Spectral sensitivity and color discrimination changes in glaucoma and glaucoma-suspect patients

Anthony J. Adams, Rosemary Rodic, Roger Husted,* and Robert Stamper

Color vision changes may occur early in the course of glaucoma and may precede visual field loss. Glaucoma suspects, having raised intraocular pressure and no diagnostic optic nerve head or visual field changes, may also have color vision loss. Unfortunately, the instruments used in the studies that have demonstrated these color vision changes were not feasible for routine clinical use; likewise, the studies did not carefully control for the effects of small pupil size and age or did not point to the underlying mechanisms responsible. We studied 19 glaucoma patients, 19 glaucoma suspects, and age-matched controls for each group by means of the Farnsworth D-15 panel test, a desaturated version of the D-15 test, and by measures of spectral increment threshold. Minor modifications of the Farnsworth D-15 panel test produce highly significant differentiation of glaucoma and glaucoma-suspect patients from age-matched normal groups. Further, spectral increment thresholds, with a two-degree spectral target flashed at either 1 or 25 Hz on a bright white background, show that both achromatic and chromatic sensitivity are significantly reduced when compared with their age-matched normals. Pupil size does not seem to be a significant factor. These results suggest that the function of two different ganglion cell populations is affected in glaucoma and that glaucoma may produce functional loss in the central foveal area earlier in the disease process than previously believed. (InVEST OPHTHALMOL VIS SCI 23:516-524, 1982.)

Key words: color vision, glaucoma, glaucoma suspects, spectral sensitivity, luminosity, color vision testing, color discrimination

It has been known for some time that color vision changes occur early in the course of glaucoma. These changes are usually described as "blue-yellow" defects, with some studies showing as much as 80% of glaucoma patients having disturbed color discrimination.1 Color vision defects may be apparent before visual field defects.2 3 Lakowski and Drance4 have also shown that about 20% of ocular hypertensive patients show severe color vision defects; they consider losses in color vision to be an important risk factor in the transition of ocular hypertension to chronic simple glaucoma.

Unfortunately, the color vision tests that have been most sensitive in detecting these blue-yellow color vision losses are not feasible for routine clinical use (e.g., FM 100 Hue test, Pickford-Nicolson anomaloscope), are...
Table I. Data for glaucoma subjects and age-matched normals

<table>
<thead>
<tr>
<th>Subject</th>
<th>Sex</th>
<th>Age (yr)</th>
<th>Acuity</th>
<th>Diagnostic results</th>
<th>Field defect</th>
<th>Treatment</th>
<th>Pupil size (mm)</th>
<th>Age-matched normal</th>
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<td>T. G.</td>
<td>M</td>
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<td>Early nasal step</td>
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<td>R. S.</td>
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<td>BS enlargement</td>
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<tr>
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<td>R. W.</td>
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</table>

OAG = open-angle glaucoma; ACG = angle-closure glaucoma; BS = blind spot.

not designed for detecting blue-yellow defects (e.g., Dvorine, Ishihara, AO pseudo-isochromatic plates), or appear to be relatively insensitive in detecting these defects (e.g., AO-HRR, F-2 plate, TMC plates). Furthermore, most studies of color vision with glaucoma patients deal with patients having a wide range of acuities and are often complicated by the color vision changes that accompany age and small pupils. Both of these latter factors can produce blue-yellow errors on color vision tests. In fact, the underlying mechanisms for the reported color discrimination changes have received little attention. Fortunately there is a growing body of evidence that psychophysical vision tests can be fashioned to selectively test achromatic (luminance) and chromatic (color) sensitivity, and that these two functions are mediated by large diameter (fast) and small diameter (slow) nerve fibers, respectively, of the ganglion cell layer. Such fast and slow neural systems have been described in a number of species and have been linked to achromatic and chromatic activity in the rhesus monkey. Selective loss of chromatic activity has been shown in diabetics and in a case of unilateral color vision loss.

The primary purpose of this study was to examine the spectral increment threshold sensitivity of glaucoma and glaucoma-suspect patients; increment threshold measures may be used to isolate chromatic from achromatic signals in the visual pathways. A secondary goal was to use an established simple clinical test of color vision on the same subjects and to use modified scoring and testing procedures that might be anticipated to reveal
more subtle disturbances of color discrimination. To this end we used the Farnsworth dichotomous panel D-15 test and a desaturated version of it, as well as a modified scoring procedure for both tests.

Our results suggest that simple modifications of a standard clinical test of color vision allows demonstration of a significant loss of color discrimination of both glaucoma and glaucoma-suspect groups when compared with their age-matched normal controls. Furthermore, the measurement of spectral increment thresholds for the same groups also demonstrated loss of both achromatic and chromatic sensitivity compared with the age-matched controls.

