Quantifying Effects of Retinal Illuminance on Frequency Doubling Perimetry

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PURPOSE. To measure and quantify effects of variation in retinal illuminance on frequency doubling technology (FDT) perimetry.

METHODS. A Zeiss-Humphrey/Welch Allyn FDT perimeter was used with the threshold N-30 strategy. Study 1, quantifying adaptation: 11 eyes of 11 subjects (24–46 years old) were tested with natural pupils, and then retested after stable pupillary dilation with neutral density filters of 0.0, 0.6, 1.2, and 1.6 log unit in front of the subject’s eye. Study 2, predicting effect of reduced illuminance: 17 eyes of 17 subjects (26–61 years old) were tested with natural pupils, and then retested after stable pupillary miosis (assessed with an infrared camera). A quantitative adaptation model was fit to results of Study 1; the mean adaptation parameter was used to predict change in Study 2.

RESULTS. Study 1: Mean defect (MD) decreased by 10 dB over a 1.6 log unit range of retinal illuminances; model fits for all subjects had $r^2 > 95\%$. Study 2: Change in MD (ΔMD) ranged from $-7.3$ dB to $+0.8$ dB. The mean adaptation parameter from Study 1 accounted for 69% of the variance in ΔMD ($P < 0.0005$), and accuracy of the model was independent of the magnitude of ΔMD ($r^2 < 1\%$, $P > 0.75$).

CONCLUSIONS. The results confirmed previous findings that FDT perimetry can be dramatically affected by variations in retinal illuminance. Application of a quantitative adaptation model provided guidelines for estimating effects of pupil diameter and lens density on FDT perimetry. (Invest Ophthalmol Vis Sci. 2005;46:235–240) DOI:10.1167/iovs.04-0264

Perimetric testing is used clinically to detect visual field abnormalities and to monitor change during the course of management of a patient. Ability to detect perimetric defects is limited by normal between-subject variability, which is due in part to variations in preretinal factors such as refractive status, pupil diameter, and density of the crystalline lens.\(^1\) Goldmann’s standardization\(^2\) of kinetic perimetry reduces the effects of preretinal factors by requiring proper refraction and by using a background luminance for which sensitivity should adhere to Weber’s law for most subjects with clear ocular media and pupil diameters of 3 mm or greater. Adherence to Weber’s law ensures that sensitivity will be relatively unaffected by change in retinal illuminance.\(^1\) Ability to monitor change over time is greater when account is taken of preretinal factors.

When clinical testing employs alternate forms of perimetric stimuli, it is useful to estimate the extent to which preretinal factors affect sensitivity. An alternate form of perimetry, referred to as Frequency Doubling Technology (FDT) perimetry, reduces the effect of refractive error by using measuring contrast sensitivity for low-spatial-frequency sinusoids,\(^3,4\) although correction of refractive error is still required for optimal performance.\(^5\) FDT perimetry uses high-frequency flicker,\(^6\) for which high mean luminances are required to reach the Weber region.\(^7\) Previous studies\(^8–10\) have demonstrated that results of FDT perimetry can be dramatically affected by changes in retinal illuminance (e.g., lenticular density or pupil diameter) and optical scatter (e.g., cataract).

Pupil diameter can be highly variable across subjects; for the 100 cd/m² mean luminance of the FDT perimeter, pupil diameter in a normal population\(^11\) varies from 2 mm to 7 mm. The present study varied retinal illuminance in normal eyes over the range of retinal illuminances expected in clinical populations (normal variations in pupil diameter and lenticular density, as well as pharmacologic mydriasis). The data were analyzed using a quantitative two-parameter adaptation model for the effects of retinal illuminance. A single adaptation parameter was estimated by analyzing effects of mean luminance on FDT perimetry for volunteers with healthy eyes and clear ocular media (Study 1); then the model was used to predict effects of change in retinal illuminance (Study 2). The analysis provided clinical guidelines for estimating effects of preretinal factors on FDT perimetry.

METHODS

Subjects

Subjects were recruited from the faculty and staff of the State University of New York, State College of Optometry, and were experienced visual field testers with normal ophthalmic examinations and best-corrected visual acuity of 20/20 or better. In Study 1, 11 eyes of 11 subjects ranging in age from 24 to 46 years (mean ± 1 SD = 33 ± 8) were fixed to fit the key parameters for a model of effects of retinal illuminance. In Study 2, 17 eyes of 17 subjects (26 to 61 years, 43 ± 11) were tested to assess the ability of the model to predict effects of reduced illuminance. The study followed the tenets of the Declaration of Helsinki and was approved by the State University of New York, State College of Optometry Institutional Review Board. After the purpose and procedures for the study were discussed with each subject, written informed consent was obtained before testing.

