ABNORMAL MAXIMUM LINE DISPLACEMENT SENSITIVITY AND FREQUENCY-OF-SEEING CURVES FOR A MOTION STIMULUS IN GLAUCOMA

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Abstract

Purpose: To investigate frequency-of-seeing (FOS) curves and maximum line displacement (LDmax) sensitivity differences between glaucomatous eyes and normals.

Method: Twenty-nine normal eyes, 28 glaucoma suspect and 29 POAG eyes underwent motion sensitivity testing in the superotemporal field. FOS curves were generated for a line stimulus undergoing displacements 0-18 min.arc. Motion thresholds and slopes of the FOS curve were obtained by probit analysis. Responses to greater magnitudes of displacement were analyzed to determine sensitivities to LDmax.

Results: Similar to previous findings, minimum motion thresholds were abnormal in 6/28 suspect and 22/29 glaucomatous eyes, and the slopes of the FOS curves were abnormally shallow in 14/28 of the suspect and 21/29 glaucomatous eyes at the test location. In 28/29 of the normal controls, the response rate showed no drop-off at the maximum displacements. However, 8/28 suspect and 14/29 of the glaucomatous eyes had abnormally reduced responses to the maximum displacement (18 min.arc). Overall, LDmax was significantly lower in the suspect and glaucoma groups compared to controls, with 8/28 (29%) suspect eyes and 14/29 (48%) glaucomatous eyes having LDmax less than 18 min.arc compared with 1/29 (3%) controls (p<0.0005, ranked test). This drop-off contributed to the shallowing of the probit slope.

Conclusions: This study has identified differences in the motion FOS response between glaucomatous eyes and normals, which may not be evident on analysis of the threshold alone. Abnormal shallowing of the slope of the FOS curve may be associated with LDmax abnormalities in glaucomatous eyes for line displacement motion. Responses are decreased for larger amplitudes of displacement as well as for the minimum thresholds for displacement.

Introduction

We have previously used a line displacement test to identify glaucomatous loss of motion sensitivity1-4. These findings have been confirmed by other workers using line stimuli5 and random dot kinetograms6-11.

These studies concentrated on differences in the motion threshold between groups. Our investigations of motion displacement threshold abnormalities in glaucoma were obtained using a line displacement test to obtain a motion frequency-of-seeing (FOS) curve. FOS curves describe the relationship between the probability of seeing a stimulus and a stimulus parameter. An advantage of FOS curve analysis is that it may

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identify further differences between normals and glaucomatous eyes that may not be evident on analysis of the threshold alone. We previously noted a lessening of the slope of the psychometric curve of motion in some patients with glaucoma. In some cases, this co-existed with a decreased response rate for larger amplitudes of displacement, as well as for the minimum thresholds for displacement.

The aim of this study was to investigate maximum line displacement (LDmax) sensitivity and the slope of the motion FOS curve differences to determine if these factors can improve the separation of controls from glaucoma above that achieved by analysis of the threshold alone.

Methods

Testing strategy

We measured motion sensitivity using a line displacement test presented in the superotemporal field in order to obtain motion displacement thresholds (MDT). This site was chosen because previous results had identified significantly elevated MDTs at this location in glaucoma patients, with good separation between patients and controls. The MDT test was performed using a computer-generated line stimulus presented on a monochrome monitor (Phillips green monochrome P31 monitor, pixelation 300×920, frame rate 50 Hz). The view distance was 1.24 m. The width of the stimulus was formed by addressing two horizontal pixels. The stimulus subtended 2°-by-2 min.arc in size and the background 8×10°, as measured directly from the display. The line stimulus was presented in the superotemporal field at 15° eccentricity on the 30° meridian. The luminance of the background was 7 cd/m² and the stimulus 27 cd/m².

The subject viewed a fixation target and was instructed to press a response button when movement was seen. A warning tone was sounded, followed by 1.5 seconds during which the stimulus was stationary. During the following two seconds, the stimulus (if it were to move), would undergo sudden oscillatory displacements at 2.5 Hz, beginning at a random time after the start of this interval. If the subject pressed the response button before stimulus movement had begun, this was counted as a false-positive response.

