False-Negative Responses in Glaucoma Perimetry: Indicators of Patient Performance or Test Reliability?

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**Purpose.** To study whether false-negative answers in computerized glaucoma perimetry indicate the patient’s ability to perform perimetry or test result reliability.

**Methods.** A retrospective evaluation was performed of visual field test results obtained with a perimetry program (Humphrey 30-2 Sita Standard; Humphrey Instruments, San Leandro, CA) in 70 consecutive patients with unilateral glaucomatous field loss. Frequencies of false-negative answers were compared between the two eyes of each patient and related to amount of visual field damage in the glaucomatous eyes using linear regression analysis.

**Results.** Frequencies of false-negative answers were higher in eyes with field loss. The intrapatient intereye difference was 6.6% on average ($P < 0.0001$). In seven subjects with false-negative frequency of 5% or more in both eyes, the mean difference was 12.7% between eyes. The differences in false-negative answers depended significantly on the amount of field loss in the glaucomatous eyes ($P = 0.0003$). Larger differences were seen in patients with advanced field loss in the affected eye.

**Conclusions.** The increased frequencies of false-negative answers in eyes with field loss were strongly associated with field status. The higher false-negative frequencies in eyes with glaucomatous field loss compared with unaffected eyes may be explained by the increased variability in threshold values typically found in such eyes. False-negative answers in patients with glaucoma therefore represent eye rather than patient status. (Invest Ophthalmol Vis Sci. 2000;41:2201–2204)

Threshold perimetry is the most important method to diagnose and identify progression of glaucoma. Many patients find visual field testing difficult, however, particularly when eyes with field loss are tested. When manual perimetry was standard, the examiner assessed patient cooperation. When computerized automated perimetry was introduced, the role of the perimetrist in patient surveillance was diminished. Instead, methods intended to estimate patient reliability were built into most computerized perimetry programs.1-2 Catch trials were introduced to measure frequencies of false positive (FP) and false-negative (FN) answers. High rates of FP indicated “trigger-happy” patients, whereas high rates of FN were thought to indicate inattentive patients or periods of inattention during an examination.2,5

An FN catch trial answer occurs when the test subject fails to give a positive response to a stimulus shown at an intensity level expected to be seen. Several studies have reported increased rates of FN answers in patients with glaucoma.4-8 Further, random threshold variability is much larger in glaucomatous than in normal fields.9-15 and visual fatigue effects are more pronounced in glaucomatous fields.14-17 Thus, it is possible that the high frequencies of answers to FN catch trials observed in patients with glaucoma could be explained by large fluctuations of threshold values and/or by the larger visual fatigue, as suggested by Katz and Sommer.5 Recently published textbooks state that FN answers should be considered a consequence of a patient’s inattentiveness.18-20

The purpose of the current study was to determine whether the frequency of FN answers in glaucoma perimetry is a patient characteristic or reflects the status of the eye.

**Methods**

**Subjects**

This study conforms to the spirit of the Declaration of Helsinki. However, when the study was started in 1998, our university felt that our retrospective protocol had little or no impact on patient integrity and, therefore, need not be submitted to the Ethics Committee for approval.

We performed a retrospective analysis of results of pairs of visual field tests obtained with a threshold perimetry program (Sita Standard 30-2; Humphrey Instruments, San Leandro, CA). Visual field test results of consecutive patients with unilateral glaucomatous field defects who visited our glaucoma outpatient department during the first 7 months of 1999 were included. All patients had had prior experience with computerized automated perimetry. Right eyes were always examined before left eyes, according to standard clinical procedures. Patients were included in the study if the glaucoma hemifield test (GHT)1 findings were outside normal limits for one eye in at least two consecutive examinations and inside normal limits for the other. All affected eyes showed typical glaucomatous disc findings (e.g., cupping reaching the edge of the optic disc).

Supporting information is available at IOVS Online (http://www iovs arvojournals org) or as Supplementary Material in this issue.

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disc or notching). Patients with glaucoma who had concomitant eye diseases that could produce localized visual field defects (e.g., macular or retinal diseases or neurologic disorders) were excluded.

**Estimation of Frequencies of False-Negative Responses**

In automated perimetry, presentation of catch trials has been the standard method of estimating rates of FN responses. The original Humphrey full-threshold program used stimuli that were uniformly 9 dB brighter than the previously measured threshold value at the same test point location. Stimuli were exposed at random intervals. The newer test programs (Sita; Humphrey)22,23 apply a modified method in which catch trial intensities are 9 dB brighter than the estimated threshold at normal points but are even brighter relative to the threshold at test points estimated to have depressed sensitivity. Catch trials are performed randomly during the test and comprise approximately 3% of stimulus presentations. Immediately after the actual test, during the processing of test data, the intensity level of each catch trial is rechecked and compared with the final threshold calculation at that test location and its corresponding frequency-of-seeing curve. Only catch trials that should be clearly visible are included in the final estimation of frequencies of FN answers. In addition, FN answers also are extracted from the pattern and consistency of patient responses24 but only in almost normal fields that have few test locations showing severe field loss. The two types of FN data are combined during postprocessing to produce a final estimation of the frequency of FN answers using the maximum-likelihood method. These procedures decrease the risks of using FN catch trials that have intensities within the expected variability of the threshold value.

**Analyses**

Intrapatient intereye differences in FN frequencies were calculated and compared using a one-group $t$-test. The amount of field loss was estimated by mean deviation (MD).25 Linear regression analysis was used to test dependence of FN differences on MD values in the glaucomatous eyes. Student’s $t$-tests were used to analyze possible effects caused by test order (first or second eye examined). Influence of patient age on FN was tested using linear regression analyses. Frequencies of fixation losses and FP answers were recorded.

