INFORMATION TO USERS

This manuscript has been reproduced from the microfilm master. UMI films the text directly from the original or copy submitted. Thus, some thesis and dissertation copies are in typewriter face, while others may be from any type of computer printer.

The quality of this reproduction is dependent upon the quality of the copy submitted. Broken or indistinct print, colored or poor quality illustrations and photographs, print bleedthrough, substandard margins, and improper alignment can adversely affect reproduction.

In the unlikely event that the author did not send UMI a complete manuscript and there are missing pages, these will be noted. Also, if unauthorized copyright material had to be removed, a note will indicate the deletion.

Oversize materials (e.g., maps, drawings, charts) are reproduced by sectioning the original, beginning at the upper left-hand corner and continuing from left to right in equal sections with small overlaps. Each original is also photographed in one exposure and is included in reduced form at the back of the book.

Photographs included in the original manuscript have been reproduced xerographically in this copy. Higher quality 6" x 9" black and white photographic prints are available for any photographs or illustrations appearing in this copy for an additional charge. Contact UMI directly to order.

U·M·I

University Microfilms International
A Bell & Howell Information Company
300 North Zeeb Road, Ann Arbor, MI 48106-1346 USA
313/761-4700 800/521-0600

Order Number 9505270

Psychophysical analysis of foveal visual losses in glaucoma

Pierce, Gilbert Eugene, Ph.D.

The Ohio State University, 1994

U·M·I
300 N. Zeeb Rd.
Ann Arbor, MI 48106

**PSYCHOPHYSICAL ANALYSIS OF FOVEAL VISUAL LOSSES IN
GLAUCOMA**

DISSERTATION

**Presented in Partial Fulfillment of the Requirements for the Degree of
Doctor of Philosophy in the Graduate School of
The Ohio State University**

by

Gilbert E. Pierce, O.D., M.S.

**The Ohio State University
1994**

**Dissertation Committee:
P.E. King-Smith, Ph.D.
R. Jones, O.D., Ph.D.
J. Schoessler, O.D., Ph. D.
C. Ingling, Ph.D.**

Approved by

Advisor

Department of Physiological Optics

ACKNOWLEDGEMENTS

I thank my advisor, Dr. Ewen King-Smith for his guidance and teaching throughout my graduate studies. Thanks also to Drs. Ronald Jones, John Schoessler, and Carl Ingling for their time and suggestions as members of the reading committee.

I thank Dr. Bob Derick of the OSU Ophthalmology Department for providing many of the patients involved in this study.

I thank Drs. Julie Preston, Michael Earley, and Scott Grigsby for all of their love, friendship, teaching, and support.

Finally, I thank my parents, Les and Doris Pierce, without whose love and support, I never could have finished.

VITA

April 24, 1963Born - Mansfield, Ohio

May, 1985B. A., Miami University,
Oxford, Ohio

June, 1989O.D., The Ohio State University
College of Optometry
Columbus, Ohio

June, 1992M.S., The Ohio State University
Graduate School
Columbus, Ohio

PUBLICATIONS

King-Smith P.E. and Pierce G.E.(1994): Unbiased estimate of the slope of the psychometric function. Invest. Ophthal. Vis. Sci. (ARVO Supplement) 35(4), p.1259.

Earley M.J., Pierce G.E. and King-Smith P.E.(1993): Analysis of spatial, temporal, and chromatic vision in human amblyopes. Invest. Ophthal. Vis. Sci. (ARVO Supplement) 34(4), p.711.

Pierce G.E. and King-Smith P.E.(1992): An experimental comparison of yes-no and forced choice threshold measurement techniques. Optometry and Vision Science (Academy Supplement) 69(12S), p.83.

Pierce G.E. and King-Smith P.E.(1992): Yes-no or two alternative forced choice. Which is the better clinical threshold technique? Invest. Ophthalm. Vis. Sci. (ARVO Supplement) 33(4), p.964.

FIELDS OF STUDY

Major Field: Physiological Optics

TABLE OF CONTENTS

ACKNOWLEDGEMENTS	ii
VITA	iii
LIST OF TABLES	iv
LIST OF FIGURES	vi
INTRODUCTION	1
PARALLEL PATHWAYS	4
VISUAL DEFICITS IN GLAUCOMA	9
METHODS	17
RESULTS	29
DISCUSSION	94
LIST OF REFERENCES	102

LIST OF TABLES

TABLE	PAGE
1. Photometric and colorimetric calibration of the three phosphors used in the Hitachi color monitor	18
2. Log losses for all subjects	30
3. Correlation coefficients for all losses	82
4. Correlation coefficients for selectivity of losses	82

LIST OF FIGURES

FIGURE	PAGE
1. Type III Wiesel and Hubel cell	4
2. Type I and II Wiesel and Hubel cells	6
3. The visual brain	7
4. Arcuate and nasal step visual field defects	11
5. Schematic diagram of the color mixture threshold apparatus	17
6. Chromaticity diagram showing the axes of modulation in the red-green and blue-yellow color mixture threshold experiments	19
7. Stimulus color space showing polar coordinate method used to describe stimulus color	20
8. Normal red-green color mixture threshold ellipse	22
9. Normal spatial contrast sensitivity function (CSF)	26
10. Normal temporal contrast sensitivity function (de Lange curve)	27
11. Red-green and blue-yellow color mixture threshold data for glaucoma patient WT	32
12. Red-green and blue-yellow color mixture threshold data for glaucoma patient DS	33

13.	Red-green and blue-yellow color mixture threshold data for glaucoma patient AJ	34
14.	Red-green and blue-yellow color mixture threshold data for glaucoma patient RW	35
15.	Red-green and blue-yellow color mixture threshold data for glaucoma patient CN	36
16.	Red-green and blue-yellow color mixture threshold data for glaucoma patient DM	37
17.	Red-green and blue-yellow color mixture threshold data for glaucoma patient TK	38
18.	Red-green and blue-yellow color mixture threshold data for glaucoma patient LO	39
19.	Red-green and blue-yellow color mixture threshold data for glaucoma patient KD	40
20.	Red-green and blue-yellow color mixture threshold data for glaucoma patient JM	41
21.	Red-green and blue-yellow color mixture threshold data for glaucoma patient MS	42
22.	Red-green and blue-yellow color mixture threshold data for glaucoma patient NJ	43
23.	Red-green and blue-yellow color mixture threshold data for glaucoma patient MS2	44
24.	Red-green and blue-yellow color mixture threshold data for glaucoma patient KHS	45

