The Psychometric Function and Reaction Times of Automated Perimetry in Normal and Abnormal Areas of the Visual Field in Patients With Glaucoma

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Purpose. To study the relationship of reaction time to the psychometric function in normal subjects, normal sensitivity test locations in patients with glaucoma, and test locations with 10 to 20 dB loss in patients with glaucoma.

Methods. The authors tested 10 patients with glaucoma and 10 age-matched normal volunteers with the Humphrey perimeter, first with program 24-2 and then with the method of constant stimuli to generate frequency of seeing curves. At two widely separated visual field locations on the program 24-2 grid, they presented stimuli in 2-dB intervals, 10 dB either side of the program 24-2 threshold, at 0 dB and 60 dB (15 repetitions per intensity). For the patients with glaucoma, they chose a visual field location with normal sensitivity and a location in an area of 10 to 20 dB loss.

Results. Analysis of variance with post hoc <-tests showed that reaction time (RT) at the 0-dB intensity was prolonged by approximately 90 msec in the abnormal sensitivity test location of patients with glaucoma compared to the control and the glaucoma normal sensitivity groups (P < 0.0001). However, this difference was accounted for by only 4 of the 10 patients with glaucoma, reaching 100% of stimuli seen with the brightest stimulus at the moderately damaged test location. Reaction time at the frequency of seeing 50% estimated threshold showed no significant differences among the groups. Prolongation of RT from the 0-dB value was analyzed as a function of increasing attenuation of stimulus intensity. The results fit the equation RT = a + b(Intensity)^2 for all groups.

Conclusions. There is no significant difference in RT between normal subjects and patients with glaucoma either at threshold or to suprathreshold stimuli. Reaction time increases after a power function with increasing attenuation of stimulus intensity up to the threshold. Invest Ophthalmol Vis Sci. 1996;37:878–885.
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with an increase in threshold. In a study using conventional automated perimetry, Flammer and colleagues reported a significant relationship of a prolonged RT in perimetrically normal areas. In a study using conventional automated perimetry, Flammer and colleagues reported a significant relationship of a prolonged RT with an increase in threshold.

If reaction time is to be used as an outcome measure in conventional automated perimetry, the relationship of RT to threshold must be defined. If there is a constant relationship between reaction time and threshold in health and disease, one would hope this relationship could be used to help predict threshold in a more accurate and less variable way. Our goal was to determine this relationship of reaction time to the psychometric function in normal subjects, normal sensitivity test locations in patients with glaucoma, and test locations with 10 to 20 dB loss in patients with glaucoma, as well as to investigate the relationship suggested by Flammer and coworkers of a prolonged RT associated with an increase in threshold in subjects with glaucoma.

METHODS

Subjects

Ten patients with well-established primary open angle glaucoma and 10 normal volunteers gave informed consent to participate in the study. The protocol was approved by the University of Iowa Institutional Review Board. The tenets of the Declaration of Helsinki were followed. The normals were paid volunteers who were hospital employees or friends or family members of eye clinic patients. The normal subjects were matched pairwise to patients by age within 5 years. Normals were included if they had no history of eye disease except refractive error and normal results of ophthalmologic examination. They all had normal automated perimetry results using the Humphrey Visual Field Analyzer (HVFA; Humphrey Instruments, San Leandro, CA), program 24-2. If a potential normal subject had three or more adjacent points with a total deviation score at the P < 0.05 level or two adjacent points with a total deviation score at the P < 0.05 level or two adjacent points with one at the P < 0.01 level with STATPAC (Humphrey Instruments), they were excluded. Subjects also were excluded if the mean deviation index was outside the 95% confidence bound for normals. All normals had normal results on the Glaucoma Hemifield Test.

