Elevated Vernier Acuity Thresholds in Glaucoma

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PURPOSE. In 1993, Piltz et al. observed that foveal vernier acuity thresholds for achromatic targets are elevated in patients with glaucoma. This study was undertaken to explore whether such elevated thresholds are present when subject groups are measured with targets of effectively equivalent contrast. Vernier acuity measures were also obtained with short-wavelength and frequency-doubled stimuli, to assess spatial hyperacuity performance in the short-wavelength-sensitive and magnocellular pathways, respectively.

METHODS. Twenty patients with glaucoma and 19 subjects with normal vision participated. All subjects had visual acuity of 20/25 or better. Achromatic two-dot vernier thresholds were obtained for 90% contrast dots. In addition, individual contrast thresholds to the achromatic dots were measured for each subject, and vernier thresholds were measured at 4, 8, 12, and 16 times contrast threshold. Short-wavelength vernier acuity thresholds were measured for blue dots presented on a bright yellow background. The stimulus for the frequency-doubling grating vernier acuity task was a 90% contrast, 1-cyc/deg, 25-Hz sinusoidal grating.

RESULTS. The glaucoma group demonstrated significantly higher foveal vernier acuity thresholds than control subjects for the blue-on-yellow stimulus (P = 0.002) and frequency-doubling grating stimulus (P < 0.001). No significant difference in vernier acuity between groups was found for the 90% contrast achromatic dots (P = 0.1), however a significant difference was found for the normalized contrast targets (P = 0.04).

CONCLUSIONS. Vernier acuity tasks can be used to demonstrate abnormal foveal function in glaucoma. Testing with visual-function–specific stimuli may be effective in identifying such dysfunction. Vernier acuity, or other similar hyperacuity tasks that assess spatial sampling, may be useful in the detection of early glaucomatous damage, before it is detected with traditional perimetric tests. (Invest Ophthalmol Vis Sci. 2002;43:1393–1399)

Human observers are able to make exquisitely fine judgments regarding spatial alignment. Indeed, vernier alignment thresholds, for which subjects are required to spatially align a pair of lines or dots, can be as small as 2 to 5 sec arc in experienced observers, which is approximately one-thirtieth of the limit of conventional human visual acuity. Acuity of this kind is commonly referred to as hyperacuity, because thresholds are a fraction of the diameter of a foveal cone. Hyperacuity performance has generally been explained by models that involve the integration of spatial information from many retinal receptive fields at a cortical level. If input to this integrative process is reduced, because of either disease or abnormal development, it may be predicted that deficits in the ability to perform such spatial judgments would arise. Deficits in hyperacuity performance have been well documented in ambylopic and have been reported in subjects with glaucoma and those with suspected glaucoma.

In this study, we were interested in further exploring vernier acuity in glaucoma. Given the vernier acuity deficits reported by Piltz et al., and the observation that other measures of foveal function have been shown to be abnormal in glaucoma, we expected that our sample would also demonstrate deficits in vernier acuity. The first purpose of this study was to determine whether the relationship between vernier acuity and stimulus contrast differs between subjects with glaucoma and control subjects. It is well documented that hyperacuity thresholds increase with decreasing contrast according to a power law. If contrast thresholds are reduced because of disease, then deficits in vernier acuity may be due to this reduction of contrast sensitivity, rather than to altered vernier acuity per se. Furthermore, differences between the vernier acuity of normal and disease groups may be more marked when measured at low contrast. There is also the possibility that vernier acuity performance decreases more rapidly than predicted by contrast alone. In this case, it may be hypothesized that reductions in vernier acuity may represent a disruption of the spatial sampling grain, which in the case of glaucoma would arise due to ganglion cell loss. Vernier acuity measures may be affected before a decrease in contrast sensitivity is noted, or to a greater extent than predicted by contrast sensitivity assessment. To explore these issues we measured vernier acuity at normalized contrast levels (fixed multiples of contrast threshold) in both patients with glaucoma and control subjects. We were interested in determining whether differences in vernier acuity between groups are greater than predicted by possible differences in contrast sensitivity and also whether larger differences between groups are manifest at low contrast.

