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Normative Data for a User-friendly Paradigm for Pattern Electrophoretogram Recording

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Abstract

Purpose—To provide normative data for a user-friendly paradigm for the pattern electrophoretogram (PERG) optimized for glaucoma screening (PERGLA).

Design—Prospective nonrandomized case series.

Participants—Ninety-three normal subjects ranging in age between 22 and 85 years.

Methods—A circular black–white grating of 25° visual angle, reversing 16.28 times per second, was presented on a television monitor placed inside a Ganzfeld bowl. The PERG was recorded simultaneously from both eyes with undilated pupils by means of skin cup electrodes taped over the lower eyelids. Reference electrodes were taped on the ipsilateral temples. Electrophysiologic signals were conventionally amplified, filtered, and digitized. Six hundred artifact-free repetitions were averaged. The response component at the reversal frequency was isolated automatically by digital Fourier transforms and was expressed as a deviation from the age-corrected average. The procedure took approximately 4 minutes.

Main Outcome Measures—Pattern electrophoretogram amplitude (μV) and phase (π rad); response variability (coefficient of variation [CV] = standard deviation [SD] / mean $\times$ 100) of amplitude and phase of 2 partial averages that build up the PERG waveform; amplitude (μV) of background noise waveform, obtained by multiplying alternate sweeps by +1 and –1; and interocular asymmetry (CV of amplitude and phase of the PERG of the 2 eyes).

Results—On average, the PERG has a signal-to-noise ratio of more than 13:1. The CVs of intrasession and intersession variabilities in amplitude and phase are lower than 10% and 2%, respectively, and do not depend on the operator. The CV of interocular asymmetries in amplitude and phase are 9.8 $\pm$ 8.8% and 1.5 $\pm$ 1.4%, respectively. The PERG amplitude and phase decrease with age. Residuals of linear regression lines have normal distribution, with an SD of 0.1 log units for amplitude and 0.019 log units for phase. Age-corrected confidence limits ($P < 0.05$) are defined as ± 2 SD of residuals.

Conclusions—The PERGLA paradigm yields responses as reliable as the best previously reported using standard protocols. The ease of execution and interpretation of results of PERGLA indicate a potential value for objective screening and follow-up of glaucoma.

For more than 20 years, the pattern electrophoretogram (PERG) has been described as a very promising technique for detecting early losses of retinal ganglion cells (RGCs) in optic neuropathies.^{1,2} In glaucoma, the primary outcome is the death of RGCs; therefore, the PERG may have a clinical value as a direct and objective index of RGC function. Indeed, the PERG

is altered dramatically in patients with glaucoma³⁻¹² and is altered significantly in a high percentage of subjects with ocular hypertension who have normal automated standard perimetry.^{9,13-20} An abnormal PERG in glaucoma suspects may predict future impairment of the visual field.^{11,17-19} In addition, in patients with ocular hypertension, the PERG may improve after pharmacologic reduction of the intraocular pressure.²¹⁻²⁵ Furthermore, in patients with ocular hypertension, the PERG may show exacerbated losses after transient increases of intraocular pressure with a suction cup.^{26,27} Finally, comparative evaluation of techniques for early glaucoma detection shows that the PERG may have a better sensitivity and specificity than short-wavelength automated perimetry.²⁸ In glaucomatous eyes with normal standard automated perimetry, highly significant losses may be found in the PERG as well as in psychophysical tests such as frequency-doubling perimetry and short-wavelength automated perimetry.²⁰