25.	Red-green and blue-yellow color mixture threshold data for glaucoma patient JT	46
26.	Red-green and blue-yellow color mixture threshold data for glaucoma patient JN	47
27.	Red-green and blue-yellow color mixture threshold data for glaucoma patient PR	48
28.	Red-green and blue-yellow color mixture threshold data for glaucoma patient SM	49
29.	Red-green and blue-yellow color mixture threshold data for glaucoma patient VJ	50
30.	Red-green and blue-yellow color mixture threshold data for glaucoma patient JG	51
31.	Red-green and blue-yellow color mixture threshold data for glaucoma patient LH	52
32.	Red-green and blue-yellow color mixture threshold data for glaucoma patient DK	53
33.	Red-green and blue-yellow color mixture threshold data for glaucoma patient JO	54
34.	Red-green and blue-yellow color mixture threshold data for glaucoma patient AS	55
35.	Spatial and temporal contrast sensitivity functions for patient WT ...	56
36.	Spatial and temporal contrast sensitivity functions for patient DS	57
37.	Spatial and temporal contrast sensitivity functions for patient AJ	58
38.	Spatial and temporal contrast sensitivity functions for patient RW ...	59

39.	Spatial and temporal contrast sensitivity functions for patient CN	60
40.	Spatial and temporal contrast sensitivity functions for patient DM ...	61
41.	Spatial and temporal contrast sensitivity functions for patient TK	62
42.	Spatial and temporal contrast sensitivity functions for patient LO	63
43.	Spatial and temporal contrast sensitivity functions for patient KD ...	64
44.	Spatial and temporal contrast sensitivity functions for patient JM	65
45.	Spatial and temporal contrast sensitivity functions for patient MS ...	66
46.	Spatial and temporal contrast sensitivity functions for patient NJ	67
47.	Spatial and temporal contrast sensitivity functions for patient MS2 .	68
48.	Spatial and temporal contrast sensitivity functions for patient KHS .	69
49.	Spatial and temporal contrast sensitivity functions for patient JT	70
50.	Spatial and temporal contrast sensitivity functions for patient JN	71
51.	Spatial and temporal contrast sensitivity functions for patient PR	72
52.	Spatial and temporal contrast sensitivity functions for patient SM ...	73
53.	Spatial and temporal contrast sensitivity functions for patient VJ	74
54.	Spatial and temporal contrast sensitivity functions for patient JG	75
55.	Spatial and temporal contrast sensitivity functions for patient LH	76
56.	Spatial and temporal contrast sensitivity functions for patient DK ...	77

57.	Spatial and temporal contrast sensitivity functions for patient JO	78
58.	Spatial and temporal contrast sensitivity functions for patient AS	79
59.	Histogram of number of eyes with significant losses	80
60.	Scatter plot of red-green color loss vs. achromatic loss	83
61.	Scatter plot of blue-yellow color loss vs. achromatic loss	84
62.	Scatter plot of red-green color loss vs. mean spatial contrast sensitivity loss	85
63.	Scatter plot of blue-yellow color loss vs. mean spatial contrast sensitivity loss	86
64.	Scatter plot of achromatic loss vs. mean spatial contrast sensitivity loss	87
65.	Scatter plot of achromatic loss vs. mean temporal contrast sensitivity loss	88
66.	Scatter plot of red-green color loss vs. mean temporal contrast sensitivity loss	89
67.	Scatter plot of blue-yellow color loss vs. mean temporal contrast sensitivity loss	90
68.	Scatter plot of achromatic loss vs. mean deviation of the visual field	91
69.	Scatter plot of temporal mean loss vs. spatial mean loss	92
70.	Scatter plot of red-green selectivity vs. slope of the spatial visuogram	93

INTRODUCTION

Glaucoma is a disease characterized by increased intraocular pressure, excavation and atrophy of the optic nerve head, and visual field defects (Stedman's Medical Dictionary, 1990). The underlying causes of glaucoma are widely varied, but it can most commonly be attributed to either an over-production of aqueous humor by the ciliary body, or to a reduction of outflow of aqueous from the anterior chamber. Regardless of its cause, the result is destruction of the optic nerve fibers. This loss of optic nerve fibers eventually leads to a loss of visual function.

The most common visual deficit noted in glaucoma is a relative loss of sensitivity of the peripheral visual field. However, Quigley et al. (1982), have suggested that up to 50% of optic nerve fibers are damaged before visual field defects are found. Therefore, it is desirable to discover more sensitive tests for the visual losses associated with glaucoma. Possible measurements that may be of benefit include those used in this study; color sensitivity, spatial contrast sensitivity, and temporal contrast sensitivity (i.e. flicker sensitivity or de Lange curves).

While glaucoma is traditionally associated with peripheral visual losses, measurements of central (foveal) visual function have been shown to be sensitive to early optic nerve disease as well (Alvarez et al., 1994, Arden and Jacobson, 1978, Ross, et al, 1981). Specifically, measurements of losses

of blue-yellow color vision, mid-spatial frequency contrast sensitivity, and high temporal frequency flicker sensitivity have been suggested as valuable tests.

An important question to be asked is what types of optic nerve fibers are damaged in glaucoma? It has been suggested (Quigley, et al, 1987, Quigley, et al, 1988, Quigley, et al, 1989, Quigley, et al, 1991, Glovinsky et al, 1991) in anatomical studies of experimental glaucoma in monkeys, that M-cells, or the larger optic nerve fibers are selectively damaged in glaucoma. Others (Alvarez, et al., 1994) have suggested, based on psychophysical evidence, a relatively selective loss of P-cells, which are the small retinal ganglion cells.

Given the confusion concerning the types of damage associated with glaucoma, it is hoped that this study can answer two important questions: 1) can tests of central vision detect early deficits in glaucoma, perhaps before visual field loss?, and 2) which type of retinal ganglion cell, M or P is damaged more readily in glaucoma patients?

