THE EFFECT OF GLAUCOMA ON CENTRAL VISUAL FUNCTION*

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INTRODUCTION

TRADITIONALLY, THE OPTIC NERVE DAMAGE THAT ACCOMPANIES PRIMARY OPEN-angle glaucoma has been described as affecting the peripheral visual function long before central vision is reduced.[1-5] Over the past 40 years, emphasis has been placed on visual field testing as the primary method for evaluating the functional damage caused by the glaucomatous process. Indeed, none of the three major textbooks on glaucoma published during the latter part of the last decade mention any method other than perimetry for assessing visual damaged produced by glaucoma.[2-4]

Most authors agree that subjective visual symptoms or loss of central visual acuity are late manifestations of primary open-angle glaucoma.[1-4] However, some have also noted that glaucoma patients do have central visual complaints before a decrease in visual acuity is detected.[1-4] For example, Duke-Elder[5] cited a survey from the Glaucoma Clinic at the University of London showing that 66% of patients reported blurred vision or difficulty in reading. He acknowledged that glaucoma in these patients was usually well established when the symptoms appeared. However, it is hard to reconcile the high percentage of central visual complaints in these patients with open-angle glaucoma with the belief that central vision remains entirely intact until late in the course of the disease.

The belief that central visual function is affected late in the glaucomatous process is based on the use of Snellen-type visual acuity charts as the only measurement of this function. This relatively gross, subjective test measures only the resolving power of the eye at near maximum contrast.[6] However, resolving power is only one of several components of central visual perception, a complex process involving the interaction of physical, optical, media-related, retinal, cerebral, and psychologic factors.[7] Fur-

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thermore, the use of Snellen-type visual acuity assessment in patients with glaucoma who are using topical medications may be misleading. In these patients, the measurements of visual acuity may be affected by the miosis produced by pilocarpine, one of the standard therapeutic agents for glaucoma. In some cases the "pinhole" pupil acts to enhance central visual acuity, while in others (particularly in patients with nuclear sclerotic cataracts), the acuity is reduced by the miosis. In addition, patient complaints may be reduced by the fact that binocular function may mask subtle or early monocular deficits.[6]

When visual acuity is measured by Snellen-type tests, even under the most rigidly controlled, standardized conditions, one ignores other parameters that are important to everyday visual function such as color perception, ability to detect low-contrast objects, motion detection, and ability to function visually in low illumination.[6] These parameters may be adversely affected by glaucoma. As early as 1901, Javal[7] reported that, in glaucoma, the visual acuity was reduced in subdued illumination. Since World War II, advancing technology coupled with increased interest in psychophysics has resulted in the production of more sophisticated tests for measuring central visual function. The results obtained with some of these tests have challenged the traditional assumptions about the nature of the functional damage induced by the glaucomatous process. One example is the study of Campbell and Ritter.[8] This study, later confirmed by that of Weinstein and Brooser,[9] showed that the critical flicker fusion frequency is reduced in patients with glaucoma in the central as well as in the peripheral visual field.[8,9]

Additional evidence of central nerve fiber loss in glaucoma has been obtained from studies of pupillary reaction to light. One way of grossly assessing the integrity of the central visual system has been to test for an afferent pupillary defect in the presence of asymmetric disease. Since the afferent limb of the pupillomotor system has a similar distribution to cones, afferent pupillary defects can be expected to appear whenever there is asymmetric involvement of those parts of the retina or optic nerve largely subserving macular function.[10] Such defects have been noted in unilateral or asymmetric macular and optic nerve disease.[10] Afferent pupillary defects have also been noted in patients with asymmetric glaucoma and with asymmetric cupping in the absence of visual field loss, perhaps suggesting that there has been a diffuse loss of nerve fibers in the papillomacular bundle in the more affected eye.[11-13] Thompson et al[14] have studied the relationships among visual acuity, pupillary defects, and visual field defects in a variety of patients. They have shown that afferent pupillary defects occur in quantitative relationship to the total visual field

loss (at least in the central 30°), and these authors have suggested that the fibers serving macular function appear to be more important than the other retinal fibers in determining this process.[14] These pupillary findings in patients with glaucoma strongly suggest that nerve fibers mediating central visual function are adversely affected. It is not known whether these nerve fibers are affected independently or concomitantly with the peripheral nerve fibers in the glaucomatous process.

Clinically, the temporal rim of the optic nerve can often be involved in the cupping process. Since the nerve fibers mediating macular function pass through the temporal rim of the optic nerve, it is reasonable to assume that the glaucomatous process does indeed damage some of these fibers and that such damage must have some functional correlates.

Recent histologic investigations also provide evidence of loss of central nerve fibers in glaucomatous eyes. The elegant quantitative electron microscopic studies of Quigley et al[15] showed that up to 50% of nerve fibers may have atrophied before Goldmann perimetry studies or Snellen acuity tests are able to show any defect. While the nerve fibers in the superior and inferior poles of the optic nerve were observed by these authors to be more susceptible to glaucomatous damage, they also noted decreased nerve fiber density in the papillomacular bundle in patients who had 20/20 visual acuity and normal Goldmann visual field studies. They also found that, as the disease progresses, nerve fiber density continues to decrease in the entire optic nerve even though the only functional changes appear to be peripheral visual field defects. Based on these anatomic changes, it is reasonable to expect some functional decrement in central visual function early in glaucoma if we can only find more sensitive means to assess this function.

In this presentation, color perception will be shown to be a foveal function. Abnormalities of color perception in glaucomatous eyes will be demonstrated by a variety of methods. In addition, concurrent defects of both chromatic and achromatic foveal vision in patients with glaucoma will be shown. The contrast sensitivity function will be explained. Published studies of both spatial and temporal contrast sensitivity examinations in glaucoma will be summarized. Finally, two previously unpublished investigations into the temporal contrast sensitivity function in normal patients, patients with glaucoma, and patients with suspected glaucoma will show that central temporal contrast sensitivity is reduced in eyes with glaucoma and that this reduction correlates with the degree of peripheral visual field loss and with the degree of cupping of the optic nerve.

The purpose of this thesis is to examine the evidence and to demon-

strate that glaucoma damages central as well as peripheral visual function. Evidence for this hypothesis will be presented from literature review, a retrospective survey of my investigations of color perception, and the presentation of previously unpublished data from my recent investigations of the contrast sensitivity function.

EFFECTS OF GLAUCOMA UPON COLOR PERCEPTION

Color perception is thought to be largely mediated by the fovea.[16,17] Although color receptors are present across the entire retina, the highest densities of color photoreceptors are located in the foveola, with progressively decreasing densities as one moves into the parafoveal area and the peripheral retina.[16,18-21] Nerve channels for color vision have been shown to be distinct from the light sense channels.[22,23] Color perception requires a high degree of retinal integration and, because of the delicate balance of neurophysiologic interactions, has been shown to be affected early in a variety of pathologic processes of the retina and optic nerve.[24] Given the effect of glaucoma on the ganglion cells and their axons, it would seem reasonable that color vision processing may be disturbed in this disease.[25]

In fact, defects of color perception in glaucoma have been noted by several observers over the past 100 years.[16,26-31] Most of these researchers report that the blue-yellow mechanism is more often and more severely affected in glaucoma than the red-green mechanism. However, one study found that the red-green mechanism was just as often affected, at least in well-established disease.[32]

Although color perception may be normal in the presence of advanced visual field changes, most studies agree that defects in color vision correlate well with the extent of visual field damage.[16,26,32] However, a minority of studies have shown that color vision defects may be present very early in the glaucomatous process, perhaps even before visual field defects can be detected.[31,33-35] In a recent 5-year follow-up study of optic hypertensive eyes, Lakowski and Drance[31] reported that visual field defects developed in 77% of eyes that had color defects when their study began but in only 19% of the eyes without color vision defects. Motolko et al[35] studied a variety of psychophysical and electrophysiologic tests in 14 patients with asymmetry of optic nerve cupping of greater than 0.2, increased intraocular pressures (IOP), visual acuity of 20/30 or better, and normal visual fields in both eyes. They found that color vision abnormalities, as measured by the anomaloscope, were present in 93% of these patients. Therefore it appears that color vision may be affected early in

the disease process, sometimes before other visual disturbances can be demonstrated.

The assessment of color perception is prone to several problems that sometimes make interpretation and comparison of different studies difficult. Different types of color tests measure separate aspects of color perception. The commonly used screening plates (eg, Ishihara, AO pseudoisochromatic, AO-HRR) were designed to detect congenital red-green defects and may be either insensitive or relatively insensitive to blue-yellow defects.[36] Although designed for use under standard lighting conditions, these tests are often administered under uncertain illumination in the clinical setting. Both the level of illumination and the color balance of the illumination source are important factors in color discrimination.[36] Furthermore, no accurate or standardized scoring criteria exist for most of these tests. Most clinical tests of color vision examine an aspect of foveal function.[16,36] However, the color plates usually test a somewhat more variable area of the macula than the anomaloscope-type test or the color cap tests, both of which subtend visual angles of about 1° to 2°.

The color cap tests, such as the Farnsworth 100 Hue and the more abbreviated Farnsworth D-15 panel, are designed to examine color perception across a wide visual spectrum than the plate tests.[16,36] Both tests require proper illumination, and the scoring can be complex. The anomaloscopes are the standards against which other methods must be measured.[36] However, they are the most difficult to use, require a well-trained administrator, take considerable time, and are not considered feasible for routine clinical use.[36]

Several factors other than the type of test and the disease process itself may affect color perception. Color discrimination declines with age.[16,37] Most of this loss is in the blue-yellow end of the spectrum and is largely explained by the yellowing of the crystalline lens with its attendant absorption of light in the blue end of the spectrum.[24,37] Hart and Gordon[38] reported that older aphakic patients (60 to 70 years of age) had color-matching values similar to those of normal, young patients (10 to 20 years of age). A small pupil can also produce blue-yellow errors.[16,26,39] Many of the studies of color vision in glaucoma failed to control for age and pupil size, making interpretation of the blue-yellow defects found open to some question.

