Motion Perception in Glaucoma

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Purpose. This study was performed to investigate motion perception in patients with glaucoma.

Methods. A random dot motion test was used to measure three aspects of central motion perception: minimum displacement threshold (Dmin), maximum displacement threshold (Dmax), and coherence threshold (signal to noise). Motion perception was assessed in 15 patients with primary open-angle glaucoma, 23 low-risk patients in whom glaucoma was suspected, and 24 age-matched normal subjects.

Results. Central motion perception was significantly impaired in patients with glaucoma; in particular, the Dmin was nearly twice that for the normal subjects (glaucoma mean, −0.27 ± 0.24 log minutes of arc; normal mean, −0.56 ± 0.13 log minutes of arc; F = 21.79, P < 0.001). Furthermore, Dmin values fell outside the normal range in 10 of the 15 patients with glaucoma, despite normal visual acuity and normal foveal perimetric thresholds. Coherence thresholds and Dmax did not discriminate between patients with glaucoma and normal subjects. Dmin was not correlated with any indices of perimetric sensitivity, and none of the tests of motion perception showed any abnormalities in patients in whom glaucoma was suspected.

Conclusions. Central motion perception can be affected in glaucoma and may reflect preferential damage to larger retinal ganglion cells. Future work will measure Dmin in a larger population of patients with suspected glaucoma and those with glaucoma, and investigate peripheral motion perception in glaucoma.

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![FIGURE 1. Schematic representation of the three types of random dot stimuli used in the current study. For minimum displacement thresholds (D_{min}) and maximum displacement thresholds (D_{max}), the dots undergo a constant displacement in a uniform direction. For coherence thresholds, the dots move smoothly with constant speed. A subset of dots (black) move in a uniform direction, whereas the remainder move in random but constant directions.](image)

subsequently was found to vary, depending on the spatial frequency content of the stimulus and stimulus field size. The higher D_{max} values obtained with larger field sizes are thought to reflect the recruitment of larger, more eccentric neural units.

An additional component of motion processing is the detection of a subset of dots moving coherently embedded in "noise." The noise is provided by background dots, which may be replotted at random to give a scintillating appearance, or, as in the current study, dots moving at constant speed but in random directions (Fig. 1). The ratio of coherently to randomly moving dots is varied to determine the coherence threshold. Typical normal coherence thresholds are 5% to 10% and may be influenced by the paradigm adopted.

This article contains initial results from ongoing research to develop clinical tests of central and peripheral motion perception for the early detection and monitoring of glaucomatous nerve damage. One of the primary goals was to use widely available instruments. Thus, our random dot motion test was developed for the Macintosh II (Apple, Cupertino, CA) computer. We wanted to establish which test of motion perception was most sensitive to early glaucomatous nerve damage for foveal viewing. In this article, we present results for D_{min}, D_{max}, and coherence thresholds in patients with glaucoma, patients suspected to have glaucoma, and normal subjects to determine which of these aspects of motion perception best differentiates the three subject groups.

MATERIALS AND METHODS

Bright, 0.35-mm dots (100 cdm^{-2}) were positioned randomly against a dark background (0.5 cdm^{-2}) on a 13-inch high-resolution monitor. The software facilitates variation of a number of parameters, such as dot density, speed, and coherence. Furthermore, we can limit coherent dot motion to small regions of the screen, which will permit us to investigate localized peripheral motion sensitivity.

The stimulus parameters adopted for patient testing were chosen after extensive preliminary investigations in young normal subjects. The dot density was 1% (which is the percentage of illuminated pixels) for all measurements, providing a mean screen luminance of 1.5 cdm^{-2}. A density of 1% thus corresponds to greater than 3000 pixels or dots. Although reducing the dot density from 1% to 0.25% had little effect on D_{max} and D_{min} values, repeatability was substantially better for the higher dot density. Even though the dots were generated across the entire screen, the coherent motion was restricted to a 16-cm square patch. To limit any possible edge effects, the motion of the surround dots was always random. Dots that crossed the edge of the patch were wrapped around to reappear at the opposite boundary.