Apparatus

An FDT perimeter (Zeiss-Humphrey/Welch Allyn FDT Visual Field Instrument; Welch Allyn, Skaneateles, NY) was used with a threshold N-30 test strategy. Testing was conducted in a dimly lit room. In Study 1, stimulus luminance was decreased by placing neutral density filters (Wratten; Eastman Kodak Company, Rochester, NY) in front of the subject’s eye. The wavelength spectrum of the perimeter’s phosphor was measured with a spectroradiometer (SpectraScan PR-704; Photo...
retinal illuminance from pupil size, and the middle panel to compute MD from retinal illuminance. The example for a cataractous lens only includes effects of reduced effective illuminance; reduction in contrast would further reduce MD with equal losses at all pupil diameters (decrease in sensitivity parameter).

Research, Inc., Chatsworth, CA), and was used to calculate the effects of age-related changes in lens density on effective retinal illuminance.

For an 8 mm pupil, the nominal mean FDT luminance of 100 cd/m² yields an effective mean retinal illuminance of 3.4 log td. The FDT perimeter sends an error message when mean luminance drops below 85 cd/m². Because this message did not appear during any of the tests, the nominal mean luminance was considered to be within 0.1 log unit of actual luminance. Neutral density filters of 1.6, 1.2, and 0.6 log unit were used to obtain mean retinal illuminances of 1.8, 2.2, and 2.8 log td, respectively.

Procedure

Study 1. FDT perimetry was performed first with the natural pupil, and then pupillary dilation was induced by one drop of 0.5% tropicamide ophthalmic solution (Acorn Inc., Buffalo Grove, IL). After stable dilation, subjects were retested four times with mean retinal illuminances of 1.8 to 3.4 log td. A brief break was given between each test. To minimize effects of sequential testing on group means, the order of retinal illuminances was 3.4, 2.8, 2.2, 1.8 log td for the first five subjects, and 1.8, 2.2, 2.8, 3.4 log td for the remaining six subjects.

Study 2. Subjects were first tested on FDT perimetry with their natural pupil, then miosis was induced by one or two drops of 1% pilocarpine ophthalmic solution (Darby Drug Company, Westbury, NY). After stable miosis, subjects were retested on FDT perimetry. Miotic pupillary diameter was determined by imaging the eye with an infrared camera. To obtain pupil diameter, the ratio of pupillary diameter and corneal diameter on the image was multiplied by the corneal diameter measured in direct examination of the subject’s eye.

Analysis

Mean retinal illuminance for FDT perimetry was computed in trolands as a function of pupil size (Fig. 1, left panel), using the method of LeGrand12 to correct for the Stiles-Crawford effect. The effect of lens density on effective retinal illuminance was computed using the spectrum of the FDT phosphor and a set of standard cone fundamentals with macular pigment removed, for age-related14 and cataract-related15 increases in lens density. Since illuminance varies with the square of pupil diameter, the effect of change in diameter is more dramatic for smaller pupils: a 2 mm increase in pupil diameter causes retinal illuminance to increase by 0.55 log unit from 2 mm to 4 mm, but by only 0.05 log unit from 8 mm to 10 mm. For all subjects pupil diameter was judged to be at least 8 mm by direct measurement with a pupil gauge; a value of 8 mm (3.4 log td) was used for all subjects.

The mean defect (MD) versus retinal illuminance functions (Fig. 1, middle panel) were defined using a common form of two-parameter adaptation model,17,18 which has a fixed template on these axes. The two parameters scale the template vertically and horizontally. For a given retinal illuminance, I, the corresponding MD is

\[ \text{MD}(I) = \text{MD}_{\text{max}} - 20 \log \left( \frac{I}{I_0} + K \right). \]

The vertical scaling factor is \( \text{MD}_{\text{max}} \), the asymptotic maximum MD at high retinal illuminances, and will be referred to as the sensitivity parameter. Since MD is relative to mean values for age-similar controls, in the middle panel of Figure 1 \( \text{MD}_{\text{max}} \) is adjusted for each age so that MD = 0 for the mean pupil diameter, using the equations of Winn et al.13 for pupil diameter versus age, and of Pokorny et al.11 for lens density versus age. The horizontal scaling factor is \( K \), the mean retinal illuminance at which MD drops to 6 dB below \( \text{MD}_{\text{max}} \); \( K \) will be referred to as the adaptation parameter.

