolled patients were followed with PERG and OCT for at least 4 years with no less than 6 visits during this period. Some patients (13/28) received treatment during follow-up (5 in yr. 1; 3 in yr. 2; 5 in yr. 3). Initiation of therapy was based on the patients' increased awareness of their condition and concern for the associated risks that was discussed with the clinician, eventually resulting in the initiation of treatment.¹⁹ Treatment consisted of either prostaglandin analogs (n=12) or beta blockers (n=1) (American Academy of Ophthalmology Preferred Practice Pattern, Glaucoma Panel, Hoskins Center for Quality Eye Care, available in the public domain at www.aao.org/ppp). 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.

Body Tilt Equipment

The equipment for PERG recording at different positions of body posture has been previously described in detail.¹⁵ Briefly, the PERG apparatus was incorporated in a custom-built balanced frame that rotated in sync with an electronically adjustable surgical bed. A moderate (minus 10 degrees) HDT angle was chosen based on previous pilot data²⁰ to induce a measurable, transient IOP elevation while minimizing potential risks of undesirable systemic hemodynamic reactions in patients.^{21, 22} The equipment also allowed measurement of IOP at designated postures (seated baseline, HDT, seated recovery) as well as measure of brachial arterial pressure.

Experimental Protocol

The experimental protocol has been previously described in detail.¹⁵ Briefly, IOP, blood pressure and PERG were first recorded in sequence with the subjects in the seated position (baseline). Subjects' posture was then progressively (over 1 minute) changed to minus 10 degrees head-down body tilt (HDT). IOP, blood pressure and PERG were measured again in the time window 3–8 minutes after posture change. Based on previous reports, a moderate head down tilt produces a rapid (within 1 min) elevation of IOP that persists for at least 30 minutes.¹³ Finally, subjects were adjusted back to seated position (recovery) within 1 minute and all measurements repeated. PERG and pressure parameters in the recovery position are not displayed in the present study, as they were previously shown to be not significantly different from the seated baseline condition.¹⁵

PERG Recording

We used a recording paradigm optimized for glaucoma detection (PERGLA) incorporated in a commercial system (Lace Elettronica, Rome, Italy). Details of the technique have been

previously reported.^{15, 23} The PERG was simultaneously recorded from both eyes by means of skin electrodes taped on the lower eyelids. Reproducibility of measurements using this protocol is considered to be very good and suitable for monitoring changes over time.^{24–26} Intratest variability of amplitude and phase is similar between normal controls and glaucoma suspects, and does not change between the seated and HDT conditions.¹⁵ Since the PERG was recorded in response to a fast contrast-reversal (16.28 reversals/s) stimulus, response waveforms were typically sinusoidal-like, with a temporal period corresponding to the reversal rate. PERG waveforms were automatically analyzed in the frequency domain by Discrete Fourier Transform to isolate the frequency component at the contrast-reversal rate (16.28 Hz), and compute its peak amplitude in microVolt and phase in π radians. Decreasing phase values are analogues to latency delays (31 ms per 1.0 π rad).

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. OCT measurements were performed with signal strength of 7 or higher. RNFL thickness was determined at 256 points of a circular scan (diameter 3.4 mm) centered on the center of the optic disc that was repeated 3 consecutive times at each visit, exported on an electronic worksheet, and an average scan was computed. Mean RNFL thickness was evaluated from the average scan as previously described.²⁷

IOP Measurement

IOP was measured with a portable, noncontact, airpulse tonometer (Reichert PT100, Depew, NY, USA) for all conditions. For each IOP reading, the instrument calculates the average of three consecutive measures. Portable, noncontact tonometry allowed measurements in HDT position and also prevented the formation of corneal irregularities that can be generated by repeated readings with contact tonometers. Corneal surface irregularities produce scatter that degrade the stimulus contrast²⁸ and may reduce PERG amplitude.²⁹ Air pulse tonometers yield IOP values that are reproducible and comparable to those obtained with Goldmann applanation tonometry.^{30–32}

Systemic pressure measurements

Systemic blood pressure (brachial artery) was assessed with a Welch-Allyn Vital Sign Monitor 300 Series (Skaneateles Falls, NY, USA). For each body position, mean arterial blood pressure (MAP) was calculated from diastolic blood pressure (DBP) and systolic blood pressure (SBP) according to the formula $MAP = DBP + 0.42 \times (SBP - DBP)$.^{33,34} Ocular perfusion pressure (OPP) was defined as the difference between mean central artery pressure (MCAP) and IOP: $OPP = MCAP - IOP$.^{35, 36} The MCAP is linked to the MAP by a posture coefficient, as the hydrostatic effect of the blood column between the heart and the eye depends on posture.^{35, 36} Based on ophthalmodynamometric measurements of the MCAP obtained at different body positions and extrapolated to derive the posture coefficient in the seated position and at minus 10 degrees head-down body tilt, OPP_{seated} was $(MAP \times 0.74) - IOP$, and OPP_{tilted} was $(MAP \times 0.86) - IOP$.^{15, 33, 34, 37, 38}