For all trials, the dots moved in one of the four cardinal directions (ie, up, down, left, or right). All thresholds were determined with a 4-AFC staircase procedure starting well above threshold. To reach the region of threshold performance quickly, the chosen variable was decreased by 0.1 log unit for each correct response until the first incorrect response was made. Thereafter, a two-down/one-up staircase was used, wherein two consecutive correct responses decreased the variable by 0.1 log unit and each incorrect response increased the variable by 0.1 log unit. The staircase was limited by eight errors (≈25 to 35 presentations), which was considered to be a reasonable trade-off between time and repeatability. All threshold values were calculated with probit analysis.
Minimum Displacement Threshold
For the determination of $D_{\text{min}}$, a viewing distance of 320 cm was adopted, giving a patch size of 2.9°. Increasing the viewing distance, and thereby reducing the field size, had little effect on $D_{\text{min}}$ values. A given trial started with a blank screen, which was replaced by one containing a random dot pattern. Thereafter, the dots underwent four displacements, in a fixed direction, each separated by 150 milliseconds, and then disappeared. Multiple displacements were used to limit temporal uncertainty.14

Maximum Displacement Threshold
For the assessment of $D_{\text{max}}$, a viewing distance of 50 cm was used, giving a stimulus field size of 19°. The choice of this viewing distance and field size was somewhat arbitrary because $D_{\text{max}}$ values show a strong dependence on field size.15 The larger $D_{\text{max}}$ values obtained with larger field sizes are thought to be mediated by larger, more eccentric neural units. It has been speculated that larger ganglion cells may be affected preferentially in glaucoma,24-26 so a large stimulus area was used. A given trial started with a blank screen, which was replaced by one containing a random dot pattern. After 250 milliseconds, the dots underwent displacement in a fixed direction and, after an additional 250 milliseconds, disappeared. This brief presentation time was used to prevent subjects from searching for clusters of dots that might provide them with extraneous clues as to the direction of displacement.

Coherence Thresholds
To be consistent with the $D_{\text{max}}$ determinations, we adopted a viewing distance of 50 cm (19° field size). A dot speed of $10^\circ$/s was used because this gave less within- and between-subject variability than speeds of $3.2^\circ$/s and $32^\circ$/s. A given trial started with a blank screen, which was replaced by one containing a random dot pattern. A subset of coherent dots then proceeded to move in a fixed direction while the remaining dots moved in random but constant directions with a frame rate of 67 Hz. The motion persisted for 1 second, and the dots subsequently disappeared. We used a short duration because pilot studies showed that longer presentation times permitted subjects to adopt search strategies.

Subjects
Subjects were recruited from the Ocular Health Clinics at the School of Optometry, University of California at Berkeley, and the School of Optometry, Queensland University of Technology. The tenets of the Declaration of Helsinki were followed; approval for the study was obtained from the Committee for Protection of Human Subjects; and informed consent was obtained from all subjects after the procedures were explained. All testing was monocular, with the tested eye being chosen at random. Subjects wore a refractive correction appropriate for the viewing distance of each test. In addition to performing our three tests of motion perception, we measured visual acuity with a high-contrast Bailey-Lovie chart27 and letter contrast sensitivity with a Pelli-Robson chart.28,29

Sixty-two subjects participated in the study; they were 32 to 74 years of age and consisted of 15 patients with primary open-angle glaucoma, 23 patients with suspected glaucoma, and 24 normal subjects. All patients with glaucoma had visual field defects with program 24-2 on the Humphrey (San Leandro, CA) Field Analyzer. To be classified as glaucomatous, two of three key field parameters (mean defect, corrected pattern standard deviation, and glaucoma hemifield test) had to fall outside the 95% range for normal subjects. All had abnormal disks, and all but two had intraocular pressures greater than 21 mm Hg at diagnosis. Two of these patients were considered to have normal-tension glaucoma. All patients with glaucoma were taking nonmotic medication when the study was performed.

Patients with suspected glaucoma were not preselected, and all had normal visual fields. Nineteen of the patients in whom glaucoma was suspected were considered to have ocular hypertension, having had intraocular pressures of 21 mm Hg or greater in one or both eyes on at least two occasions. The remaining patients with suspected glaucoma thus were categorized because of high cup-to-disk ratios or intraocular pressure/disk asymmetries. None of the subjects had any ocular or neurologic disease other than defined in the selection criteria and were free of systemic abnormalities with known ophthalmic complications. No subjects were taking medication that was known to influence visual performance. All had visual acuities of 20/30 or better.

RESULTS
The mean results for each subject group and each test are shown in Table 1. The most significant difference occurred for $D_{\text{max}}$, for which the mean value for the patients with glaucoma ($-0.27 \pm 0.24$ log minutes of arc) was nearly twice (0.3 log units) that for the normal subjects ($-0.56 \pm 0.13$ log minutes of arc). This difference is highly significant (analysis of variance: $F = 21.79, P < 0.001$). Significant differences also were observed for $D_{\text{max}}$ ($F = 5.36, P < 0.01$) letter contrast sensitivity ($F = 6.86, P < 0.01$). No significant differences were found for coherence thresholds or visual acuity. The patients with suspected glaucoma did not differ significantly from the normal subjects on any of
TABLE 1. Mean (±SD) Values for Each Subject Group and for Each Test