PARALLEL PATHWAYS

Strong evidence exists that the mammalian visual system uses parallel processing to convey visual information. Two primary channels, the magnocellular and parvocellular, are used to carry information from the retina to the lateral geniculate nucleus, and subsequently to the primary visual cortex and visual association areas. These names, magnocellular and parvocellular come from the relative sizes of cell bodies in the two pathways at the LGN. This parallel design allows more efficient processing of the information carried in a visual scene. The magno channel can carry information about motion and coarse detail, while the parvo channel carries information about color and fine detail.

The magno channel, as the name suggests, has larger axons and cell bodies than does the parvo channel. The retinal ganglion cells that input to the magno channel are primarily Wiesel and Hubel type III cells (Wiesel and Hubel, 1966). These ganglion cells have large receptive fields due to their large dendritic spread, and are therefore sometimes referred to as parasol cells. They are also referred to as M-cells or P_{α} cells. Their receptive fields are typically 2.5 to 3 times larger than those of a parvo cell at the same retinal eccentricity (de Monasterio and Gouras, 1975). These receptive fields are spatially opponent, giving them a band-pass character, but are not color opponent. This is because both red and green (long wavelength sensitive and middle wavelength sensitive) cones input into both the center and surround

portions of the receptive field (see Figure 1). M-cells constitute about 10% of the total retinal ganglion cells, and are fairly evenly distributed throughout the retina (Bassi and Lehmkuhle, 1990).

Figure 1: Type III Wiesel and Hubel cell. This cell is spatially opponent, but achromatic. (See text for details.)

M-ganglion cells from the retina synapse in layers 1 and 2 of the dorsal lateral geniculate nucleus (the two most ventral layers). As mentioned previously, these layers contain cell bodies larger than those in the other layers, hence the name magnocellular. After synapsing in the LGN, the magno channel axons project to layer 4C α of primary visual cortex (V1). The magnocellular pathway, due to its anatomical and physiological

characteristics, is thought to carry information about luminance (especially at low spatial frequencies) and motion. It is also believed by some to be responsible for conveying information of some higher level visual functions, such as depth perception and contrast sensitivity (Livingstone and Hubel, 1988).

The retinal ganglion cells of the parvocellular channel have smaller axons and cell bodies than do the magno cells. P-cells of the retina are typically type I and type II Wiesel and Hubel cells (Wiesel and Hubel, 1966). Type I cells are both spatially and color opponent. In other words, they have center-surround organization with different cone types represented in the center than those in the surround. Type II cells are color opponent, but not spatially opponent. Figure 2 shows a schematic diagram of type I and type II cells. Type I cells are highly concentrated at the fovea and decrease gradually in number with increasing retinal eccentricity. Cells of the parvo channel are often called P-cells, midget cells, or $P\beta$ cells. The two types of P-cells combined comprise about 80% of the retinal ganglion cells (Bassi and Lehmkuhle, 1990).

P-ganglion cells synapse in the dorsal layers 3,4,5, and 6 of the LGN. As mentioned before, the cell bodies in these layers are smaller than the two ventral layers (hence the name parvocellular). After synapsing at the LGN, the parvocellular axons project to layer 4C β of primary visual cortex. P-cells can carry information about color (which M-cells do not) and also carry information about high spatial frequencies (fine detail) due to their small

receptive field size. Figure 3 shows a schematic diagram of the parallel channels of the visual system from retina to cortex.

Considerable debate exists as to how luminance information is carried to visual cortex. As the M-cells are spatially opponent, but not color

Figure 2. Type I and type II Wiesel and Hubel cells. See text for details.

opponent, it is obvious that they are capable of carrying information about luminance contrast. Several investigators have suggested that only the magno channel is capable of carrying luminance information, and that any visual percepts that are lost with equiluminant stimuli (stimuli which contain only chromatic contrast) must be carried by the magno channel (Livingstone and Hubel, 1988). However, others have demonstrated that the parvocellular channel is also capable of carrying luminance information, and that these

Figure 3. The visual brain (after Livingstone and Hubel, 1988) showing the segregation of the parallel visual pathways. See text for details.

visual percepts which disappear at equiluminance may be carried by the luminance sensitive portion of the parvocellular channel (Ingling and Martinez, 1983, Ingling and Grigsby, 1989).

There is strong evidence that the visual system maintains this parallel organization after reaching cortex. From layer 4C, the parvo pathway projects to the “blobs” and “interblobs” in layer 2 and 3 of V1. Blobs are areas that stain deeply for cytochrome oxidase, and are thought to process primarily information about color. Interblobs are regions which stain poorly for cytochrome oxidase, and are thought to process information about fine detail and form. The magno projections from 4C α are primarily to layer 4B. From V1, the magno and parvo pathways seem to maintain segregation into area V2 (see Figure 3). This segregation is somewhat maintained even in higher levels of cortex, although there are massive interconnections among the higher visual areas of the brain (Van Essen, et al, 19). This concept of parallel processing in the visual system is important in the present study, because it is well known that diseases which affect the optic nerve (including glaucoma) may selectively affect either the M or P retinal ganglion cells.

VISUAL DEFICITS IN GLAUCOMA

Glaucoma is a family of diseases of the optic nerve that results in destruction of nerve fibers. The destruction is normally thought to be caused by intraocular pressure that is significantly above normal levels. There are two significant theories of how damage to the optic nerve head occurs in glaucoma. The first theory is that the damage is due to ischemia of the nerve head. In this theory the damage is caused by an interruption in the microcirculation of the nerve head. It is the difference between the intraocular pressure and the perfusion pressure of the nerve head that is important according to this theory. The second theory is that the damage is a direct result of the mechanical pressure on the nerve head itself (Kanski, 1987).

Glaucoma is commonly diagnosed by using a combination of clinical tests. The three most important tests performed are 1) measurement of intraocular pressure, 2) ophthalmoscopic observation of the optic nerve head, and 3) threshold visual fields. Intraocular pressures above 22mm of mercury are typically thought of as cause for concern, although this is only a rough guideline. Quite often, patients can maintain a pressure in the mid-twenties or higher for long periods without suffering glaucomatous damage. Conversely, many suffer from “low-tension” or, more properly, “normal-tension” glaucoma, in which the pressure is well within the normal range,

yet glaucomatous damage does occur. In these patients, it is believed that the optic nerve can only tolerate pressures well below the upper end of the normal range. On ophthalmoscopy, a cup-disc ratio of greater than 0.5, or a “notch” in the rim tissue of the optic cup may be indicative of glaucoma. Also, an asymmetry in cup-disc ratio between the two eyes may indicate glaucomatous damage in the eye with the larger cup. Visual fields are currently the diagnostic tool of choice in glaucoma. However, this is potentially a very difficult test to evaluate.

