
Static flicker perimetry in glaucoma and ocular hypertension*

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ABSTRACT

The visual threshold for standard and flickering targets was determined and compared in 8 glaucoma patients, 8 glaucoma suspects and 13 normal controls. Using a Goldmann size III standard white light target, 25 points in the central 30° of the visual field were tested. The location of these points was designed to reflect areas of the visual field commonly affected by glaucomatous damage. The same determinations were then repeated with the test target flickering at 25 Hz. All glaucoma patients had elevation of the visual threshold compared to normal controls for both standard and flickering targets. The absolute value of threshold elevation was not significantly different between standard and flickering lights. However, when larger targets were used, flicker thresholds were an average 8 dB higher ($p < 0.05$) in the glaucoma patients compared to the normals, suggesting improved identification of glaucomatous damage with the use of larger flickering targets.

INTRODUCTION

The ability of glaucoma patients to process luminance modulated at higher temporal frequencies (flicker) is impaired: temporal contrast sensitivity is reduced (1-3) as well as critical flicker fusion frequency at many locations in the visual fields (4-6). The maximal deficit appears to occur in the frequency range of 20-40 Hz (1-3). Within this frequency range, temporal contrast sensitivity is reduced prior to the development of visual field defects (1), and the amount of reduction appears to be related to intraocular pressure even within the normal population (2).

Recent data indicate that up to 50% of the optic nerve fibers may be lost before a visual field defect can be detected using standard perimetry (7). Larger diameter fibers which project to the magnocellular layers of the lateral geniculate nucleus (8) have been found to be preferentially affected (9,10). These large fibers respond to lower contrast stimuli, have larger diameter receptive fields and higher conduction velocities than smaller fibers, and are better able to respond to higher frequencies of luminance modulation (11,12).

The loss of sensitivity at higher temporal frequencies may be related to the loss of larger diameter optic nerve fibers. Therefore, the sensitivity of standard static perimetry in detecting visual damage might be improved if the targets were temporally modulated in the 20-40 Hz range. In this study, we tested the hypothesis that static perimetry employing targets flickering at 25 Hz would detect visual field defects in glaucoma patients and glaucoma suspects better than static perimetry using standard targets. We also studied the effect of target size on the identification of glaucomatous defects using flicker perimetry.

MATERIALS AND METHODS

The study was designed and conducted in compliance with the recommendations of the

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Declaration of Helsinki for the use of humans in scientific research. Subjects consisted of 8 glaucoma patients, 8 glaucoma suspects and 13 normal controls. Glaucoma patients and suspects were recruited from the population attending the glaucoma clinic at West Virginia University. Normal controls were volunteers among the clinic staff and patient companions who underwent a general eye examination to rule out media opacities, glaucoma, and optic nerve or macular disease. The subjects' average age and pupil size are outlined in Table 1. Visual acuity in all subjects was 20/40 or better. Glaucoma patients had intraocular pressure greater than 21 mm Hg prior to the initiation of treatment, and optic nerve head damage or visual field defects in one or both eyes. Glaucoma suspects had intraocular pressure greater than 21 mm Hg in one or both eyes, but no definitive optic nerve head damage or visual field defects. Glaucomatous damage of the optic nerve was diagnosed prior to enrollment in the study if erosion or notching of the

nerve rim, or a cup-to-disc ratio in excess of 0.6 were seen on stereoscopic fundus examination using a 90-diopter lens. The visual field obtained by full-threshold static automated perimetry was considered abnormal if there was evidence of arcuate or nasal defects, or generalized depression in excess of 4 dB not explained by media opacities or a small pupil, and which have been documented on at least two consecutive occasions prior to the study. Both optic nerve and visual field damage criteria were in accordance with what we regularly use in the clinical evaluation of glaucoma patients. Written informed consent was obtained after the nature of the procedure was fully explained. To familiarize them with static automated perimetry, normal subjects were given a demonstration test performed with the Vision Monitor (Metrovision, Inc., Lille, France), a static projection perimeter with flicker generation capability. All subjects had their eyes tested twice during the same visit. For the initial test, the target

