Influence of Fixation Accuracy on Threshold Variability in Patients With Open Angle Glaucoma

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Purpose. To evaluate the contribution that fixation errors make to the overall variability of perimetric responses in patients with glaucoma.

Methods. Frequency of seeing curves were established, with and without fixation error correction, at two locations in each of 14 patients with glaucoma and good visual acuity. One location corresponded to a relatively normal region of the visual field, whereas the second corresponded to a region in which there was a sensitivity deficit. All patients had an acuity of better than 20/63 (except one whose acuity was 20/100). The locations of the first and fourth Purkinje images of a collimated infrared source were used to give a measure of eye position, during each stimulus presentation (accuracy 10 minutes of arc).

Results. Considerable variation was found in patient fixation accuracy. In the worst case, fixation was within 30 minutes of the target in only 7% of presentations, whereas in the best, it was within this range in more than 60%. No relationship was found between accuracy of fixation and extent of loss. The gradient of the frequency of seeing curve was found to be shallow at regions of reduced sensitivity, a finding that supports the recognized relationship between variability and sensitivity deficit. A recalculation of the frequency of seeing curves, using only those responses in which the patient's fixation was within a specified range (<60 minutes of arc), did not show a meaningful reduction in variability at either location.

Conclusions. It is concluded that fixation errors, though contributing to variability, are not the major cause of the increased variability seen at locations with reduced sensitivity. Invest Ophthalmol Vis Sci. 1996;37:444-450.

In automated static perimetry, the differential light sensitivity is measured with a bracketing strategy. Although repeat measures of this threshold show a small amount of variability in normal patients, variability is increased greatly in patients with glaucoma.1-7 Heijl et al8 have reported that patients with loss of 8 to 18 dB will show variability (95% confidence limits) that approaches the measurement range of the Humphrey Visual Field Analyzer (0 to 40 dB). This increase in variability makes it difficult to differentiate between nonsignificant random variations in the visual field and true progression. It often requires results of several visual field tests, taken during a period of time, before a decision can be made on whether the visual field has deteriorated.8,9

The causes of this increased variability are unknown, although various researchers have suggested that it is the result of a reduced number of nerve fibers,5 increased susceptibility to fatigue,10 and poor fixation control.2,11,12

The isolated scotomata found in the visual fields of patients with glaucoma often have steep sensitivity profiles, and small inaccuracies of fixation can result in a stimulus falling inside a deep scotoma from a normal area or vice versa. In the presence of steep sensitivity profiles, inaccuracies of fixation can, therefore, result in an increase in variability when multiple estimates of threshold are made. A relationship between the number of edges in the visual field and test--
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retest variability has already been demonstrated, and the effects of fixation instability quantified in both normal experienced observers and patients with glaucoma.

The sensitivity and variability at a given location in automated perimetry are well described by the frequency of seeing (FOS) curve. This S-shaped curve gives the percentage of stimuli seen at a range of intensities that straddle the threshold. The threshold sensitivity is normally defined as the intensity at which 50% of the stimuli will be seen. The variability is represented by the gradient of the FOS curve—steep gradients represent little variability, and shallow gradients reveal large amounts of variability. The gradient can be represented by the standard deviation of the curve, although other researchers have chosen to use interquartile range and a threshold coefficient based on a linear regression of the central section of the FOS curve.

The purpose of this study was to test the hypothesis that fixation errors contribute to increased variability. This study uses a two-dimensional eye position recorder to measure fixation accuracy during the presentation time of the perimetric stimulus. It then reports on the effect of excluding responses in which the fixation was inaccurate on the gradient of the FOS curve.

METHODS

Patients

Our sample contained 14 clinically stable patients with glaucoma (9 men, 5 women), whose average age was 75.2 years (range, 61 to 88 years). All patients had established glaucomatous visual field defects, as detected by previous Octopus perimetry. This visual field loss included isolated paracentral scotoma, arcuate defects, and altitudinal hemifield loss. Acuity in each patient was better than 20/63 (except in one, in whom it was 20/100), and each had an absence of any other known ocular, neurologic, or systemic disease likely to affect the visual field. All eyes were phakic, all media were clear, and all patients had undergone full-threshold perimetry. The study was approved by the University Hospital of Wales Ethical Committee, and it was conducted in accordance with the tenets of the Declaration of Helsinki. Informed consent was obtained from each patient.