The second purpose of this study was to evaluate the utility of visual-function–specific vernier tasks for the measurement of foveal deficits in glaucoma. Perimetric tasks that evaluate specific ganglion cell populations have been demonstrated to be superior to standard automated perimetry (SAP) for the detection of early vision loss associated with glaucoma (for example, Refs. 18–24). Two examples of these newer perimetric tests are short-wavelength automated perimetry (SWAP) and frequency-doubling technology perimetry (FDT). SWAP assesses function of the short-wavelength–sensitive pathways, whereas FDT measures magnocellular pathway function. Two explanations are commonly used for the enhanced ability of these tests to detect glaucomatous visual field loss. It has been proposed that early glaucomatous damage is selective for larger optic nerve fibers and is therefore more likely to affect magnocellular neurons. Because the small bistratified ganglion cells known to subserve the short-wavelength–sensitive pathway are the largest of the ganglion cells that project to the parvocellular layers of the lateral geniculate nucleus, early loss of these fibers is also predicted by the large-axon hypoth-
es. Alternately, because both magnocellular and short-wavelength-sensitive neurons are sparsely represented within the retina, deficits are apparent earlier in these pathways because of reduced redundancy, even if all ganglion cells are lost with equal probability. It is possible that ganglion cell loss in more sparsely represented systems severely disrupts vernier acuity. To explore this possibility, we measured vernier thresholds for a two-dot short-wavelength stimulus and for a frequency-doubling grating (low-spatial-frequency, sinusoidal, rapidly counterphasing) vernier alignment task, in both normal observers and those with glaucoma.

**METHODS**

**Subjects**

Twenty subjects with glaucoma (mean age, 66.9 ± 9.6 years) and 19 control subjects (mean age, 53.1 ± 15.8 years) participated. Subject groups were approximately, but not exactly, age matched, as vernier thresholds have been shown to be largely independent of aging; however, recent studies demonstrate some deterioration with aging. It is possible that ganglion cell loss in more sparsely represented systems severely disrupts vernier acuity. To explore this possibility, we measured vernier thresholds for a two-dot short-wavelength stimulus and for a frequency-doubling grating (low-spatial-frequency, sinusoidal, rapidly counterphasing) vernier alignment task, in both normal observers and those with glaucoma.

Subjects with glaucoma were recruited from the Glaucoma Service of the Devers Eye Institute. Normal subjects were recruited from staff of the Devers Eye Institute, as well as among spouses and friends of patients. To be included in the study, all subjects were required to have refractive errors of less than ± 4.00 D sphere and less than 2.00 D of astigmatism, best corrected visual acuity of 20/25 or better, no history of diabetes or other systemic disease known to affect ocular function, and no current medications known to affect visual field sensitivity or contrast sensitivity. Normal control subjects were required to have normal findings in a eye examination (including slit lamp biomicroscopy of the anterior segment and ophthalmoscopy of the macula and optic nerve), IOP of less than 21 mm Hg, and normal visual fields when tested using the Visual Field Analyzer 24-2 Full-Threshold test strategy (Humphrey Instruments, San Leandro, CA). Patients with glaucoma were required to have a clinical diagnosis of primary open-angle glaucoma, a history of IOP greater than 22 mm Hg before treatment, and a previously documented glaucomatous visual field loss (abnormal Glaucoma Hemifield Test result or Pattern Standard Deviation [PSD] indices worse than the 5% probability level) as established with the visual field analyzer (Humphrey Instruments) 24-2 or 30-2 threshold procedure in the eye to be tested. The median mean deviation (MD) in the patients with glaucoma was −4.17 dB (range, 1.7 to −21.33) and the median PSD was 4.29 dB (range, 1.42-15.87).

Before testing, all subjects provided written informed consent in accordance with a protocol approved by the Legacy Health Systems Institutional Review Board and in accordance with the tenets of the Declaration of Helsinki.

Subjects participated in a single test session of approximately 45 minutes duration. All measures were made monocularly and tested foveal vision. Only one eye was assessed in each subject. The test eye was assigned randomly, both for the control subjects and for those subjects with bilateral glaucoma in which both eyes met the visual acuity and other inclusion criteria. In the remainder of the patients with glaucoma, the eye tested was the one that met the inclusion criteria.