Visual fields for assessment and diagnosis of glaucoma are typically done with an automated perimeter. There are several advantages of automated perimetry over manual. The most significant advantages are good repeatability, good detectability, and easy follow-up (Flammer, et al., 1985). What makes the assessment of visual fields in glaucoma difficult is that there is really no definitive type of field loss in glaucoma. Drance (1991) has found that a diffuse loss of sensitivity throughout the visual field may precede localized defects, although others have found that this is not the case (Heijl; 1989). It has been suggested (Lachenmayr, et al., 1990) that diffuse loss of sensitivity may be strongly related to intraocular pressure level.

Among localized visual field defects, arcuate losses (due to nerve fiber bundle losses), and nasal steps (loss of sensitivity in the inferior nasal quadrant) are the “classical” field losses associated with glaucoma (Drance, 1985). These two types of field loss are shown in Figure 4. The most common defect is of the superior arcuate (Bjerrum) type (Hart and Becker 1982). While visual field loss is still the most common criterion for

beginning treatment, it is well known that there may be a significant loss of optic nerve fibers before a visual field defect is detected (Quigley et al., 1989).

Figure 4. Arcuate (A) and nasal step (B) visual field defects. These are the two most common localized visual field deficits in glaucoma.

Recently other clinical tests have been shown to be effective in detection of glaucoma. These include contrast sensitivity (Korth et al, 1989), pattern electroretinograms (Odom et al, 1990), and blue-on-yellow perimetry (Johnson et al, 1993a and b).

EVIDENCE FOR SELECTIVE M CELL LOSS

Anatomical, psychophysical and electrophysiological evidence have all been used to suggest that the large (M) cells are selectively damaged in both experimental and human glaucoma. Quigley et al. (1987) showed a relatively selective reduction of large cell axons anatomically in experimental glaucoma in monkeys (though no fiber size was completely spared). This was also demonstrated in post-mortem histological studies in human glaucoma (Quigley et al., 1988). Glovinsky et al. (1991, 1993) also reported a greater loss of large than small cells (both at the fovea and in peripheral retina) in experimental glaucoma, especially in early and middle stages of the disease. A selective blockage of axonal transport to the magnocellular layers of the LGN (suggesting selective damage to large cells or their axons) has also been demonstrated in experimental glaucoma (Dandona, et al., 1991)

Psychophysical evidence used to support a selective loss of large cells typically involves the use of motion or flicker perception. Tyler et al. (1981) showed that 90% of the glaucomatous and ocular hypertensive eyes studied had flicker sensitivity losses at temporal frequencies of 30-40 Hz prior to any visual field loss. Casson et al. (1993), using temporal modulation

perimetry, showed flicker sensitivity losses throughout the visual field in glaucoma patients and ocular hypertensives. Breton, et al. (1991) reported temporal contrast sensitivity losses centered at a frequency of 15 Hz in glaucoma patients. Tytla, et al. (1990) demonstrated temporal contrast sensitivity losses in primary open angle glaucoma patients and in some ocular hypertensives. Brussel et al. (1986) used a technique known as multi-flash campimetry to show a loss of temporal resolving power in glaucomatous eyes. Tyler et al.(1984) demonstrated that losses of flicker sensitivity are correlated moderately well with intraocular pressure in normal observers, suggesting that elevated IOPs may affect temporal contrast sensitivity. With regard to motion sensitivity, deficits have also been shown in glaucoma and ocular hypertension (Fitzke, et al. 1989; Silverman et al., 1990). As both motion and flicker sensitivity are thought to be mediated primarily by the magno pathway, all of these reports suggest damage primarily to M cells.

Electrophysiological evidence may also suggest a relatively selective destruction of large cells. As with psychophysical data, high temporal frequency losses have also been demonstrated with pattern electroretinograms (Trick, 1985; Odom, et al., 1990) Also, Schmeisser and Smith (1989), using VEPs have shown losses in sensitivity to high temporal frequencies.

EVIDENCE FOR SELECTIVE P CELL LOSS

Contrary to the above evidence, a large body of evidence, primarily but not exclusively psychophysical, exists suggesting a relatively selective loss of P ganglion cells from the optic nerve in glaucoma. Much of this evidence implies a loss of type II Wiesel and Hubel cells signaling blue-yellow color vision, but there is also evidence for an early loss of type I cells, signaling red-green opponent processes.

Among the evidence for blue-yellow losses, most was obtained using threshold perimetry. Heron, Adams and Husted (1988) tested central visual fields for the short wavelength sensitive (blue) pathways in glaucoma patients and ocular hypertensives. They found evidence for both local and diffuse loss of blue sensitive processes. Johnson et al. (1989) found that short wavelength sensitive field losses were slightly more frequent than field losses measured with white-on-white perimetry in glaucoma patients. Hart et al. (1990) found that for moderately mild visual field defects, blue-on-yellow perimetry showed greater impairment than white-on-white, while for deeper defects, the two types showed nearly equivalent losses. This would suggest that the blue-yellow chromatic loss precedes the achromatic loss. Flanagan et al. (1990) found that early primary open angle glaucoma patients had abnormal visual field scores which were twice as great with blue-on-yellow perimetry than with white-on-white perimetry. Sample et al. (1993) showed that short wavelength sensitive visual fields tests identified early functional losses in ocular hypertensive eyes at greatest risk for developing primary

open angle glaucoma. Possibly the most convincing evidence is from Johnson et al. (1993 a and b) who showed that blue-on-yellow perimetry is superior to white-on white perimetry both at diagnosing glaucoma and in following changes in sensitivity over time. In fact, the evidence for the value of blue-on-yellow visual fields in glaucoma is so strong that Humphrey instruments has begun manufacturing auto-perimeters with blue-on-yellow capabilities built in. Previously the perimeters would have to be individually modified for this purpose.

Other evidence for blue-yellow losses is found in spectral sensitivity measurements (Yamazaki et al., 1988, Zwas et al., 1991, Tamaki et al., 1991), visual evoked potentials (Korth et al, 1994) and in measurements using common clinical techniques, such as Farnsworth-Maunsell 100 Hue test (Pooinsawmy et al., 1980, Sample et al., 1986, Lakowski and Drance, 1979, Hamill et al., 1984, Drance et al., 1991) and the Pickford anomaloscope (Airaksinen et al., 1986, Motolko et al., 1982, Hamill et al. 1984, Drance et al., 1981).