Eye Position Recorder

Eye position was monitored with a video camera that captured a magnified image of the eye during each stimulus presentation. Images were digitized and then viewed on a computer monitor (640- × 480-pixel resolution) on which the first and fourth Purkinje images of a collimated infrared light source could be seen clearly. The x and y coordinates of the central pixel within each of the Purkinje images were extracted manually and stored in a computer file. The relative positions of these two images were used to give a measure of eye position accurate to within 10 minutes of arc in horizontal and vertical meridians across a measuring range of ±8°. This technique of recording eye position was selected because it is noninvasive, accurate, and relatively insensitive to translational eye movements.

A large dichromatic mirror placed in front of the patient’s eye allowed the recorder’s imaging path and the patient’s viewing path to be separated. The patient had an uninterrupted view of the visual field screen extending to 25° in all meridians.

Perimetric Testing

All patients first underwent full-threshold visual field testing that covered the central 24° of the visual field, with stimuli arranged on a 6° square matrix centered 3° from the vertical and horizontal midlines using a modified Henson CFA3000 (Tinsley Medical Instruments, Croydon, UK) visual field analyzer. The stimuli were green light-emitting diodes that subtended an angle of 0.5° at the eye. Double determination of the thresholds were made at every test location (52 in all). The fixation target for perimetric testing was a 2-mm white spot (angular subtense 20 minutes of arc).

On the basis of the results from the full-threshold test, two locations were selected for establishing FOS data. One location was in a region of the visual field in which there was no indication of any localized sensitivity loss, whereas the second was located at the edge of a localized defect in which the threshold measure indicated some sensitivity deficit. To ensure that the resultant FOS curves were not truncated by the maximum intensity limit (300 cd/m²) of the perimeter, locations at which the sensitivity deficit was severe were avoided. The two locations were well separated from each other and were in different quadrants of the visual field.

Frequency of seeing data were composed of 20 presentations at each intensity level ranging from 8 dB above to 8 dB below the previously established threshold (2-dB steps, 180 presentations at each location). Each patient responded by pressing a response button for each presentation seen. Stimulus intensity and location were randomized to ensure that patients could not predict the location and intensity of the next presentation.
Recording of Fixation Error

Before collecting the FOS data, each patient performed a series of calibration movements to four light-emitting diode targets placed 1° from the fixation target along the 0°, 90°, 180°, and 270° meridians. Data from these fixations were used to establish the relative positions of the first and fourth Purkinje images for central fixation and the horizontal and vertical scaling factors relating the relative pixel locations of the first and fourth Purkinje images to eye position measured in minutes of arc from the central fixation point.

Data were used to calculate the magnitude (minutes of arc) of the horizontal, vertical, and resultant fixation errors during each stimulus presentation. The magnitude of the resultant error was merged with patient response and stimulus data to create a file in which the stimulus location, intensity, patient response, and fixation error were stored. Extracted data from this file were input into the software package SPSS, on which a probit analysis was performed to estimate the threshold (50% seeing) and variability (standard deviation) of each FOS trial. Probit analyses were conducted on all data and on data in which the resultant error was less than 60 minutes of arc.

RESULTS

Fixation accuracy of all 14 patients is shown in Figure 1. In patient RH, only 7% of the trials had a fixation error of less than 30 minutes of arc. In patient NB, more than 60% of the trials had a fixation error of less than 30 minutes of arc. Many of the patients had fixation errors of more than 1° for a significant number of trials.