**High-Contrast Vernier Acuity**

Figure 1A illustrates the achromatic two-dot vernier target, which consisted of two black-dot targets presented one above the other, with a slight horizontal displacement. Each dot was 12 min arc, with the vertical separation between the two dots being 8 min arc. The dots were presented at 90% contrast, on a uniform background of 45 cd/m², at a viewing distance of 9.87 m. Stimuli were presented on a gamma-corrected 21-in. color monitor (Trinitron GDM-500PS; Sony, Tokyo, Japan) and were generated using a VSG 2/4 graphics card (Cambridge Research Systems, Kent, UK).

Figure 1B illustrates the short-wavelength vernier target. Two dots of 24 min arc were presented with a vertical separation between the dots of 16 min arc. The dots were generated as white dots on a black computer screen (21-in. model VB 21300 GLS high-intensity gray scale monitor; Siemens, Erlangen, Germany), which was viewed at a distance of 8.97 m. To generate the blue-on-yellow stimulus conditions necessary for assessment of the short-wavelength-sensitive pathway, light from the computer screen was passed through a blue filter (440-nm interference filter; Omega Optical, Brattleboro, VT) then reflected off a beam splitter. The beam splitter was used to superimpose the blue dots on a uniform, bright-yellow background (OG530 filter; Schott, New York, NY). The luminance of the resultant blue dots was 2.1 cd/m² displayed on a 150-cd/m² yellow background. This stimulus and background combination has been shown to isolate the short-wavelength-sensitive mechanisms effectively.

Figure 1C illustrates the frequency-doubling grating vernier acuity target. Stimuli were generated on the color monitor described earlier. The stimulus display consisted of two black-dot targets presented one above the other, with a slight horizontal displacement. Each dot was 12 min arc, with the vertical separation between the two dots being 8 min arc. The dots were presented at 90% contrast, on a uniform background of 45 cd/m², at a viewing distance of 9.87 m. Stimuli were presented on a gamma-corrected 21-in. color monitor (Trinitron GDM-500PS; Sony, Tokyo, Japan) and were generated using a VSG 2/4 graphics card (Cambridge Research Systems, Kent, UK).
horizontally displaced from the upper grating. The maximum allowable vernier displacement was 0.5 cycle of the grating, because of the repetitive nature of the sinusoidal stimulus.

Vernier acuity thresholds were measured for each of the three targets (achromatic dots, blue-on-yellow dots, and frequency-doubled grating) using a two-alternate forced-choice technique. For the dot targets, the location of the upper dot was constant, whereas the lower dot was slightly displaced, either to the left or right of the upper dot. The subject was required to indicate the direction of displacement (left or right) by pressing a button. Similarly, for the grating stimulus, the subject’s task was to determine whether the lower grating was displaced to the left or right, relative to the upper grating. Thresholding was achieved using a staircase procedure that terminated after four reversals. Vernier displacements were increased by 25% after an incorrect response and decreased by 25% after three successive correct responses. The result of a single staircase was determined as the mean of the last two reversals. The three-up, one-down staircase paradigm converges to the 79% correct response level. Two staircases were randomly interleaved for each stimulus, with the final threshold being taken as the average of the results of the two staircases.

**Normalized Contrast Vernier Acuity**

To determine thresholds at effectively equivalent contrast for all subjects, contrast detection thresholds were measured for the achromatic dot targets. The stimulus parameters were the same as illustrated in Figure 1A. A yes–no paradigm was used, with subjects required to press a button when they detected the presence of the stimulus. Thresholds were obtained using a staircase procedure that terminated after four reversals. Contrast was increased by 25% after an incorrect response and decreased by 25% after three successive correct responses. Two staircases were randomly interleaved, with the final threshold being taken as the average of the results of the two staircases.

Vernier acuity for the achromatic dot targets (Fig. 1A) was measured for dots of contrast equal to 4, 8, 12, and 16 times each subject’s contrast detection threshold. Thresholds were measured using the same two-alternate forced-choice paradigm combined with a three-up, one-down staircase as used in the high-contrast vernier acuity task. Two staircases were run for each contrast level, and all contrast levels were interleaved simultaneously.