**Methods**

*Subjects.* The 19 glaucoma subjects (14 primary open angle) were each individually age matched to
within 4 years with a normal subject. Similarly, 19
glaucoma suspects were each age matched to nor-
mal subjects. Glaucoma subjects were defined as
having applanation of intraocular pressures (IOPs)
greater than 22 mm Hg on two or more occa-
sions, with diagnostic optic nerve head and/or vi-
sual field defects. (Clinical details of each subject
are shown in Table 1.) Glaucoma suspects were
defined as having IOPs of greater than 22 mm Hg
on two or more occasions, without any diagnostic
optic nerve head or field changes and without hav-
ing received any treatment for the raised IOP.
Normal subjects were recruited on the basis of
normal retinal and optic nerve head findings, IOP
less than 22 mm Hg, no crystalline lens changes
greater than grade two nuclear sclerosis, and cor-
rected acuity better than 20/40 (glaucoma and
glaucoma-suspect patients were included on the
same lens, retinal, and acuity criteria). No aphakic
or intraocular lens subjects were included in the
study. In addition to the control subjects used to
age match the glaucoma and glaucoma-suspect
patients, normal subjects were also studied on the
modified clinical Farnsworth D-15 panel color vi-
sion test.

Tests.
Farnsworth dichotomous panel D-15 test. This
test, originally designed to identify observers with
moderate and severe color vision loss, contains 15
color caps taken from the Munsell color circle
with approximately equal hue steps; each has the
same saturation (chroma) and lightness (value).
The subject is asked to “arrange the caps in order
according to color” and typically does this in less
than 1 min. The standard scoring practice to iden-
tify “test failures” requires that two “major” errors
be made, each resulting in colors across the color
circle being placed side by side (Fig. 1, a). We had
noted in pilot studies that patients with retinal
disorders frequently made multiple errors that did
not meet this “pass-fail” criterion, whereas nor-
mals rarely made more than one single-place er-
or. Consequently, for this study we adopted the
pass-fail criterion as follows: test failure results
when a subject makes more than one single-place
eror or any error greater than single-place (Fig. 1,
b). In this study we also used a desaturated version
of the test (each color cap was of the same hue and
lightness but was less saturated by two steps in the
Munsell notation) and applied the same pass-fail
criterion; we anticipated that the desaturated ver-
ion would result in an increased error score. Both
tests were administered monocularly under a
MacBeth Easel lamp. Test order was reversed for
each successive subject to avoid favoring one ver-
sion of the D-15 test. Each subject was also tested
with the AO-HRR plates under the MacBeth
Easel lamp.

Achromatic and chromatic sensitivity test. The
detection of flicker increments of spectral light on
a white background is mediated by chromatic
pathways for low flicker rates and by achromatic
pathways for high alternation rates. In our exper-
iments a 2 deg, centrally fixated spectral test spot
was viewed against a large (10 degree), 1270 tro-
land, white (color temperature ~3200° K) back-
ground. After adapting for 3 min to the white
background, the observer decreased the radiance
of the test spot until it no longer flickered. Three
such settings were averaged at each spectral wave-
length tested. The spectral sensitivity measures
allow an estimate of absolute sensitivity loss. In
our experiments, the 1 Hz flicker was used at 460,
500, 550, and 600 nm for chromatic sensitivity
measures and the 25 Hz flicker was used at 460,
550, and 650 nm for achromatic sensitivity mea-
sures. All measures were made on a portable two-
channel, Maxwellian-view optical system with the
single light source (tungsten halogen ophthalmosco-
pe bulb) filament focused to a 1 mm image in
Fig. 2. Spectral sensitivity of glaucoma subjects (n = 19, mean age 51.5 ± 15.8 years) and their age-matched normals (n = 19, mean age 51.6 ± 15.6 years). Solid lines (through the normal data), From a separate study of 11 young normals (mean age 24 years) under identical test conditions, except thresholds were determined at 20 nm intervals across the spectrum. The log difference between glaucoma and normal subjects is shown in the lower panels. A, Chromatic increment thresholds for a 2 deg circular target flashed at 1 Hz on a 1270 photopic troland white background and foveally fixated. Open symbols, Means for the glaucoma subjects shown in Table I; filled symbols, means for the age-matched normals. Error bars indicate ±1 standard deviation for the normals (the standard deviation was always less than 0.3 log units at each wavelength). B, Achromatic increment thresholds for a 25 Hz test target. All other conditions are as described in A. Standard deviations never exceed 0.23 log units for the normals. At 460 nm, seven of the glaucoma subjects were unable to see 25 Hz flicker in the test target at the maximum intensity available. Consequently, comparisons with normal values at this wavelength are less meaningful.

the plane of the subject's pupil. Intensity was controlled by a 4 neutral density Inconel wedge; for wavelength control the half-bandwidth of the interference wedge was approximately 12 nm. Field stops at the focal point of the Maxwellian lens provided the test and background stimuli.