After a suitable instruction period, subjects underwent a test which consisted of ten presentations each of ten different displacements in 2 min.arc intervals from 0-18 min.arc in a random order. The test included ten presentations of a 0 min.arc displacement (stationary target catch trials) and if the subject pressed the button to 0 min.arc displacement, this was recorded as a false-positive response.

The experimenter observed the subject for the duration of the test to ensure reliable fixation throughout.

Subjects

We tested 29 control subjects and 42 patients. The controls underwent testing in one randomly selected eye. Twenty-seven patients had one eye meeting either POAG (n=14) or glaucoma suspect criteria (n=13) and underwent testing in this eye only. Fifteen patients had POAG in one eye and a glaucoma suspect fellow eye, and under-
Maximum line displacement sensitivity and frequency-of-seeing curves

went testing of both eyes in a randomized order. Because these patients were contributing both eyes to the study, we performed two independent analyses of the data: the first using data from both eyes of these patients, then re-analyzing using data from only one eye selected at random from each of these patients. We present the data using both eyes of these patients, as all statistically significant results reported in this study were confirmed using both analyses and did not differ at the \( p < 0.05 \) level of significance.

Control eyes had normal ocular examination and normal Humphrey HFA 24-2 fields (defined as a normal Glaucoma Hemifield Test with global indices within 95% CI for normal subjects with no hemifield clusters of depressed points). Glaucomatous eyes had documented intraocular pressures >21 mmHg with typical glaucomatous optic disc cupping and documented glaucomatous visual field defects on the Humphrey 24-2 field.

Glaucoma suspect eyes had at least one of the following: glaucomatous optic disc cupping, clinical evidence of retinal nerve fiber layer defects, or a documented intraocular pressure >21 mmHg on at least one occasion, in the presence of a normal Humphrey 24-2 field (defined as normal or borderline Glaucoma Hemifield Test in the absence of any clusters of depressed locations in either hemifield).

A field was defined as glaucomatous on the Humphrey 24-2 if at least one hemifield contained a cluster of a minimum of three adjacent depressed points on the STATPAC 2 pattern deviation plot with one point having a probability of \( p < 1\% \) and two adjacent points having a probability of \( p < 2\% \). According to this cluster definition, 7/29 glaucoma eyes had scotomas within the MDT test site, and the remaining 22/29 glaucomatous eyes had normal Humphrey 24-2 field thresholds at the motion test site.

The Humphrey 24-2 mean defects (MDs) of the glaucomatous eyes ranged from -14.2 to -1.3 dB (median -4.6 dB), and the glaucoma suspect eyes from -4.2 dB to +1.8 dB (median -0.7 dB). The MDs of the glaucoma eyes and suspect eyes were significantly lower than the Humphrey 24-2 MDs of the control eyes (range -2.7 to +2.5 dB, median 0.05 dB) at the \( p < 0.05 \) level. Although all suspects had Humphrey 24-2 fields that fulfilled our definition of normality, five (of 28) had a depressed MD, one had a depressed PSD, and five had a depressed CPSD at the \( p < 0.05\% \) level.

The mean age of the controls was 58.7 ± 10.5 years, with a range of 31.3 to 74.9 years. The mean age of patients with glaucoma suspect eyes tested was 60.9 ± 11.5 years (range 30.6 to 78.8 years) and POAG eyes tested was 62.9 ± 10.7 years (range 30.6 to 78.8). The age of the groups were closely matched and did not differ significantly at the \( p < 0.05 \) level.

Analysis

FOS curves of the subjects’ responses to the motion stimulus were generated, and the data imported to SPSS for Windows (release 6.0, SPSS Inc. Chicago, IL). Probit analysis generated the slope of the FOS curve and the MDT which corresponded to a 50% FOS of the probit fitted curve.

