Glaucomatous Visual Field Damage

Luminance and Color-Contrast Sensitivities

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Using a modified Humphrey perimeter, we evaluated 16 eyes with primary open-angle glaucoma and visual field loss (defects 0.5–3.0 log units in depth), and 14 normal eyes. Each eye was tested twice in random order with conventional luminance-increment static perimetry and with the perimeter modified to produce a high-luminance yellow adapting background and a blue test stimulus. The background was a broad-spectrum light of 500 nm and above (yellow), while the stimulus was a broad-spectrum light of 500 nm and below (blue). Paired comparisons were made between conventional and blue/yellow sensitivities for every point examined (1184 points in 16 diseased eyes and 1036 points in 14 normal eyes). Defect depths were determined by using the age-corrected norms distributed in the Humphrey Statpac software. In glaucomatous eyes, blue/yellow sensitivity showed greater impairment than did conventional perimetric sensitivity, in which defect depths were less than 1.0 log unit. However, for defects greater than 1.0 log unit in depth, conventional perimetric sensitivity and blue/yellow sensitivity showed equivalent degrees of damage. Receiver operating characteristic (ROC) analysis was used to compare the ability of blue/yellow and of conventional perimetry in distinguishing between glaucomatous and normal eyes. Results indicated that although blue/yellow color-contrast perimetry may be more sensitive for the detection of incipient glaucomatous damage, in the manifest stages of visual field damage blue/yellow color-contrast perimetry is no more sensitive than is conventional (luminance-increment) perimetry for defining the extent of glaucomatous visual field defects.


Threshold static perimetry has become a standard method for measuring glaucomatous damage to the visual field. However, it has been recognized for some time that perimetry is a relatively insensitive test, in that it detects glaucomatous damage only after a significant proportion of nerve fiber bundles already have been damaged.1,2 It has been known also that the acquired dyschromatopsia of ocular hypertension frequently is detectable at a time when visual field defects may be either absent or at only very early stages of development.3–8 This form of dyschromatopsia consists predominantly of a loss of discrimination between blue and yellow hues and their intermediate mixtures. Acquired dyschromatopsias are usually detected and characterized by using tests of color vision in which colored test objects are centrally (foveally) viewed. The dyschromatopias of ocular hypertension and glaucoma have been reviewed recently in depth.9,10

Unfortunately, while the sensitivity of color vision tests for the detection of early glaucomatous abnormalities may be higher than that of conventional visual field testing, color tests lack specificity. Although there has been some evidence to suggest that the presence of a dyschromatopsia in ocular hypertension may be a useful predictor of incipient damage to the visual field,5,8,11 as yet there is no single color vision test that supports the clinical diagnosis of glaucoma in the way that conventional perimetry can. There have been attempts to improve the specificity of color testing by extending the examination to the extrafoveal visual field.7,12–16 Among studies of glaucomatous patients, these attempts have included heterochromatic flicker photometry and heterochromatic luminance-increment static perimetry. Although the results have not been conclusive, some investigators have reported that the use of short-wavelength stimuli increased the sensitivity for detection of visual field defects in glaucoma.7,13,15,16 We have reported contradictory results. In a group of glaucoma patients

359
we were unable to identify a clear advantage in kinetic color-contrast perimetry over conventional methods of perimetry for defining the topography of established glaucomatous visual field defects. In patients with advanced disease, it even appeared that static blue/yellow color perimetry was less sensitive for characterizing glaucomatous defects.

In the work reported here we have attempted to identify the source of these apparent contradictions. To do this we tested the hypothesis that the use of blue/yellow color contrast between the test object and the adapting surround increases the sensitivity of static perimetry in the characterization of glaucomatous visual field defects of moderate depth. For this purpose, we recruited a group of patients with glaucomatous visual field defects that were known to be restricted to localized areas in the central visual field. All patients were selected for having areas of the visual field where perimetric sensitivity remained apparently normal and other areas that clearly were diseased. Our intent was to compare two different perimetric tests over areas of the visual field that demonstrated a broad range of glaucomatous damage, from minimal to severe. The tests compared were conventional threshold static perimetry by program 30-2 of the Humphrey automated perimeter, and threshold static perimetry in the same pattern but with a high-luminance background of yellow color (wavelengths greater than 500 nm) and projected stimuli of a contrasting blue color (wavelengths less than 500 nm). The question we wished to answer was whether glaucomatous defects of any depth produce a greater or lesser depression of blue/yellow color-contrast sensitivities, as compared to conventional luminance increment sensitivities.