Statistics

The criterion for mean RNFL thinning beyond chance was obtained from published data by Budenz et al, 2008³⁹ using the method detailed in the appendix of that publication. In brief, the first 3 measurements and the 3 last measurements of the follow up series were averaged, and their difference represented the RNFL change, a conservative approach to minimize sampling variability. The test-retest tolerance limit for mean RNFL thickness (table 2 of Budenz et al, 2008³⁹) was multiplied by the square root of 2/3 obtaining 5.4 μm as a two-sided change in RNFL thickness beyond chance. This value is more than 4 times the rate of normal age-related mean RNFL thinning.⁴⁰ Logistic regression was used to create a prediction equation for the risk of RNFL thinning ($>5.4 \mu\text{m}$ from baseline to follow up) in which PERG and hemodynamic measurements at baseline and change upon HDT were allowed entry in a backward stepwise fashion. In this pilot study we relaxed the p-value for inclusion in the model to 0.2 as recommended as a model building strategy.⁴¹ One randomly selected eye from each participant was included in this analysis. Both selected eyes and contralateral eyes met the study criteria for glaucoma suspect.

Results

A subpopulation of GS displayed significant mean RNFL thinning after 5 years

Figure 1 compares baseline RNFL mean thicknesses with corresponding changes for randomly selected eyes of 28 GS patients monitored 5.0 ± 0.73 years. Changes larger than 5.4 μm significantly ($P < 0.05$) exceed the intervisit test-retest variability criterion for mean RNFL thickness changes.³⁹ In our GS patient population, eyes with reduction of mean RNFL thickness larger than 5.4 μm (9/28, 32%) have been defined as “thinners, T”, as opposed to “non-thinners, NT” that had changes equal to or less than 5.4 μm . The mean loss of RNFL thickness in T was $-8.18 \mu\text{m}$ (SE 1.02), whereas in NT was $-0.685 \mu\text{m}$ (SE, 0.687). Both T and NT had baseline RNFLT in the normal range⁴² with no significant difference between them (t-test, $P = 0.21$). Also, in both T and NT the baseline RNFLT was not correlated with RNFLT change (T: $R^2 = 0.014$; NT, $R^2 = 0.026$). To corroborate Budenz et al, 2008³⁹ criterion of significant thinning, we performed linear regression analysis of the mean RNFL thickness over age^{43,44, 45} for all measurements of the longitudinal series. The average slope of mean RNFLT in thinners was $-0.1641 \mu\text{m/yr}$ (SE, 0.016; 95% C.I., -0.1 , -0.196), corresponding to a $-8.2 \mu\text{m}$ loss over 5 years – in very good agreement with $-8.18 \mu\text{m}$ mean RNFLT loss we measured. Sectorial RNFLT analysis showed that the inferior quadrant had a steeper slope ($-0.162 \mu\text{m/yr}$, SE, 0.053) compared to other quadrants (superior: $-0.114 \mu\text{m/yr}$, SE, 0.033; nasal: $-0.142 \mu\text{m/yr}$, SE, 0.021; temporal: $-0.115 \mu\text{m/yr}$, SE, 0.039). The average slope of mean RNFLT in non-thinners was $-0.029 \mu\text{m/yr}$ (SE, 0.018; 95% C.I., 0.01, -0.064).

Baseline PERG amplitude and phase and their changes upon HDT

Figure 2A compares PERG amplitude of similarly-aged controls (SAC), non-thinners (NT), and thinners (T) in the seated position and during HDT posture. Univariate ANOVA did not reveal a significant difference among groups in the seated position ($P = 0.08$). In the tilted position, however, there was a significant ($P = 0.0025$) difference between groups (SAC $>$ NT, $P = 0.001$; SAC $>$ T, $P = 0.0075$). A two-way repeated measures ANOVA of factors Group

(SAC, NT, T) and Posture (seated, HDT) on the dependent variable PERG amplitude revealed that there was a significant effect of group ($P=0.0098$), posture ($P<0.001$) and an interaction between group and posture ($P=0.02$).