Table 1. Summary of Subject Data and Stimulus Characteristics

Stimulus Type and Size	Number Eyes	Number Subjects	Age (years) Mean \pm S.D.	Pupil Size (mm) Mean \pm S.D.
25 arc min Standard				
Normal	23	12	40.0 \pm 7.9	4.9 \pm 0.7
Suspect	12	8	50.7 \pm 16.0	5.0 \pm 2.0
Glaucoma	14	8	61.4 \pm 10.5	4.5 \pm 2.4
25 arc min Flicker				
Normal	25	13	40.1 \pm 7.5	4.9 \pm 0.7
Suspect	12	8	50.7 \pm 16.0	5.0 \pm 2.0
Glaucoma	14	8	61.4 \pm 10.5	4.5 \pm 2.4
10-degree Flicker				
Normal	18	9	39.9 \pm 8.2	5.0 \pm 0.6
Suspect	7	4	47.9 \pm 15.2	4.3 \pm 2.0
Glaucoma	8	5	61.0 \pm 13.2	4.8 \pm 2.5
Ganzfeld Flicker				
Normal	14	7	41.3 \pm 8.2	5.0 \pm 0.6
Suspect	5	3	57.0 \pm 13.5	4.6 \pm 2.9
Glaucoma	7	4	59.3 \pm 12.0	4.8 \pm 2.5

was a steady circular spot of white light, approximately 25 arc min in diameter. Subsequently, the same target was made to flicker at 25 Hz (25 flashes/sec). Standard perimetry always preceded flicker perimetry. If both of a patient's eyes were tested, the right eye was tested first. Target luminance could be changed in 1 dB steps between 0.25 and 318 cd/m². Background luminance was 10 cd/m². In the case of standard targets, stimulus duration was 300 ms, and a staircase method with a 4-1-1-1 rule was employed for threshold measurements. The mean luminance attenuation at each tested point was considered as the threshold value at that location. In the case of flickering targets, thresholds were determined using a method of ascending limits: target luminance began at its lowest level (32 dB attenuation), and was increased at a rate of 1 dB per second until it was seen by the patient. The flicker threshold was determined by averaging 2 trials at each point. Both standard and flickering targets were projected at 25 locations in the visual field, commonly affected by glaucomatous damage (Figs 1-3).

In addition to standard and flicker testing with a 25 arc min target at the 25

locations shown in Figs 1-3, participating subjects were invited to undergo further testing using larger flickering targets. No selection of subjects was attempted for this part of the experiment, and participation was optional. A subgroup consisting of 5 glaucoma patients, 4 glaucoma suspects and 9 normal controls was tested. Larger flickering targets consisted of a 10° stimulus projected at 9 central locations as illustrated in Fig 4, and a ganzfeld stimulus which subtended the entire cupola.

Statistical analysis

Results from both eyes of normal subjects, but only those from affected eyes of glaucoma suspects and glaucoma patients were analyzed. Analysis of the results for both 25 arc min and 10° test targets proceeded in 2 steps. First, a multivariate analysis of covariance (MANCOVA) was performed using data from each eye. As it was not possible to control for correlation between eyes of the same subject, age, or pupil size by using different experimental groups, these variables were used as covariates, so that their effects could be statistically controlled for (13-14). The MANCOVA tested whether a significant difference existed,

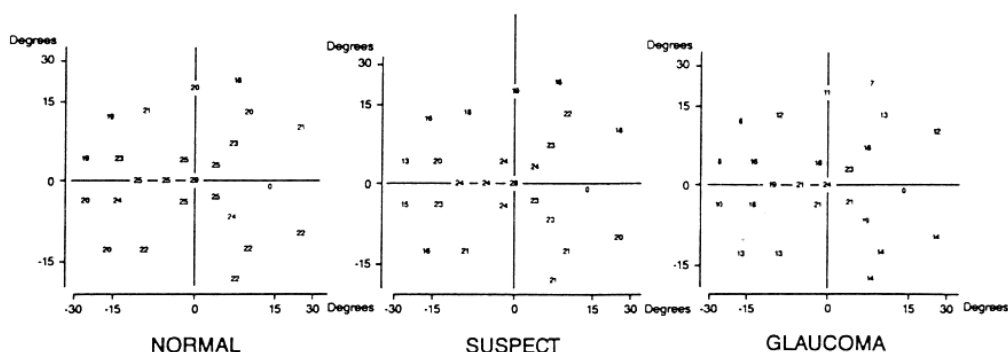


Figure 1. Mean threshold (dB of attenuation) for standard 25 arc min targets, as measured at 25 points in each

of the 3 subject groups. The scales represent results from all eyes, with left eyes rotated into right ones.