The mean value for the adaptation parameter from Study 1 was used to predict effects of reduced retinal illuminance in Study 2. The effect of reduced illuminance was computed as \( \Delta \text{MD} \), the difference between the subject’s initial MD and the MD under miosis. The \( \Delta \text{MD} \) for a given miosis pupil diameter was predicted from the adaptation parameter for natural pupils from 2 mm to 7 mm (representing normal between-subject variability in pupil diameter).14

The predicted and measured effects of miosis were first compared with the linear regression of measured versus predicted \( \Delta \text{MD} \) to estimate the percent of variance in measured \( \Delta \text{MD} \) that could be accounted for with the adaptation parameter. Then agreement between data and predictions was analyzed with a standard method for comparing measurement methods17; accuracy of the prediction (difference between measured and predicted \( \Delta \text{MD} \)) was plotted against the mean \( \Delta \text{MD} \) (average of measured and predicted \( \Delta \text{MD} \)), and linear regression was used to determine whether accuracy varied across values for mean \( \Delta \text{MD} \).

The effect of retinal illuminance was characterized in terms of the MD, a clinical index of overall sensitivity provided by the FDT perimeter as a weighted average relative to age-matched norms. The dB units used by the FDT perimeter are different from the dB units used in conventional perimetry. In a range of basic studies of spatial vision, 1 dB is considered to equal 0.05 log unit change in Michelson contrast.19 In conventional perimetry, sensitivity is reported in terms of the log ratio between the maximum stimulus and the threshold stimulus, with 1 dB equal to 0.10 log unit change in Weber contrast. The version of the FDT perimeter that we chose used a proprietary method to compute ‘dB’ from stimulus contrast, for which a change by 1 dB is usually near an 0.05 log unit change in contrast, but can approach 0.10 log unit.19 For comparisons across stimuli we used the definition of 1 dB equals 0.05 log unit of Michelson contrast. For the luminance increments used in conventional perimetry, Weber contrast equals Michelson contrast, and the “25 dB” stimulus is 100% Weber contrast. Sensitivities were converted from conventional perimetric units to 0.05 log Michelson contrast by first subtracting 25 dB from the instrument printout, then doubling the remainder (for 20 dB per log unit contrast).

Since the FDT method of computing dB units is proprietary, it is not possible for a clinician to readily determine the actual stimulus contrast.
corresponding to a given sensitivity. To quantify our results in a way familiar to clinicians, we analyzed the data in terms of MD, assuming that in all cases 1 dB equals 0.05 log unit change in contrast; this will tend to slightly underestimate the effects of retinal illuminance on sensitivity measured with FDT perimetry. We assessed this effect by comparing our results with those of Membrey et al., who computed their own index for FDT sensitivity by converting dB values into luminance values using equations provided by the manufacturer.

**RESULTS**

**Study 1: Estimating Adaptation Parameter**

Data for individual subjects are shown in Figure 2, with fits of the two-parameter adaptation model. In all cases, MD decreased by at least 10 dB when retinal illuminance was lowered by 1.6 log unit. The fit parameters had a mean of $2.32 \pm 0.11$ log td (range, 2.21–2.54 log td) for the adaptation parameter ($K$), and $1.6 \pm 0.21$ dB (range, $-2.7$ to $+5.6$ dB) for the sensitivity parameter ($MD_{max}$); for all subjects the predictions accounted for at least 95% of the variance in the data (solid circles). Data for the initial MD with natural pupil (open circles) are plotted for a retinal illuminance of 3.25 log td, corresponding to a 5.7 mm diameter at the group’s mean age of 33 years. For all subjects, the initial MD with natural pupil was within 3 dB of the predicted value (mean difference $0.1 \pm 1.4$ dB, $t = 0.27, P = 0.79$).