I have participated in a detailed study of color vision mechanisms in patients with primary open-angle glaucoma and in those with elevated IOP without detectable visual field changes (glaucoma suspects).[40] The patients' ages ranged from 17 to 68 years. These patients were matched to control patients in whom there was no more than a 4 year difference in

age. All patients had visual acuities better than 20/40 and, at most, early nuclear sclerosis of the crystalline lens. The patients with glaucoma were chosen so that none had advanced glaucomatous damage.

One purpose of the study was to evaluate three clinically useful color vision tests for their ability to identify color vision disturbances in a glaucomatous population. A further purpose of the study was to define scoring criteria for these tests that might improve their sensitivity and specificity.

Finally, the spectral increment threshold sensitivity (the sensitivity to narrow wavelength bands across the visible spectrum) was examined in patients with glaucoma and "ocular hypertension." Spectral increment thresholds can help isolate the chromatic (color) from the achromatic (luminance) pathways, which appear to be mediated by small-diameter (slow) and large-diameter (fast) neurons of the ganglion cell layer.[40-42] Since glaucoma does affect the ganglion cells, it was hypothesized that there might be a selective loss of one of these functions, which has been shown in diabetics and other persons with acquired color vision loss.[43,44]

Nineteen patients with primary open-angle glaucoma or chronic angle-closure glaucoma after iridectomy, 19 with ocular hypertension, and 38 normal subjects age-matched to each of the patients in the two groups were selected according to the criteria cited previously. Pupil size was measured before testing. Each patient was tested monocularly with the American Optical-Hardy-Ritter-Rand (AO-HRR) color plates (both screening and diagnostic), Fransworth D-15 panel, and a Farnsworth D-15 panel whose caps had been desaturated by two steps in the Munsell notation. These tests were all performed under the MacBeth Easel Lamp. A modified scoring technique was used for the two D-15 panels. A fail score was given if a subject made more than one single-place error *or* any error greater than a single-place.

The results are summarized in Table I. Thirty-seven percent of the glaucoma patients failed the AO-HRR screening plates while only 5% of the age-matched normal subjects failed this test. Only 11% of the glaucoma patients and none of the normal subjects failed the diagnostic plates of the AO-HRR test. In the Farnsworth D-15 panel with conventional scoring, only 4 of the 19 glaucoma patients, 1 of the glaucoma suspect subjects, and none of the age-matched normal subjects had abnormal scores. With the modified scoring, 10 of the 19 glaucoma patient, six of the glaucoma suspect subjects, and none of the normal subjects failed. The difference from the normal group is statistically significant at the $P < 0.001$ level for the glaucoma group and at the $P < 0.01$ level for the group of glaucoma suspect subjects by the Fisher Exact Probability test.

TABLE I: CLINICAL COLOR VISION TESTS*

DIAGNOSIS	D-15 (%)	DESATURATED D-15 (%)	AO-HRR SCREENING (%)	AO-HRR DIAGNOSTIC (%)
Glaucoma	53	78	37	11
Age-matched normal subjects	0	11	5	0
Glaucoma suspect eyes	32	58	21	0
Age-matched normal subjects	0	11	0	0

*Adapted from Adams et al.[40]

For the desaturated version of the D-15 panel, 14 (78%) of the glaucoma patients, 11 (58%) of the glaucoma suspect patients, and 1 (11%) of the age-matched normal patients failed. These differences are statistically significant at the same levels as those for the unmodified D-15 test. Only 5 of the 19 glaucoma patients and none of the glaucoma suspect patients had small pupils ($\leq$ 2 mm). No statistically significant difference could be found in the failure rates between glaucoma patients with small pupils and those with pupils larger than 2 mm.

These results suggest that a simple, rapid, clinically feasible test, the desaturated Farnsworth D-15, identifies color vision defects in more than half of the glaucoma patients with only modest visual field defects while failing only a few normal subjects. Because the caps used in this test subtend an angle of 1.5° at 50 cm, the distance used in this study, the results strongly suggest a defect in macular, if not foveal, function in these patients with glaucoma. The test also fails over one half of the glaucoma suspect patients. Long-term follow-up will be necessary to determine if patients suspected of having glaucoma who fail the color vision test are the ones, as in the study by Drance et al,[26] who will go on to develop the full picture of primary open-angle glaucoma.

The same groups of patients and normal subjects were tested for chromatic and achromatic sensitivities. A 2°, centrally fixated, spectral test spot against a 10°, 1270 Troland, white background was used with the light source (~ 3200° K) focused to a 1-mm image in the subject's pupil. A 3-minute adaptation period was given each eye. Chromatic sensitivity was measured at 460, 500, 550, and 600 nm with the flicker frequency at 1 Hz. The achromatic sensitivity was measured at 460, 550, and 600 nm with the flicker frequency at 25 Hz. The brightness of the test spot was decreased by the subject until the flicker just disappeared. The average of three test runs for each frequency and wavelength was considered the final value. Details of the methodology and results have been reported elsewhere.[40] Only the results will be summarized here.

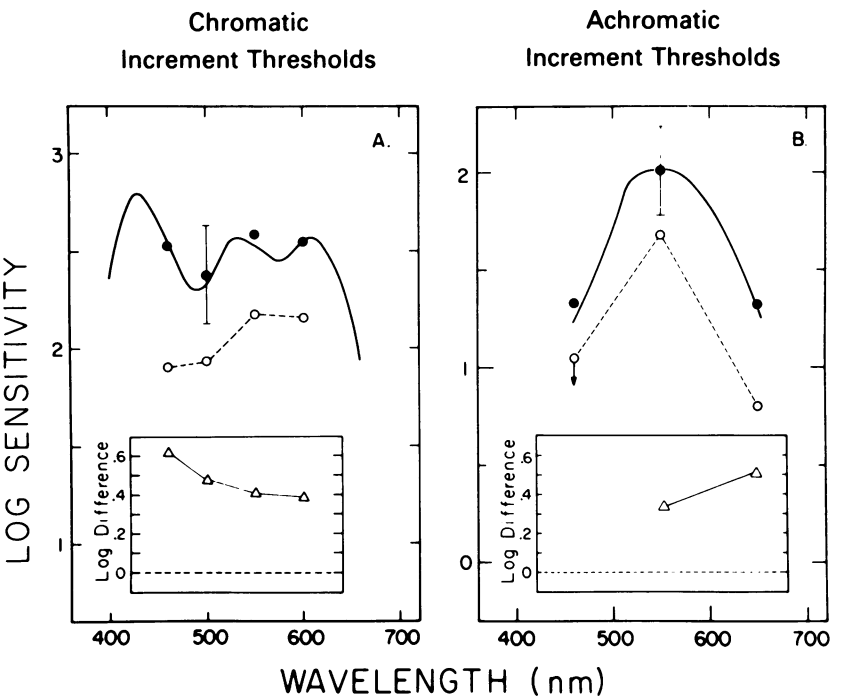

FIGURE 1

Average spectral sensitivities of *glaucoma patients* and age-matched control patients. *Black solid line,* Normal values are indicated for separate group of young, normal subjects tested identically except at 20-nm intervals across spectrum. *Lower box,* Log differences, is plotted between glaucoma patients and age-matched control patients. *Open circles,* Data are indicated for glaucoma patients. *Closed circles,* Mean values are indicated for age-matched control subjects. *Error bars,* ± SD for normal subjects (always less than 0.3 log unit) are shown. A: Chromatic increment thresholds for 2° circular target flashed at 1 Hz. B: Achromatic increment thresholds for 2° circular target flashed at 25 Hz. At 460 nm, 7 of the 19 glaucoma patients were unable to see 25-Hz flicker at maximum target intensity, making comparisons unmeaningful with normal values at this wavelength (from Adams et al[40]).

The results show a loss of both achromatic and chromatic sensitivity for the glaucoma patients as well as for some of the glaucoma suspects as compared with the age-matched normal subjects (Fig 1). The magnitude of this loss was about 0.6 log units for chromatic sensitivity and about 0.4 log units for achromatic sensitivity. The differences at all wavelengths tested are statistically significant at the $P < 0.01$ level compared with normal subjects. This is somewhat surprising because achromatic sensitivity has been thought to be normal in patients with glaucoma.[16] Glau-