To establish whether there was a relationship between fixation accuracy and visual field loss, two characteristics of the visual field data were extracted from the records of each patient. The first is a measure similar to mean defect (MD), which is an indicator of the extent of loss, whereas the second measures whether the defect encroaches to within 5° of the fixation point. The MD values are shown in Figure 2. Although the sample size was not large, there was no

† There is no normative data base for this experimental setup. Decibel values should be used solely for comparison between patients rather than as a measure of loss.
obvious relationship between fixation error and MD. Three of the patients (TM, RH, LA) had severe defects that encroached to within 5° of the fixation point. Fixation accuracy of these three patients, again, did not appear to be different from that of the other patients ($P = 0.39$, Mann–Whitney test).

Frequency of seeing curves obtained from all test locations were found to fall into three different categories on the basis of both the sensitivity (50% seeing point on the FOS curve) and the curve’s standard deviation. The FOS curve presented in Figure 3a is from a location at which the sensitivity was within the normal range. This type of response, characterized by a relatively steep FOS curve, was found at every location where there was no sensitivity deficit. The 95% confidence limits of the fitted curve are narrow, and the frequency of seeing extends from 0% to 100% across the tested range of 18 dB. The curve in Figure 3b represents one of two types of responses obtained from locations at which there was a reduction in sensitivity. It was found at 11 of the 28 (39%) locations and is characterized by a shallower gradient (increased SD of the FOS curve) and a widening of the 95% confidence limits. The FOS curve in Figure 3c represents the other type of response found in areas of reduced sensitivity (3 of 28 [11%] locations). In the example given, the frequency of seeing never exceeded 23%. In the other two patients, the maximum was 16% (TM) and 48% (NB). When a probit fit was possible (only in patient KC), it resulted in a shallow curve (large SD) and wide 95% confidence limits.

The relationship between the sensitivity and variability (SD of the FOS curve) is shown in Figure 4. Results show both increased variability with lowered sensitivity and increased scatter of results with lowered sensitivity. There is a strong positive correlation between sensitivity and the SD of the FOS curve ($r = 0.65, P < 0.001$).

As an example, the effect of removing responses from which the fixation error was greater than 60 minutes of arc is shown in Figure 5 for normal and defective locations of one patient (GMM). This patient was selected on the basis of the number and size of his fixation errors; 47% of responses had an error greater than 60 minutes of arc at normal and defective locations. In this case, the tested hypothesis predicted a steepening of the FOS curve when responses collected with large errors were removed. The gradient of the FOS curve, at the defective location, actually became slightly shallower (greater variability) with fixation error correction. At the normal location, it became slightly steeper. Neither of these changes was significant (SPSS parallelism chi-square analysis of the probit function).

Results from all locations in all patients in whom

FIGURE 3. The three types of frequency of seeing curve seen in the data. Type a comes from a relatively normal location, whereas types b and c come from locations in which there is a sensitivity deficit.
a probit fit could be made by SPSS are shown in Figure 6. Rather than show all the individual FOS curves, Figure 6 presents the data in the form of change in variability (SD of FOS curve of all trials minus SD of FOS curve of trials in which the fixation error is less than 60 minutes). Data are organized with the most accurate fixator on the right and the most inaccurate of the left. Data for each location have been tested for parallelism (SPSS parallelism chi-square analysis of the probit function), and those that reveal significant change in the slope of the FOS curve are shown. Only five sets of data show significant change in the FOS curve gradient; four become steeper and one becomes flatter. Of these five sets of data, four come from locations with normal sensitivity, and only one comes from a location with reduced sensitivity. Large changes seen at the defective locations of patients RH, JA, KC, and NB are not significant because of the wide range of confidence limits attached to the probit analysis. Analysis of the data from the whole group shows that there is no significant difference in the change in SD of the FOS between the normal and defective locations ($P = 0.84$, paired $t$-test).

**DISCUSSION**

Detecting clinically significant visual field change is hampered by the large amount of variability found in perimetry. This study has investigated the contribution that fixation errors make toward overall variability. Data on the accuracy of fixation during stimulus presentation (Fig. 1) demonstrate that many patients have difficulty in maintaining accurate fixation. Similar findings were presented in an earlier article that also reported a poor relationship between measures of fixation accuracy and the Heijl–Krakau method of estimating fixation accuracy. This poor relationship was ascribed to the relatively large size of the blind spot and to inaccuracies in locating its center at the beginning of the examination.