In order to obtain a measure of the sensitivity to maximum line displacements, we identified the largest magnitude of line displacement coinciding with the optimal response rate (LDmax).
Results

Minimum motion displacement thresholds

Table 1 shows the minimum MDTs and the slope indices for the groups. Similar to our previous findings, the MDTs were significantly elevated in the glaucomatous eyes (Mann-Whitney U test, \( p < 0.0001 \)) and in the glaucoma suspect eyes (\( p < 0.001 \)) compared to controls.

An MDT cut-off of nine was used, which was derived from previously published normative data and has been shown to achieve good separation of normal from glaucomatous eyes\(^2,4\). Using this cut-off, 22/29 glaucomatous eyes and 6/28 suspect eyes had abnormally elevated MDTs at the test location. No control eyes had an MDT above this level.

The slope indices were also significantly lower in the glaucoma eyes (Mann-Whitney U test, \( p < 0.0001 \)) and in the glaucoma suspect eyes (\( p < 0.005 \)) compared to the controls, indicating a shallowing of the FOS in the patients as a group at the location tested. Slopes of the FOS curves were abnormally shallow (defined as outside the control mean \( \pm 1.96 \text{ SD} \)) in 14/28 of the suspect and 21/29 glaucomatous eyes.

Frequency-of-seeing curves and maximum line displacement sensitivity

Figures 1a and b show typical normal FOS curves obtained from controls with a normal minimum displacement threshold and steep slopes of the probit-fitted FOS curve. There is no drop-off of the response rate at the maximum displacements, and LD\(_{\text{max}}\) is 18 min.arc (the maximum displacement tested). In 28/29 of the normal controls, the response rate showed no drop-off at the maximum displacements. Only one control showed a drop-off of the response rate at the maximum displacement tested, resulting in an LD\(_{\text{max}}\) of 16 min.arc.

However in the glaucomatous eyes and suspect eyes, we commonly identified a drop-off of the response rate at the larger displacements tested. This resulted in LD\(_{\text{max}}\) values of less than 18 min.arc (Fig. 1d) and contributed to the shallowing of the calculated values of the probit FOS slope seen in the glaucomatous eyes and suspects. In some cases the drop-off in the response rates at the larger displacements was more marked, resulting in diminished LD\(_{\text{max}}\) values of 14 min.arc or less (Figs. 1e, f and g). This fall off in the response rates for the larger displacements could be severe (Figs. 1f and g).

Table 1. Summary statistics for the motion thresholds (min.arc) and slope indices of the frequency-of-seeing curves by group

<table>
<thead>
<tr>
<th>Group</th>
<th>Normals (29 eyes)</th>
<th>Glaucoma suspects (28 eyes)</th>
<th>Glaucoma patients (29 eyes)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Motion threshold (min.arc)</td>
<td>5.9±1.7 (2.6-8.9)</td>
<td>8.7±3.4 (5.0-17.6)</td>
<td>12.9±5.8 (5.2-34.2)</td>
</tr>
<tr>
<td>Slope of probit-fitted FOS</td>
<td>0.50±0.27 (0.23-1.29)</td>
<td>0.31±0.16 (0.14-0.64)</td>
<td>0.19±0.06 (0.05-0.32)</td>
</tr>
</tbody>
</table>

Values shown are mean ±1 SD. Figures in brackets indicate minimum and maximum values.
Figure 2 shows the observed difference in the distribution of LD_{max} values between the glaucomatous eyes and the control group. Overall group values of LD_{max} were significantly lower in the glaucomatous eyes (Mann-Whitney U test, $p < 0.0001$) and in the suspect eyes ($p < 0.01$) compared to controls. Fourteen/29 (48%) glaucoma eyes had LD_{max} less than 18 min.arc, and 8/28 (29%) suspect eyes had LD_{max} less than 18 min.arc compared with only 1/29 (3%) controls (Fig. 2).

In six suspect eyes and three glaucomatous eyes, a decreased response rate to larger amplitudes of displacement (represented by a LD_{max} under 18 min.arc) was detected even though the minimum displacement thresholds remained within normal limits (see examples in Figures 1d and e).