Results

Farnsworth panel D-15 tests. When the conventional scoring method (see Methods) was applied to the D-15 test, only four of the glaucoma subjects and one of the glaucoma suspects failed the test. However, Table II shows that 10 of 19 glaucoma subjects failed with the modified scoring method and six of 19 glaucoma suspects also failed. No age-matched normals failed with this procedure. The difference between glaucoma and normal subjects is highly significant (p < 0.0001, Fisher exact probability test); the difference between glaucoma suspects and normals is significant at better than the 0.01
level by the same test. The desaturated version of the D-15 test caused 78% of the glaucoma patients and 58% of the glaucoma suspects to fail. By comparison, the age-matched normal group had about 11% failures. Both groups are significantly different from their age-matched normals (glaucoma, p < 0.0001; glaucoma suspects, p < 0.01, Fisher exact probability test). In fact, better estimates of the failure rate in the normal population for both the D-15 and desaturated D-15 tests can be estimated from our larger study of normals (mean age 35 years), where we estimate approximately 1% and 3% failures, respectively. We believe the failure rate in the normal population is likely to be less than this for the under-50 age group and greater than this for those over 65.

One of the few clinically feasible alternatives to the D-15 test in detecting retinal disease is the AO-HRR plate test. From Table I it can be seen that fewer glaucoma patients and glaucoma suspects fail the AO-HRR screening test than the D-15 tests. Furthermore, most of those who fail go on to pass all the diagnostic plates of this test, including all the glaucoma suspects. Although the AO-HRR screening test fails significantly more glaucoma subjects than normals (p < 0.02, Fisher exact probability test), the test does not reveal significantly different performance (at the 0.05 level) between those with small pupils (Fisher exact probability test, p = 0.37). Further, none of the glaucoma suspects had miotic pupils and their color vision test results also differed significantly from those of normals.

**Achromatic and chromatic sensitivity.** To what extent do the clinical results above have a parallel in the sensitivity of achromatic and chromatic processing? One might anticipate some loss of chromatic processing, but there is little expectation of a loss in achromatic or luminosity sense. In fact, spectral luminosity is generally reported as normal for glaucoma patients (see for example, Pokorny et al., 14 p. 292). Our results suggest a loss of both achromatic and chromatic sensitivity for glaucoma and glaucoma suspects compared with their age-matched normals. Fig. 2, A, shows up to a four times (0.6 log unit) loss of chromatic sensitivity for the glaucoma subjects, with the greatest loss in the short-wavelength (blue-violet) end of the spectrum. When compared with that of the age-matched normals, a two to three times loss of sensitivity (0.3 to 0.5 log units) was noted in achromatic sensitivity for the glaucoma subjects (Fig. 2, B). The difference at all wavelengths is statistically significant (p = 0.0005 to 0.005 for chromatic and p < 0.01 for achromatic, t test) when compared with that of age-matched normals.

Fig. 3 shows that glaucoma suspects are also significantly different from their age-matched normals (p < 0.05 at all wavelengths except 550 nm for achromatic sensitivity, where p < 0.10 by t test). Here the magnitude of the difference from normals for chromatic and achromatic sensitivity is reduced when compared with that in the glaucoma subjects.

The data presented in Figs. 2 and 3 do not answer the question of whether the chromatic and achromatic sensitivity losses occur in the same subjects. In fact, those subjects who showed reduction in achromatic activity also showed reduced chromatic sensitivity. There are a number of ways of showing this. For example, for the glaucoma subjects the chromatic sensitivity at 550 nm (C550) correlates well with the achromatic sensitivity at the same wavelength (r = 0.71), and of the
Fig. 3. Spectral sensitivity of glaucoma-suspect subjects (n = 19, mean age 53.6 ± 14.8 years) and their age-matched normals (n = 19, mean age 52.8 ± 14.6 years). A, Chromatic increment thresholds for the same conditions as in Fig. 2, A. Open symbols, Means for the glaucoma suspects; filled symbols, means for the age-matched normals. Error bars indicate ±1 standard deviation for the normals (standard deviation always less than 0.31 log units). B, Achromatic increment thresholds. Conditions as in Fig. 2, B. Standard deviations never exceed 0.23 log units for the normals. At 460 nm, five of the glaucoma suspects and two of the age-matched normals were unable to see 25 Hz flicker at the maximum intensity available. Consequently, comparisons at this wavelength are less meaningful. Solid lines as in Fig. 2. The log differences between glaucoma suspects and normal subjects are shown in the lower panels.