**RESULTS**

Figure 2 shows the geometric mean (±SE) vernier threshold for the glaucoma and control groups for each of the three vernier targets. Individual data are represented by the open circles for the control subjects and open triangles for the glaucomatous observers. The left panel shows data for the achromatic dots (90% contrast), the middle panel shows data for the blue-on-yellow dots, and the right panel shows data for the frequency-doubling grating. Three of the patients with glaucoma and two of the control subjects were unable to determine reliably the direction of displacement at the maximum horizontal separation for the blue-on-yellow target. A further patient was unable to see the blue-on-yellow stimulus; hence, the mean represents data of 16 patients and 17 control subjects. The mean vernier threshold for the frequency-doubling grating stimulus was derived from the results of 16 patients with glaucoma and 17 control subjects. Four patients with glaucoma and two control subjects were unable to determine the direction of displacement when the separation was maximal. The maximum displacement is limited by the repetitive nature of the sinusoidal stimulus for the frequency-doubling task and by the width of the display for the blue-on-yellow task. The glaucoma group had significantly higher thresholds than the control subjects for the blue-on-yellow stimulus (t-test on log-transformed data, df = 32, P = 0.002), and frequency-doubling grating stimulus (t-test on log-transformed data, df = 31, P < 0.001), but not for the achromatic dot targets (t-test on log-transformed data, df = 57, P = 0.09).

The contrast thresholds for detection of the achromatic dot targets appear in Figure 3 as geometric means (±SE) of the two subject groups. Individual data for the subjects are also presented. The glaucoma group’s mean contrast threshold was significantly higher than that of the control group (t-test on log-transformed data, df = 57, P = 0.01).

Figure 4 shows the results for the achromatic two-dot vernier acuity target as a function of normalized contrast, with which thresholds were measured at 4, 8, 12, and 16 times each individual’s contrast threshold. Geometric means (±SE, filled symbols) and individual data (open symbols) are presented. A two-way repeated measures ANOVA on the log-transformed data revealed a statistically significant difference in performance between the control and glaucoma groups (P = 0.04). There was no statistically significant interaction between subject group and contrast level (P = 0.08), indicating that the decline in performance with decreasing contrast was similar between the two groups. However, paired t-tests of the log-transformed data at each individual contrast level show the following probabilities: 4 times contrast threshold (P = 0.15), 8 times contrast threshold (P = 0.005), 12 times contrast threshold (P = 0.59) and 16 times contrast threshold (P = 0.10). If a Bonferroni correction is applied to adjust the probability levels for multiple comparisons, thereby requiring a
probability of 0.0125 for significance, only the thresholds at eight times contrast threshold are significantly different between groups.

Figure 5 compares performance on the vernier tasks in the patients with glaucoma with the global indices (MD and PSD) returned from their most recent visual field assessments with the Visual Field Analyzer (Humphrey Instruments) 24-2 or 30-2 threshold procedure. Spearman rank order correlation coefficients are also shown. Vernier acuity performance was not significantly correlated with either of the global indices for any of the vernier tasks.

**DISCUSSION**

In this study, we found a significant increase in both foveal contrast thresholds and vernier acuity thresholds in subjects with glaucoma. This confirms a number of previous studies that demonstrate abnormal foveal performance in glaucoma. More specifically, our measurement of decreased foveal vernier acuity performance in subjects with glaucoma agrees with that reported by Piltz et al. Generally, glaucoma is considered to be a condition that predominantly affects the peripheral visual field, in that foveal abnormalities are not usually found early in glaucoma by using perimeteric paradigms. This is supported in the present study by the finding of no significant correlations between vernier acuity performance and the global indices produced by the visual field analyzer in our patients with glaucoma. It has been argued that this may be due, in part, to the logarithmic scale used to measure luminance increment sensitivity in glaucoma, because many more ganglion cells must be lost foveally than peripherally to detect a 3-dB loss of visual field sensitivity.

It is well documented that vernier acuity thresholds decrease with increasing stimulus contrast according to a power law. Because of the dependence of vernier acuity on contrast, deficits in vernier performance may manifest in disease simply because of reduced contrast sensitivity rather than a reduction in vernier acuity per se. When achromatic targets of normalized contrast were used, a difference in contrast sensitivity between the groups was still found, however, indicating a genuine loss of foveal vernier acuity in glaucomatous observers. That this loss was not statistically demonstrated with the 90% contrast achromatic targets (Fig. 2, left) is probably due to the poor power of the t-test performed, in comparison with the ANOVA analysis (Fig. 4). This difference in power is most directly attribut-

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**FIGURE 3.** Mean contrast thresholds (± SE) for the control (●) and glaucoma (▲) groups.