Univariate ANOVA of PERG phase (Fig. 2B) showed that there was a significant ($P=0.019$) difference among groups in the seated position (SAC>NT, $P=0.043$; SAC>T, $P=0.0052$). In the tilted position, there was no significant difference among groups ($P=0.19$). A two-way repeated measures ANOVA of PERG phase showed that there was a significant effect of group ($P=0.03$) but no effect of tilt ($P=0.21$) or interaction between group and posture ($P=0.87$).

Baseline systemic and ocular pressures and their changes upon HDT

Figure 3A compares IOP of SAC, NT, and T groups during seated and HDT posture. Univariate ANOVAs did not show group differences in both seated and HDT posture. However, a two-way repeated measures ANOVA of factors Group and Posture revealed a strong effect of posture ($P<0.001$). In all subjects' groups there were significant ($P=0.01$) IOP elevations upon HDT posture (SAC: +3.72 mm Hg; NT: +3.7 mm Hg; T: +4.04 mm Hg).

Figure 3B compares mean arterial pressure (MAP) of SAC, NT and T groups during seated and HDT postures. Univariate ANOVAs showed that there was a significant ($P=0.035$) difference among groups in the HDT posture (SAC<T, $P=0.0109$). A two-way repeated measures ANOVA of factors Group and Posture revealed that there was a significant ($P=0.046$) effect of posture but no interaction between Group and Posture.

Figure 3C compares OPP of SAC, NT, and T groups during seated and HDT posture. Univariate ANOVAs showed significant ($P=0.0093$) group differences in the HDT posture (SAC<T, $P=0.0024$). A two-way repeated measures ANOVA of factors Group and Posture revealed a significant effect of Group ($P=0.048$) a strong effect of Posture ($P<0.001$), as well as a strong interaction between Group and Posture ($P<0.001$). There were significant ($P=0.01$) OPP elevations upon HDT posture in NT (+6.96 mm Hg) and T (+7.83 mm Hg) groups but not in the SAC group.

Baseline PERG and systemic/ocular pressures as predictor of RNFL thinning

As both PERG and systemic/ocular pressures showed baseline and posture-dependent changes in thinners and non-thinners, we performed a multivariate statistical analysis to understand if RNFL thinning could be predicted based on baseline variables. Backwards stepwise logistic regression isolated 4 relevant variables (PERG amplitude seated, PERG phase seated, PERG phase HDT, and MAP HDT). Corresponding coefficients of the logistic regression equation are summarized in Table 2.

The logistic regression determined a prediction equation able to discriminate ($P=0.007$) eyes with RNFL thinning from eyes with unchanged RNFL with an area under the ROC curve of 0.89 (SE=0.07). This estimate was obtained using the same data from which the model was constructed. In Figure 4 the PERG variable (a linear combination of seated PERG amplitude/phase and PERG phase upon HDT) is plotted against MAP upon HDT. The

separation graph between T and NT displayed in Figure 4 shows that T appear to be separated from NT by diagonal line with 1 false negative and 5 false positives. We did not have an independent validation sample; however, repeating the logistic regression on the eyes non-selected for randomization discriminated eyes with RNFL thinning from eyes with unchanged RNFL with an area under the ROC curve of 0.833, SE=0.087 (supplementary Figure S1).

Retrospective analysis of baseline clinical characteristics of thinners and non-thinners

A relevant question to ask was whether RNFL thinning could have been predicted based on the baseline risk profile of patients. Retrospective analysis of baseline characteristics summarized in Table 3 shows that 5/9 (55%) of T and 8/19 (42 %) of NT received treatment during the follow up period. The difference in the frequency of treatment between the two groups was not statistically significant ($P=0.13$, Fisher exact test). Thinners, compared to non-thinners, were relatively older, had a thinner cornea, a larger disk cupping, thinner RNFL, and worse visual field MD/PSD. However, these differences were small and not statistically significant. There was no significant correlation between CCT and RNFL thickness in Thinners ($R=0.33$, $P=0.39$). The calculated OHTS risk score (<http://ohts.wustl.edu/risk/calculator.html>) also was relatively higher in T vs. NT but the difference not statistically significant. According to the OHTS risk calculator, the risk of developing glaucoma after 5 years was similar in thinners ($14.4 \pm 4.4\%$) and in non-thinners ($13.5 \pm 4.1\%$).

Overall, retrospective analysis of baseline risk profile was consistent with the prediction of RNFL thinning based on HDT-induced neurovascular changes but was per se insufficient to predict thinners from non-thinners.