Red-green color vision losses, corresponding to damage to type I retinal ganglion cells, have also been demonstrated in early glaucoma. Motolko et al. (1982) found, using an anomaloscope, that six out of fourteen early glaucoma patients showed a disturbance in red-green matching. Lakowski and Drance, as mentioned previously, found significant error scores on the 100 Hue testing all color ranges in glaucoma patients. Red-green flicker has also been shown to be sensitive to early glaucoma (Brussel et al., 1989). Alvarez et al (1994), using the color mixture threshold

technique, found that both red-green and blue-yellow chromatic losses preceded achromatic losses in early glaucoma.

Thus, there is significant confusion and disagreement as to what type of nerve fibers are lost first in glaucoma. It is the aim of this study to help identify the types of nerve fibers affected by measuring chromatic and achromatic thresholds (color-mixture thresholds) as well as spatial and temporal contrast sensitivity functions.

METHODS

The experiments performed on each patient included color-mixture thresholds (red-green and blue-yellow), (Vingrys and King-Smith, 1986, King-Smith et al., 1987, Grigsby et al., 1991) spatial contrast sensitivity functions, and temporal contrast sensitivity functions (de Lange curves). It has been demonstrated (Grigsby et al., 1991) that the combination of these four tests can discriminate well between large and small cell losses in optic nerve disease.

COLOR-MIXTURE THRESHOLDS

Color mixture thresholds were measured using the method of King-Smith et al., 1987, and Sellers et al., 1986. The stimuli were 1 degree foveal test spots generated on a Hitachi 2719 color television monitor driven by a North-Star Horizon computer (see Figure 5 for a schematic of the system).

Figure 5. Schematic diagram of the Color Mixture Threshold apparatus.

The spots were presented for 200msec on a uniform background of 50cd/m². Table 1 gives the photometric and colorimetric calibration of the red, green, and blue phosphors of the color television display. The monitor was viewed from a distance of 2m at which it subtended 10° by 8°. The monitor was surrounded by a white screen subtending 30° by 20° which matched the monitor in color and luminance. One degree test spots of a wide variety of colors and luminances were generated using Motorola MC1495 analog multipliers allowing independent modulation of the three television phosphors. Red, green, and blue phosphor positions in C.I.E. color space are shown in Figure 6.

TABLE 1

Photometric and colorimetric calibration of the three phosphors used in the Hitachi color monitor measured with a Pritchard 1980 photometer. (from King-Smith et al. 1987)

Phosphor	1931 CIE chromaticity coordinates			Photopic Luminance (cd/m ²)
	x	y	z	
Red	0.617	0.345	0.038	11.0
Green	0.334	0.581	0.085	32.7
Blue	0.162	0.081	0.757	5.6
Combination (white)	0.315	0.313	0.372	49.3

The outputs of the combination of the three phosphors can be described by using a sphere denoting a three dimensional color space (Figure 6). The outputs of each phosphor are represented by the axes of the sphere (Vingrys and King-Smith, 1986). By using this color sphere, both increments and decrements of the outputs of the three phosphors may be visualized. In relation to the output creating the achromatic background luminance of 50cd/m^2 , the output of each phosphor may be either increased or decreased. In this manner, test spots of any color and luminance which fall within the sphere may be generated.

Figure 7: Stimulus color space showing polar coordinate method used to describe stimulus color (ϕ = red/green angle, θ = blue/yellow angle). (modified from Vingrys and King-Smith, 1986).

In this polar coordinate system, any stimulus may be described by three parameters: the angle subtended between the R and G axes (ϕ), the angle subtended by the R/G plane and the blue axis (the blue-yellow angle θ), and the length of the vector OP. The vector OP describes the contrast amplitude and is defined by:

$$\overline{OP} = \sqrt{R^2 + G^2 + B^2} \quad (1)$$

where R, G, and B are the individual phosphor contrasts, which are defined as:

$$R = \Delta R / R_b \quad G = \Delta G / G_b \quad B = \Delta B / B_b \quad (2)$$

where ΔR , ΔG and ΔB are the differences between the stimulus and background luminance for each phosphor, and R_b , G_b , and B_b , are the background phosphor luminances.

Two types of color mixture thresholds were measured on each patient, red-green, and blue-yellow. During the red-green color mixture threshold measurements the blue phosphor is maintained at its background output level. The red and green phosphors are independently modulated to produce stimuli that fall only in the red-green plane of the color sphere. All stimuli in this test can then be plotted two dimensionally, i.e. contrast of the green phosphor is plotted as a function of contrast of the red phosphor (see Figure 8).

In this two-dimensional coordinate system, it can be readily seen that both incremental (1st quadrant) and decremental (3rd quadrant) stimuli may be generated. In the first quadrant, the outputs of both the red and green

phosphors are being increased, producing spots of a higher luminance than the background. In the third quadrant, the outputs of both phosphors are being decreased, producing spots of a lower luminance than the background. In the second quadrant, the green phosphor output is increased, while the red phosphor output is decreased. Similarly, in the fourth quadrant, the red phosphor output is increased, while the green phosphor output is decreased.

Figure 8: Normal red/green color mixture threshold ellipse (from King-Smith, et al, 1987).

In this manner, stimuli which do not differ from the background luminance,(equiluminant stimuli) but are merely “greener” or “redder” than the background may be generated. For observers with normal color vision an equiluminant red spot falls on a line at an angle of about -20° , while an equiluminant green spot falls at an angle of about 160° . Modulation along this equiluminant line should provide a constant stimulation of the blue cones, and thus modulate only the red and green cones. This equiluminant line falls on the r-g (constant b cone stimulation) line in C.I.E. color space.

For the blue-yellow color mixture thresholds, blue contrast refers to the output of the blue phosphor, while yellow contrast refers to the combination of the outputs of the red and green phosphors. As with the red-green mixtures, stimuli can be either incremental or decremental in luminance relative to the background, or may be equiluminant with respect to the background. The blue-yellow equiluminant angle may also be represented in C.I.E. color space (Figure 6).