Despite its great potential as an objective test for the earlier diagnosis and monitoring of progression of early stages of glaucoma, the PERG has been virtually ignored in the ophthalmologic practice. A likely explanation is that the PERG is a difficult response to record. As compared with the ordinary flash ERG, the PERG amplitude is smaller by a factor of 100 or more. In addition, with ordinary corneal electrodes embedded in a contact lens or in a speculum, the visibility of the pattern stimulus is somehow impaired. To avoid interference with vision, corneal electrodes consisting of tiny threads of carbon fibers or tiny gold laminae may be inserted into the conjunctival fornix or leaned on the corneal surface after topical anesthesia. The use of these electrodes requires a skilled operator and compliance from patients for stable recordings. In addition, the use of these electrodes may not be extended to all subjects, and prolonged recording sessions may cause corneal damage. Overall, these obstacles contributed to the present disrepute of the PERG technique, described in some reports as “unreliable for clinical purposes.”²⁹⁻³¹

An alternative method of recording the PERG without the shortcomings described above is by means of skin electrodes taped on the lower eyelids. This method drastically eliminates the problem of (1) optical degradation of the pattern stimulus, (2) electrode stability, (3) dependency on a skilled operator, and (4) patient compliance. An obvious drawback of noncorneal electrodes, as compared with corneal electrodes, is the reduction of signal amplitude by a factor of 2 to 3.³²⁻³⁴ Nevertheless, responses with a high signal-to-noise (S/N) ratio may be obtained provided that (1) the spatial-temporal characteristics of the stimulus are chosen to maximize response amplitude, (2) the averaging is adequate to reduce the noise level, and (3) the response evaluation is performed in the frequency domain to isolate automatically the signal (response component at the frequency of contrast reversal) from the noise (at frequencies different from that of contrast reversal).³⁵ This approach also eliminates the need for an experienced operator to interpret the response waveform.

This paper describes a paradigm for recording a robust and reliable PERG in a fast and automatic way. Normative data are provided for a population of 93 healthy individuals of different age. Preliminary results have been previously reported in abstract form (Porciatti V, Ventura LM. Electrophysiological screening for glaucoma: normative data with a non-invasive, fast, and fully automatic version of the pattern ERG called PERGLA. Presented at: The Association for Research in Vision and Ophthalmology Annual Meeting, May 4–10, 2002; Ft. Lauderdale) (Porciatti V, Ventura LM. Objective screening for retinal ganglion cell function in glaucoma with a fast and non-invasive version of the PERG. Presented at: American Academy of Ophthalmology Annual Meeting, October, 2002; Orlando).

Materials and Methods

Electrode and Subject Placement

A sketch of the electrode and subject placement is displayed in Figure 1A–E. A small patch (approximately 1 cm²) of the skin of the central forehead, of the temples, and lower eyelids is gently cleansed with electrode skin preoperative preparation pads (containing 70% isopropyl alcohol and pumice) to reduce skin impedance at less than 5000 Ohm. Five skin electrode cups (9 mm diameter) are filled with conductive jelly and taped (surgical tape, 1.5 × 1.5 cm) over the cleansed skin. The central forehead electrode is placed 3 cm above the bridge of the nose. The temporal electrodes are placed 3 cm lateral to the lateral canthus. For lower-eyelid electrodes, the upper margin of the electrode is kept 5 mm below eyelashes. The subject leans his or her chin and forehead over a chin rest placed in front of a television display, placed at 30 cm distance from the subject's eyes. To record the PERG, the subject fixates with both eyes on a target at the center of the pattern display. The television display is contained within a Ganzfeld bowl to provide a fixed amount of background adaptation (4 cd/m²). Pupils are undilated.

Characteristics of the Pattern Stimulus and Signal Conditioning

The recording system is an adaptation of an existing commercial set up for visual electrophysiology (Glaide; Lace Elettronica, Pisa, Italy). The pattern stimulus consists of a black–white horizontal bar grating with a square-wave profile, displayed on a television monitor (14.1-cm diameter circular field). When subjects look at the center of the patterned field from a 30-cm viewing distance, the pattern covers a circular retinal area with a 25° diameter centered on the fovea. The mean luminance of the display is 40 candela/m², the spatial frequency of the grating is 1.6 cycles/degree, and the contrast of the grating is 98%. The contrast is defined as the difference in luminance between light and dark bars, divided by the sum of their luminance. The bars alternate in counterphase at 8.14 Hz (temporal period, 122.8 milliseconds; 2 contrast reversals per period) without changes in mean luminance. Electrical signals from skin electrodes are fed into a 2-channel differential amplifier (eyelid active, ipsilateral temple reference, forehead common ground), amplified (100,000 fold), filtered (1–30 Hz), and digitized with 12-bit resolution at 4169 Hz. The electrode impedance is evaluated automatically, and a light-emitting diode indicates whether the impedance is acceptable (less than 5000 Ohm).