Discussion

This longitudinal study on 28 glaucoma suspects shows that 9/28 of them developed significant mean RNFL thinning over 5 years while 19/28 did not. Both thinners and non-thinners had normal RNFL thickness at baseline, and in both groups the magnitude of RNFL change was unrelated to baseline RNFL thickness. The rate of change of mean RNFL thickness in the group of thinners ($-0.164 \mu\text{m/yr}$) was in the range of that reported by Miki et al, 2014 (mean $-2.02 \mu\text{m/yr}$)⁴⁴ for glaucoma suspects eventually developing visual field damage. However, none of the RNFL thinners in the present study developed visual field defects over the observation period.

The present study showed that both RNFL thinners and non-thinners, compared to similarly-aged controls, had significantly lower tilted PERG amplitude and delayed seated PERG phase. Previous cross-sectional results of our group¹⁵ also demonstrated posture-dependent PERG losses in glaucoma suspects. Thinners also had significantly higher MAP and estimated OPP compared to controls. Combining PERG variables with hemodynamic variables for randomly selected eyes at different posture in a logistic regression model predicted thinners from non-thinners with an area under the ROC curve of 0.89 ($P=0.007$). To ensure that the results were consistent, analyses were repeated on the eyes not originally selected with similar results. This represents a novel and potentially important finding, as

assessment of posture-dependent neurovascular variables may potentiate risk-assessment in the clinical management of glaucoma. We retrospectively compared baseline risk factors between thinners and non-thinners. A few of these variables (Table 3) showed borderline significant ($0.1 > p > 0.05$) differences between the two groups, but were not themselves sufficient to discriminate between thinners and non-thinners. According to the OHTS risk calculator, the risk of developing glaucoma after 5 years was similar in thinners (14.4 %) and in non-thinners (13.5%).

While the present study suggests that posture-dependent neurovascular variables have predictive value on future RNFL thinning, it does not provide clear insights about the corresponding causative mechanisms. Body inversion is known to be associated with a host of manifestations relevant to glaucoma, including IOP elevation, increased pressure of the central retinal artery and of the cerebrospinal fluid, vasoconstriction of the retinal arterioles, and orbital congestion.^{33, 35, 36, 46–48, 49, 50} Body inversion is also known to be associated with optic nerve dysfunction as shown by loss of PERG signal,^{14, 13} loss of VEP signal,^{7, 14} as well as loss of psychophysical visual function.¹¹ Prolonged head-down posture may cause irreversible ischemic damage in the optic nerve.¹²

This study has some limitations that need to be pointed out. First, the patients' sample was small. Second, some of the patients were treated during the follow up. IOP-lowering treatment may improve PERG amplitude⁵¹ and alleviate the magnitude of RNFL thinning. While IOP-lowering-dependent PERG amplitude improvement does not represent an issue as treatment was initiated after baseline PERG data were collected, IOP-lowering-dependent alleviation of RNFL thinning might have changed the status of some patients with borderline significant RNFL thinning from Thinners to Non-Thinners. This however, was unlikely the case as Fig. 1 shows that borderline non-Thinners were not treated. As treatment was administered in both Thinners and Non-Thinners, treatment did not significantly contribute to the logistic regression model. Third, the logistic regression model did not have an independent validation sample; however, logistic regression analysis on measurements of either fellow eyes or the average of the two eyes gave similar results. Fourth, RNFL thickness data were obtained with Stratus OCT that was available when the study was initiated; Stratus OCT had insufficient lateral resolution for detailed focal RNFL analysis. We cannot exclude that assessment of the region of maximal thinning with a current state-of-the-art OCT instrument might have produced somewhat different results.

Altogether, this study provides promising pilot data for a full-scale clinical trial to test the hypothesis that a HDT provocative test may help to potentiate risk-assessment in glaucoma suspects. A randomized clinical trial (NCT02390284), including HDT provocation in glaucoma suspects has been initiated at Bascom Palmer Eye Institute.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1.

Changes of mean RNFL thicknesses over ~ 5 years in randomly selected eyes of 28 glaucoma suspects. Initial and final RNFL thicknesses were the average of first 3 and last measurements of the longitudinal series, respectively. Note that 9/28 eyes had losses of RNFL thickness larger than 5.4 μm , which represents the $\pm$ 95% confidence interval of the normal intervisit test-retest variability of mean RNFL thickness according to Budenz et al, 2008. In both thinners and the non-thinners, the initial mean RNFL thickness was in the normal range according to Budenz et al., 2007. In both thinners and the non-thinners, there was no significant correlation between initial RNFL thickness and change of RNFL thickness (Non thinners, $R^2=0.026$; thinners, $R^2=0.014$). Thirteen patients (red symbols) received IOP-lowering drops during the follow-up period.

Figure 2.