Thresholds were measured for each stimulus using ZEST (King-Smith et al., 1994), a modification of QUEST (Watson and Pelli, 1983). ZEST is an acronym for “zippy estimation by sequential testing,” and is an efficient adaptive psychophysical method. To describe briefly, it is a Bayesian adaptive procedure in which the use of prior knowledge (in the form of the prior probability density function, or pdf) is used to help determine the intensity of the subsequent stimulus (Pierce, 1992). Each stimulus is presented at the **mean** of the prior pdf (as opposed to the **mode** in QUEST). After the observer’s response, the prior pdf is multiplied by a likelihood

function (either a “yes” or “no” function based on the observer’s response) to calculate a new probability density function, the posterior pdf. This then becomes the prior pdf for the next stimulus which is presented at its mean value. After a given number of trials (in the case of this study, 8) the measurement is terminated, and the threshold estimate is the mean of the final posterior pdf.

For the color mixture thresholds, 32 different stimuli are used (16 each for red-green and blue-yellow mixtures). In addition two blank trials are included in each cycle, to monitor a false-positive response rate. Any experiment with a false positive rate of greater than 15% was repeated. Each of the 32 stimuli corresponds to a given mixture of phosphor contrasts, which in turn corresponds to a given angle in either the red-green or blue-yellow color space. Once the threshold for each of these stimuli is determined, an ellipse is fitted to the plotted data using a least-squares method (Figure 8). In the typical ellipse, the length can be considered a measure of color sensitivity, and the width a measure of luminance sensitivity. This is because the long axis of the ellipse normally falls near the equiluminous angle, so modulation along this axis would be changing the color of the stimulus without affecting its luminance. Similarly, the short axis, or width of the ellipse, typically falls at an angle where the phosphors are being either brightened or dimmed equally, changing the luminance of the stimulus without affecting its color. Thus, the observer’s sensitivities to both chromatic and achromatic contrast differences can be determined by this method. The chromatic sensitivity is determined solely by function of

the parvocellular pathway. The achromatic sensitivity is determined by contributions from both the magnocellular and parvocellular pathways (Ingling and Grigsby, 1990, Ingling and Martinez, 1983). Length, width, and length-width ratios can typically be used as measures of chromatic sensitivity, achromatic sensitivity, and selectivity of visual loss, respectively. In cases where the length is not a good indicator of chromatic sensitivity (cases where the ellipse is nearly round or is elongated along the luminance axis) the pre-determined angle of -20° is used to determine the chromatic (color) sensitivity. In these cases, 45° is used as the angle to determine achromatic (luminance) sensitivity.

SPATIAL CONTRAST SENSITIVITY FUNCTIONS

Spatial contrast sensitivity functions (CSFs) were measured for each patient using sine-wave gratings generated on a Tektronix 608 oscilloscope (P31 phosphor). The oscilloscope was driven by a North Star Horizon computer. The screen subtended 3.5° by 2.75° at the two meter viewing distance. The monitor was surrounded by a screen measuring 20° by 30° which matched the luminance of the oscilloscope screen. Contrast thresholds were determined for gratings ranging from 1 cycle/degree to 25 cycles /degree (11 spatial frequencies in all). All gratings were matched in space average luminance (50cd/m^2). Gratings were presented for 0.5 seconds within a rectilinear temporal envelope. Thresholds were determined in 8 trials using the ZEST procedure previously described. A cutoff frequency was also measured for each eye at 89% contrast. As with the color-mixture

thresholds, only experiments with false positive rates of less than 15% were accepted. Sensitivities were compared to age-matched normal data to determine the extent and type of loss. Figure 9 shows a typical normal CSF curve.

Figure 9: Normal spatial contrast sensitivity function (CSF)

TEMPORAL CONTRAST SENSITIVITY MEASUREMENTS

Temporal contrast sensitivity functions (deLange curves) were measured on the same apparatus as the spatial CSFs. A uniform field flicker of 1 second total duration was presented in a raised cosine envelope. Sensitivities were measured for sinusoidally temporally modulated stimuli

flickering from 1 to 30 Hz (11 temporal frequencies). A flicker fusion frequency was measured as well. Thresholds were again determined using ZEST, and data were again compared to age matched norms to determine loss. Figure 10 shows a typical deLange curve.

Figure 10: Normal temporal contrast sensitivity function (deLange curve)

SUBJECTS

During the current study, ten patients were recruited from the Ohio State University College of Optometry and Department of Ophthalmology. Both eyes of each subject were tested using the four procedures described above. Seven of the subjects were currently being treated for glaucoma. The diagnosis of glaucoma in these patients was based on the clinical decision making process of the clinician that was treating them. All patients had elevated intraocular pressures (pre-treatment of 22mm Hg or greater), optic nerve head cupping (vertical C/D of 0.6 or greater, or notching of the rim of the cup), and visual field loss (significant Mean Deviation, Corrected Pattern Standard Deviation or both on Humphrey 24-2 or 30-2 threshold visual field programs). The 3 glaucoma suspects included had elevated IOP and cupping, but without significant visual field defects. All patients had best corrected visual acuity of 20/40 or better in each eye, had no significant media opacities, and had no diabetes. No patients using miotic medications for the treatment of glaucoma were included in the study.

Previous data collected in our lab were also included in the analysis. Twenty eyes of fourteen glaucoma patients were measured over the last several years on all four of the above mentioned tests. These patients all had similar inclusion criteria to the patients which were tested during the current study.

RESULTS

Results for the 24 subjects included in the study are summarized in table 2. Log losses for all of the measurements are shown in the table with all significant losses ($P < 0.05$) from age matched normals marked with an asterisk.

Color mixture threshold ellipses for all subjects are displayed in Figures 11-34. In each figure, the red-green color mixture data are shown in the left panel, and the blue-yellow color mixture data are shown in the right panel. Results for the right are plotted with diamonds and solid lines, and results for the left eye are plotted with squares and dotted lines. Age matched normal averages, and 98th percentile age matched normals are plotted with dashed lines and labeled on each ellipse. The log chromatic loss, log luminance loss, and log chromatic/luminance ratio (C/L) for each subject are listed in table 2.

