Effects of Blur and Repeated Testing on Sensitivity Estimates with Frequency Doubling Perimetry

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PURPOSE. To investigate the effect of blur and repeated testing on sensitivity with frequency doubling technology (FDT) perimetry.

METHODS. One eye of 12 patients with glaucoma (mean deviation [MD] mean, −2.5 dB; range, 0.5 to −4.3 dB) and 11 normal control subjects underwent six consecutive tests with the FDT N30 threshold program in each of two sessions. In session 1, blur was induced by trial lenses (−6.00, −3.00, 0.00, +3.00, and +6.00 D, in random order). In session 2, only the effects of repeated testing were evaluated. The MD and pattern standard deviation (PSD) indices were evaluated as functions of blur and of test order. By correcting the data of session 1 for the reduction of sensitivity with repeated testing (session 2), the effect of blur on FDT sensitivities was established, and its clinical consequences evaluated on total- and pattern-deviation probability maps.

RESULTS. FDT sensitivities decreased with blur (by <0.5 dB/D) and with repeated testing (by ~2 dB between the first and sixth tests). Blur and repeated testing independently led to larger numbers of locations with significant total and pattern deviation. Sensitivity reductions were similar in normal control subjects and patients with glaucoma, at central and peripheral test locations and at locations with high and low sensitivities. However, patients with glaucoma showed larger deterioration in the total-deviation-probability maps.

CONCLUSIONS. To optimize the performance of the device, refractive errors should be corrected and immediate retesting avoided. Further research is needed to establish the cause of sensitivity loss with repeated FDT testing. (Invest Ophthalmol Vis Sci. 2003;44:646–652) DOI:10.1167/iovs.02-0532

The frequency doubling technology device (FDT; Welch-Allyn, Skaneateles, NY) examines the central visual field by using low-spatial-frequency sine-wave-grating stimuli that are counterphase flickered at high temporal frequency. Because the contrast of such gratings is affected little by defocus, these stimuli should be relatively resistant to blur. Although the manufacturer’s instructions suggest that refractive errors within ±7.00 D need not be corrected, the effects of blur on FDT sensitivities have not been reported.

Owing to the smaller number of stimulus locations, visual field tests with the FDT device are much faster than those typically performed with standard automated perimetry. The instrument has been shown to perform well in detecting visual field loss resulting from glaucoma and neurologic disorders. Because of its portability and the short test durations, it is regarded as an attractive alternative to standard automated perimetry in applications such as glaucoma screening. Although refractive errors can be corrected by using the patient’s spectacles or trial lenses, these are not always available, and their use lengthens the time required to prepare a subject for a visual field test. Moreover, spectacles and trial lenses may occasionally cause rim artifacts at peripheral test locations that can lead to diagnostic errors. To determine the benefits and disadvantages of correcting refractive errors for FDT examina-

METHODS

Subjects

Twelve patients with early open-angle glaucoma (mean age, 52.8 years; range, 34–70; mean deviation [MD] mean, −2.5 dB, range, ±0.5 to ±4.3) were recruited from the Eye Care Centre of the QEII Health Sciences Centre. All patients had a clinical diagnosis of primary open-angle glaucoma with characteristic optic disc or visual field changes. Eleven control subjects (mean age, 52.8 years, range 34–79) with a normal ophthalmic examination and a negative family history of glaucoma were recruited from patients’ spouses and hospital staff. One randomly selected eye of each participant was examined. Study eyes had a best corrected visual acuity equal to or better than 20/25 and refractive errors within ±3.50 DS (spherical error) and ±3.00 DC (cylindrical error). All subjects were experienced with conventional threshold perimetry, and most had previously performed threshold tests on the FDT device. The study adhered to the tenets of the Declaration of Helsinki and was approved by the ethics committee of the Health Sciences Centre. All subjects gave informed consent to participate in the study.