<table>
<thead>
<tr>
<th></th>
<th>Normals (n = 24)</th>
<th>Glaucoma Suspects (n = 23)</th>
<th>Glaucoma Patients (n = 15)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>56.1 ± 10.6</td>
<td>56.0 ± 10.7</td>
<td>61.6 ± 8.5</td>
</tr>
<tr>
<td>Visual acuity (log minutes of arc)</td>
<td>-0.03 ± 0.07</td>
<td>0.00 ± 0.08</td>
<td>0.05 ± 0.14</td>
</tr>
<tr>
<td>Letter contrast sensitivity (log sensitivity)</td>
<td>1.71 ±0.14</td>
<td>1.74 ±0.11</td>
<td>1.60 ±0.13*</td>
</tr>
<tr>
<td>Dmin (log minutes of arc)</td>
<td>-0.56 ±0.13</td>
<td>-0.53 ±0.14</td>
<td>-0.25 ±0.23†</td>
</tr>
<tr>
<td>Dmax (log minutes of arc)</td>
<td>1.74 ±0.09</td>
<td>1.74 ±0.06</td>
<td>1.67 ±0.09*</td>
</tr>
<tr>
<td>log coherence threshold</td>
<td>-1.11 ±0.12</td>
<td>-1.13 ±0.16</td>
<td>-1.01 ±0.16</td>
</tr>
</tbody>
</table>

* Significantly different from normal group (P < 0.01).
† Significantly different from normal group (P < 0.001).

The results for the three tests of motion perception are shown in Figure 2. The 95% confidence limits for the normal subjects were calculated (mean ± 1.96 SD) and are shown as shaded areas. Dmin values for 10 of the 15 patients with glaucoma (67%) fell outside the normal range. Three patients with glaucoma exhibited abnormal coherence thresholds, whereas two showed abnormal Dmax values. Although letter contrast sensitivity was significantly lower in the group with glaucoma, only two patients with glaucoma had values that fell outside the normal range.

DISCUSSION

We examined three aspects of central motion perception using random dot stimuli in patients with glaucoma, patients with suspected glaucoma, and normal control subjects. Central motion perception was impaired significantly in the patients with glaucoma, most notably for Dmin, when other central measures, including visual acuity and foveal perimeter thresholds, were normal. Although this is an interesting finding, it is not compelling evidence supporting the measurement of Dmin as a screening test for glaucoma because 5 of 15 patients had normal thresholds; however, the test may have some value in monitoring patients on a longitudinal basis. We plan to extend our studies to the assessment of Dmin in areas of the visual field where early glaucomatous defects occur.

Abnormal Dmin values may be interpreted in light of visual system function and recent anatomic studies of neural damage in nonhuman primate experimental glaucoma. Chronic elevation of intraocular pressure in primates has been shown to preferentially damage larger retinal ganglion cells and larger optic nerve fibers. Preliminary investigations of glaucomatous human eyes suggest a similar pattern of nerve damage. Therefore, it appears that chronic open-angle glaucoma may preferentially damage the larger retinal ganglion cells that project to the magnocellular layer of the lateral geniculate nucleus. Lee, Wehrhahn, Westheimer, and Kremers measured responses to step displacements from macaque ganglion cells that projected to either the parvocellular or magnocellular layers of the lateral geniculate nucleus, and they computed the displacement thresholds (corresponding to 75% probability of detection). For 40% luminance contrast, displacement thresholds were approximately 0.05 log minutes of arc per decade of life.

Although a statistically significant difference was found between Dmax values in patients with glaucoma and normal subjects, only two patients with glaucoma had values that fell outside the normal range.
Nakayama and Silverman suggested that $D_{\text{min}}$ and $D_{\text{max}}$ are not mediated by a single neural subunit, and this hypothesis has been supported by recent investigations showing the different temporal characteristics of $D_{\text{min}}$ and $D_{\text{max}}$. The resistance of $D_{\text{max}}$ to glaucomatous damage also may result from redundancy in our stimulus. Control studies show that reducing the field size from 19° to 9.5° in normal young subjects decreases $D_{\text{max}}$ values by only 0.15 log minutes of arc (1.82 versus 1.67 log minutes of arc, respectively). This is substantially smaller than the range of normal values (0.40 log minutes of arc) determined in the current study. Therefore, substantial neural loss may occur before abnormal $D_{\text{max}}$ values are observed.