The spatial and temporal contrast sensitivity measurements for all subjects are shown in figures 35-48. The spatial CSFs are plotted in the left half of each figure, and the temporal CSFs (deLange curves) are plotted in the right half of each figure. The top panel of each plot is the actual contrast sensitivity measurement. Shown below the measurements are the spatial and temporal visuograms. Visuograms are calculated by taking the ratio of age matched normal data/patient data for each measured frequency. Losses in sensitivity will plot as positive values in the visuogram. Right eye data are

plotted with diamonds and solid curves, and left eye data are plotted with squares and dotted curves. Age matched normal curves are shown for comparison.

TABLE 2

Log losses for red-green and blue-yellow color mixture thresholds, and spatial and temporal contrast sensitivity functions for all patients included in the study. Right eye is listed first for each patient. If only one eye was tested, it is marked R or L. Significant losses are marked with an asterisk (*). C/L ratios selective for luminance and slopes selective for low frequencies are marked with a pound sign (#)

	RED-GREEN			BLUE-YELLOW			SPATIAL		TEMPORAL	
SUB	COL	LUM	C/L	COL	LUM	C/L	MEAN	SLOPE	MEAN	SLOPE
WT	-.036	-.06	.024	-.242	-.024	-.228	-.076	-.003	.09	-.001
	-.086	.09	-.176	-.132	.066	-.198	.256	.024	.248	.003
DS	0	-.253	.234*	.053	-.098	.151	-.107	-.001	.057	.014*
	.049	-.045	.104	.123	-.168	.301*	.031	-.002	.036	.014*
AJ	-.076	-.142	.066	-.033	-.101	.067	.138	.002	.201*	-.008
	-.106	.008	-.114	-.073	-.031	-.043	.179	.010	.293*	-.010
RW	.244*	.163	.081	.12	.104	.026	.496*	.046*	.205	.006
	.454*	.433*	.031	.45*	.344*	.096	.583*	.025	.614*	.011
CN	-.06	-.01	-.059	.156	.018	.138	.019	-.009	.146*	.005
	.02	.13	-.109	.166*	.148	.018	.329	.027	.227*	.009
DM	-.05	-.078	.017	-.163	-.143	-.02	-.096	-.025	.182	.010*
	-.02	-.128	.107	-.203	-.053	-.16	-.133	-.015	.121	.012*
TK	-.13	-.068	-.053	-.143	-.093	-.05	-.179	-.020	-.09	.001
	-.09	-.038	-.063	-.113	-.013	-.11	.144	.008	-.047	.001
LO	-.033	-.079	.036	-.107	-.14	.033	-.066	.009	.019	.001
	.027	.041	-.014	-.087	.02	-.107	-.346	-.035*	-.095	-.001

TABLE 2
(continued)

SUB	RED-GREEN			BLUE-YELLOW			SPATIAL		TEMPORAL	
	COL	LUM	C/L	COL	LUM	C/L	MEAN	SLOPE	MEAN	SLOPE
KD	.102	-.077	.179*	-.099	-.076	-.023	.432*	.011	.099	-.003
	.032	-.027	.059	-.039	-.056	.0147	.044	.002	.12	-.002
JM	.077	-.049	.126	.093	-.02	.113	-.078	.007	-.144	.007
	-.133	-.099	-.034	-.187	-.09	-.087	-.051	-.012	-.191	.002
MS(R)	.152	.123	.028	.024	.184	-.17	.502*	.040*	.435*	-.005
NJ(L)	.216*	.121	.095	.075	.164	-.089	-.115	-.025#	-.159	-.003
MS2	.401*	.067	.323*	.199	.086	.113	.13	.006	.516*	-.026#
	.551*	.217	.323*	.379*	.216	.163	.30	.030	.564*	-.020#
KHS(R)	.969*	.059	.921*	.878*	.103	.774*	.279	-.013	.064	.008
JT(L)	1.79*	1.42*	.37*	1.623*	1.413*	.21	1.233*	.157*	.962*	.033*
JN(L)	.144	.137	.007	.329*	.089	.241	.77*	.048*	.148	.033*
PR	-.158	.053	-.211#	.001	.044	-.043	-.115	-.014	-.316	-.003
	.212	.533*	-.321#	.401*	.534*	-.143	.761*	.001	.436*	.007
SM	.486*	.051	.436*	.289*	.009	.280*	.040	.004	.265	.013*
	.436*	.011	.426*	.399*	-.011	.410*	-.009	.004	.309*	.009
VJ	1.381*	.934*	.446*	1.391*	.87*	.52*	1.024*	.030	1.031*	.040*
	.861*	.474*	.386*	.571*	.43*	.15	.682*	.024	.744*	.011*
JG(R)	1.480*	.689*	.72*	1.557*	.549*	1.208*	.935*	.111*	.382*	.013*
LH(R)	.303*	.08	.223*	.241	.172	.07	.583*	.011	.152	-.011#
DK	.114	.207	-.093	-.071	.139	-.199	.136	.004	.073	.015*
	.214*	.207	.017	.069	.139	-.079	.458*	.026*	.095	.020*
JO(R)	.98*	.612*	.367*	.777*	.667*	.110	1.041*	.093*	.796*	.023*
AS	.644*	.147	.497*	.549*	.179	.371*	.340*	.017*	.015	-.004
	.474*	.257*	.217*	.389*	.289*	.101	.236	.003	.025	-.006

Figure 11: Red-green and blue-yellow color mixture threshold data for glaucoma patient WT. Right eye data are plotted with diamonds and solid curves. Left eye data are plotted with squares and dotted curves. Age matched normal average and 98th percentile age matched normal data are plotted for comparison.

Figure 12: Red-green and blue-yellow color mixture threshold data for glaucoma patient DS. Right eye data are plotted with diamonds and solid curves. Left eye data are plotted with squares and dotted curves. Age matched normal average and 98th percentile age matched normal data are plotted for comparison.

Figure 13: Red-green and blue-yellow color mixture threshold data for glaucoma patient AJ. Right eye data are plotted with diamonds and solid curves. Left eye data are plotted with squares and dotted curves. Age matched normal average and 98th percentile age matched normal data are plotted for comparison.

Figure 14: Red-green and blue-yellow color mixture threshold data for glaucoma patient RW. Right eye data are plotted with diamonds and solid curves. Left eye data are plotted with squares and dotted curves. Age matched normal average and 98th percentile age matched normal data are plotted for comparison.