Procedures

The study eyes were examined with the N30 threshold test (software version 2.60, Welch-Allyn). This program examines 19 test locations, covering the visual field to an eccentricity of 30° nasally and 20° temporally. The central test location is circular (diameter, 10°), whereas the remaining 18 locations cover squares of 10° × 10°. The FDT perimeter presents vertical sine-wave-grating stimuli (spatial frequency 0.50 cyc/deg for the central stimulus, 0.25 cyc/deg for the peripheral stimuli), which are counterphase flickered at 25 Hz. The

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Stimuli are presented for 0.7 seconds, including ramped onsets and offsets, on a display set at optical infinity. Stimulus contrasts are varied according to the rules of a modified binary search (MOBS) procedure, and subjects are instructed to press a button as soon as any shimmering is detected on the test area, which is of uniform luminance (70–100 cd/m²). A visor shields the fellow eye from ambient light.

Tests were performed during two separate sessions, each consisting of six consecutive tests, separated by rest periods of approximately 8 minutes. Each test lasted approximately 5 minutes. The first test of each session was completed with the optimal refractive correction, determined from the subjects' spectacles. This correction was incorporated into a trial frame, with full-aperture (diameter, 37 mm) trial lenses. During the subsequent five tests in session 1, refractive blur was induced by trial lenses, worn by the subject in random order.

Analysis
The combined effects of induced blur and repeated testing (session 1) were investigated by evaluating the FDT MD and pattern standard deviation (PSD) indices as functions of blur and of examination order. The data from session 2 were analyzed to assess the effects of repeated testing on sensitivity and on the total- and pattern-deviation probability maps. To summarize the probability maps, scores ranging from 0 to 4 were assigned to each test location, depending on the significance level of the deviation values (>5%, <5%, <2%, <1%, and <0.5%, respectively) and summed across the 19 locations (see Figs. 1 and 2 for examples). The average total- and pattern-deviation summary scores were evaluated as functions of test order. In addition, we derived the number of normal controls and glaucoma patients who would have been misclassified (false-positives and -negatives, respectively) by using an arbitrary criterion of a total-deviation score of 2 or more as the cutoff for positive test outcomes.

To isolate the effect of blur, the sensitivity data from session 2 were subtracted from the corresponding data in session 1, separately for each patient and each test location. The results of test 3 in session 2, for example, were subtracted from those of test 3 in session 1 (Fig. 3). The resultant differences were assumed to be caused by blur (order-corrected blur effects).

Differences between the effects of blur on central versus more peripheral test locations were evaluated by stratifying test locations into sets of central locations (including the central stimulus and its four neighbors) and peripheral locations (consisting of the remaining 14 locations). To investigate whether the effect of blur varies with sensitivity, test locations were stratified into two equal-sized groups according to the average sensitivity measured during session 2.
To evaluate the effect of blur on the total- and pattern-deviation probability maps, the order-corrected blur effects (point-wise sensitivity differences between corresponding tests of sessions 1 and 2) were added to the sensitivities of test 1 in session 1, separately for each patient and each test location (Fig. 4).

A database containing these results was analyzed by the manufacturers of the device against the normative values of the commercial software, so that the effects of blur on the probability maps could be estimated without the confounding effects of repeated testing. Similar to the analysis of test order effects, we evaluated the average total- and pattern-deviation scores as functions of induced refractive error and derived the number of misclassified test results.

**RESULTS**

**Global Analysis: Effects of Blur and Repeated Testing on Visual Field Indices**

The FDT MD (an index of overall visual field loss) deteriorated with refractive blur (Fig. 5), both in patients with glaucoma and in normal control subjects. Although the different blur conditions had been induced randomly during tests 2 to 6 of session 1 (Pearson $\chi^2$, $P = 0.19$), the data revealed a concurrent decrease in sensitivity with repeated testing (Fig. 6).