Patients with glaucoma were recruited from previous studies in which they had taken HVFA tests that showed test locations in one eye with visual field damage in the 10- to 20-dB range (P < 0.005 for pointwise total deviation with STATPAC analysis) and test locations with normal results (P > 0.05) with the total deviation plot. All patients with glaucoma had undergone threshold automated perimetry within the preceding 2 months. All patients with the clinical diagnosis of primary open angle glaucoma had open angles on gonioscopy. They had an intraocular pressure greater than 21 mm Hg during their course, along with glaucomatous optic disc changes, glaucomatous visual field defects, and no other apparent mechanism of glaucoma. All patients were receiving treatment for intraocular pressure control, but none were using a miotic. Patients with primary open angle glaucoma were excluded if they had any other disease known to cause visual loss. All subjects had corrected visual acuity of 20/25 or better, pupil diameter of at least 3 mm when tested, spectacle correction not exceeding 6.00 D (equivalent sphere), and previous experience with automated perimetric examinations.

Testing Strategy

Conventional automated perimetry was first performed with the HVFA with program 24-2 using the manufacturer’s recommendations (except for three subjects in whom program 30-2 was performed). These programs test the central 21° or 27° of the visual field with stimuli spaced 6° apart; in addition, the 24-2 program tests one stimulus above and one stimulus below the nasal horizontal at 27°. We used a Goldmann size III (4 mm²) object on a 31.5-asb background. The size of the stimulus was fixed, and the threshold to differential light intensity was estimated at each test point with a staircase procedure. Each subject’s appropriate near correction was used. Rest breaks were given when requested.

Frequency of seeing curves were measured by controlling the HVFA with a custom program run by a personal computer (Hewlett Packard [Palo Alto, CA] Vectra 486, 33 mHz). At two different test locations, stimuli were presented in 2-dB intervals up to and including 10 dB from either side of the estimated (HVFA program 24-2) threshold, with 15 repetitions at each stimulus intensity. All presentations of stimulus intensity and location were randomized. To determine false-positive and false-negative responses, 60-dB and 0-dB stimuli were presented 20 times at each location. Therefore, each location was tested a total of 205 times. To prevent subjects from concentrating their entire attention on the two tested points, eight random additional locations of normal or near normal vision were tested with three repetitions of the 0-dB stimulus for a total of 24 extra trials. These 434 trials produced approximately a 30-minute test. This constraint was added to simulate usual clinical testing time of two 30-2 tests. All subjects were asked to respond as quickly as possible to the stimuli and were reminded two more times during testing to respond to the stimuli as quickly as possible. Reaction time for each trial was measured as the time between the beginning of the 200-msec stimulus presentation to the subject’s button-pressing response. If the subject did not respond within 2 seconds, the stimulus was considered
Additionally, we tried to choose high enough sensitivity test locations that were not greatly different from neighboring test points. In other words, we avoided test locations that were doubly determined by the total deviation plot (P > 0.05); the other point came from a normal area of visual field as determined from fixation in the glaucoma patient's normal sensitivity test location. In patients with glaucoma, one of the two points tested came from an area of normal visual field as determined by the total deviation plot (P > 0.05); the other point came from an area of the patient's visual field at which there was 10 to 20 dB of visual field loss. All selected test locations had a P < 0.005 total deviation score. We tried to use test locations that were doubly determined and thresholds that were not greatly different from neighboring test points. In other words, we avoided testing locations at steep edges of visual field defects because of their known high test–retest variability. Additionally, we tried to choose high enough sensitivities in the normal sensitivity test location of patients with glaucoma to match the thresholds of the controls.

To balance the location of the test presentations, these two points were along the vertical meridian at the Cartesian coordinates (0,9) and (0, –9). In patients with glaucoma, one of the two points tested came from a normal area of visual field as determined by the total deviation plot (P > 0.05); the other point came from an area of the patient's visual field at which there was 10 to 20 dB of visual field loss. All selected test locations had a P < 0.005 total deviation score. We tried to use test locations that were doubly determined and thresholds that were not greatly different from neighboring test points. In other words, we avoided testing locations at steep edges of visual field defects because of their known high test–retest variability. Additionally, we tried to choose high enough sensitivities in the normal sensitivity test location of patients with glaucoma to match the thresholds of the controls.