The mean effect of retinal illuminance is shown in Figure 3, along with the adaptation model fit to the group means from Study 1 and for the data of Membrey et al. The adaptation parameter ($\pm 1$ SEM) was $2.53 (\pm 0.24)$ log td for the mean FDT CS data of Membrey et al., and $2.32 (\pm 0.16)$ log td for our mean FDT MD data; this 0.19 log unit difference did not reach statistical significance ($t = 0.78, P > 0.4$). By comparison, adaptation parameters for fits to the Membrey et al. data for the standard size III perimetric stimulus and for letter contrast sensitivity ($0.95$ and $0.47$ log td, respectively) were significantly lower than for FDT perimetry ($t > 3.9, P < 0.005$).

**Study 2: Predicting Effect of Reduced Illuminance**

Retinal illuminance varied across subjects by 1.1 log unit under miosis; miotic pupil diameters ranged from 1.1 to 4.2 mm. The change in MD under reduced retinal illuminance ($\Delta$MD) ranged from $-7.3$ to $+0.8$ dB (mean, $-2.8$ dB).

Figure 4 shows FDT results for the subject with the lowest retinal illuminance (1.1 mm pupil). With normal illuminance (natural pupil), MD was $+0.1$ dB and all locations were scored as normal. Under reduced retinal illuminance (miotic pupil), MD was $-7.3$ dB and was below the 99.5% confidence limit for normal; sensitivity at all but one visual field location was flagged as abnormal. For individual locations, the sensitivity losses for this subject under reduced retinal illuminance ranged from $-5$ dB to $-17$ dB, with a median of $-10$ dB.

Figure 5 shows predicted and measured effects of retinal illuminance as $\Delta$MD versus miotic pupil diameter for the subjects in Study 2. Curves show predictions for the mean adaptation parameter from Study 1 ($log K = 2.32$ log td), assuming...
natural pupil diameters from 2 mm to 7 mm and a standard 32-year-old lens density. All subjects had ΔMD within 1 dB of this predicted range. Note that only the adaptation parameter (log K) and natural pupil diameter affect the predictions, because the sensitivity parameter (MDmax) does not affect ΔMD.

Predicted and measured values for ΔMD are compared in Figure 6. The left panel shows results of linear regression assuming a 5.7 mm natural pupil diameter.11 predicted ΔMD accounted for 69% of the variance in measured ΔMD. The right panel shows analysis of agreement17: measured ΔMD averaged slightly greater than predicted (measured − predicted = 0.9 ± 1.5 dB, t = 2.41, P = 0.028) and was independent of ΔMD (r² < 2%, P > 0.60).

DISCUSSION

The present study confirmed previous reports8,9 that sensitivity measured with FDT perimetry can be dramatically affected by change in retinal illuminance. The range of retinal illuminances we used was similar to that encountered clinically: for a population ranging from patients with small (2 mm) pupils and dense lenses to patients with dilated pupils and clear lenses, the expected clinical range of retinal illuminances is 2.1–3.4 log td. The range of mean retinal illuminances used with our subjects was 1.8–3.4 log td for Study 1 and 2.0–3.3 log td for Study 2.

The success of the model over this range of retinal illuminances provides guidelines for clinical use of FDT perimetry. Normal variability in pupil size is large; a systematic study of effects of retinal illuminance in a large population found pupil diameters ranging from 2–7 mm near 100 cd/m².11 This normal variability represents a 0.9 log unit variation in retinal illuminance across observers; for the adaptation model this range of variability provides guidelines for potential effects of mydriatic agents on FDT perimetry. When the natural pupil diameter is at least 5 mm at the 100 cd/m² mean illuminance, FDT sensitivity should increase by no more than 1 dB under pharmacological mydriasis, even in eyes with relatively dense lenses. When the natural pupil diameter is small, effects of mydriasis on FDT MD should be substantial: 2–4 dB at 3 mm and 4–7 dB at 2 mm. By comparison, effects of normal moment-to-moment fluctuations in natural pupil size should have minimal effect on within-test variability: ±0.2 mm fluctuations around a 4 mm mean diameter should vary FDT sensitivity by no more than 0.5 dB, even for relatively dense lenses. For FDT perimetry, the effects of pupil size should be greater for a dense lens, and the effects of lens density should be greater for small pupil diameters. The normative database provided with the instrument presumably incorporates normal tendencies toward higher lens density and smaller pupil diameter with age. For assessing a patient relative to instrument norms, it would be useful to make comparisons including pupil diameter and lens density. For clinical trials, requiring stable
dilation may improve the ability of FDT perimetry to detect glaucomatous loss.