Our study also demonstrated that the ability to maintain accurate fixation varied among patients (Fig. 1). Some patients maintained accurate fixation, whereas others made errors greater than 60 minutes of arc in the majority of trials. During the experiment, the perimetrist, who was in attendance throughout, actively encouraged the patient to maintain accurate fixation. Available to the perimetrist was the magnified video image of the eye stored on the recorder. Although there were no formal procedures in which the perimetrist reported on the patient’s fixation accuracy, it was our opinion that the perimetrist’s subjec-
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Figure 6. Change in the standard deviation of the frequency of seeing curve after the removal of responses for which the error in fixation was greater than 60 minutes of arc. Positive values indicated a steepening of the curve (less variability), whereas negative values indicated a shallower curve (more variability). Solid bars represent data from regions in which there was a sensitivity deficit, whereas lightly shaded bars represent locations in which sensitivity was within the normal range. Data in this figure have been organized with the most accurate fixator on the right and the least accurate fixator on the left. *Change is significant at $P = 0.05$. **Change is significant at $P = 0.01$.

There was no obvious relationship between the extent of visual field loss and fixation accuracy. Patients with severe visual field loss, encroaching to within $5^\circ$ of the fixation point, were no more inaccurate in their fixation than those with relatively mild paracentral defects. Because all patients had reasonably good acuity, we suggest that a patient’s fixation accuracy is unlikely to be compromised until the fovea becomes involved.

The tested hypothesis of this article—that fixation errors contribute to increased variability—predicts a greater change in variability in patients with large numbers of fixation errors (those toward the left side of Fig. 6). It also predicts a greater change at defective locations, at which there are likely to be steep sensitivity gradients, than at normal locations. Data in Figure 6 show no obvious trend from left to right. Although the change for locations with field damage tends to be greater than it is for normal locations, this change occurs in both directions, and it reaches statistical significance in only one instance.

Heafliger and Flammer\textsuperscript{14} undertook a study that compared variability at the edge of the physiological blind spot, where the gradient of sensitivity was steep, with that at the border of glaucomatous defects. They found that although variability was increased at the edge of the blind spot—a finding that lends support to the hypothesis that fixation errors are partially responsible for the increased variability in glaucoma—it was greater still at the edge of the glaucomatous defect, where the gradients were shallower. This finding is difficult to explain on the basis of the fixation error hypothesis.

Previous reports\textsuperscript{16–18} have noted good correlation between variability and sensitivity, and they also have noted that this relationship holds for normal visual fields (center and periphery), cataract, persons with suspected glaucoma, and patients diagnosed with glaucoma. Chauhan et al\textsuperscript{17} pointed out that even if there is good correlation, it is difficult to predict the amount of variability from the threshold values in patients with glaucoma. They suggested that unrecognized factors may influence variability. Our results support their observation. At the normal sensitivity range of values (25 to 30 dB), there is little spread in the standard deviations, whereas at the 15- to 25-dB range, the spread is much greater (Fig. 4). Below 15 dB, the spread reduces because of intensity limitations.
of the equipment. Olsson et al. studied the influences of age and test point eccentricity on increased variability. They found that neither factor correlated with variability.

This study was designed to determine whether the increased variability seen on visual field testing of patients with glaucoma could result from poor fixation. Though substantiating the relationship between sensitivity deficit and variability, results have been unable to show a significant reduction in variability when fixation errors in excess of 60 minutes of arc are removed. This finding leads to the conclusion that whereas local visual field sensitivity influences variability, fixation errors may have only a minor influence. It is likely that factors besides sensitivity and fixation errors are responsible for the variability observed in our study. Further research is required to quantify these factors.

Key Words

eye movements, fixation accuracy, glaucoma, visual fields

References