Nine glaucoma patients with the lowest C550 sensitivity, all of whom are at least 2 standard deviations from the mean of the age-matched normals, seven are also in the group of nine who have the lowest achromatic sensitivity at the same wavelength (L550). A similar correlation is seen for the glaucoma suspects for the same functions (r = 0.89); of the nine subjects with the lowest C550, six are also in the group of nine who have the lowest L550.

With the instrumentation used to measure spectral sensitivity, pupil size should not have influenced the results, since all the light passes through a 1 mm beam focused at the subject’s pupil. Although unlikely, it is conceivable that the subjects with a miotic pupil may find the beams from the test and background stimuli partially obstructed during part of the test. In fact, we find no significant difference in the results for the five subjects who had miotic pupils when compared with the other glaucoma subjects. For the chromatic sensitivity the difference was less than 0.1 log units at all wavelengths and reached a maximum of only 0.14 log units at 550 nm for the achromatic sensitivity.

Discussion

Both glaucoma patients and glaucoma suspects, as groups, show significantly reduced
chromatic and achromatic sensitivity, demonstrating that both color and luminosity functions are altered. Inasmuch as chromatic and achromatic activity are carried by two different populations of ganglion cells, each with different conduction velocities and firing patterns (tonic or phasic), the results suggest that our glaucoma and glaucoma-suspect groups both have changes in integrity of these pathways. It is generally accepted that foveal function is not affected until late in the glaucomatous process. Since these testing conditions isolate the central two degrees of the fovea, retinal changes in this region may be an earlier component of visual loss associated with glaucoma than previously thought. The high percentage of glaucoma-suspect failures is surprising. It could simply be that the raised IOP alone results in these changes. It may also be that these changes are a very early sign of glaucoma; if this is the case, we could have been dealing with a higher percentage of patients destined to develop glaucoma than expected from other studies. A less likely explanation is that the decreased spectral sensitivity is simply associated with the gene for abnormal aqueous dynamics.

The task for the D-15 and desaturated D-15 tests is essentially a saturation discrimination task. This is particularly obvious with the desaturated test, which has pastel-colored caps. In the visual system there is evidence for separate pathways for chromatic or color signals and achromatic or brightness (whiteness) signals. The difference between the achromatic and chromatic signals in the visual system should provide an estimate of saturation discrimination. Consequently, patients whose signal for chromaticity is considerably different than the signal for achromaticity would be expected to have good saturation discrimination. Thus if we take a ratio of the achromatic sensitivity to the chromatic sensitivity (i.e., subtract the log sensitivities), the ratio ought to predict the relative discrimination ability of the patient. We did this for the 550 nm spectral thresholds by identifying the four glaucoma patients who had the highest predicted saturation discrimination (highest ratio) and the four with the lowest predicted saturation discrimination (lowest ratio). The four with the highest predicted saturation discrimination all passed the D-15 test and the four with the lowest predicted saturation discrimination all failed the D-15 test ($p < 0.04$, Fisher exact probability test). A similar analysis for the glaucoma suspects revealed that the four with the highest predicted saturation discrimination all passed the D-15 test and three of the four with the lowest saturation discrimination failed the D-15 test. The Fisher exact probability statistic ($p < 0.07$) fails to reach normal levels of significance ($p < 0.05$); nevertheless, the trend is the same as for the glaucoma subjects. It is interesting to note that if we simply look at the chromatic thresholds or the achromatic thresholds in isolation, neither of them alone shows a significant correlation with the performance on the D-15 test.

Longitudinal studies are necessary to determine whether these kinds of color vision tests identify those glaucoma suspects at high risk for subsequent glaucoma.

Previous studies have shown that glaucoma patients and glaucoma suspects may have reduced color discrimination. Unfortunately, these color vision changes are most commonly identified by tests that are difficult to incorporate into clinical practice (about 20 to 30 min is required to test and score the FM 100 Hue test, and the Pickford-Nicolson Anomaloscope is expensive and complicated enough to place it out of the realm of routine office procedure). The Farnsworth dichotomous D-15 panel test generally requires less than a minute of actual testing time for each eye, excluding instructions and scoring. By conventional scoring, four of our glaucoma subjects would have failed the test; one of the glaucoma suspects would have failed. Modified scoring, in our study, improved test sensitivity without significant loss of specificity. Ten of 19 glaucoma patients, all with good acuity, and six of 19 glaucoma suspects failed with the modified scoring procedure. The desaturated version of the D-15 test with the modified scoring was even more sensitive (failing 14 of 18 glaucoma patients and 11 of 19 glaucoma suspects). We are unable to ac-
count for these results on the basis of pupil size or age.

REFERENCES