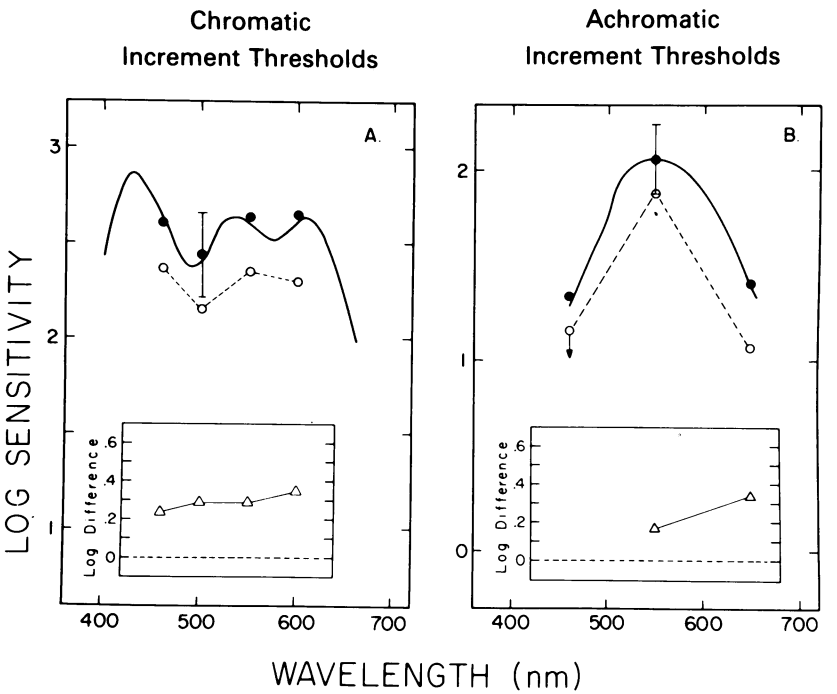

FIGURE 2

Averge spectral sensitivities of *glaucoma suspects* and age-matched control patients. *Black solid line*, normal values are indicated for separate group of young normal patients tested identically except at 20-nm intervals across spectrum. *Lower box*, Log difference is plotted between glaucoma patients and age-matched control patients. *Open circles*, Data are indicated for glaucoma suspect patients. *Closed circles*, Mean values are indicated for age-matched control subjects. *Error bars*, ± SD for normal subjects (always less than 0.3 log unit) are shown. A: Chromatic increment thresholds for 2° circular target flashed at 1 Hz. B: Achromatic increment thresholds for 2° circular target flashed at 25 Hz. At 460 nm, 5 of 19 glaucoma suspect patients and 2 of age-matched normal subjects were unable to see 25-Hz flicker at maximum target intensity, making comparisons with normal values at this wavelength difficult if not impossible (from Adams et al[40]).

coma suspect subjects also showed statistically significant differences from normal subjects in both types of sensitivity ($P < 0.05$) at all wavelengths tested except at 550 nm for achromatic sensitivity ($P < 0.10$) (Fig 2). Those subjects who showed decrease in achromatic sensitivity also showed decrease in the chromatic sensitivity. These findings have been supported by the recent study of Flammer and Drance.[45] They studied patients with suspected glaucoma with the 100-Hue test and the Octopus perimeter using the quantitative retinal sensitivity program. Their results

showed a significant correlation between defective color perception and decreased retinal light sensitivity in the central, paracentral, and midperipheral parts of the visual field.

The results of the study by Adams et al[40] suggest that patients with primary open-angle glaucoma and chronic angle-closure glaucoma after iridectomy have defects in both color- and brightness-processing pathways of the central 2° of the macula despite relatively early visual field changes. Since these two pathways appear to be mediated by two distinctly different populations of ganglion cells, both types of ganglion cells seem to be affected.[40] The results cannot be attributed to age or small pupils. Since congenital blue-yellow defects are extremely rare in the general population (< 0.0001%), it is reasonable to conclude that these changes are acquired as a result of the glaucomatous process.[46] Coupled with the results of the other studies cited in this section, there apparently is little doubt that the central visual pathways mediating both color and brightness are affected early in the glaucomatous process.

EFFECT OF GLAUCOMA ON CONTRAST SENSITIVITY

INTRODUCTION

Schade[47] pioneered the use of spatial frequency and contrast sensitivity testing as a means of assessing visual function. However, Campbell is credited with spurring the current surge of interest in this method. Measurement of contrast sensitivity is not just another laboratory oddity. Campbell and Maffei[48] have stated, "The ability of men and other animals to perceive the details of objects and scenes is determined to a large extent by how well their visual systems can discern contrasts."

A complex sound can be analyzed by its component auditory frequencies. Similarly, a visual stimulus can be dissected into component visual frequencies. This process is known as Fourier analysis.[49] By looking at the constituent parts of visual perception, it becomes possible to better understand how vision works. The visual system of man and most animals appears to be made up of many different channels or pathways, each of which is tuned to selectively respond to a given dimension of visual stimuli.[48] The information obtained from each channel is then integrated into a total image. Each channel responds best to some unique range of stimulus characteristic(s) along the continuum of the dimensions of that particular stimulus. For example, psychophysicists have been able to identify different channels that respond selectively to the wavelengths in the visible spectrum. The identification of neural channels that specifical-

ly respond to stimuli that vary in orientation or frequency demonstrate the anatomic and physiologic correlates of this principle.[47]

TERMINOLOGY

Before discussing how contrast sensitivity testing can be used to examine the effects of glaucoma on visual function, it is necessary to first define the terms used in this area of psychophysics. Contrast is the term used to describe the difference in luminance between two visible areas. The measurement of how well one can detect that a difference exists between two adjacent areas of different luminance is called *spatial contrast sensitivity*. Similarly, contrast can also exist between two objects seen sequentially. The measurement of how well one can detect that a difference exists between two areas of different luminance presented sequentially is called *temporal contrast sensitivity*.

Spatial contrast sensitivity is usually measured by the use of a grating—alternating light and dark bars. The number of alternating pairs per degree of visual angle is designated as the spatial frequency and is recorded in cycles per degree. The term "mean luminance" is the average of the luminance of the lighter and darker bars. Conceptually, the bars are said to vary (or modulate) around the mean luminance. The difference in luminance between the darker and lighter bars relative to the mean luminance is the contrast. If the change from Darker to lighter bars is abrupt, the pattern formed is called a squre-wave grating. If the transition from lighter to darker bars is gradual, the pattern is a sine-wave grating. Most tests of spatial contrast sensitivity utilize sine wave patterns since this technique has many advantages for physiologic studies.[45]

For temporal contrast sensitivity studies, the intensity of a light is alternately varied between two levels. The number of times per second that the alternation takes place is the temporal frequency. The mean luminance is the average of the luminances of the brighter and darker lights, and the lights are said to vary (modulate) on either side of the mean luminance. The difference in luminance between the brighter or darker light and the mean luminance is the contrast. As with spatial patterns, the transition from darker to lighter can be abrupt (square-wave flicker) or gradual (sine-wave flicker) wit the sine-wave modulation being the more commonly used.

The smallest difference in luminance that will either make a pattern appear as alternating bars rather than a homogeneous gray field (for spatial contrast testing) or make sequential lights appear as a flicker rather than a steady light (for temporal contrast testing) is the contrast threshold. The threshold of contrast is measured for each of several frequencies. The

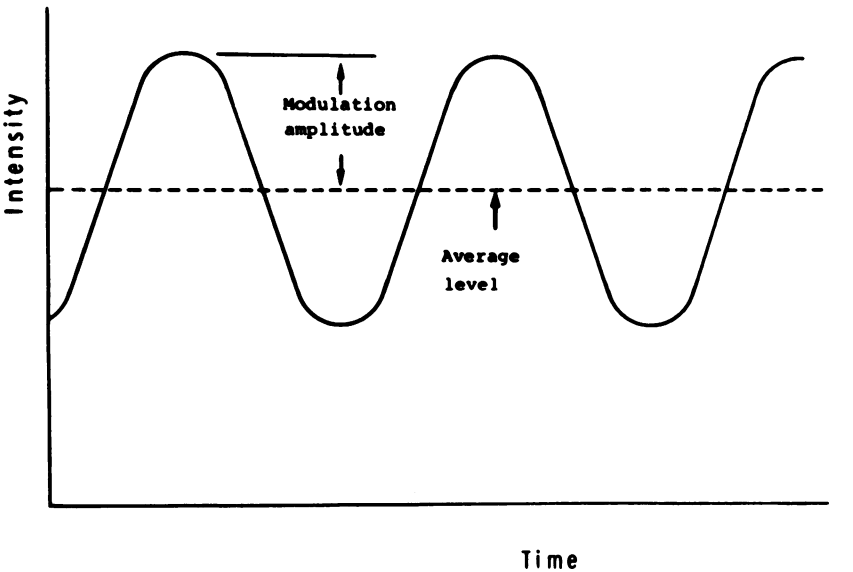

FIGURE 3
Diagrammatic representation of sinusoidal flicker used in temporal contrast sensitivity testing. Average level equals mean luminance. Modulation amplitude equals contrast (from Kayawawa F, Yamamoto T, Motokazu I[85]).

results are plotted as the contrast sensitivity (reciprocal of threshold) against the frequencies tested and is called the modulation transfer function (Figs 3 and 4). The plot in a normal person looks like an inverted U. The term "visuogram" was coined by Bodis-Wollner[50] to describe the plot of contrast sensitivity compared with the theoretic normal curve.