Pattern electroretinogram amplitude (A) and phase (B) recorded in the seated (blue bars) and head-down (red bars) position from randomly selected eyes of Similarly-Aged Controls (SAC, n=11), RNFL non-thinners (NT, n=19), and RNFL thinners (T, n=9). Bars represent the mean and the SEM. Note that the PERG amplitude and phase tend to be smaller in RNFL thinners compared to RNFL non-thinners and similarly-aged controls. Also note that the PERG amplitude decreases upon HDT in non-thinners and thinners but not in controls.

Figure 3.

A: Intraocular pressure (IOP), B: mean arterial pressure (MAP) and C: ocular perfusion pressure (OPP) measured in the seated (blue bars) and head-down (red bars) position in randomly selected eyes of similarly-aged controls (SAC, n=11), RNFL non-thinners (NT, n=19), and RNFL thinners (T, n=9). Bars represent the mean and the SEM. Note in A that IOP increases in all groups upon HDT. Also note in B and C that MAP and OPP tend to be higher in the thinners group compared to non-thinners and similarly-aged controls. Note in C that OPP tends to increase upon HDT in non-thinners and thinners but not in controls.

Figure 4.

Relationship between posture-dependent PERG amplitude and phase coefficients (PERG component) and Mean Arterial Pressure upon head-down posture (MAP on tilt) in randomly selected eyes of a population of 28 glaucoma suspects who were followed at least 4 years with OCT. Larger, filled symbols represent eyes that developed mean RNFL thinning larger than $5.4 \mu\text{m}$ (grey, $P < 0.05$; black, $P < 0.01$). Small open symbols represent eyes without significant RNFL thinning. Coefficients were obtained by backward logistic regression. Note the relatively good separation between RNFL thinners and non-thinners.

Table 1

Baseline characteristic of glaucoma suspects

		N. of subjects (%)
Gender	Males	10 (38%)
	Females	18 (62%)
Race	Caucasian	22 (79%)
	African American	5 (17%)
	Other	1 (3%)
Ethnicity	Non-Hispanic	16 (59%)
	Hispanic	12 (41%)
Family history of glaucoma		15 (52%)
		Mean (SD)
CCT (μm)		535.7 (38.5)
Age (years)		57.3 (8.7)
IOP (mm Hg)		15.7 (3.1)
vCDR		0.54 (0.13)
RNFL thickness (μm)		101.3 (11.4)
MD (dB)		-0.83 (1.46)
PSD (dB)		1.82 (0.64)

CCT: central corneal thickness; IOP: intraocular pressure; vCDR: vertical cup-to-disk ratio; MD: Humphrey visual field 24-2 Mean Deviation; PSD: Humphrey visual field 24-2 Pattern Standard Deviation.

Table 2

Summary of logistic regression parameters

Variable	Coefficient	(SE)	P-value*
PERG_amp_seated	−5.216	(2.765)	0.024
PERG_phase_seated	−18.226	(9.324)	0.014
PERG_phase_HDT	5.956	(5.358)	0.20
MAP_HDT	0.202	(0.100)	0.005
Constant	4.792		

Table 3

Retrospective analysis of baseline characteristics of glaucoma suspects

		Thinners (N)	Non-Thinners (N)	Total (N)
Gender	Male	3	7	10
	Female	6	12	18
Race	Caucasian	8	14	22
	African American	1	4	5
	Other	0	1	1
Ethnicity	Non-Hispanic	5	11	16
	Hispanic	4	8	12
Family History		5	10	15
Topical treatment		5	8	13
		Mean (SD)	Mean (SD)	P value
Age (years)		62.3 (5.2)	56.04 (9.7)	0.09
CCT (mm)		527.80 (39.50)	542.26 (37.43)	0.36
IOP (mmHg)		15.0 (1.8)	15.1 (3.17)	0.93
vCDR		0.60 (0.07)	0.51 (0.14)	0.08
MD (dB)		-1.41 (1.72)	-1.29 (3.61)	0.93
PSD (dB)		1.99 (0.74)	1.72 (0.54)	0.283
RNFL Thickness (μm)		98.01 (13.08)	103.15 (9.65)	0.253
OHTS risk calculator (points)		9.7 (2.10)	7.84 (2.78)	0.09

CCT: central corneal thickness; IOP: intraocular pressure; vCDR: vertical cup-to-disk ratio; MD: Humphrey visual field 24-2 Mean Deviation; PSD: Humphrey visual field 24-2 Pattern Standard Deviation; RNFL: Retinal Nerve Fiber Layer Thickness; OHTS: Ocular Hypertension Treatment Study.