Materials and Methods

Patient Selection

Patients with primary open-angle glaucoma were selected from those being cared for in our clinics. Patients were selected on the basis of having the following: documented elevations of intraocular pressure (pressures of 23 mmHg or greater on three or more occasions); pathologic cupping of the optic disc; and characteristic glaucomatous visual field defects, including paracentral scotomas, nasal steps, or arcuate scotomas. Visual field defects were confirmed both by conventional manual kinetic perimetry with a Goldmann perimeter, and by threshold static perimetry with program 30-2 of the Humphrey visual field analyzer. All visual fields were evaluated by Statpac analysis (commercial software provided by the Allergan Humphrey Co., San Leandro, CA) prior to patient enrollment, and visual fields were required to have at least one location of statistically normal sensitivity in three of the four quadrants of the visual field. This requirement ensured that each patient contributed both apparently unaffected as well as diseased visual field locations to the study data. Only one eye was selected for each patient included in the study. Patients were required to have gonioscopically open angles and no known attributes of secondary glaucoma, such as corneal angle deformity, peripheral anterior synechias, or other evidence of ocular inflammatory disease. No restrictions were placed on patient medications or surgical history for glaucoma.

Aphakic and pseudophakic patients were excluded from the study, as were those with evidence of congenital (ie, red/green) dyschromatopsias. No restriction was placed on visual acuity; however, no patients with media opacities or pupillary miosis sufficiently dense to depress the visual field were included. Depression was assessed by comparing the total deviation and pattern deviation numeric and probability plots with the Statpac analysis program. A diffuse defect found on the total deviation probability plot (multiple adjacent locations spread evenly across the central visual field with \( P < 0.05 \)) but not found on the pattern deviation probability plot was taken as evidence of visual field depression by media opacity or miosis.

Normal Subjects

A group of normal subjects, recruited from the professional and technical staff of our department, was included in the study for purposes of comparison. Normals were defined as those with no known history of ocular disease, with visual acuity of 20/30 or better, and with visual field examinations by Humphrey program 30-2 showing no evidence of disease. Statpac analysis was used to assess visual field status; no eye was included if performance reliability was below the Statpac standard necessary to allow comparison with the database of normals. Normal eyes were excluded from the study if two or more locations had \( P < 0.05 \% \) on the total deviation probability plot, or if four or more locations had \( P < 1\% \).

Sixteen glaucoma patients and 14 normal subjects were included in the study. Informed consent was obtained from all participants. One eye of each participant was studied. No attempt was made to match the participants for age, but suitable corrections for age-related variations in perimetric sensitivities and ocular media absorption of blue light were made.

Color Vision Testing

All participants were screened for dyschromatopsia with Lanthony’s New Color Test (NCT). This test
was chosen as an alternative to the Farnsworth-Munsell 100-hue because of the considerable time savings it offers. Only the first step (the separation phase) of the NCT was used. It was found that this test could be completed reliably for one eye in less than 5 min.

Perimetric Tests

All of the threshold static perimetry was done with the 30-2 program of the Humphrey automated perimeter, but short-term fluctuations were not measured. All test data were submitted to analysis by the Statpac program. Kinetic perimetry with the Goldmann instrument was used only to confirm the presence of glaucomatous visual field defects and to screen for the presence of nonglaucomatous defects, such as those obeying the vertical meridian.