BACKGROUND

When the normal visuogram is examined, one can seen that the highest frequency that the human eye can perceive is about 45 cycles per degree (cpd) and that the human eye is most sensitive to low-contrast objects in the frequency range of 3 to 5 cpd.[50] In contrast, the cat has its peak sensitivity at about 0.3 cpd; therefore cats require more contrast to see the higher-frequency components of an image.[50]

In the visual system of the cat, it has been shown that in the ganglion cell layer of the retina each "X" cell is sensitive to a specific spatial frequency range and each "Y" cell is sensitive to a specific temporal frequency range.[51] Cells in the visual cortex may also be specialized to

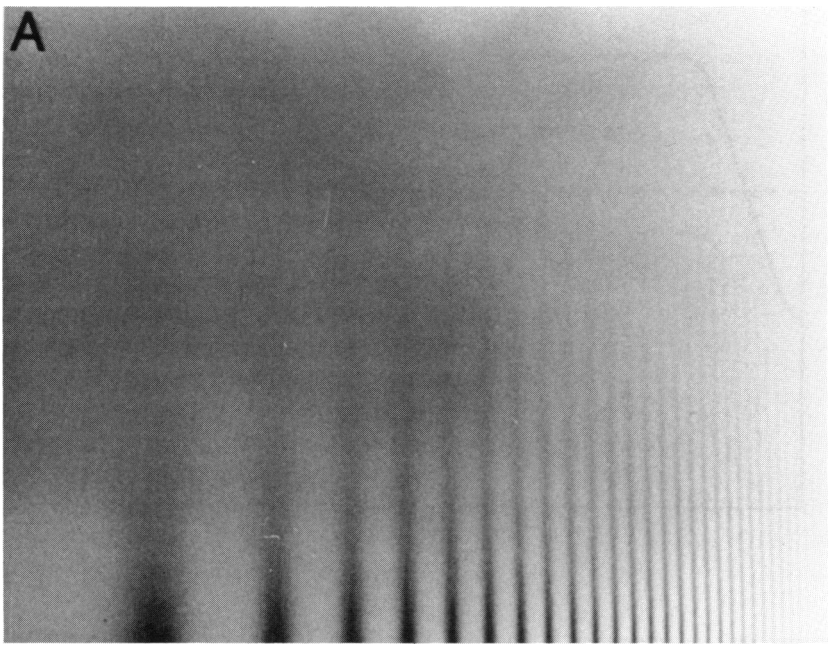

FIGURE 4
A: Series of sinusoidal gratings of increasing spatial frequency from left to right. Contrast increases from top of page to bottom. Note that gratings of different frequency are seen at different levels on page and that, if one were to connect points of detection of grating pattern for each spatial frequency, the line would trace an inverted U shape (from Campbell and Maffei[48]).

respond to specific frequencies. If the striate cortex of the monkey is removed, the animal shows markedly decreased ability to respond to contrast patterns at all frequencies.[52] In the human being, using visual evoked potential recordings from the brain, a direct relationship between the amplitude of the evoked response and the contrast levels of gratings has been shown.[45] These studies strongly suggest that the visual system is specifically geared toward receiving contrast and frequency information.

Ginsberg[47] has shown that any complex monochromatic image such as a portrait can be broken down into contrast patterns of different frequencies. Identification of an object requires only a few low spatial frequencies. To discriminate details and sharpness, the higher frequencies are

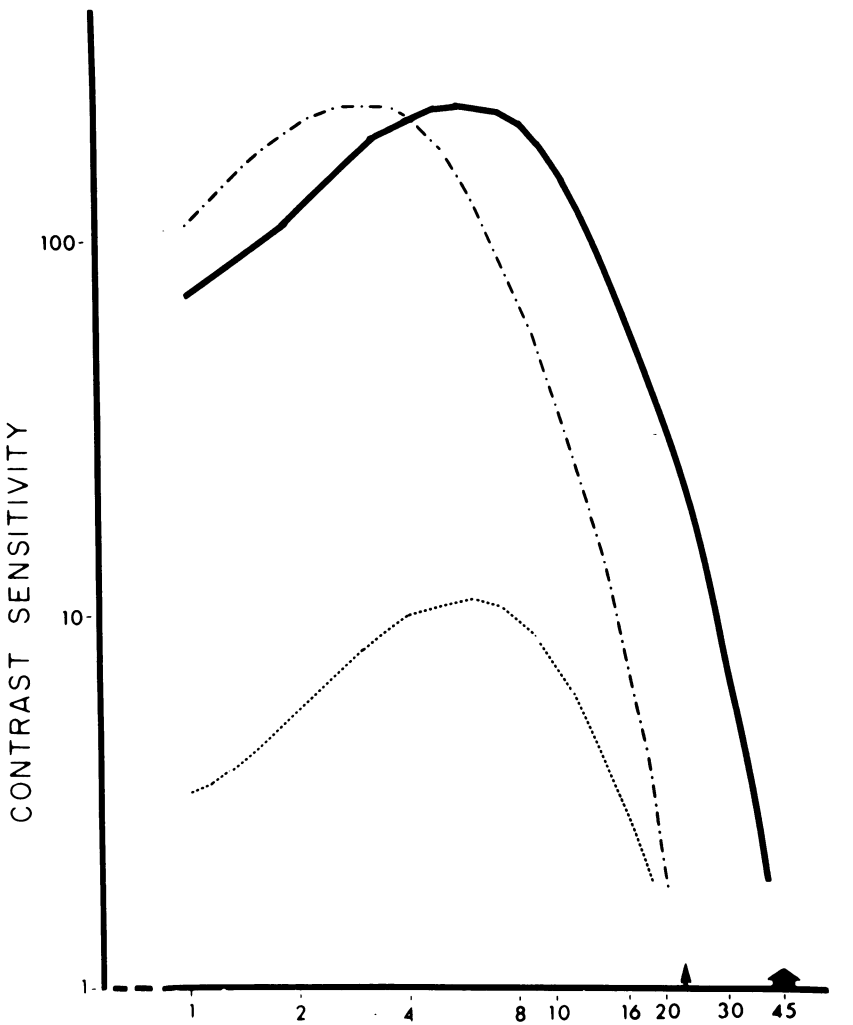

FIGURE 4 (Cont'd)

B: Spatial modulation transfer function (spatial contrast sensitivity) as plotted from test similar to that in A. Normal contrast sensitivity function is represented (*solid line*). Function from eye with loss of contrast sensitivity, mainly in high frequencies, is illustrated (*dotted-dashed line*). Function from eye with loss of contrast sensitivity for all frequencies is represented (*dotted line*) (from Bodis-Wollner[51]).

required as well.[47] Presumably the retina, and perhaps even the proximal cerebral cortex, respond to the spatial and temporal frequency components of an image, and the distal cortex integrates the component parts into the total image.[3]

Many factors can influence the contrast sensitivity function. A physiologic variation in contrast threshold exists among normal persons, especially for the lower frequencies.[47] Refractive errors and corrective lenses reduce the sensitivity for contrast, especially at the higher frequencies.[47] The lower frequencies are hardly affected. Age also seems to have an effect on the contrast sensitivity.[54,55] Investigations by Sekuler and coworkers[54] and Arundale[55] have shown that there is a reduction in sensitivity for the lower frequencies in the very young and the elderly (> 70). However, Arundale[51] showed a decreased high-frequency response in the aged. Adaptation can decrease contrast sensitivity. Finally, pupil size can affect the contrast sensitivity for higher frequencies, with the optimum sensitivity at 3 mm, and decreased sensitivity with both miosis and mydriasis.[56] Of course, similar problems plague other subjective methods of visual assessment such as visual acuity and perimetry.

The measurement of visual acuity using the Snellen test approximates the highest detectable spatial frequency at maximum contrast. Normal Snellen acuity only measures the visual threshold to the higher spatial frequencies but tells nothing about the relative sensitivity over the whole range of spatial frequencies.[47] A patient can have normal visual acuity and still be aware of the poor "quality" of an image. This degradation of the "quality" of the image may be due to a loss of contrast sensitivity at given frequencies that do not affect the resolution at maximum contrast.[47]

That patients with pathologic conditions of the visual pathways can have subjective visual complaints about the quality of central vision despite a normal Snellen acuity test has been well documented.[51,56,57] Some of these complaints have been shown to relate to decreased contrast sensitivity.[57]

Several different clinical conditions have been noted to affect the contrast sensitivity function. Among them are the use of soft contact lenses, the presence of amblyopia, cataract, corneal opacity, anoxia, optic nerve disease, or macular disease, or neurologic problems.[47,50,58-68] Each condition tends to affect the contrast sensitivity curve in a different way. Media opacities and artificial central scotoma tend to reduce sensitivity to the entire range of frequencies.[69,70] Refractive errors, amblyopia, anoxia, multiple sclerosis, other types of optic nerve disease, macular lesions, and cerebral lesions tend to reduce sensitivity to the higher frequencies and leave the lower frequencies relatively unaffected. Conversely, the sensi-

tivity to the lower frequencies is depressed by glaucoma and by certain retinal lesions.[50]

SPATIAL CONTRAST SENSITIVITY IN GLAUCOMA

Campbell and Green[71] were the first to measure contrast sensitivity using sinusoidal gratings generated on an oscilloscope. For the next decade, most research in this field was done with some form of video display system, thus relegating most investigation to the laboratory. In 1978, Arden[62] developed six printed sinusoidal grating plates that could be used as a rapid, portable, and clinically useful tool to evaluate the contrast sensitivity function. For the first time, contrast sensitivity could come out of the psychophysics laboratory and into the clinical setting. The Arden plates consist of photographs of sinusoidal gratings at six different frequencies (0.2, 0.4, 0.8, 1.6, 3.2, and 6.4 cpd at the suggested testing distance of 50 cm). The contrast increases logarithmically from the top of the page to the bottom. The tester gradually moves a gray cover down the plate until the subject first notes the sinusoidal pattern. At that point a score is read at the side of the plate. The scores may be treated for each plate individually or summed to give a total score. No special training is needed to administer the test.

Arden contrast plates have been found to be at least as good as Snellen visual acuity tests for screening and for identification of visual loss in patients with retrobulbar neuritis caused by multiple sclerosis.[66,67,72] Indeed, Skalka[73] found that the Arden grating test was more sensitive for detecting visual loss caused by optic nerve and macular disease than either Snellen acuity tests or acuity as measured with the visual evoked potential.