This order effect was confirmed in session 2, which showed a similar decline in sensitivity with repeated testing in normal control subjects and patients with glaucoma (Fig. 7). A comparison between the first tests of sessions 1 and 2 showed a small learning effect. Although all subjects were experienced with standard automated perimetry and most had performed threshold tests on the FDT before, the MDs were slightly higher in session 2 in both groups of subjects (mean difference [95% CI]; 0.52 dB, [0.3–1.0 dB], $P = 0.04$, paired $t$-test). During both sessions, the PSD (a global index for localized visual field loss) showed little or no systematic change with repeated testing in normal control subjects and patients with glaucoma (Figs. 6, 7). Blur led to a slight reduction of PSD in the normal control group, but there was little or no effect on PSD in the patients with glaucoma (Fig. 5).

**Point-wise Analysis**

**Effect of Repeated Testing.** The point-wise analysis of the data from session 2 confirmed that sensitivities declined with repeated testing, similarly at central and peripheral test locations (Fig. 8) and at locations with different levels of sensitivity (Fig. 9).

The total- and pattern-deviation analyses classified a larger number of test locations as outside normal limits, and their significance levels increased (Fig. 10). In the group of normal control subjects, this led to a large increase in false-positive test outcomes. Although the sensitivity reductions were similar at locations with high and low sensitivities, repeated testing had a more marked effect on the probability maps of the patients with glaucoma compared with the normal control subjects (Fig. 10).

**Effect of Blur.** The point-wise comparison between the data of sessions 1 and 2 isolated the effect of blur on FDT sensitivity. Hyperopic blur (caused by adding negative trial lenses) appeared to degrade sensitivity slightly more than myopic blur. Whereas the differences were small and well within 2 SEM, blur reduced sensitivities slightly more at the five most central test locations compared with the peripheral ones (Fig. 11a). Locations with high sensitivity were affected to an extent similar to those with low sensitivities (Fig. 11b). The higher sensitivities measured in session 2, which were probably due to a learning effect, led to a small apparent reduction with 0.00 D blur (Fig. 11b).

Although the increase in average total-deviation score was modest in our normal control group, hyperopic blur (negative lenses) led to larger numbers of false-positive test outcomes (Fig. 12). Both myopic and hyperopic blur conditions increased the total-deviation scores more markedly in the glaucoma group than in the normal control subjects. The effect of blur on the pattern-deviation maps appeared more complex, in that pattern-deviation scores appeared to increase with myopic blur and decreased with hyperopic blur (Fig. 12).

**DISCUSSION**

The data in this study show that sensitivity estimates of the FDT instrument decreased with repeated testing and under the influence of blur. Although small, these changes may suffice to increase the number of false-positive test outcomes.
FIGURE 5. (a) MD and (b) PSD for tests 2 to 6 of session 1 as a function of blur. Data from test 1 (always performed without blur) were omitted from these figures. Blur was induced in random order. Error bars, ± SEM.

FIGURE 6. (a) MD and (b) PSD for the six tests of session 1 as a function of test order. Test 1 was always performed without blur, whereas tests 2 to 6 were performed with blur. Error bars, ± SEM.

FIGURE 7. Results of session 2 (control experiment without blur). Reduction of MD was apparent in normal control subjects and patients with glaucoma (a), and the PSD increased slightly (b). Error bars, ± SEM.
In standard automated perimetry, even small refractive errors can reduce sensitivity, particularly to small stimuli. With the Goldmann size III stimulus, the sensitivity reductions have been estimated to be between 0.8 and 1.5 dB/D of defocus. Furthermore, test locations near fixation are affected more than those in the periphery of the field. In comparison, the blur-induced sensitivity reductions of FDT sensitivity in this study were smaller (<0.5 dB/D) and affected central and peripheral test locations to a similar extent (Fig. 8).

Although the measurement scale of the FDT perimeter provides clinicians with data similar to those of the more familiar Humphrey Field Analyzer (Humphrey Instruments, San Leandro, CA), the techniques have different variability characteristics. It therefore may not be meaningful to compare the blur-induced reductions of sensitivity in our study to those previously published for conventional perimetry. To give a clinically interpretable assessment of the influence of blur on FDT thresholds, the probability maps were recalculated after removing the effects of repeated testing from the data. The order-corrected data show that in normal control subjects, refractive blur, on average led to only small increases in the number of test locations with abnormal total deviations and in their significance levels. However, averages can mask clinically important effects in small groups of subjects. Although the small sample in our study precluded a formal analysis of sensitivity and specificity of the FDT, we calculated the number of test results that would have led to misclassifications (false-positive and -negative test outcomes), by using an arbitrary criterion of two or more locations with a total-deviation probability less than 5% (or one or more locations at \( P < 0.02 \) or lower). These data show that even small changes in the sensitivity estimates can reduce the specificity of the test.