We used the clinically available summary index MD, assuming that 1 dB equals an 0.05 log unit change in contrast, whereas in fact the FDT perimeter uses values between 0.05 and 0.10 log unit according to a proprietary formula. To evaluate the potential effect of our use of 0.05 log unit for all dB values, we compared our data with those of Membrey et al., who used equations provided by the manufacturer and computed average contrast sensitivity by converting dB values into luminance values. The adaptation parameter we derived by fitting the adaptation model to their group mean sensitivities was slightly higher than for our mean MD data, but this did not reach statistical significance. By comparison, the adaptation parameters for the fits to the data of Membrey et al. for conventional perimetry and for contrast sensitivity were much lower than for FDT perimetry. The clinically available MD index was sufficiently accurate for results of Study 1 to be consistent with Membrey et al.’s direct calculation of sensitivity, and for predicted AMD to account for most of the variance in measured AMD in Study 2.

The mean luminance of cathode-ray tubes (CRTs) can vary during the course of a day as well as across days. We did not measure CRT mean luminance for each test, so our value for mean luminance (100 cd/m²) is imprecise. The FDT perimeter provides a warning if mean luminance drops 0.1 log unit below nominal luminance, and this never occurred during the experimental period. Variability in mean luminance during the course of the experiment was expected to be lower than the normal SD for the adaptation parameter, given the consistency between values of the adaptation parameters for our data and those of Membrey et al.

Differences were found in adaptation parameters derived by fitting data for different types of stimuli (Fig. 3), consistent with the analysis of Graham and Hood concerning effects of temporal and spatial frequency on adaptation to mean retinal illuminance. They analyzed data on the mean retinal illuminance required for Weber’s law to hold, demonstrating a systematic increase in the adaptation parameter with spatial and temporal frequency. Temporal modulation for FDT perimetry is restricted to a high temporal frequency, so a high value for the adaptation parameter is expected. Conventional perimetry measures sensitivity to increments which include lower temporal frequencies in their amplitude spectra, consistent with a lower value for the adaptation parameter. Contrast sensitivity measured with letter charts corresponds to lower retinal illuminance than for FDT perimetry. At 25 Hz, the temporal frequency used by our FDT perimeter, Figure 6 of Graham and Hood, indicates that a retinal illuminance of 3.1 log td is required for Weber’s law to hold. Our mean value of the adaptation parameter is consistent with their analysis, since a retinal illuminance of 3.1 log td gives sensitivity within 0.6 dB of maximum (MD_max).

Our analysis indicated that the effect of reduced retinal illuminance on FDT sensitivity is related to the use of a high temporal frequency, which requires high retinal illuminances in order for contrast sensitivity to adhere to Weber’s law. FDT perimetry compensates for this in part by use of a tenfold higher mean luminance than for conventional perimetry, but our analysis showed that the mean luminance for FDT was still not high enough to ensure that Weber’s law applies. Furthermore, the high mean luminance used for FDT perimetry may lead to adaptation anomalies. The original motivation for use of a high temporal frequency for FDT stimuli was to tap nonlinear ganglion cells, but recent work has shown that nonlinear ganglion cells cannot mediate frequency doubling.

We concur with the assessment of previous studies that use of lower temporal frequencies is advisable, and provide a method to quantitatively express retinal illuminance for new perimetric stimuli.

Abnormal results on FDT perimetry are not necessarily indicative of visual field loss, since they may also be caused by a small pupil or a dense lens. This can limit the usefulness of FDT perimetry for glaucoma screening in an older population, where small pupils and dense lenses could cause high false alarm rates. For example, a screening of elderly patients with FDT perimetry found that 60% of eyes with abnormal FDT results had cataract as their only ocular problem. When FDT is used in screening, it is important to recognize that MD values of −4 dB or worse may be caused by pupillary miosis and/or a dense lens. Furthermore, pupillary dilation can be expected to improve sensitivity by 2 dB or more.

To increase consistency and stability of clinical findings with FDT perimetry, pre-receptor factors should be controlled. When using FDT perimetry to follow a patient, it is
preferable that pupil size be held relatively constant across visits, either by using stable dilation on all visits or by always using the natural pupil for FDT testing. If mydriatics are used for only some of a series of FDT tests, or if diameter of the natural pupil varies from visit to visit, the potential effects of this should be considered in clinical decision-making. When comparing a patient’s data with age norms, pupil size and lens density should be taken into account: higher sensitivity is expected when the lens is clear and the pupil is large, and lower sensitivity for small pupils and/or dense lenses.

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References