In a preliminary study of 90 normal eyes, 7 eyes with ocular hypertension, 15 with early glaucoma, 12 with moderate glaucoma, and 16 with advanced glaucoma, Arden and Jacobson[74] reported that the loss of contrast sensitivity, as measured by the sum of the scores from their photographic grating plates, correlated well with the extent of visual field damage. In their study, there was little overlap with normal subjects, at least for the moderate and advanced glaucoma groups. Their study also suggested that the higher frequencies (3.2 and 6.4 cpd) appeared to be preferentially lost in glaucoma patients. This was in contrast to expectation because the paracentral area of the retina, whic was thought to be affected earlier in glaucoma than the central area, is more likely to cause loss of the lower frequencies.[74]

Sokol et al,[75] using the same test, were unable to confirm that patients with glaucoma had any different scores than their age-matched normal

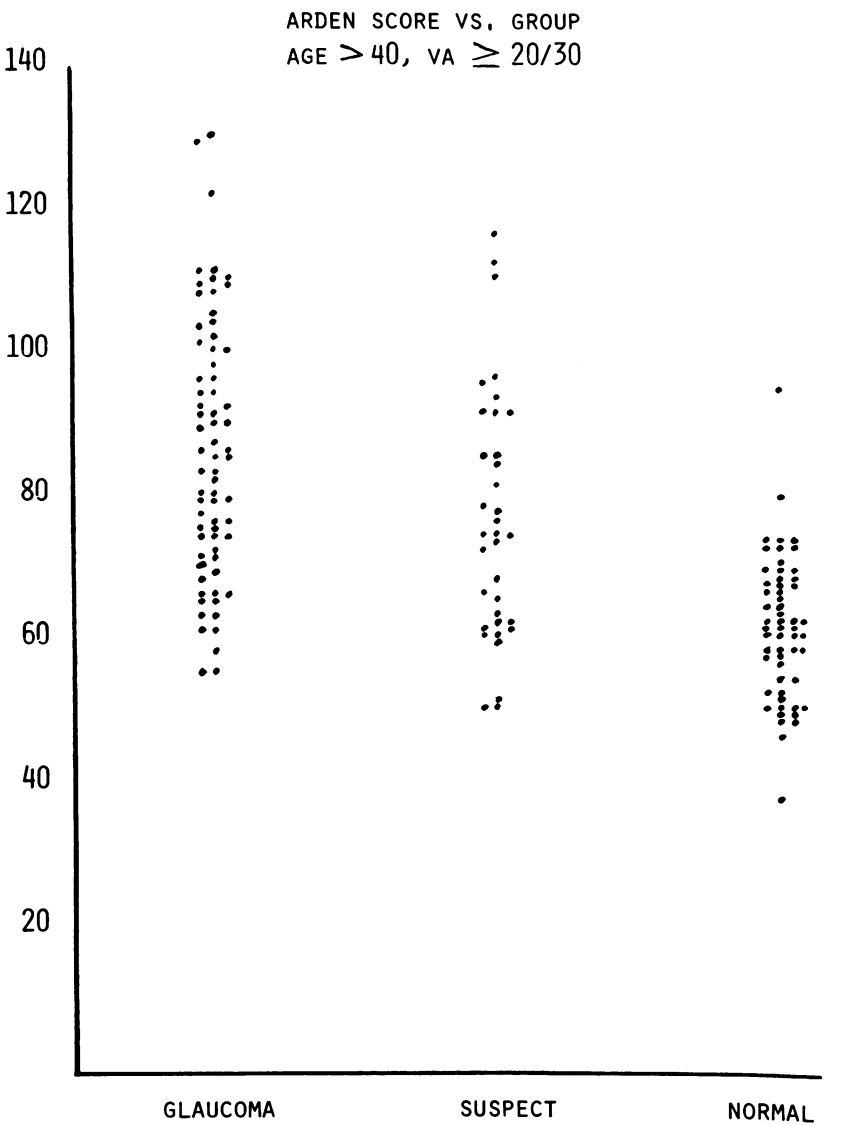

FIGURE 5
Arden grating score by diagnostic group. Total scores from six Arden plates are plotted for glaucoma, suspected glaucoma, and normal eyes in subjects with visual acuity of 20/30 or better and aged 40 years or more. Note generally higher (poorer) scores for eyes with glaucoma, intermediate scores for glaucoma suspect subjects, and considerable overlap with normal subjects (from Stamper et al[77]).

TABLE II: RESULTS OF ARDEN TESTING IN SUBJECTS OLDER THAN 40 YEARS* (VISUAL ACUITY 20/30 OR BETTER)

CUTOFF SCORE	FALSE-POSITIVE FINDINGS (%)	FALSE-NEGATIVE FINDINGS (%)
60	61	4
65	39	10
70	21	19
74	9	28
80	4	39

*Adapted from Stamper et al.[77]

counterparts. Unlike the study of Arden and Jacobson,[74] these authors found a significant decrement with age and a high false-positive rate in normal subjects over 50 years of age. This finding was similar to that found by Skalka.[76]

Stamper and associates[77] studied 95 normal eyes, 75 eyes with proved glaucoma, and 46 eyes suspected of being glaucomatous using the Arden plates. They found a statistically significant loss of contrast sensitivity in the glaucomatous eyes and in the glaucoma suspect eyes as compared with the normal eyes. However, the distributions among the three groups overlapped so that no cutoff scores could be found that satisfactorily separated the groups (Fig 5, Table II). In contrast to the findings of Arden and Jacobson,[74] the higher frequencies did not appear to be affected any more than the lower frequencies. Like Arden and Jacobson,[74] they found no age-dependent trends, and pupil size did not appear to adversely affect the scores. They found the test to be reproducible, with little or no intertester variability.

Vaegan[78] reported that the Arden test could be made more sensitive with a forced-choice format. This investigator stated that the forced-choice form of the Arden test was "much better" at detecting glaucoma than the Arden format and that only one forced-choice plate was necessary to distinguish the glaucomatous from the normal eyes. His study showed a roughly equal loss at all spatial frequencies tested. The forced-choice format was less affected by age than the standard Arden test. Unfortunately, Vaegan[78] had only six patients, and no large-scale study has been published.

To date, all investigations of glaucomatous eyes using spatial contrast sensitivity do suggest that a defect in spatial contrast sensitivity is present and that this defect may occur relatively early in the disease. However, the testing format of the Arden gratings has given variable results and has not proved to be of great diagnostic specificity. Furthermore, the Arden

plates subtend a visual angle of 30° at 50 cm, making it difficult to use this test as a means of demonstrating loss of function limited to the central retinal area.[75] However, both macular lesions, eg, with macular degeneration and a 3° artificial central scotoma can depress the spatial contrast sensitivity function; this suggests that the loss of spatial contrast sensitivity in glaucoma may be due to the effect of the disease on central visual processes.[65,69,70]

TEMPORAL CONTRAST SENSITIVITY IN GLAUCOMA

The temporal contrast sensitivity function bears a similar relationship to the critical flicker fusion frequency (CFF) as the spatial contrast Snellen function does to Snellen visual acuity. The CFF is the maximum frequency that can be detected as a flicker at maximum contrast. The normal human CFF measured centrally is about 45 cycles per second (c/s). 8 The CFF for the paracentral field is slightly higher.8 Temporal contrast sensitivity is usually measured by two methods: (1) An evenly illuminated target of 2° to 4° is alternated between the darker and brighter phases (diffuse flicker). (2) A sinusoidal bar pattern is presented in a 2° to 4° target, and the bar pattern is alternated so that the darker bars become the brighter and vice versa (counterphase flicker).

A decrease of the diffuse flicker sensitivity in the paracentral field of the glaucomatous eye was demonstrated by several studies reported between 1947 and 1962.[8,9,79] Each of these studies confirmed that flicker fusion testing of the visual field in the central 30° tends to be a more sensitive means of detecting glaucomatous damage than standard tangent screen testing. Campbell and Ritter[8] and Miles[79] emphasized that flicker sensitivity in the paracentral visual field out to 30° is more likely to be depressed in glaucoma than the central CFF. It is interesting that a review of the data from both studies shows that the central CFF is frequently reduced even in cases of early glaucoma. Unfortunately, the number of patients studied in each of these investigations were small and the size of the target was not specified exactly.

Reduced temporal contrast sensitivity in the central 4°, both for diffuse flicker targets and for counterphase targets, was demonstrated in eyes with ocular hypertension and primary open-angle glaucoma by Atkin et al.[80] These authors used a single frequency (8 Hz) for both types of testing situations and a 1.2 cpd pattern in the counterphase studies. They recorded the threshold of flicker at which the patient detected the flicker 50% of the time. While the overlap between the glaucomatous eyes and the control eyes was significant when each method (counterphase and diffuse flicker) was considered alone, these authors noted that an average

of the scores from the two methods could readily distinguish between glaucomatous and control eyes. They called this average score the dynamic response coefficient (DRC). The results did not appear to be correlated with pupil size since the scores of the pilocarpine-treated patients did not differ from those on other medications. An age factor was detected, showing a decrease of about 1.4 dB per 20 years. However, the numbers were small (only 11 patients with glaucoma). Nevertheless, the results do suggest that the temporal contrast sensitivity function has clinical utility as a sensitive indicator of damage to the visual system caused by glaucoma.

Using the pioneering method of de Lange, Tyler[81] tested the flicker sensitivity of 41 patients with early glaucoma and 12 normal subjects. The stimulus was a 5°, homogeneous flickering field equiluminant with the surround that could be modulated by the patient to increase or decrease the contrast (Fig 6). Thresholds for flicker detection were determined at 5, 10, 20, 30, 45, and 50 Hz, both for central fixation and for an area of the retina that was 14° eccentric to fixation and 45° above the horizontal meridian in the temporal visual field. Thus both macular and Bjerrum areas were tested.