Signal Processing

The PERG waveform is obtained by averaging 600 artifact-free time periods of 122.8 milliseconds in duration (sweeps), in synchrony with contrast alternation. Two independent response blocks of 330 sweeps each are recorded. For each block, the first 30 sweeps are rejected from the average to eliminate the spurious effect of the stimulus onset and to allow a steady-state recording. Fixation time lasts approximately 1.30 minutes, during which time the subject is allowed to blink freely. Sweeps containing spurious signals originating from eye blinking or gross eye movements are automatically rejected over a threshold voltage of ± 25 μ V. Typically, 5 to 50 spurious sweeps per recording are rejected. The number of rejections has no effect on the averaged waveform, although the recording time is somewhat longer when the rejection rate is higher. After a brief pause, a second PERG block is recorded. The first and the second PERG blocks are superimposed automatically to have a visual indication of response consistency and then averaged. An index of response consistency is computed automatically by the coefficient of variation (CV = standard deviation [SD] / mean × 100) of PERG amplitude and phase of the 2 blocks. Typically, the CVs of amplitude and phase are of the order of 10% and 1.5%, respectively. For occasional larger variabilities, the operator may acquire additional blocks of 300 sweeps to reduce the CV. An example of PERG waveforms simultaneously recorded in the 2 eyes is displayed in Figure 1F. Because the PERG has been recorded in

response to relatively fast alternating gratings, the response is typically steady state; that is, it has a sinusoidallike waveform with a frequency corresponding to the reversal rate. Steady-state responses are analyzed best in the frequency domain by digital Fourier transform to isolate the harmonic component at the contrast-reversal rate (16.28 Hz) and to compute its amplitude in μV and phase in π rad. To avoid inherent discontinuity of phase data around the value modulo (2π rad), readings smaller than 1π rad were reconstructed automatically (unwrapping) with an additive constant of 2π .³⁵ At the reversal rate of 16.28 Hz, a phase shift of 0.1π rad corresponds to a latency change of 3.1 millisecond. To facilitate the clinical interpretation of results, amplitude and phase data also were expressed in deviation from normal. Figure 1G shows a polar diagram representing deviations of amplitude and phase from age-predicted averages. The origin of axes represents zero deviation. One division on the deviation plot represents 1 SD unit, and the box represents the 95% confidence boundary (± 2 SDs) of amplitude and phase. In the example of Figure 1G, the PERGs of the 2 eyes have an amplitude and phase slightly 'better' (greater) than the normal age-corrected average, and a very small interocular asymmetry. The noise amplitude deviates approximately -10 SD from the normal average.

A "noise" response is obtained simultaneously with the PERG by multiplying alternate sweeps by $+1$ and -1 before averaging, thereby canceling the stimulus-evoked response and leaving the background activity.³⁶ The noise waveform also is submitted automatically to digital Fourier transform to isolate the 16.28-Hz component. The average amplitude of the noise waveform was $0.08 \pm 0.03 \mu\text{V}$, which is of the same order as that of the noise obtained by recording a blank response (with the stimulus occluded; see below). Under the present experimental condition, the noise index was independent of age (Pearson, 0.0117 [right eye], $P = 0.91$; Pearson, -0.019 , $P = 0.865$).