Discussion

In accordance with our previous findings, this study identified a significant elevation in the minimum motion thresholds in glaucoma patients compared with normals. However, the aim of this study was to look for differences in the response rate to large...
amplitudes of line displacement motion, which may exist between glaucoma patients and normals.

In all but one control, the response rate showed no drop-off at the maximum displacement tested. In the glaucoma patients, nearly 50% showed a significant drop-off in the response rate at the maximum magnitude of line displacement. This was manifested as a reduction in the largest displacement coinciding with the optimal response rate (LDmax) in the glaucomatous eyes and suspect eyes which, as a group, were significantly smaller for the glaucomatous eyes and controls. This effect contributed to the shallowing of the slope of the FOS curve. F and g. FOS curves of glaucomatous eyes with abnormally elevated MDTs with a more severe drop-off of the response rate at the larger displacements tested (16 and 18 min.arc) resulting in an LDmax of 14 min.arc.

The finding of an impaired response to larger amplitudes of line displacement in glaucoma has not been reported previously, since until now, previous studies have concentrated on the minimum motion threshold. We examined motion FOS curves in this study, as this technique allows us to identify further differences between normals

Fig. 1d-g. FOS curves of d. a suspect eye, and e. a glaucomatous eye with MDTs of 8.2 and 8.5 min.arc, respectively, both within the normal range. However, there is a falling off of the response rate at the maximum displacement tested indicated by an LDmax of d. 16 min.arc and e. 14 min.arc. This contributes to the shallowing of the slope of the FOS curve. F and g. FOS curves of glaucomatous eyes with abnormally elevated MDTs with a more severe drop-off of the response rate at the larger displacements tested (16 and 18 min.arc) resulting in an LDmax of 14 min.arc.

In all but one control, the response rate showed no drop-off at the maximum displacement tested. In the glaucoma patients, nearly 50% showed a significant drop-off in the response rate at the maximum magnitude of line displacement. This was manifest as a reduction in the largest displacement coinciding with the optimal response rate (LDmax) in the glaucomatous eyes and suspect eyes which, as a group, were significantly smaller for the glaucomatous eyes and controls. This effect contributed to the shallowing of the FOS curve seen in glaucomatous and suspect eyes. In the glaucomatous eyes, the impaired maximum line sensitivity coexisted with elevated minimum motion thresholds, because of the high proportion of elevated minimum motion thresholds in this group. However, in the suspects we identified an equivalent number of eyes (6/28) with impaired maximum line sensitivity in the presence of normal minimum motion thresholds as those eyes with elevated minimum thresholds. This suggests that impaired sensitivity to large displacements may be an early feature of the impaired motion response in glaucoma.

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Fig. 2. Bar chart of the frequency of LDmax values between the groups. For the controls, 28/29 had an LDmax of 18 min.arc. Eight/28 (29%) of the suspect eyes and 14/29 (48%) of the glaucomatous eyes had an LDmax of less than 18 min.arc.

and glaucoma eyes which may not be evident on analysis of the threshold alone.

This approach has previously been useful in conventional perimetry, as FOS curve abnormalities such as a lessening of the slope, have been identified in glaucoma by a number of researchers.13-18.

The cause of the impaired response to LDmax observed in our glaucoma patients remains unknown. Although a number of mechanisms may be proposed, one possibility is that the motion target may be stimulating a sparsely represented subpopulation of ganglion cells with minimal overlapping receptive fields. Glaucomatous ganglion cell loss would result in a thinning of the receptive field overlap in this sparsely represented system, according to the reduced redundancy hypothesis.19 As a consequence, large displacements of the line stimulus from its starting position would result in the stimulus falling outside the receptive field. This would manifest as a failure to perceive the apparent motion at large amplitudes of displacements, with a consequent falling-off of the response rate.

Further work is required to investigate this effect and to examine whether abnormalities of LDmax detection could be useful in improving the sensitivity and specificity of motion testing in glaucoma.

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References