Tyler[81] found a decreased temporal contrast sensitivity in both central and peripheral retinal test areas in patients with both ocular hypertension and glaucoma compared with control subjects (Table III). A preponderance of high-frequency losses (> 30 Hz) was found in the peripheral locus compared with the central locus, where losses tended to be more in the midfrequencies (10 to 30 Hz). Furthermore, 60% of this glaucomatous patients showed losses in the midfrequencies and not as much in the lower (< 10 Hz) or higher (> 30 Hz) frequencies. This loss of midfrequency temporal contrast sensitivity was termed "notch loss." Therefore, losses of contrast sensitivity could be found despite a normal CFF—a situation similar to that found in those eyes with decreased spatial contrast sensitivity and normal Snellen test acuity. At 30 Hz, the degree of loss of temporal contrast sensitivity correlated with the degree of visual field loss.

Tyler[81] found the temporal contrast sensitivity function to be relatively insensitive to age and refractive error. However, his oldest normal subject was aged 68 years whereas the glaucoma patients ranged up to 78 years of age. Comparing five eyes with their fellow eyes, the interocular comparisons were good, with the eye having the higher IOP always showing greater loss.

With my collaborators, I undertook to confirm Tyler's work and to further refine the testing situation so as to develop a clinically useful

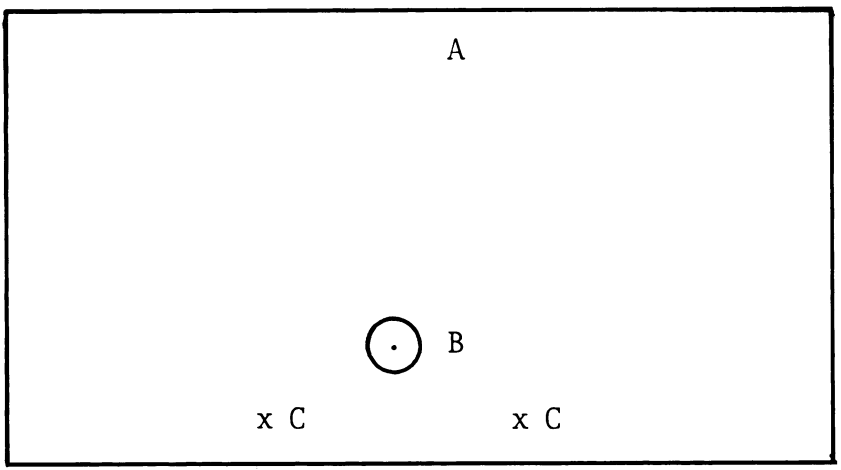

FIGURE 6
Diagrammatic representation of Tyler's apparatus. A: Surround, equiluminant across entire field and equivalent to mean luminance of B. B: Central stimulus of 5° is illuminated by 25 LEDs that could be modulated around mean luminance by patient to increase or decrease contrast. Frequency of alternation was controlled by tester. C: Two spots inferiorly that, when fixated, placed "central" stimulus into superior Bjerrum area nasal and temporal to fixation. (Tyler's original work used only temporal fixation spot.)

method of measuring temporal contrast sensitivity. The questions that our studies addressed were as follows: (1) Is there a sharp cutoff between normal and glaucomatous patients? (2) Which is more sensitive in detecting glaucomatous damage—central or peripheral testing? (3) Are there one or two of the frequencies that are most reliable in identifying glaucomatous damage. Towards this end, two separate, sequential investigations were undertaken. In each of the studies, the patients were carefully monitored in regard to their visual field, visual acuity, IOP, and optic nerve status.

MATERIALS AND METHODS

STUDY I

The first study utilized Tyler's[81] apparatus (Fig 6). This consisted of a homogeneous, equiluminant, steady field (a roentgenographic view box) lighted by voltage-controlled incandescent bulbs behind a diffusing surface placed 40 cm from the subject's eye. In the center of the surround was an equiluminant circle creating a uniform field 2.5 cm in diameter,

TABLE III: TEMPORAL CONTRAST SENSITIVITY IN GLAUCOMA AND OCULAR HYPERTENSION*

	PATIENTS (%) SHOWING LOSS IN CENTRAL FIELD	PATIENTS (%) SHOWING LOSS IN PERIPHERAL FIELD
Glaucoma	77	100
Ocular hypertension	83	86

*From Tyler.[81]

subtending 5° of visual angle. The central field was illuminated by 25 high-luminance, light-emitting diodes with a linear current-luminance function. A steady DC electrical signal controlled the mean luminance at 40 cd/m^2. A two-decade, ten-turn potentiometer controlled the added amplitude of sinusoidal modulation and, combined with an additional one-decade range switch, allowed control of modulation from 0.1% to 100% contrast.

The subject was asked to look either at a fixation dot in the center of the stimulus field or at one of two dots located 15° nasal and temporal to fixation and inferiorly at the 315° and 225° meridians. This projected the stimulus onto fixation, 15° superonasally and 15° superotemporally in the Bjerrum area, respectively. Two frequencies (25 Hz and 40 Hz) were tested at each locus. The potentiometer was adjusted by the tester to show flicker and then was slowly adjusted by the patient or tester until the subject was satisfied that the flicker had just disappeared. Two readings usually sufficed for each frequency in each locus. In the rare instance when the two readings differed by more than 10%, a third reading was taken. The runs were averaged. The tester was unaware of the subject's clinical classification.

Normal subjects were classified as such after complete ophthalmologic examination. Their visual acuity was 20/30 or better (all but two eyes were 20/20 or better). Forty-four eyes from 23 subjects were examined. Ages ranged from 25 to 71 years, with a mean age of 40.4 years.

Glaucoma suspects were patients with IOPs over 22 mm Hg on at least two occasions and who had no other ocular pathologic condition and open anterior chamber angles. Goldmann visual fields were normal by the Armaly-Drance screening method or showed only early, nondiagnostic defects such as a slightly enlarged blind spot or mild generalized contraction. The optic nerve heads showed normal or only suspicious cupping; no patients had diagnostic cupping. Twenty-two eyes of 11 patients were examined. The ages ranged from 28 to 83 years with a mean age of 59 years.

TABLE IV: MEAN TEMPORAL CONTRAST SENSITIVITY*

EYES	NO	CENTRAL	SUPERIOER BJERRUM AREA	
			NASAL	TEMPORAL
At 25 Hz				
Normal	44	279.8 (105.7)	385.2 (111.7)	372.3 (121.1)
Suspect	22	400.5 (93.7)†	489.8 (126.8)‡	457.3 (118.3)‡
Glaucoma	45	549.4 (156.8)†§	732.8 (199.2)†§	715.6 (209.4)‡§
At 40 Hz				
Normal	44	675.0 (106.3)	659.4 (107.8)	623.0 (132.7)
Suspect	22	757.9 (102.8)‡	742.7 (150.7)‡	730.1 (158.0)‖
Glaucoma	45	914.9 (100.5)†§	909.3 (104.7)†§	895.0 (116.1)†§

*Sensitivity recorded as 500 per log unit, eg, 1000 = detection at 100% contrast, 750 at 31% contrast, 500 at 10% contrast, 250 at 3.1% contrast, and 0 at 1% contrast (± SD).
†$P < 0.001$ compared to normal subjects (Student's *t*-test).
‡$P < 0.01$ compared to normal subjects (Student's *t*-test).
§$P < 0.001$ compared to suspects (Student's *t*-test).
‖$P < 0.02$ compared to normal subjects (Student's *t*-test).

Patients with glaucoma had IOPs over 22 mm Hg on at least two occasions as well as a diagnostic Goldmann visual field defect or pathologic cupping or both. Forty-five eyes of 28 patients were examined. The ages ranged from 22 to 81 years with a mean age of 58.8 years.

The results were analyzed by the Student's *t*-test for unpaired groups and by chi-square.

RESULTS

The results of this study are summarized in Tables IV and V. Patients with glaucoma showed decreased temporal contrast sensitivity in the central 5° field and in both superonasal and temporal visual field at 15° eccentricity to both 25-Hz and 40-Hz flicker ($P < 0.001$). The mean values of the temporal contrast sensitivity measurements for the glaucoma suspect eyes were significantly reduced from those of normal subjects at both 25 and 40 Hz in all three retinal areas, although the level of significance was less than that of glaucomatous eyes compared with normal eyes. However, when evaluating the percentage of eyes that had scores greater than 2.3 standard deviation (SD) from the mean (corresponding to the 99% confidence level or 1% false-positive level), no significant difference was found between normal eyes and glaucoma suspect eyes. No significant difference in sensitivity was found between the central and either of the two peripheral measurements. Good interocular and test-retest reliability could be demonstrated.

Although the test showed good specificity, only 50% to 70% of the

TABLE V: PERCENTAGE OF EYES WITH ABNORMAL TFS (> 2.3 SD FROM MEAN)

EYES	NO	CENTRAL (%)	SUPERIOR BJERRUM AREA	
			NASAL (%)	TEMPORAL (%)
At 25 Hz				
Normal	44	0	0	2
Suspects	22	5 (NS)*	14 (NS)*	5 (NS)*
Glaucoma	45	62†§	71†§	62†§
At 40 Hz				
Normal	44	0	0	0
Suspects	22	5 (NS)*	14 (NS)*	14‡
Glaucoma	45	60†§	60†§	51†‖

*Not significant by chi-square compared with normal subjects.
†$P < 0.001$ by chi-square compared with normal subjects.
‡$P < 0.02$ by chi-square compared with normal subjects.
§$P < 0.001$ by chi-square compared with glaucoma suspects.
‖$P < 0.01$ compared with glaucoma suspects.

patients with glaucoma showed abnormal sensitivity. No correlations could be found with age, Snellen visual acuity results, or presence or absence of shallow scotomata in the areas tested. Surprisingly, among the normal subjects and the glaucoma suspect subjects, a significant correlation was found ($r = 0.6$) between lower sensitivity and higher IOP. The significance of this finding is not clear.