**FIGURE 4.** Mean vernier acuity thresholds (± SE) for the achromatic twodot vernier acuity target, as a function of normalized contrast (4, 8, 12, and 16 times each individual's contrast threshold) for the control and glaucoma groups.
able to the fourfold increase in data used in the ANOVA. One plausible explanation for the significant decrease in vernier acuity is that it represents a disruption of spatial sampling, due to ganglion cell loss. Because of this, it may be expected that vernier performance is correlated with contrast sensitivity losses resulting from ganglion cell loss. No correlation was found between vernier acuity and depth of visual field defect, however, as assessed by standard perimetric indices (Fig. 5). This noncorrelation may, in part, reflect that standard perimetric indices are weighted by performance in the peripheral visual field, whereas vernier acuity is dependent on function in the central visual field. However, we also found losses in vernier acuity that were independent of central losses in contrast sensitivity (Fig. 4). As such, vernier acuity deficits may occur in some patients with glaucoma despite the presence of normal contrast sensitivity.

We did not find evidence for a more rapid decrease in vernier acuity performance with reducing contrast in glaucoma, when compared with that in control subjects. This is illustrated by the similar shapes of the curves in Figure 4, as well as the absence of a significant interaction between contrast and subject group in the ANOVA analysis of the data represented in Figure 4. When the thresholds at each contrast level were considered separately, the glaucoma group performed significantly worse than the control group at eight times contrast threshold. No significant difference was found at the other contrast levels. It is possible that, at low contrast, both groups had more difficulty with the task, resulting in a reduction in the ability to distinguish between the groups. However, the spread of the data at four times contrast threshold does not demonstrate relatively increased variability. Nevertheless, it is possible that testing at inter-

**Figure 5.** Individual vernier acuity thresholds for the subjects in the glaucoma group, plotted against their MD and PSD indices returned by their most recent visual field analyzer threshold tests. Data are for (top) the 90% contrast achromatic dot targets, (middle) the blue-on-yellow targets, and (bottom) the frequency-doubling grating stimulus. r = Spearman rank order correlation coefficient.
mediate contrast may provide some advantage over testing at high contrast for the purpose of distinguishing between individuals with glaucoma and those with normal vision. In particular, larger differences are expected to be manifest between the groups when they are tested at the same absolute contrast level (rather than equivalent contrast), because the glaucoma group should demonstrate a reduction in vernier threshold due both to their reduced contrast sensitivity and to a genuine reduction in vernier performance.

Similar to the findings of Piltz et al., we found considerable overlap between the vernier thresholds of normal control subjects and patients with glaucoma when measured with static achromatic stimuli. Differences between the groups were more marked when visual-function-specific stimuli (short-wavelength spots and frequency-doubling gratings) were used. The nature of our short-wavelength stimulus necessitates its detection by short-wavelength-sensitive mechanisms, which are known to be affected early in glaucoma. The frequency-doubling grating vernier task used in this study is likely to be detected by magnocellular mechanisms, which are also known to be affected in glaucoma. It is unclear whether magnocellular or parvocellular pathways mediate the detection of static achromatic vernier tasks, however, it seems likely that the magnocellular pathway is primarily involved at low contrast. Although thresholds on the two visual-function-specific tasks investigated were elevated beyond what is generally considered to be hyperacuity in both normal and glaucomatous observers, these stimuli may have advantages for the detection of spatial sampling changes due to retinal ganglion cell loss, because the neural pathways responsible for their detection are sparsely represented. It should be noted, however, that patients with glaucoma are likely to have reduced contrast sensitivity for both the short-wavelength and frequency-doubling grating tasks. We did not equilibrate contrast between the control and glaucoma groups for the assessment of short-wavelength and frequency-doubling grating vernier acuity and therefore do not know how much of the difference between the groups can be explained by differential contrast sensitivity.

Although further validation of the utility of vernier acuity or other similar hyperacuity measures to detect glaucomatous visual dysfunction is needed, these measures may provide an indirect measure of ganglion cell sampling and may have the potential to reveal dysfunction before traditional visual field assessment.

References