A hybrid form of blue/yellow color contrast static perimetry was performed with a special modification to a Humphrey automated perimeter equipped with a background illumination system capable of a sustained luminance of 315 apostilb. The housings for the background illumination bulbs were fitted with Kodak (Rochester, NY) Wratten yellow filters (no. 8). With the yellow filters in place, the background luminance was attenuated to 198 apostilb. The projector of this perimeter was equipped with a clip-on Ealing interference filter no. 35-5289, producing a blue stimulus of wavelengths below 495 nm. In comparison to conventional luminance perimetry with the 30-2 program at a background luminance of 31.5 apostilb and with a size III test object, it was found that the blue/yellow instrument with a 198 apostilb yellow background and a size V blue test object gave sensitivity values of comparable numerical magnitude in visual fields obtained from normal eyes.

All tests for a given patient were confined to one eye, and were completed within less than one half day of testing. Patients initially underwent dyschromatopsia classification by the Lanthony NCT, followed by static perimetry with the conventional and the blue/yellow methods. The order of perimetric testing was randomized by coin toss. All data from the Humphrey instrument were transferred to a spreadsheet program in a desktop computer for further statistical analysis. Age-related norms for threshold static perimetry by conventional luminance perimetry were taken from the data distributed within the Statpac program of the Humphrey instrument.

Scatter plots compared the paired observations for luminance- and color-contrast sensitivities at each location in the visual field for each individual patient as well as for the aggregate body of merged data. The depth of glaucomatous defect in the visual field was defined as the difference between the observed value in the patient and the value expected for the age-related norm. This value was plotted as a function of the similar statistic for the blue/yellow color contrast perimetric data. The color data were first corrected for age-related ocular media absorption of blue light (see full description in Results). The corrected values then were subtracted from the age-related sensitivity values of the Statpac data base. If there were a difference in the susceptibility of the two perimetric functions (luminance- and color-contrast sensitivity) to glaucomatous damage, the plot of one defect type against the other would produce a line with a slope of value other than one. However, if luminance- and color-contrast perimetry do not differ significantly from one another in their response to damage by the glaucomatous process, the slope is expected to have a value close to unity.

As an additional means of analysis, receiver operating characteristic (ROC) analysis was used to compare the ability of color-contrast and luminance perimetry to separate glaucoma patients from normal subjects. A review of this method has been provided by Massof and Emmel. ROC analysis is a criterion-free statistical technique derived from signal detection theory. It treats the normal data set as noise and the patient data set as noise plus signal. An ROC curve plots the cumulative noise-plus-signal data versus the noise data. The area under the ROC curve (Pd) represents the difference between the two distributions. Pd equals 0.5 for identical distributions. A discrimination index (Pd) is calculated by the formula Pd = 2(0.5 - Pd). A Pd value of 1.0 denotes perfect separation between patients and normals, while a Pd value of 0 represents 0 discrimination value. For this study we used the Monte Carlo method to calculate Pd for each point in our data set, comparing visual field defect depths for the two perimetric testing methods. The defect depth comparisons for each visual field point in the glaucoma data set were compared to the distribution of similarly computed “defect depth” comparisons in the normal data set. As in the scatter plot analysis, all raw data was age-corrected before applying ROC analysis.

Results

Sixteen glaucoma patients (ages 47–87 yr, mean 68 yr) and 14 normal subjects (ages 24–65 yr, mean 36 yr) were included in the study. Figure 1 summarizes the results of color vision testing with the Lanthony NCT for the first 10 normal eyes and 15 glaucomatous eyes. The separation phase of the NCT tests the ability to differentiate between colored caps of varying levels of color saturation ("chroma") and caps that have varying brightnesses in a neutral gray series. Half of the normals were unable to differentiate between grays and the most desaturated (chroma 2)
blue-purple caps, but otherwise made no systematic errors. Glaucoma patients, however, showed a strong pattern of blue/yellow dyschromatopsia, as marked by the percentages of subjects confusing purple-blue and yellow caps with grays. (Male patients with identifiable congenital dyschromatopias in a red-green axis had been excluded from this study.) While none of the normals missed the chroma 4 purple-blue cap, 47% of glaucomatous eyes showed a dyschromatopsia at this moderate level of color saturation. The NCT test was performed primarily in order to exclude from the study patients with evidence of congenital dyschromatopsia. The results showed a characteristic and expected degree of acquired blue/yellow hue discrimination defect among glaucomatous eyes.