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Data Analysis

Frequency of seeing curves for each subject were constructed as cumulative Gaussian functions, and a least squares fit was calculated. The threshold was defined as the stimulus intensity corresponding to the 50% frequency of seeing of the fitted curves. The standard deviation of the cumulative Gaussian function and the coefficient of determination or goodness of fit ($r^2$) were calculated for each frequency of seeing curve. The mean RT at the frequency of seeing threshold and the 0-dB intensity also were computed. The difference between the frequency of seeing thresholds and the 24-2 thresholds was calculated. Prolongation of RT from the value found at 0 dB was analyzed as a function of increasing attenuation of stimulus intensity. In other words, we analyzed prolongation (RT$_{pi}$) from the RT of the 0-dB stimulus at various intensities related to threshold by plotting RT prolongation against increasing stimulus attenuation to threshold (for each value, RT$_{pi} = RT_i - RT_{0\text{dB}}$, where RT$_0$ is the mean RT in msec at stimulus intensity, and $i$ dB and RT$_{0\text{dB}}$ is the mean RT for the 0-dB stimulus).

**Statistical Analysis**

Subjects' data files were imported into Systat (SPSS Inc., Evanston, IL) and SigmaStat (Jandel Scientific, San Rafael, CA) for further statistical analysis. The primary outcome variables were normally distributed using the Kolmogorov–Smirnov test, ($P > 0.05$), except the $r^2$ values of the normal subjects. All had similar variances using the Levene Median test, ($P > 0.05$) except those that failed the above tests for normality and homoscedasticity (in which case, we performed ANOVA on ranks with post hoc tests using the Student–Newman–Keuls method). Statistical significance was set at $P < 0.05$.

The relationship between threshold and RT was analyzed. The simplest equation yielding a fit for this function with an $r^2$ greater than 0.9 from another study on normal subjects' RT change with visual field eccentricity was $RT = a + b(\text{Intensity})^3$. Therefore, we used this equation to fit our data. Linear regression analysis on ranks with post hoc tests using the Student–Newman–Keuls method. Statistical significance was set at $P < 0.05$.

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**TABLE 1.** Estimates of Thresholds (in dB) by the Standard Staircase Procedure of the Humphrey Program 30-2 Test and the Calculated 50% Frequency of Seeing Thresholds (in dB) for the Different Groups

<table>
<thead>
<tr>
<th></th>
<th>Glaucoma</th>
<th></th>
<th>Normal</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Staircase</td>
<td>FOS</td>
<td>Staircase</td>
<td>FOS</td>
</tr>
<tr>
<td>Mean</td>
<td>27.8</td>
<td>28.0</td>
<td>15.1</td>
<td>14.6</td>
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<tr>
<td>SD</td>
<td>2.78</td>
<td>3.62</td>
<td>3.51</td>
<td>9.01</td>
</tr>
<tr>
<td>Minimum</td>
<td>23.0</td>
<td>20.1</td>
<td>9.0</td>
<td>2.9</td>
</tr>
<tr>
<td>Maximum</td>
<td>31.0</td>
<td>32.0</td>
<td>21.0</td>
<td>26.9</td>
</tr>
</tbody>
</table>

FOS = frequency of seeing curve 50% threshold; Normal = glaucoma patient test location of normal sensitivity.
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was used to determine the relationship between the standard deviation of the frequency of seeing curve and threshold and the frequency of seeing curve goodness of fit ($r^2$) and threshold.

RESULTS

The mean age of the patients was 60.2 ± 9.0 years, and of the normal controls it was 59.8 ± 7.9 years. The age difference between the groups was not statistically significant ($P = 0.77$). As expected, the threshold estimates using the 4 dB–2 dB staircase strategy of the 24-2 program of the HVFA and the results of the frequency of seeing curve thresholds were lowest in the normal subjects and in the patients with glaucoma in areas of normal visual field sensitivity and highest in patients with glaucoma in areas of abnormal visual field sensitivity (Table 1). Frequency of seeing curve thresholds of the normal subjects' two test locations did not show a significant difference ($P = 0.48$, paired $t$-test). Visual field thresholds from the HVFA 24-2 test (staircase algorithm) and the frequency of seeing curve thresholds were compared by computing the differences in values. Differences were not statistically significant among the patients with glaucoma and the normals (Table 1). False negatives—no response to the 0-dB stimulus—were uncommon (total of three) except for the abnormal sensitivity test location in the patients with glaucoma. They occurred here because in six subjects, the brightest stimulus (0 dB) was not seen 100% of the time. False positives—responses to the 60-dB stimulus—were also rare; no subject had more than two (total of five).