Although this form of contrast sensitivity testing produced results that promised clinical usefulness, the clinical value was diminished by the detailed nature of the testing procedure, the need for a trained tester, and the relatively low sensitivity. However, this study did demonstrate that testing the central 5° was about as sensitive a method for detecting temporal contrast defects as was testing involving the peripheral retinal areas. Studies by others had shown that forced-choice testing could produce more reliable results.[78,82]

To find a simple, rapid method of measuring contrast sensitivity that does not required a trained tester and that more clearly distinguishes the glaucomatous patient from the normal subject, and to further examine the effect of glaucoma on central visual function, my co-workers and I have studied the temporal contrast sensitivity technique utilizing a forced-choice staircase process in patients with glaucoma and ocular hypertension and in normal subjects. The staircase method determines a threshold by increasing the stimulus in large steps until the threshold has been passed, then reducing the stimulus intensity in extremely small steps until the threshold is passed again, then increasing again until the threshold has been satisfactorily identified by this bracketing technique. A

similar process occurs in the opposite direction if the threshold has been passed on the first stimulus try. We have correlated the findings with the degree of visual field loss and cupping.

STUDY II

All subjects had visual acuity equal to or better than 20/30, no (or only minimal) lens changes, and no other ocular diseases. Fifteen persons with normal eyes, IOPs of less than 21 mm Hg, normal Goldmann perimetry (class 0), and an average age of 55.8 years were classified in the normal group. Sixteen patients with IOPs greater than 22 mm Hg on three or more occasions, nonpathologic cupping, normal Goldmann perimetry (class 0), and an average age of 51.3 years were classified as glaucoma suspects. Twenty-one patients with open-angle glaucoma, cupping of at least one optic nerve, and nonspecific (class 1) Goldmann field defects were classified as group 1. The average age was 57.2 years. Seventeen patients with early open-angle glaucoma, cupping of the optic nerve, and early specific defects of the visual field were classified as group 2 and had an average age of 65.2 years. Group 3 comprised six glaucomatous patients with moderate visual field defects. Group 4 contained four patients with open-angle glaucoma and advanced visual field loss. Because groups 3 and 4 were small, they were combined for the purposes of analysis; their combined average age was 73.6 years.

APPARATUS

The testing apparatus was developed by Tyler, and was a further refinement of his original testing equipment. The new apparatus consisted of a 40-cm square amorphous surround consisting of a photograph of tan rocks illuminated from behind by four incandescent bulbs and a diffusing panel to provide a steady, equiluminant field. In the center was a round, 2.5-cm diameter diffusing sheet illuminated by 25 light-emitting diodes providing a steady, equiluminant, uniform stimulus. A dark fixation spot was located in the center of the stimulus (Fig 7). The light sources were controlled by a steady DC signal giving a mean luminance of 50 cd/m^2. The amplitude and frequency of modulation of the sinusoidal flicker were controlled by a small home computer. The apparatus was viewed from a forehead and chin rest at a distance of 28.5 cm, giving a 5° central flickering field.

Five frequencies were tested: 2.5 Hz, 5 Hz, 10 Hz, 20 Hz, and 28 Hz. The threshold for each frequency was determined by a rapid staircase method programmed into the computer. The patient indicated whether or not the flicker was seen with a forced-choice, yes-no system. The entire

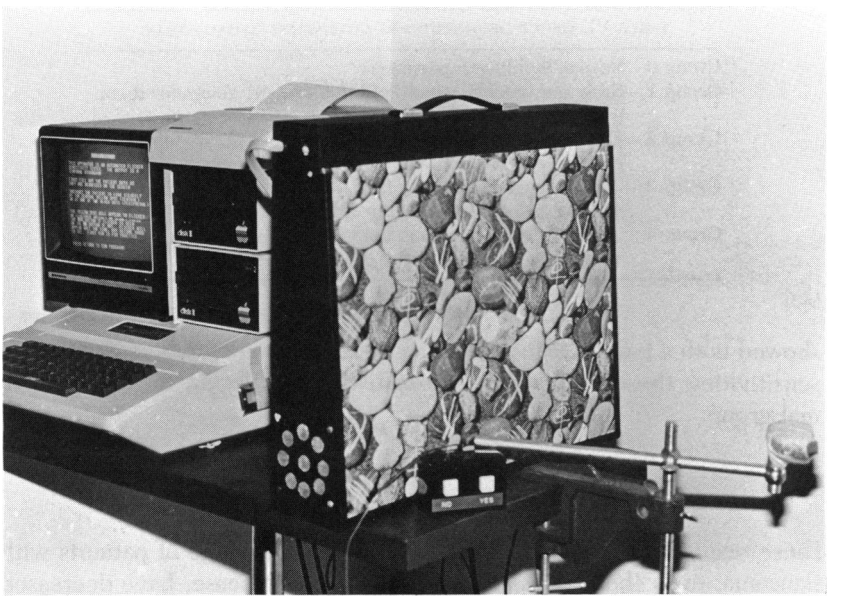

FIGURE 7
Temporal contrast sensitivity apparatus developed by Tyler.

test took about ten minutes per eye and could be easily administered by an inexperienced tester with only a few minutes' training. The tester was masked from the clinical classification of the subject.

Measurements were made of the level of modulation (contrast) required for detection of flicker at each frequency. Results were recorded in hundredths of a log unit (one-tenth dB) as the number of 1/100ths of a log unit below the theoretic normal threshold. The results were analyzed by the Student's *t*-test for unpaired groups, the chi-square test, and Pearson correlations.

RESULTS

The results are summarized in Tables VII through IX and in Figs 8 and 9. The mean flicker sensitivity for each of the glaucoma groups was lower than for the normal group at frequencies of 10 Hz and above. This reduced sensitivity was statistically significant at the 0.01 level or less for all visual field classifications. Similarly, the precentage of subjects with abnormal flicker sensitivity (> 2.3 SD from mean) was also significantly higher for each visual field classification. While glaucoma suspects

TABLE VI: GROUP DEFINITIONS BY GOLDMANN VISUAL FIELDS

Group 0	Normal Goldmann perimetry
Group 1	Early nonspecific visual field defects, eg, generalized contraction, enlarged blind spot
Group 2	Early specific glaucomatous defects, eg, nasal step and/or early arcuate defect, and/or Bjerrum scotoma
Group 3	Moderate glaucomatous field defects; visual field loss involving at least one quarter of the visual field
Group 4	Advanced glaucomatous field defects; visual field loss involving at least one half of the visual field

showed both a lower mean sensitivity and higher percentage of abnormal sensitivities, these values were not statistically different than in the normal group.

DISCUSSION

These results demonstrate that a significant percentage of patients with glaucoma, even those in the early stage of their disease, have decreased sensitivity to temporal contrast sensitivity (flicker sensitivity) in the central 5° of the visual field. The amount of loss and the percentage of patients with such loss directly correlate both with the degree of peripheral visual field loss and with the degree of optic nerve cupping. These observations suggest that the defect in central functioning progresses concurrently with the rest of the disease process.

While the findings could be related to the increasing ages of the different groups, earlier studies by Tyler[81] suggest that temporal contrast sensitivity is not particularly affected by age. Other conditions, including

TABLE VII: MEAN FLICKER SENSITIVITY*
(PERCENT ABNORMAL AT 20 Hz)

GROUP	NO	AVERAGE SENSITIVITY (dB)†	ABNORMAL TFS‡ (%)
Normal	15	−2.1	7
Suspects	16	−2.69	25
Glaucoma (1)	21	−5.14§	50§
Glaucoma (2)	17	−5.76§	82§
Glaucoma (3-4)	10	−10.1§	100§

*Sensitivity recorded as number of dB below theoretic normal mean.
†Db below theoretic mean for young normal subjects.
‡Percentage > 2.3 SD below theoretic mean.
§Statistically significant at < 0.01 level.

TABLE VIII: MEAN CONTRAST SENSITIVITY FOR EACH GROUP AND FREQUENCY (MEAN BELOW NORMAL THRESHOLD IN dB ± SD)

FREQUENCY (Hz)	NORMAL (n = 15)	SUSPECTS (n = 16)	GLAUCOMA (1) (n = 21)	GLAUCOMA (2) (n = 17)	GLAUCOMA (3-4) (n = 10)
2.5	−0.73 (1.87)	−1.50 (2.53)*	−2.41 (3.10)*	−1.76 (4.24)*	−4.2 (2.82)‡
5	−0.14 (2.45)	−1.00 (3.92)*	−1.67 (3.22)*	−2.18 (4.48)*	−3.5 (3.60)§
10	−4.00 (1.84)	−1.75 (3.49)*	−2.81 (3.01)†	−3.06 (3.07)†	−6.5 (2.46)‡
20	−2.10 (2.68)	−2.69 (2.68)*	−5.14 (3.29)†	−5.76 (4.29)†	−10.1 (4.36)‡
30	−1.60 (2.61)	−3.38 (2.52)*	−4.60 (3.50)†	−5.63 (3.05)‡	−10.3 (3.96)‡

*Not significant.
†$P < 0.01$ compared to normal subjects by Student's t-test.
‡$P < 0.001$ compared to normal subjects by Student's t-test.
§$P < 0.02$ compared to normal subjects by Student's t-test.

media opacity, amblyopia, and retinal disease, have been shown to decrease temporal contrast sensitivity.[83-87] However, patients with significant lens changes, amblyopia, and retinal disease were excluded from this study.

The findings confirm those of Atkin et al[80] who showed abnormalities in temporal contrast sensitivity in patients with glaucoma and in those with ocular hypertension. However, they found losses predominating in the lower frequencies while our study shows losses in the higher frequencies. This discrepancy remains unexplained.