Subjects

Subjects of this study were a mixed population of individuals (63 white, 23 Hispanic, 4 Asian-American, 1 Indian-American, 2 black) of both genders (56 males, 37 females) and of different ages (range, 22–85 years; mean $\pm$ SD, 43.5 ± 18 years). Subjects were free from systemic or ocular diseases as assessed by routine ophthalmologic examination and had best-corrected Snellen visual acuity of 20/20 or better. Individuals with myopia of more than 4 diopters (D) were excluded because the ERG is reduced in high myopia.³⁷ Subjects had refractive errors smaller than ± 3.5 spherical D, ± 2.0 cylindrical D, which were corrected for the viewing distance (30 cm). In all subjects, the Jaeger visual acuity for near was corrected to J1+. The methods applied in the study adhered to the tenets of the Declaration of Helsinki for the use of human subjects in biomedical research. Institutional review board/ethics committee approval was obtained for this study, and informed consent was obtained from each subject before recording.

Operators

Operators were the senior author, 1 research fellow, and 4 medical students who rotated in the laboratory.

Results

Figure 2 is a scatterplot of amplitude and phase of the PERG recorded from both eyes of 93 subjects ranging in age from 22 to 85 years. Open symbols represent right eyes, and closed symbols represent left eyes. Thick lines represent the regression lines, and thin lines represent the 95% confidence intervals.

Amplitude data could be best fitted with a linear regression line on log-log coordinates. Phase data could be fitted best with a linear regression line on linear-linear coordinates. For both

amplitude and phase, the slope of regression was virtually identical by analyzing separately the right and left eyes. For the statistical analysis, only 1 eye (left eye) per subject was included. For amplitude data, the equation of the regression line for the left eyes was $\log(\text{Amp}) = 0.583 - 0.357 \times \log(\text{Age})$; $R = 0.53$; $P < 0.001$. For phase data, the equation of the regression line for the left eyes was $\text{Phase} = 1.99 + 0.0027 \times \text{Age}$; $R = 0.514$; $P < 0.001$. For both amplitude and phase, the distribution of residuals was not significantly different from normality (amplitude: Kolmogoroff-Smirnoff distance = 0.076, $P = 0.22$; phase: Kolmogoroff-Smirnoff distance = 0.063, $P = 0.48$). The SD of residuals was ± 0.10 log units for amplitude and ± 0.019 log units for phase. The 95% age-corrected confidence limits of normality have been defined as ± 2 SD of residuals above and below the amplitude and phase predicted for the subject's age according to the linear equations described above. In practice, the lower confidence limit of age-corrected amplitude is: $10^{(\log(\text{Predicted Amp}) - 2 \times 0.10)}$. This value is 36.9% lower than the amplitude predicted from regression of amplitude data and is well above the noise level for all ages. The lower confidence limit for phase is: $10^{(\log(\text{Predicted Phase}) - 2 \times 0.019)}$. This value is 8.4% lower than the phase predicted from regression of phase data.

The left panel of Figure 2 also shows an estimate of the average noise level (described in more detail in "Methods"). On average, the noise amplitude was smaller than the average PERG signal by a factor of more than 10.

Variability and Repeatability

We measured the PERG variability both within one session and between sessions. We identified 4 main sources of variability: intrinsic, same day, test-retest, and operator dependent. All variabilities are expressed as CV ($\text{SD} / \text{Mean} \times 100$) of amplitude and phase between 2 responses recorded in the same session or in different sessions.

Intrinsic Variability—Evaluation of intrinsic variability is necessary to establish whether a response is reliable and to provide an index of variance for the statistical comparison of the differences between serial responses. Intrinsic variability is defined as the CV of 2 consecutive partial averages of 300 sweeps, divided by $\sqrt{2}$. Adjustment by a $\sqrt{2}$ factor was required to compare the CV of intrinsic variability with the CVs of the other sources of variability (calculated on averages of 600 sweeps).

Same-Day Variability—The PERG was recorded twice during the same day (at least 4 hours apart). During the interval, the electrodes were kept in place but disconnected from the recording system, and the subjects were free to roam indoors.