Coherence thresholds were abnormal in only 3 of 18 patients with glaucoma (17%), a lower proportion than reported by Silverman, Trick, and Hart. They found that motion coherence thresholds fell outside the normal range in 16 of 37 (43%) patients with glaucoma and 3 of 14 (21%) patients with ocular hypertension. There are, however, several important methodologic differences between the stimuli used in their study and those used in ours. The stimulus adopted by Silverman, Trick, and Hart covered an area of 60° X 60°, which may have facilitated recruitment of more eccentric motion mechanisms. Their stimulus, however, contained only 100 dots, giving a dot density (0.03 dots/deg²) that was substantially lower than ours (7.0 dots/deg²). With such a low dot density, it is possible that a significant number of the coherent dots may have been moving within or across visual field defects. Coherence thresholds may become elevated because of sampling limitations rather than deficits in motion mechanisms per se. Although the background dots in the current study moved smoothly, those of Silverman, Trick, and Hart were relocated randomly every 90 milliseconds, producing a perception of white noise. In our experience, it is relatively easy to detect as few as two or three coherent dots against this type of background, particularly for long stimulus durations, and very low thresholds can be achieved by normal subjects.

Drum, Breton, Massof et al; Drum, Severns, O'Leary et al; and Drum, Quigley, and Roros used stimuli similar to those used by Silverman, Trick, and Hart in the development of a technique referred to as "pattern discrimination perimetry." The subject is required to detect a patch of uniform dots embedded in a field of counterphasing random dots. The visibility of the patch can be manipulated by varying the spatial and temporal coherence (ie, regularity of the pattern). A regular checkerboard pattern represents 100% coherence, whereas a completely random pattern has 0% coherence. Drum, Severns, O'Leary et al found that patients with glaucoma had equivalent deficits for pattern discrimination perimetry and con-
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They concluded that pattern discrimination and light detection are mediated by different mechanisms that can be damaged differentially in glaucoma. They acknowledged, however, that the test is demanding for the subject and there are limitations resulting from spatial uncertainty and the restricted dynamic range of the test.

Motion Perception in Patients With Suspected Glaucoma

Although patients with glaucoma tended to perform worse than the normal subjects in all of our tests of motion perception, abnormalities were not shown in our patients with suspected glaucoma. This finding is not unexpected, considering that these patients with suspected glaucoma were not preselected, with the only inclusion criterion being referral for additional evaluation after a primary care examination. The patients with ocular hypertension in our group showed only modest elevations in intraocular pressure. Those studies that have shown evidence for visual dysfunction in patients with suspected glaucoma have used high-risk or carefully screened patients. The risk of glaucoma increases as the level of intraocular pressure increases; even so, the incidence of glaucomatous field loss developing in patients with ocular hypertension has been estimated to be as low as 1% per year.

We are investigating Dmin in a larger population of patients with ocular hypertension.

Dmin, Visual Fields, and Visual Acuity

We compared Dmin values with visual field sensitivity as measured with the 24-2 program on the Humphrey Field Analyzer in the patients with glaucoma. Dmin values were correlated poorly with the mean deviation (R = 0.32) and pattern standard deviation (R = 0.03). Furthermore, a weak correlation (R = 0.25) was observed between the Dmin and foveal threshold measured on the Humphrey Field Analyzer. Foveal thresholds were abnormal in only 4 of the 18 patients with glaucoma; however, the perimetric target has a relatively large diameter (0.43°). It has been shown that targets of these dimensions saturate the fovea, and sensitivity is not decreased until significant neural loss has occurred.

Although all the patients with glaucoma had a visual acuity that fell within normal limits, a significant correlation (R = 0.74, P < 0.001) was found between Dmin and visual acuity (see Fig. 3). We were concerned that this was an artifact; however, control experiments assessing the effects of induced refractive error and reduced target luminance on Dmin have suggested that this is unlikely. Figure 4 shows the mean variation in visual acuity and Dmin induced by myopic blur of up to 2.00 diopters in four normal subjects. Optical blur affects visual acuity more than Dmin, resulting in a line with a slope of 0.69, substantially flatter than that found for the patients with glaucoma (Fig. 3). This is consistent with previous studies that have shown that displacement thresholds are relatively unaffected by optical degradation. Similarly, reducing retinal illumination by a factor of 10 using neutral density filters had little effect on Dmin in normal subjects. A nonartifactual relationship therefore may exist between Dmin and visual acuity in glaucoma and warrants additional investigation in a larger patient population.
SUMMARY

We have shown that motion perception is disrupted in patients with glaucoma. D_{min} values were elevated in 10 of 15 patients with glaucoma with normal visual acuity and were unrelated to visual field loss. We propose that this finding represents psychophysical evidence for preferential loss to large retinal ganglion cells. The current study was limited to foveal motion thresholds, but future work will investigate peripheral motion perception in patients with glaucoma.

Key Words

glaucoma, motion perception, D_{min}, magnocellular pathway, retinal ganglion cells

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