Intratest variability, illustrated by the standard deviation of the frequency of seeing curve, was lowest in normal subjects, intermediate in the areas of normal sensitivity of patients with glaucoma, and highest in test locations of 10 to 20 dB loss in patients with glaucoma (see Figs. 1, 2). The differences between these groups were highly significant ($P < 0.006$, ANOVA with post hoc $t$-tests). Frequency of seeing curve standard deviations for the two locations tested in normal subjects did not show a significant difference ($P = 0.17$). We found a negative linear relationship between the frequency of seeing curve standard deviations and threshold for the patients with glaucoma, but this was statistically significant only for the test location of normal sensitivity ($P < 0.005$, Fig. 3). No significant relationship was found for the normal subjects over the small range of intensities of the normal test locations.

The $r^2$ value, representing the goodness of fit of the frequency of seeing curves, also was significantly different among the three groups ($P < 0.01$, ANOVA with post hoc $t$-tests). Again, the two normal test points did not differ significantly. A linear relationship was found between the frequency of seeing goodness of fit and the 50% frequency of seeing curve threshold for the patients with glaucoma (test location of normal sensitivity, $P < 0.0001$, $r^2 = 0.22$; abnormal sensitivity location, $P < 0.0001$, $r^2 = 0.54$) (Fig. 4). As with the standard deviations, we found no significant relation-
ship in the normal subject's $r^2$ values and threshold for the small range of intensities tested.

We evaluated the mean RT at both threshold (50% frequency of seeing) and 0-dB intensity (Tables 2, 3). The RT at threshold was approximately 200 msec longer than for the suprathreshold, 0-dB stimulus. Surprisingly, at the 50% frequency of seeing curve threshold, there was no significant difference among the groups of test locations (Table 2). However, at the 0-dB intensity for the test location with 10 to 20 dB loss, patients with glaucoma had higher RTs by ap-
TABLE 2. Reaction Time Values at the 50% Frequency of Seeing Thresholds for the Different Groups

<table>
<thead>
<tr>
<th>Glaucoma</th>
<th>Normal</th>
<th>0, 9</th>
<th>0, -9</th>
</tr>
</thead>
<tbody>
<tr>
<td>'Normal'</td>
<td>Abnormal</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>663.0</td>
<td>620.2</td>
<td>680.1</td>
</tr>
<tr>
<td>SD</td>
<td>79.7</td>
<td>75.5</td>
<td>90.5</td>
</tr>
<tr>
<td>Minimum</td>
<td>534.1</td>
<td>482.9</td>
<td>536.9</td>
</tr>
<tr>
<td>Maximum</td>
<td>768.9</td>
<td>760.3</td>
<td>811.0</td>
</tr>
</tbody>
</table>

Reaction time values are in msec.

proximately 90 msec than normal subjects \((P = 0.045, \text{ Table 3})\). A linear regression analysis of percent seen at 0 dB at the glaucoma test location, with 10 to 20 dB loss versus its RT, reveals a significant slope to the regression line \((P = 0.014, \text{Fig. 5})\). When the most outlying test point is excluded, the significance level falls \((P = 0.09)\). This relationship shows at least some of the high RT at 0 dB is accounted for by the percent of stimuli seen at 0 dB. If we compute the RT only for the subjects who reached 100% at 0 dB, the mean value falls from 528 msec to 478 msec. This leaves a non-statistically significant trend of increases in RT to the 0 dB stimulus from 438 msec and 434 msec in the control subjects to 460 msec in the normal sensitivity test location of the patients with glaucoma to 478 msec at the abnormal sensitivity test location \((\text{ANOVA, } P = 0.57)\).