The testing situation used in this study is relatively rapid, simple to administer, and repeatable. The apparatus can be made relatively inexpensively. Other simple tests such as the Arden plates have shown a defect in contrast sensitivity in patients with glaucoma, but these plates do not satisfactorily distinguish these patients from the normal group.[75,77] In answer to the first question posed for our studies, the test reported here does seem to better, although not perfectly, distinguish between most normal and glaucomatous eyes. The second question was answered by study I in which we showed that testing the central 5° appears to be as

TABLE IX: PEARSON CORRELATIONS (r) OF TFS LOSS WITH CUP/DISC RATIO AND GOLDMANN FIELD LOSS

TFS loss *vs* C/D ratio	$r = 0.63$*
TFS loss *vs* Goldmann field loss	$r = 0.59$*
Goldmann field loss *vs* C/D ratio	$r = 0.59$*

*$r > 0.29$ = significant at $P < 0.01$. TFS values adjusted for pupil size.

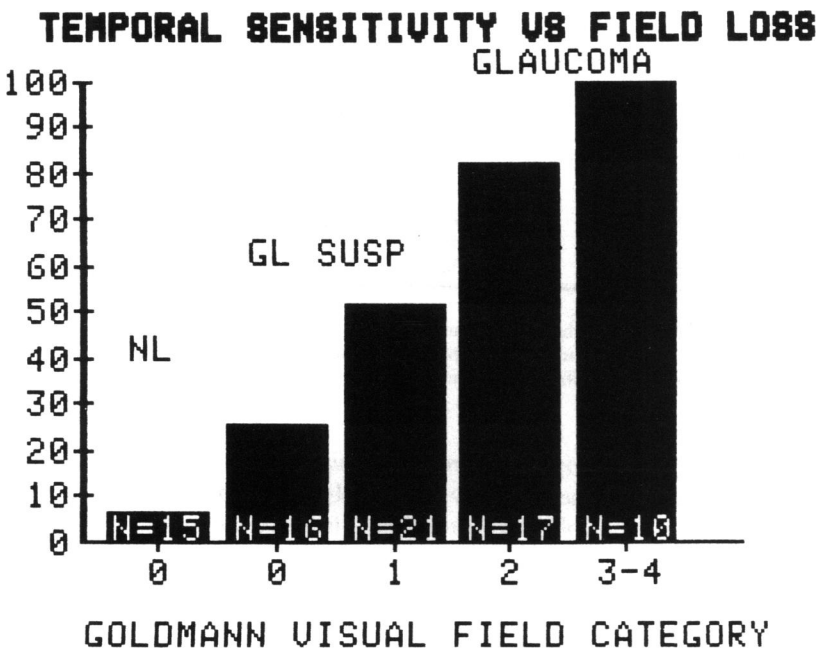

FIGURE 8
Temporal contrast sensitivity *vs* visual field. Note correlation between percentage of eyes in each group showing > 2.3 SD below mean normal sensitivity and degree of field loss (Table VII). Flicker sensitivities also correlated well with cup-to-disc ratio (Table IX).

sensitive for detecting the changes produced by glaucoma as testing paracentral areas of the retina. Finally, the midfrequencies of the temporal spectrum from about 10 to 30 Hz appear to be the most reliable in identifying glaucomatous damage.

Whether or not the detection of defects in contrast sensitivity, either spatial or temporal, will have the same prognostic implications as the detection of defects in color vision, eg, will require a long-term follow-up study. Such a study is currently under way with special attention being paid to the fate of the ocular hypertensive patients with abnormal temporal contrast sensitivity. Further studies are also necessary to define the place of contrast sensitivity measurement in diagnosis and management of glaucoma. Regardless of the prognostic or diagnostic value of these tests, the results obtained with their use underscore the fact that disruption of macular function may occur early in the course of glaucoma.

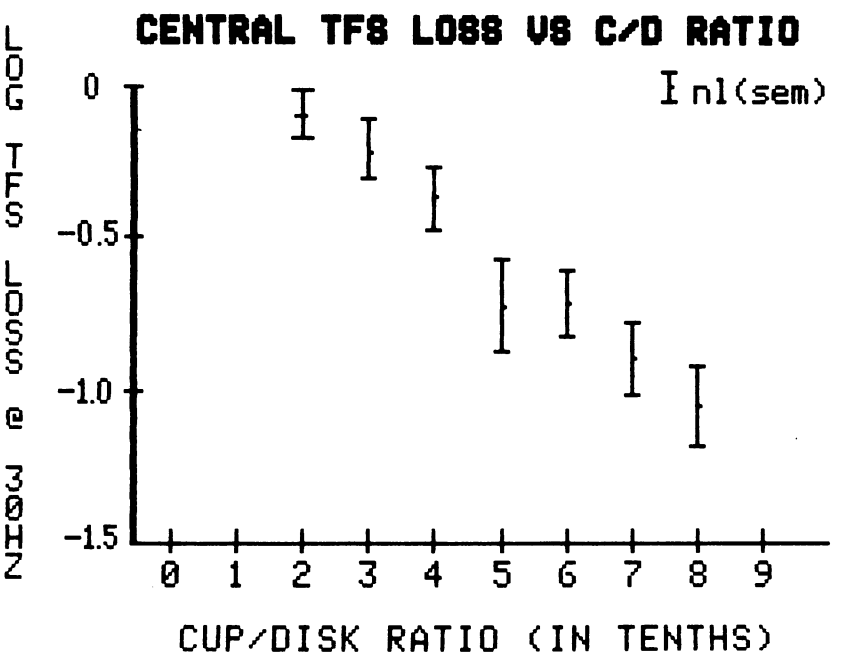

FIGURE 9
Plot of log loss of temporal contrast sensitivity (TFS) at 30 Hz against cup-to-disc ratio of patients with glaucoma or suspected glaucoma. Data are shown as mean log loss of contrast sensitivity ± standard error of the mean (SEM). Mean and SEM of normal group are shown (upper right of plot).

SUMMARY AND CONCLUSIONS

Glaucoma has traditionally been thought to affect peripheral visual function in its early stages and to spare central visual function until late in the disease process. The basis for this assumption has been the reliance on Goldmann-type perimetry, a rather sensitive method for assessing the peripheral visual function, and on Snellen-type visual acuity measurements, a rather insensitive method of assessing central visual function. This belief has persisted despite frequent complaints from patients with glaucoma that their central vision is disturbed. Over the past two decades, several investigations of central visual functions and their anatomic substrate have challenged this assumption.

Histologic studies of the nerve fiber layer in eyes with glaucoma suggest that the number of ganglion cells subserving macular function is decreased even in early stages of the disease. In addition, afferent pupil-

lary defects (a gross measurement of macular nerve fiber function) may also be present in eyes with early glaucoma.

Several studies have demonstrated that color perception (largely mediated by the fovea) is defective in glaucoma. Furthermore, defects in color perception may even precede the development of visual field abnormalities. Seventy-eight percent of patients with early glaucomatous visual field defects were found to have a defect in color perception when tested with a desaturated D-15 color panel that tests only the central 1.5°. In addition, both chromatic and achromatic foveal perception channels are defective in eyes with glaucoma and even in some eyes of those with suspected glaucoma.

Contrast sensitivity has become recognized as an important component of visual function. Partial loss of contrast sensitivity may cause a degradation in the quality of perception even though the Snellen visual acuity remains normal. Although contrast sensitivity is not entirely a macular function, it has been shown that as little as 3° of disturbance of the macula (eg, with macular degeneration or with an artificial central scotoma) will reduce the contrast sensitivity, suggesting that this modality is indeed mediated to a significant extent by this portion of the retina. Spatial contrast sensitivity appears to be reduced in patients with glaucoma. However, because of overlap and lack of a sharp cutoff measurement, present testing procedures fail to allow a clear distinction between the glaucomatous and normal populations.

Although reduced temporal contrast sensitivity has been demonstrated in glaucomatous eyes by others, I undertook a systematic investigation of this function in a large group of patients with glaucoma and with suspected glaucoma. The first part of the investigation revealed that temporal contrast sensitivity at 25 and 40 Hz is reduced in patients with glaucoma and in some who are glaucoma suspects. The central 5° and the Bjerrum area seem to be equally affected. The second part of the investigation used a simpler, automated, rapid staircase, forced-choice method of assessing temporal contrast thresholds at several different frequencies. This investigation showed that glaucoma produces a decrease in the temporal contrast sensitivity of the central 5° and that the loss of sensitivity was more frequent and consistent in the 10- to 30-Hz range of frequencies. Furthermore, the degree of decreased contrast sensitivity in the central visual field correlated extremely well with the degree of peripheral Goldmann visual field loss and with the degree of cupping in these patients.

This review of previous studies and the results of my investigations into color vision and contrast sensitivity provide strong support for the hy-

pothesis that (1) central visual function is affected by the glaucomatous process, (2) central visual function may be damaged early in the course of the disease process, and (3) such loss of function progresses as the disease progresses.

Therefore, careful assessment of central visual function is as important for evaluating the patient with glaucoma and with suspected glaucoma as assessment of the peripheral visual function. Simple, clinically practical tests of color perception such as the Farnsworth D-15 or, preferably, the desaturated version of this test are available and should become part of the routine evaluation for glaucoma. Despite the useful information that they provide, tests for contrast sensitivity functions are not quite ready for routine clinical use. Further studies should bring improvements in the testing of this method, enabling the clinician to better assess the full extent of visual changes induced by glaucoma and, armed with this knowledge, to better diagnose and manage this important disease process.

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