**RESULTS**

Seventy patients with glaucoma (28 men and 42 women) who had unilateral glaucomatous visual field defects were identified and included in the analysis. Thirty-four patients had field defects in the right eye and 36 in the left eye. Mean age was 70 years, ranging from 41 to 83 years. The eyes with glaucomatous field defects represented a wide range of glaucomatous damage from very subtle defects to extensive field loss; MD values ranged from $-29.39$ to $0.01$ dB, (mean: $-11.99$ dB). MD values of the eyes without field loss ranged from $-4.52$ to $+2.21$ dB (mean: $-0.68$ dB).

In 84% (59/70) of patients, FN frequencies were higher in the eye with field defects. The intrapatient intereye difference of FN frequencies was 6.6% on average, showing higher frequencies in the glaucomatous eyes. This difference was significant ($P < 0.0001$, Fig. 1).

An increased number of such answers in the glaucomatous eyes caused intrapatient differences of FN responses. No patients showed high frequencies in both eyes concurrently. Only seven patients had frequencies higher than 5% in both eyes. In these patients the FN difference was 12.7% on average.

The difference in FN frequencies between healthy and glaucomatous eyes could be explained by the amount of field loss as expressed by the MD value in the affected eye ($P = 0.0003$). Larger intereye differences were seen in patients who had more advanced visual field loss than in eyes with subtle loss in the glaucomatous eye (Fig. 2).

Patient age did not influence the frequency of FN answers. Age slopes were small and insignificant, with an increase of 0.05% per year of age ($P = 0.30$) in normal eyes and a decrease of 0.07% per year of age ($P = 0.64$) in eyes with field loss.

FN response rates were unaffected by the order of testing. Eyes with field loss showed 9.7% FN answers on average when tested first, and 8.4% when tested second. The corresponding numbers were 2.2% and 2.6%, respectively, in the eyes without field loss.

Frequencies of FP answers were small and well within acceptable limits. The average FP was 2.5%, ranging from 0% to 15%. FP frequencies did not differ between healthy and glaucomatous eyes; the mean difference was 0.8%. Fixation losses were 9.2% on average, ranging from 0% to 59%. Nineteen of the 140 eyes (13.6%) showed Fixation losses more than 20%, 14 of
Differences in False Negative responses between healthy and glaucoma eyes (%)

MD values in glaucoma eyes (dB)

-30 -25 -20 -15 -10 -5 0 5

FIGURE 2. Influence of amount of glaucoma field loss on intereye intrapatient differences of false-negative responses was large and significant, \( P = 0.0003 \).

them in unaffected eyes. The average FN frequency in these 19 eyes was 5.6%.

DISCUSSION

We studied perimetric test results of patients with unilateral glaucomatous visual field defects to investigate whether FN responses reflect patient test performance or if they are more dependent on visual field status. Our results showed that intrapatient differences in FN frequencies were caused by increases in such responses in glaucomatous eyes and that they were associated with the amount of field loss. Patients were included without applying restrictions to any of the reliability indices.

Originally, the false-negative response parameter was intended to reflect patient reliability in computerized perimetry.\(^2\)\(^-\)\(^\)\(^5\) Previous studies, however, have observed elevated frequencies of FN responses in patients with glaucoma compared with normal subjects.\(^4\)\(^-\)\(^8\) If the false-negative rate were primarily an index of patient performance, similar frequencies would be expected in both eyes of the same patient, at least in tests performed the same day. Still, some textbooks consider FN answers to be reflective of a patient’s inattentiveness.\(^18\)-\(^20\) although some texts question whether FN answers in patients with glaucomatous visual field loss are due solely to patient inattentiveness. Lachenmayr and Vivell,\(^18\) and Anderson and Patella,\(^5\) discuss the effect of increased threshold variability on FN responses in glaucomatous visual fields. Weitzman and Caprioli,\(^26\) and Budenz,\(^20\) discuss the possibility that increased FN answers may be caused by perimetric visual fatigue. Choplin and Russell\(^19\) refer to fixation loss as a likely explanation for increased frequencies of FN in glaucoma eyes. We have previously demonstrated an association between large test–retest threshold fluctuations and increased frequencies of FN responses,\(^27\) and, it is likely that the larger frequencies of FN answers in glaucomatous eyes can be explained by this increased variability of threshold values. Thus, in glaucomatous eyes, FN catch trials have considerably less than 100% probability of being seen. The Sita programs use an improved catch trial method designed to reduce the number of FN catch trials presented at questionable intensities. The frequency of FN responses was also smaller with Sita than with the Humphrey full-threshold strategy, but even with the precautions included in the Sita program, its false-negative response rate does not provide a fair estimate of patient inattention.

Thus, our results suggest that current FN catch trial methods are inadequate for estimating patient attentiveness in perimetry in eyes with glaucomatous visual field loss. Instead the frequency of false-negative responses in eyes with glaucomatous visual field defects is associated with amount of field loss. This means that improved patient instructions and more intense supervision may not improve test results.

It would be desirable to have a method for estimation of FN that does not rely on catch trials, similar to the one used in Sita for estimation of frequencies of false-positive responses.\(^28\) Unfortunately, no such methods are available or have been suggested. The FN index obtained with catch trials can be considered an indicator of reliability of test result, with high FN frequencies associated with low precision in threshold estimates probably explained by the increased threshold variability in glaucomatous eyes. The field status, however, provides similar information.

References