Figure 2 shows the perimetric results in gray-scale format for one glaucoma patient. The image to the left is from the conventional 30-2 perimetric examination, while the image to the right is from the blue/yellow variation of the test. An arcuate defect in the superior Bjerrum region of the visual field was found by both methods of testing. This was a moderate defect; its range of sensitivity depression generally was 0.5–1.0 log units. Seen qualitatively, the two gray-scale displays show a more prominent defect with blue/yellow testing. This difference was seen in the numerical displays as well. Four points in the superonasal quadrant that were depressed by less than 5 dB on conventional testing were found to be depressed by more than 10 dB on the blue/yellow test.

An advanced defect is illustrated in the case of Figure 3. A maximum luminance defect was found by
conventional testing over the entire superonasal quadrant and most of the superotemporal quadrant. Only four locations in the superior hemifield were depressed by less than 0.5 log units. Comparison of the gray-scale displays confirms the topographic features of the defect. Although the blue/yellow results seem to show greater generalized depression of the inferior hemifield, there is no apparent difference in the shape of the defect as mapped by the two methods.

These differences, seen by qualitative comparisons alone, cannot be interpreted as meaningful. Quantitative comparisons are needed to measure the sensitivity of one perimetric method as compared to the other. We wished to determine whether the magnitude of pathologic change by one test was consistently different from that of the other. For this purpose, we pooled the data from all patients studied. The pooling of data from all visual field locations of all patients allowed comparisons between the two tests as a function of degree of glaucomatous damage. To allow for comparison of data from multiple patients of differing ages, a relative age-correction factor for ocular media absorption of blue light was applied to all data for blue/yellow perimetric sensitivities. This factor, ranging from approximately 2 to 6 dB of blue/yellow sensitivity, was taken from the function shown in Figure 4. This function was generated by a least squares polynomial regression fit to data for age-dependent ocular absorption of blue light in normal eyes. These data have been previously reported, and were kindly provided to us by the authors. The age correction factor for each subject was applied to the raw blue/yellow perimetric sensitivity values prior to calculating the blue/yellow sensitivity defect for each location.

The comparison of static perimetric defects detected by conventional luminance testing to those found by blue/yellow testing for 14 normal and 16 glaucomatous eyes is shown in Figure 5. The data were plotted for each visual field location included in the examinations. Program 30-2 has 76 test object locations. The two points that may fall within the physiologic blind spot were excluded from consideration, so that 74 points were included for each visual field. For the visual fields of the 14 normal eyes, 1036 data points were plotted, and for the 16 glaucoma eyes, 1184 data points were plotted. The curves superimposed on the scatter plots were computed by a least squares polynomial regression. Each test point was considered an independent observation solely for the purpose of solving the polynomial regression equation, and not for inferential tests of significance.

The values in Figure 5 are expressed as "defects:" the differences between expected and observed sensitivity values. Negative defects represent observations of sensitivity that exceeded the expected values. The curves fit to these data have gently rising slopes that
increase with increasing levels of perimetric defect. In the lower left tails of these curves, corresponding to those visual field sensitivities showing the least evidence of disease, the slopes are relatively flat. With increasing depths of visual field defect, the curves increase in slope. Qualitatively, this increasing slope illustrates that for relatively less affected visual field locations, there is a greater apparent effect of disease on blue/yellow sensitivity than on conventional perimetric sensitivity. This greater effect is seen as a shift and a rightward spread of the points at the lower end of the curve for glaucomatous eyes, when compared to the distribution of points from normal eyes. For the normal eyes, the calculated global means and standard deviations for perimetric “defects” were +1.7 ± 2.3 dB for conventional sensitivities and -2.3 ± 4.0 dB for blue/yellow sensitivities. For the normal eyes the global distribution of conventional defects was statistically normal (confirmed by Komolgorov-Smirnov one sample test, P < 0.001). Note that the variability of data for blue/yellow testing was approximately twice that for conventional testing.