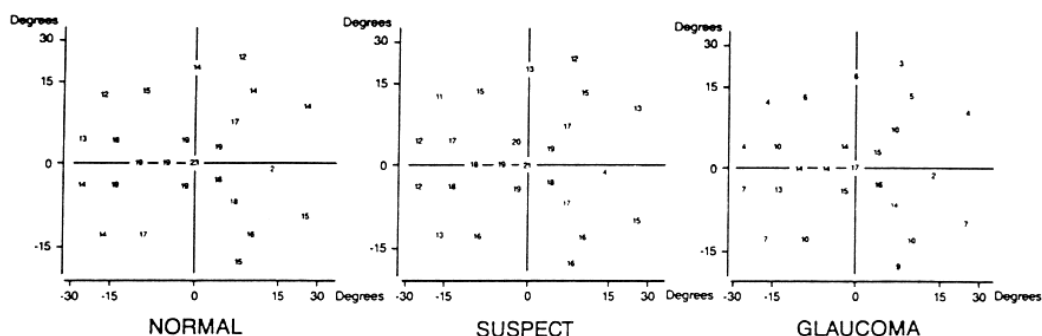


Figure 2. Mean threshold (dB of attenuation) for flickering 25 arc min targets, as measured at 25 points in each

of the 3 subject groups. The scales represent results from all eyes, with left eyes rotated into right ones.

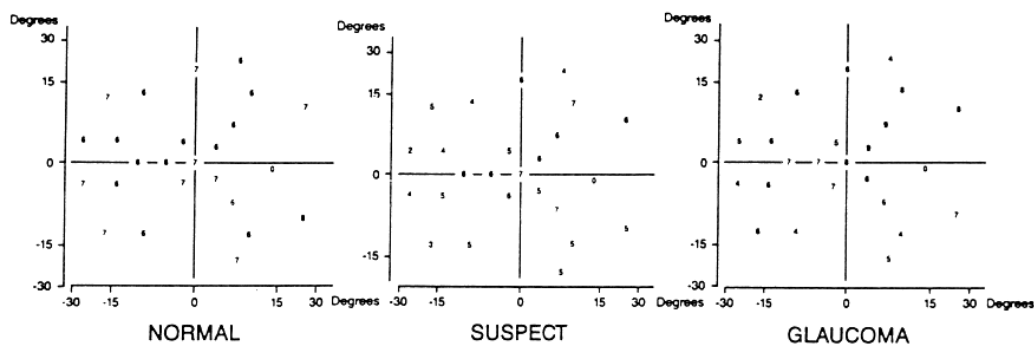


Figure 3. Mean difference (dB of attenuation) between standard and flicker thresholds for 25 arc min targets in the 3

subject groups. The scales represent results from all eyes, with left eyes rotated into right ones.

adjusting for the covariate matrix of the group, target location, target type, age and pupil size. Second, if the MANCOVA was significant, it was followed by analyses of covariance (ANCOVA) of repeated measures and Tukey post hoc comparisons for each stimulus location. Three effects were tested: the effect of group (glaucoma patient, glaucoma suspect or normal control), target type (standard or 25 Hz flicker), and the interaction of group and target type. An ANCOVA was used to analyze the results obtained with the full-field flicker target.

RESULTS

The value scales representing the mean thresholds for standard and flickering targets, as well as the mean difference between them at each tested point in the 3 subject groups are shown in Figs 1-3. The effects of group and target type on the threshold value were statistically significant, but their interaction was not (Group: Hotelling-Lawley trace = 2.22; $F = 2.09$, $df = 50, 94$; $p = 0.0011$; Target type: Hotelling-Lawley trace = 4.95; $F = 9.5$; $df = 25, 48$; $p < 0.0001$; Group-Target interaction: Hotelling-Lawley trace =

1.55; $F = 1.46$; $df = 50, 94$; $p = 0.057$). This was true at all points except the blind spot (ANCOVA, $p < 0.05$). Glaucoma patients had elevated thresholds compared to normals on all but 3 points with standard targets, and 2 points with flickering targets (Tukey, $p \leq 0.05$). The ability of the static visual fields to correctly identify the groups as normal or abnormal was determined for each target type. The confidence limit for abnormality was set as 2 standard deviations above the mean threshold. To be classified as abnormal, a visual field had to have 6 or more abnormal points ($p < 0.05$). Using this criterion, no normal eye was identified as abnormal with either standard or flickering targets. All 14 glaucomatous eyes were identified as abnormal with standard targets, and 11 (79%) with flickering targets. In the suspect group, 5 of 12 eyes (42%) were identified as abnormal with standard targets, and 2 (17%) with flickering targets (Table 2).