In the glaucoma group, the effects of blur on the total-deviation probability maps were larger. Even minor sensitivity reductions may suffice to increase the significance level of an already abnormal test location, whereas a larger change may be necessary to alter the status of a test location with normal sensitivity. The effect of blur on pattern-deviation maps appeared to be more complex. With negative blurring lenses, the pattern-deviation scores decreased slightly, whereas they rose with positive blur.

Sensitivity reductions with repeated visual field examinations have been reported, with conventional perimetry as well as with the FDT device. Such changes may be sensory (i.e., caused by genuine sensitivity reductions over time) or behavioral (when subjects tend to establish more conservative response criteria over time). Hypotheses relating to sensory change to explain the reduced FDT sensitivity of the second tested eye include central adaptation to the properties of the FDT stimulus, incomplete light adaptation of the tested eye, effects related to the dark adaptation of the nontested eye shielded by the visor of the device (Flanagan JG, Forrest AL, Simpson T, ARVO Abstract #2163, 2002), and binocular inhibition resulting from the unequal luminance presented to both eyes.
FIGURE 10. Average total- and pattern-deviation scores increased with repeat testing (session 2) in (a) control subjects and (b) glaucoma patients. Numbers below the abscissa state the number of subjects who had false-positive (nfp, a) or false-negative (nfn, b) outcomes, with a total-deviation score of 2 or more was used as an arbitrary cutoff criterion.

FIGURE 11. Effect of blur on central and peripheral test locations (a) and on locations with high and low sensitivity (b). Dotted horizontal line: no change. The reduction at 0.00 D is due to a learning effect between the two sessions. Error bars, ±SEM.

FIGURE 12. Effect of blur on average total- and pattern-deviation scores (order-corrected data) in (a) control subjects and (b) glaucoma patients. Numbers below the abscissa state the number of subjects who had false-positive (nfp, a) or false-negative (nfn, b) outcomes, with a total-deviation score of 2 or more used as an arbitrary cutoff criterion.
eyes. Although our study was not designed to investigate this question, sensitivities decreased continuously throughout both sessions, suggesting that dark adaptation of the contralateral eye may be involved. The low ambient illumination of our test room (~7 lux) would not have sufficed to prevent continuing dark adaptation of the contralateral eyes.

The commercial FDT device corrects for the sensitivity reduction with repeated testing, when evaluating the results of the second tested eye against its normative database. However, the manufacturer's guidelines suggest that the instrument should be restarted for tests of the contralateral eye if more than 3 minutes have elapsed after completion of the first test. Our data suggest that order effects may persist for longer than 3 minutes, which is of some importance when guidelines for examination with the FDT device are proposed. To increase specificity, diagnostic and screening tests are often repeated if the initial result is positive, and reductions in FDT sensitivity with repeated testing may interfere with this approach. Further work is needed to establish whether sensitivity reductions with repeated FDT testing also occur with the briefer suprathreshold screening tests and whether they can be prevented by using different examination protocols (e.g., higher levels of room illumination and/or longer rest breaks).

Whether patients with small or moderate refractive errors should wear a correction largely depends on the motivation for the test. The sensitivity reductions caused by small levels of blur are unlikely to give rise to many false-positive results when decision criteria are applied that yield extremely high specificity (in mass screenings for glaucoma, for example). In clinical practice, however, where greater emphasis is placed on the sensitivity (in mass screenings for glaucoma, for example), it may well be enhanced when refractive errors are corrected. It may also be prudent to consistently correct refractive errors in patients who perform FDT examinations for monitoring of ocular hypertension or glaucoma.

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References