Reaction times of subjects were transformed by subtracting the value at 0 dB from the observed RT at each stimulus intensity. We called this value the RT prolongation. This was then analyzed as a function of increasing attenuation of stimulus intensity. The results fit the equation \(RT = a + b(\text{Intensity})^n\) \((\text{Fig. 6})\). The goodness of this fit was greater than 0.90 in the normal sensitivity test locations and was 0.58 in the abnormal location of the group with glaucoma.

DISCUSSION

Flammer and coworkers\(^9\) studied covariates of long-term fluctuation in normals, glaucoma suspects, and patients with glaucoma.\(^9\) They reported a relationship between reversible changes in threshold and reversible changes in the short-term fluctuation, intraocular pressure, and reaction time. They concluded that RT varied inversely with threshold. Our data on short-term fluctuation shows RT at threshold does not significantly differ in normal areas of the visual field in patients with glaucoma or in areas of moderate optic nerve damage compared with age-matched controls. However, we did find a trend for an increase in RT, not at threshold, but to the 0-dB stimulus for the subjects with glaucoma. This trend was accounted for primarily by the finding that the 0-dB stimuli were not seen at a 100% frequency in all subjects with glaucoma \((\text{Fig. 5})\). In other words, in our subjects, RT to the 0-dB stimulus was related to the percent of stimuli seen.

In 1879, Hall and von Kries\(^13\) studied nine locations in the visual field and found RT increased with visual field eccentricity and with decreasing light intensity. Their results have been confirmed many times.\(^4-7\) Our similar results demonstrate these well-known relationships in the setting of clinical threshold automated perimetry. Our new finding is the power function type relationship \((RT = a + b(\text{Intensity})^n)\) —is true not only for normal subjects but also for patients with optic nerve damage from glaucoma. Because this relationship is constant in normal subjects and in patients with glaucoma, it may aid in the prediction of threshold from the RT results from testing with suprathreshold stimuli, function as a reliability criteria \(\text{poor subjects and malingerers would be expected to have highly variable RTs},\) and serve as an index of test fatigue.

A major problem facing conventional automated
perimetry today is highlighted by our results showing that variability in conventional automated perimetry increases substantially with sensitivity loss. Our data show this variability to be low for test locations in normal subjects, with subjects’ “seen” responses occurring over a 6- to 8-dB range. Our results confirm those of others that variability is high in patients with glaucoma with moderate visual field loss.9,14-17 Also, our results showing a rise in variability in normal areas of the visual field in patients with glaucoma are similar to previous reports.2,10-20 In particular, our results of variability using frequency of seeing curves in glaucoma with 15 repetitions per test location mirror those of Chauhan and colleagues,9 who used five repetitions per location. With a decrease in sensitivity, we also found variability increased, the slope of the frequency of seeing curve flattened, and the goodness of fit worsened. We were disturbed to find that this flattening of the frequency of seeing curve slope was so pronounced in 6 of the 10 patients that 100% seen was not reached, even with the 0-dB stimulus. Because retest variability is high in conventional automated perimetry, we plan to use simulations with our RT data to determine whether RT can be used to help predict threshold. For example, if we limit “seen” responses to those with a short RT, this should shift the threshold to a higher intensity with an associated reduction in variability.

In conclusion, threshold variability in areas of 10 to 20 dB loss is very high and increases with increasing threshold. Threshold variability is significantly increased in test locations of normal sensitivity of the visual fields of glaucoma patients. Suprathreshold, but not threshold, RT is prolonged in areas of moderate glaucomatous damage. However, this is primarily because of failure of most subjects to reach 100% seen at the 0-dB stimulus. Reaction time increases after a power function from suprathreshold to threshold intensities.

Key Words

glaucoma, perimetry, reaction times, visual testing

Acknowledgments

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References

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