Virtually every point in the least affected areas of the glaucomatous visual fields shows a greater reduction in blue/yellow sensitivity than in conventional sensitivity, when compared to the data for normal eyes. This means that even the points that show no depression by conventional perimetry often have a measurable reduction by blue/yellow testing. Comparing normal and glaucoma eyes for all locations having less than 1.0 log unit depression by conventional perimetry, the blue/yellow defect for normals was -2.30 ± 3.93 dB (mean ± SD), while that for glaucoma was +2.70 ± 4.63 dB (student t-test P < 0.001). This means that for locations with less than 10 dB of conventional defect, glaucoma eyes show (on average) 5 dB more blue/yellow defect than do normal eyes.

Where the extent of glaucomatous damage was greater, however, the two perimetric functions varied at nearly equal rates. Above defect depths of 10 dB (1.0 log unit) by conventional perimetry, the slope of the comparison curve is near unity. For defects greater than 1.0 log unit, the two types of sensitivities show quantitatively similar behavior.

The mean “defect” level for normal eyes of 1.7 dB represents a systematic error in all the data relative to the expected values in the Statpac database. The level of tolerance specified by the Humphrey Company for calibration of the instruments used in compiling their normative data base was ±1.0 dB. On average, our instrument appears to have been out of calibration by approximately 1.0–1.7 dB, relative to the Statpac data. Since this was a systematic error in all sensitivity measurements, it could not have had any effect on the study outcome or on the ROC analysis, which follows.

Figure 6 shows the result of ROC analysis. This scatter plot compares the discrimination indices for blue/yellow color-contrast and conventional perimetry for each of the 74 visual field locations included in the study. The discrimination index ($P_d$) expresses...
Inspection of the data for glaucoma eyes in Figure 5 suggests that there are two distinctly different types of degradation of blue/yellow sensitivity. The first type, represented in the nearly horizontal portion of the fitted curve, is a diffuse change in color vision that involves the entire central visual field, and that appears to be present in areas where defects by conventional testing are not evident. The second type, represented by the steeply rising portion of the curve, is a focal form of loss, occurring simultaneously in the areas of damage defined by conventional perimetric testing. This latter type of damage to color vision occurs to the same extent as damage to luminance-contrast mechanisms. This finding is in excellent agreement with the observations of Drance,\(^5\) who has pointed out that there seem to be two distinct types of glaucomatous damage to visual function, one diffuse and the other focal.

Diffuse and focal forms of damage have been observed in photographic studies of the retinal nerve fiber layer in patients with glaucoma.\(^22,23\) The two forms of damage are highly correlated with visual field measures of diffuse and focal defects in function.\(^23\) The diffuse type of damage, which seems to occur in the visual field prior to the onset of focal perimetric defects, is reflected in global depressions of the central visual field, including functional deficits in stimulus strength. The same pattern of results was obtained, showing a rising curve with a shallow tail to the left and a steep portion to the right, with a slope of about 1.0.

**Discussion**

The blue/yellow method of color perimetry used in this study is a hybrid design in which the contrast between the stimulus and its adapting surround represents a mixture of both luminance and spectral contrast components. By using barrier filters for the background and test object that are spectrally mutually exclusive, and by using relatively high-luminance background levels, we have attempted to weight the hybrid function towards the color-contrast component. If blue/yellow color-contrast sensitivities are more sensitive to damage than conventional sensitivities, one would expect this hybrid mixture to produce some measurable increase in susceptibility of the blue/yellow hybrid sensitivity values to damage by the glaucomatous process. While our results indicate that blue/yellow perimetry is more sensitive than conventional perimetry in the detection of moderate damage to visual function (up to 1.0 log units), it appears to offer little or no additional advantage in following defects of greater depth. This result seems to be uniform for patients of all ages and for every subject studied.

We found that a size V blue test object on a 198 apostilb yellow adapting background was necessary for blue/yellow perimetry to achieve sensitivities with numerical values similar those obtained with a size III test object at the standard settings for luminance perimetry. Therefore, the question arose as to whether the different test object size and background intensity could account in part for the differing behavior of the blue/yellow and conventional sensitivities in response to glaucomatous damage. Accordingly, the experiment was reproduced on eight of the glaucomatous patients, while reducing the test object to a size III and the background intensity to 19.8 apostilb for the blue/yellow part of the test. These parameters represented a 1 log unit reduction in adapting level and approximately a 1 log unit equivalent reduction in stimulus strength. The same pattern of results was obtained, showing a rising curve with a shallow tail to the left and a steep portion to the right, with a slope of about 1.0.