Test-Retest Variability—The PERG was recorded on the same subject in 2 different sessions (at least 1 week apart) by the same operator.

Operator-Dependent Variability—The PERG was recorded on the same subject in 2 different sessions (at least 1 week apart) by 2 different operators.

All variabilities are summarized in Table 1.

Analysis of these data indicates that the main source of variability is intrinsic to the response itself. Repeating the test during the same day, or on different days with the same or different operators, does not change substantially the coefficient of variation. Phase variability, as compared with amplitude variability, is typically smaller (by a factor of 4 to 8 in our paradigm).

Interocular Asymmetry

In addition to PERG amplitude and phase, interocular asymmetry in these measures may offer additional information about early RGC dysfunction. For example, if a disease progresses asymmetrically as with glaucoma,³⁸ then the amount of asymmetry may be expected to be abnormally high even before the PERG amplitude and the phase may exceed the 95% confidence limits of normal controls. In Figure 3, amplitude and phase data of one eye are plotted against corresponding values of the other eye. The PERGs of the 2 eyes were highly correlated (amplitude, $R = 0.87$; phase, $R = 0.92$). To have a normalized index of interocular asymmetry, the PERGs of the 2 eyes are automatically compared, and the CV of amplitude and phase between the 2 eyes are calculated. Average interocular asymmetries in amplitude and phase ($n = 93$) were $9.8 \pm 8.8\%$ and $1.5 \pm 1.4\%$, respectively. Interocular asymmetry in amplitude and phase did not depend on age (amplitude: $R = 0.15$, $P = 0.15$; phase: $R = 0.08$, $P = 0.4$).

A question to ask is whether the interocular asymmetry in normal subjects reflects a real difference between the responses of the 2 eyes or merely a difference resulting from the statistical variability of the responses of the 2 eyes. One way to address this point is to determine whether the sign and the amount of intereye differences (the right eye minus the left eye) are maintained in the test–retest paradigm. If the intereye difference reflects a real difference in the response of the 2 eyes, one would expect that the sign and the amount of difference would be maintained in the test–retest condition. If, conversely, the intereye differences were the result of random variability, one would expect a random change in the sign and the amount of difference between the test and retest. We correlated the differences in amplitude between the 2 eyes (the right eye minus the left eye) of the baseline PERG with corresponding differences of the retest PERG. The differences were linearly correlated ($R = 0.7$; $P = 0.002$; $n = 26$), indicating that interocular differences reflect real differences between the 2 eyes, rather than random fluctuation.

One possible flaw in evaluating PERG interocular asymmetries would be that the recording electrode in one eye picks up the electrical signals originating in the other eye. This indeed has been reported to occur using gold foil corneal electrodes.^{39,40} We have addressed this issue by recording the PERG in 6 different normal subjects with 1 of the 2 eyes occluded. The PERG of the occluded eye had an average amplitude of $0.084 \pm 0.03 \mu\text{V}$, which is virtually identical to the average noise index of the normal population. This indicates that under our recording conditions, the PERG is not significantly contaminated by the activity originating in the contralateral eye.

Discussion

The aims of this study were to describe a paradigm for robust and reliable PERG recording and to provide the confidence limits for a population of normal individuals of different ages. This paradigm is fundamentally different from the standard PERG⁴¹ and has been given the acronym PERGLA to emphasize its primary use as a clinical tool for early detection and follow-up of glaucoma patients. The set of experimental conditions are synthesized from well-described elements that already existed in isolation in the literature.

As compared with standard PERG techniques,⁴¹ the PERGLA appears to be patient and user-friendly, because it does not require topical anesthesia, uncomfortable corneal electrodes, skilled operators, patient compliance, or the interpretation of response waveforms. The entire procedure takes approximately 4 minutes and can be carried out by a trained technician. Amplitude and phase deviations from age-corrected normal averages are readily evaluated on a polar diagram. In addition, indices of response consistency, noise, and interocular asymmetry

are provided simultaneously. These indices may represent important supplementary information for the statistical significance and the clinical interpretation of the response.