The value scales representing the mean threshold at each of the 9 points tested with the 10° flickering targets in the different groups are presented in Fig 4. MANCOVA indicated a significant effect of patient group on the threshold value (Hotelling-Lawley trace = 5.75; $F = 4.15$; $df = 18, 26$; $p = 0.0005$). Each of the 9 points showed threshold elevation (ANCOVA, $p \leq 0.05$) in the glaucoma group compared to normals and glaucoma suspects (Tukey, $p < 0.05$). Using a criterion of abnormality as 3 or more points with threshold elevation of 2 or more standard deviations above the mean ($p < 0.05$), no normal eyes were identified as abnormal, while all glaucomatous eyes and 2 of 7 (29%) suspect eyes were identified as abnormal (Table 2).

In the case of full-field flicker, the

Table 2. The Percentage of Eyes Identified as Abnormal Using Standard and Flicker Test Targets *

Stimulus Type and Size	Glaucoma	Suspect	Normal
25 arc min Standard	100 %	42 %	0 %
25 arc min Flicker	79 %	17 %	0 %
10-degree Flicker	100 %	29 %	0 %
Ganzfeld Flicker	100 %	40 %	0 %

mean threshold differed significantly between patient groups (ANCOVA, $F = 35.54$; $df = 2, 19$; $p = 0.0001$). The glaucoma group had threshold elevation relative to both the normal and suspect groups (Tukey, $p < 0.05$). Using a criterion of abnormality as threshold elevation of 2 or more standard deviations above the mean, all normal eyes were identified as normal, and all glaucomatous eyes, as well as 2 of 5 (40%) glaucoma suspect eyes, were identified as abnormal (Table 2).

DISCUSSION

Visual field defects were observed in glaucoma patients and some glaucoma suspects using either standard or 25 Hz flickering targets. However, there was no statistically significant difference in the depth of the defects either throughout the field or at any single location. While the flicker threshold was elevated in glaucoma patients relative to normals, the elevation was not larger than that obtained with standard targets (Fig 5).

The elevation in flicker threshold at 25 Hz in glaucoma patients and some glaucoma suspects is consistent with evidence that flicker sensitivity is reduced in glaucoma (1-6). However, it is

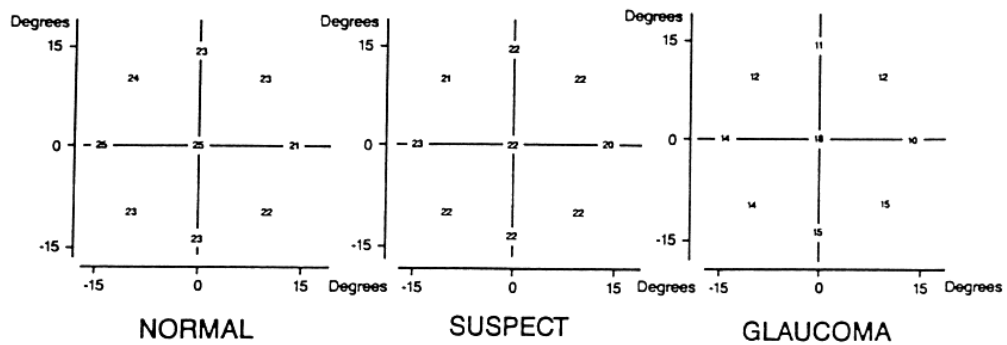


Figure 4. Mean threshold (dB of attenuation) for flickering 10° targets, as measured at 9 central points in each of

the 3 subject groups. The scales represent results from all eyes, with left eyes rotated into right ones.