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such as reduced contrast sensitivity, kinetic isopter constriction, and reduced blue/yellow color contrast detection.6,8,23 While the diffuse changes appear earlier in the course of glaucomatous damage and therefore are more sensitive detectors of disease, they still lack the diagnostic specificity that focal defects provide. The greater diagnostic specificity of the focal type of damage lies primarily in the geometrically specific patterns corresponding to the distribution of retinal nerve fiber bundles. If early changes in color discrimination in the visual field are found also to have some focal attributes, ie, defects matching the nerve fiber pattern, then a truly more sensitive test for defining early glaucomatous damage could be developed. However, if the early changes in color discrimination have no such focal characteristics, then color testing may be no better than any other test that detects the diffuse form of damage.

The two differing forms of glaucomatous damage, focal and diffuse, may also explain the apparent discrepancies between our earlier observations17,18 and those reported by other investigators.7,13,15,16 When studying patients with advanced visual field defects by using a manual kinetic method of color contrast perimetry, we were unable to detect any appreciable advantage of color contrast methods for mapping the topography of glaucomatous visual field defects.17 Static hybrid color contrast perimetry was also no more sensitive than conventional perimetry for defining the depth of advanced defects.18 It now seems clear that in visual fields having manifest, focal defects of greater than moderate depth (1.0 log unit or more by conventional perimetry), color perimetry is unlikely to give any advantage over conventional visual field testing. In part this appears to be due to a lesser dynamic range of blue/yellow visual field function in the later stages of disease. The diffuse loss of color discrimination that occurs in the earlier stages of the disease leaves behind a relatively small residuum of color-contrast function that subsequently decays in parallel with conventionally measured perimetric sensitivity in the later course of disease.

Drum and colleagues also reported that the greater part of short-wavelength sensitivity loss in glaucoma is spatially diffuse, and stressed the importance of differentiating between preretinal absorption effects and the purely neural effects of disease induced loss of color function.24 Heron et al, differentiating between absorptive and neural defects in short wavelength sensitivity, found a specifically neural basis for glaucomatous damage to color vision.7 Sample and co-workers subsequently reported careful studies for which the effects of aging on ocular media absorption were controlled, confirming that the short-wavelength sensitivity loss in glaucoma has a neural basis.25-27

The hybrid type of color perimetry used for the current study is not suited ideally to the detection of color-contrast deficits. Although we have weighted our blue/yellow method towards the detection of color-contrast function, we have not eliminated entirely the possibility that luminance-contrast mechanisms played a significant role in determining the color contrast sensitivities. For instance, the yellow background luminance of 198 apostilb is not sufficiently bright to saturate middle- and long-wavelength-sensitive cone function, so that for the blue stimuli, there was probably some middle-wavelength cone intrusion. While this effect may have diminished differences between color-contrast and luminance sensitivities, it would not have enhanced them, nor would it have explained the curved relationship we found showing differing effects of disease on lesser affected, compared to more affected, areas of the visual field.

A better measure of the relative effects of glaucomatous damage on luminance and blue/yellow color-contrast visual functions would be provided by a comparison of conventional threshold static perimetric functions with a more isolated measure of color-contrast perimetric sensitivities. We have reported previously a method of color-contrast threshold sensitivity determinations that uses a color video tangent screen.17,28 This method uses heterochromatic flicker photometry to arrive at luminance-matched combinations of stimulus and surround for color-contrast perimetric testing. Although our prior work with that instrument was performed with kinetic perimetry, we are in the process of modifying it to allow for automated threshold static determinations of color-contrast sensitivity. The importance of continued study of color-contrast function in glaucoma has been stressed in the work of Drance et al,11 who show that color vision deficits in patients with ocular hypertension can be important predictors of subsequent glaucomatous visual field damage.

Key words: glaucoma, perimetry, color vision, dyschromatopsia, color contrast

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