Although several studies compared the PERG obtained with different electrodes to establish which yielded the maximal response amplitude,³⁴ little is known about the response noise under different conditions. The strength of a response, however, depends more on the S/N ratio than on the absolute amplitude. The PERG recorded with the present paradigm has an average amplitude of 1.1 μV and an average noise of 0.08 μV , resulting in an average S/N ratio of 13.7. This value can be considered high in the field of evoked potential recording under most circumstances.⁴² In our paradigm, a low noise level was obtained by averaging 600 sweeps (reducing the noise by a factor of 25) and by isolating the response component (at the reversal frequency) from unwanted biologic activity such as that generated by the eye muscles, eye movements, and electroencephalography (occurring mainly at frequencies different from the reversal rate). A further element that may have helped to reduce the noise was the use of a narrow rejection window ($\pm 25 \mu\text{V}$), which allowed for the discarding of most of the unwanted activity generated by eye blinks. This setting is narrower by a factor of 4 as compared with that commonly accepted in standard conditions.⁴¹ Setting a narrow rejection window was possible because the active and the reference electrode had matched impedances, thereby exploiting the characteristics of the common-mode rejection of the differential amplifiers.

The PERG signal was maximized by choosing spatial-temporal conditions that yield maximal amplitude in normal subjects.³⁵ Interestingly, these conditions are the same as those under which glaucoma patients and monkeys with experimental glaucoma display the earliest and largest PERG losses.^{9,13,14,25,43} Thus, the beneficial effects of optimizing the spatial-temporal conditions are reflected on both the S/N ratio and the test sensitivity for screening of glaucoma.

In addition to a favorable S/N ratio, PERG reliability depends on the trial-to-trial variability of the signal itself and the reproducibility of the response in the test–retest. We have computed several intrasession and intersession indices of response variability, also taking into account the effect of changing the operator. Under all conditions, the coefficient of variation in amplitude is well within 10%, and that of phase is well within 2%. The CVs of intrasession variability and test–retest variability are of the same order of magnitude as those reported in the literature using corneal electrodes, experienced operators, and stringent technical controls.^{44,45}

In normal controls, the PERG amplitude and phase decrease (latency increases) with increasing age, in agreement with several previous reports.^{35,46–49} Age-related PERG changes may result in part from reduction of retinal illuminance⁵⁰ resulting from senile miosis and from reduction in image contrast resulting from increased light scattering in optical media.^{48,51} When the response is normalized for senile miosis,^{35,46,47,49,52} however, and senile lenses are substituted with pseudophakic implants,³⁵ the PERG of aged subjects is still substantially reduced and delayed as compared with the PERG of younger subjects. This indicates, at least in part, an age-dependent loss of retinal ganglion cells (for review, see Neufeld and Gachie⁵³). With the present paradigm, PERG amplitude data could best be fitted with a linear regression line on log–log coordinates, whereas phase data are best fitted on linear–linear coordinates. Because residuals had normal distribution, regression analysis allowed the prediction of age-corrected averages of amplitude and phase as well as the 95% confidence limits of normality (± 2 SD of residuals). What is important for the clinical application is that the lower 95% confidence interval for amplitude is well above the noise level, thereby allowing a suitable amplitude range for detection of abnormal responses and evaluation of progressive response deterioration.