not in agreement with previous work which has demonstrated improvement in identifying glaucomatous defects using temporally modulated stimuli (1,3). Our failure to get improved identification of glaucoma patients with flicker perimetry is unlikely to be due to the choice of the temporal frequency value (25 Hz), as others have used a 20-40 Hz frequency range (1-3). However, as there is spatio-temporal reciprocity in visual processing, temporal frequency and target size may covary. Therefore, improved discrimination of glaucoma patients from normals may be achieved with an optimal combination of these variables. Other procedural variations might account for the lack of a difference between standard and flicker perimetry in the ability to detect glaucoma defects. While Tyler (1,2) and Stamper (3) determined sensitivity to modulation depth (temporal contrast), we determined sensitivity to flicker luminance increments. We also employed different strategies for threshold determination in the flicker and standard conditions (ascending limits and staircase, respectively). While we cannot exclude these dissimilarities as explanations, we think that target size,

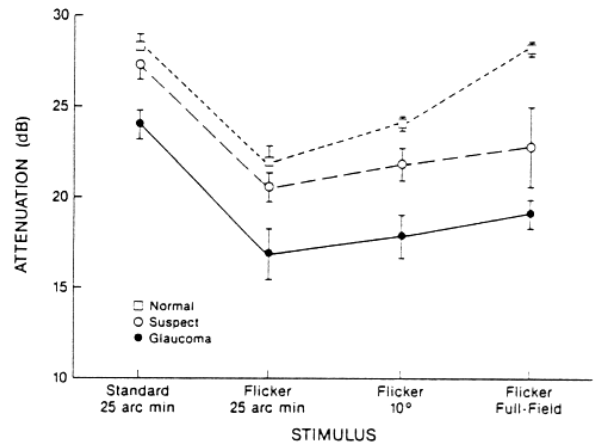


Figure 5. Mean visual threshold (dB of attenuation) for different target types and sizes, adjusted for correlation between eyes of the same subject, age, and pupil size. Vertical bars represent standard errors of the mean.

or its interaction with temporal frequency is a more likely one.

It is possible that our failure to find improved detection of visual field loss using flicker perimetry may in some way be related to the age differences between the groups. One may hypothesize an interaction of temporal frequency, age, and glaucoma, such that the effects of age and glaucoma on temporal frequency balance each other.

While this possibility cannot be excluded, our use of statistical controls for the effects of age makes it unlikely. Similarly, it is possible that our sample sizes were not large enough to detect differences in flicker sensitivity between the groups. However, we presume that if this is true, the magnitude of the differences is unlikely to be clinically significant.

The studies which have examined sensitivity losses with temporal modulation (1-6) have used target sizes much larger than those used in automated perimetry (several degrees vs less than 60 arc min, respectively). In our study, when the target size was increased to 10° , the difference in flicker threshold between normals and glaucoma patients increased from about 3-8 dB to about 6-12 dB. In addition, the variance of the thresholds was smaller with larger targets, thus permitting easier detection of abnormality. However, for full-field flicker testing, the difference in threshold between normals and glaucoma patients did not increase any further (Fig 5), but remained about the same as with the 10° targets (approximately 9 dB).

Much, if not all, of the difference observed in the detection of glaucomatous defects in psychophysical studies involving temporal modulation may be attributable to target size or to its interaction with temporal frequency. A large fraction of the larger ganglion cells is destroyed in glaucoma (9,10). In primates, larger ganglion cells project to the magnocellular layers of the lateral geniculate body (8). Magnocellular layers and the ganglion cells which project to them have larger receptive fields and higher contrast sensitivity than cells of the parvocellular layer (11,12). Consequently, in normal eyes, large, low

contrast targets are more easily detected by ganglion cells which project to the magnocellular layers. In eyes damaged by glaucoma, where large ganglion cells are selectively destroyed, the response elicited by low contrast or small increments of large targets should be reduced. These effects may be increased by temporal modulation.

Normal increment sensitivity increases with target size up to a critical size (15,16) which varies with eccentricity (17). This effect depends, in part, on the number of retinal elements stimulated. In glaucoma, ganglion cells are destroyed. Therefore, in the same retinal area, there would be fewer elements and less summation. The critical size would increase and the threshold for a target smaller than the critical size would be elevated. Using kinetic perimetry, DuBois-Poulsen (18) observed that spatial summation was disturbed in glaucoma patients. Our future projects will aim at determining if spatial summation is disturbed in static perimetry, and if flickering and standard targets differ in their summation characteristics.

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