Little is known on normative data for PERG interocular asymmetries. Hull and Drasdo⁴⁸ measured the intereye ratio for the transient PERG in response to reversing checkerboards with

30' checks. They found that the average intereye amplitude ratio (worse eye divided by better eye) was 0.85 ± 0.07 , which corresponds to a CV of approximately 8%. This value is of the same order of magnitude as the CV of interocular amplitude asymmetry found in the present study ($9.8 \pm 8.8\%$). With the PERGLA paradigm, the 95% confidence limit of interocular difference in amplitude is 0.13 log units. Interestingly, this value is close to that reported for interocular differences in visual acuity in normal subjects (0.16 logarithm of the minimum angle of resolution).⁵⁴ As far as we know, no data on interocular PERG phase asymmetry are available in the literature. The 95% confidence limit of interocular difference in phase determined in the present study is 0.02 log units only.

In conclusion, the PERG recorded with the PERGLA paradigm seems to be as robust and reliable as the PERG obtained using standard protocols with corneal electrodes, experienced operators, and stringent technical requirements. The use of skin electrodes, automatic analysis, and expression of data as deviation from age-corrected norms extends the use of the technique to operators with minimal training. The technique appears particularly promising for the screening of glaucoma. Preliminary results obtained on a large population of glaucoma suspects (with abnormal optic disc appearance and normal Humphrey visual field) showed that the PERG was abnormal in amplitude, phase, or interocular asymmetry in nearly 50% of them (Ventura LM, Porciatti V, Parrish RK II. Over 50% of glaucoma suspects with increased disk cupping and normal visual field have abnormal function of retinal ganglion cells. Abstract presented at: American Academy of Ophthalmology Annual Meeting, October, 2002; Orlando). This figure may originate in part from nonspecific PERG reductions,⁵⁵ and therefore may overestimate the number of persons who may have or may experience glaucomatous dysfunction. Finally, with the PERGLA paradigm, the response reproducibility is small enough to encourage the use of serial PERGs for monitoring progression of glaucomatous neuropathy and the effects of treatment to lower the intraocular pressure.

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Figure 1.

Electrode montage, subject positioning, and examples of response and deviation plots. **A**, Skin preparation with a cleansing pad. **B**, Positioning of a flat cup electrode on the lower eyelid with surgical tape. **C**, Placement of active (eyelids), reference (temples), and ground (forehead) electrodes. **D**, Subject positioning before the visual stimulus. **E**, Sketch of the visual stimulus inside the Ganzfeld bowl. **F**, Pattern electroretinogram (PERG) waveforms recorded simultaneously from the right and left eyes of a representative normal subject. The label rev on the x-axis indicates the time of contrast reversal. **G**, Polar diagram representing deviations of amplitude (y-axis) and phase (x-axis) from age-predicted averages. The origin of axes represents zero deviation. One division on the grid represents 1 standard deviation (SD) unit, and the box represents the 95% confidence boundary of amplitude and phase. The amplitude of the noise level deviates approximately -10 SD from the average normal PERG amplitude. For further explanation, see text.

Figure 2. Age-dependent pattern electroretinogram (PERG) changes. Scatterplots of PERG amplitude (left) and phase (right) as a function of age. Open symbols represent right eyes, and closed symbols represent left eyes. Thick regression lines for both right and left eyes are shown superimposed. Thin lines represent the corresponding 95% confidence intervals. For further explanation, see text.

Figure 3. Interocular pattern electroretinogram (PERG) asymmetry. Amplitude (left) and phase (right) data of the left eyes (OS) are plotted against corresponding data of the right eyes (OD). Scatterplots show the regression lines (thick) as well as the 95% confidence intervals (thin lines). For further explanation, see text.

Table 1

Summary of Variability and Repeatability of the Pattern Electroretinogram Recorded According to the Pattern Electroretinogram for Glaucoma Paradigm (See Text for Explanation)

Source of Variability	Coefficient of Variation and Standard Deviation		Number of eyes
	<i>Amplitude</i>	<i>Phase</i>	
Intrinsic	6.9 ± 4.9	0.85 ± 0.75	186
Same-day	6.3 ± 3.4	1.3 ± 0.05	12
Test–retest	8.2 ± 5.0	1.7 ± 1.4	52
Operator-dependent	8.5 ± 9.3	1.4 ± 1.5	16