Figure 15: Red-green and blue-yellow color mixture threshold data for glaucoma patient CN. Right eye data are plotted with diamonds and solid curves. Left eye data are plotted with squares and dotted curves. Age matched normal average and 98th percentile age matched normal data are plotted for comparison.

Figure 16: Red-green and blue-yellow color mixture threshold data for glaucoma patient DM. Right eye data are plotted with diamonds and solid curves. Left eye data are plotted with squares and dotted curves. Age matched normal average and 98th percentile age matched normal data are plotted for comparison.

Figure 17: Red-green and blue-yellow color mixture threshold data for glaucoma patient TK. Right eye data are plotted with diamonds and solid curves. Left eye data are plotted with squares and dotted curves. Age matched normal average and 98th percentile age matched normal data are plotted for comparison.

Figure 18: Red-green and blue-yellow color mixture threshold data for glaucoma patient LO. Right eye data are plotted with diamonds and solid curves. Left eye data are plotted with squares and dotted curves. Age matched normal average and 98th percentile age matched normal data are plotted for comparison.

Figure 19: Red-green and blue-yellow color mixture threshold data for glaucoma patient KD. Right eye data are plotted with diamonds and solid curves. Left eye data are plotted with squares and dotted curves. Age matched normal average and 98th percentile age matched normal data are plotted for comparison.

Figure 20: Red-green and blue-yellow color mixture threshold data for glaucoma patient JM. Right eye data are plotted with diamonds and solid curves. Left eye data are plotted with squares and dotted curves. Age matched normal average and 98th percentile age matched normal data are plotted for comparison.

Figure 21: Red-green and blue-yellow color mixture threshold data for glaucoma patient MS. Right eye data are plotted with diamonds and solid curves. Left eye data are not available for this patient. Age matched normal average and 98th percentile age matched normal data are plotted for comparison.

Figure 22: Red-green and blue-yellow color mixture threshold data for glaucoma patient NJ. Right eye data are not available for this patient. Left eye data are plotted with squares and dotted curves. Age matched normal average and 98th percentile age matched normal data are plotted for comparison.

Figure 23: Red-green and blue-yellow color mixture threshold data for glaucoma patient MS2. Right eye data are plotted with diamonds and solid curves. Left eye data are plotted with squares and dotted curves. Age matched normal average and 98th percentile age matched normal data are plotted for comparison.

Figure 24: Red-green and blue-yellow color mixture threshold data for glaucoma patient KHS. Right eye data are plotted with diamonds and solid curves. Left eye data are not available for this patient. Age matched normal average and 98th percentile age matched normal data are plotted for comparison.

Figure 25: Red-green and blue-yellow color mixture threshold data for glaucoma patient JT. Right eye data are not available for this patient. Left eye data are plotted with squares and dotted curves. Age matched normal average and 98th percentile age matched normal data are plotted for comparison.

Figure 26: Red-green and blue-yellow color mixture threshold data for glaucoma patient JN. Right eye data are not available for this patient. Left eye data are plotted with squares and dotted curves. Age matched normal average and 98th percentile age matched normal data are plotted for comparison.

Figure 27: Red-green and blue-yellow color mixture threshold data for glaucoma patient PR. Right eye data are plotted with diamonds and solid curves. Left eye data are plotted with squares and dotted curves. Age matched normal average and 98th percentile age matched normal data are plotted for comparison.

Figure 28: Red-green and blue-yellow color mixture threshold data for glaucoma patient SM. Right eye data are plotted with diamonds and solid curves. Left eye data are plotted with squares and dotted curves. Age matched normal average and 98th percentile age matched normal data are plotted for comparison.

Figure 29: Red-green and blue-yellow color mixture threshold data for glaucoma patient VJ. Right eye data are plotted with diamonds and solid curves. Left eye data are plotted with squares and dotted curves. Age matched normal average and 98th percentile age matched normal data are plotted for comparison.

Figure 30: Red-green and blue-yellow color mixture threshold data for glaucoma patient JG. Right eye data are plotted with diamonds and solid curves. Left eye data are not available for this patient. Age matched normal average and 98th percentile age matched normal data are plotted for comparison.

Figure 31: Red-green and blue-yellow color mixture threshold data for glaucoma patient LH. Right eye data are plotted with diamonds and solid curves. Left eye data are not available for this patient. Age matched normal average and 98th percentile age matched normal data are plotted for comparison.

Figure 32: Red-green and blue-yellow color mixture threshold data for glaucoma patient DK. Right eye data are plotted with diamonds and solid curves. Left eye data are plotted with squares and dotted curves. Age matched normal average and 98th percentile age matched normal data are plotted for comparison.

Figure 33: Red-green and blue-yellow color mixture threshold data for glaucoma patient JO. Right eye data are plotted with diamonds and solid curves. Left eye data are not available for this patient. Age matched normal average and 98th percentile age matched normal data are plotted for comparison.

Figure 34: Red-green and blue-yellow color mixture threshold data for glaucoma patient AS. Right eye data are plotted with diamonds and solid curves. Left eye data are plotted with squares and dotted curves. Age matched normal average and 98th percentile age matched normal data are plotted for comparison.

Figure 35: Spatial and temporal contrast sensitivity functions for glaucoma patient WT. Data for right eye are plotted with diamonds and fit with solid curve. Data for left eye are plotted with squares and fit with dotted curve. Age matched normals are plotted with hourglasses (and error bars) and fit with dashed curve. Log loss compared to normal are shown in the spatial and temporal visuograms below each contrast sensitivity curve.

Figure 36: Spatial and temporal contrast sensitivity functions for glaucoma patient DS. Data for right eye are plotted with diamonds and fit with solid curve. Data for left eye are plotted with squares and fit with dotted curve. Age matched normals are plotted with hourglasses (and error bars) and fit with dashed curve. Log loss compared to normal are shown in the spatial and temporal visuograms below each contrast sensitivity curve.

Figure 37: Spatial and temporal contrast sensitivity functions for glaucoma patient AJ. Data for right eye are plotted with diamonds and fit with solid curve. Data for left eye are plotted with squares and fit with dotted curve. Age matched normals are plotted with hourglasses (and error bars) and fit with dashed curve. Log loss compared to normal are shown in the spatial and temporal visuograms below each contrast sensitivity curve.

Figure 38: Spatial and temporal contrast sensitivity functions for glaucoma patient RW. Data for right eye are plotted with diamonds and fit with solid curve. Data for left eye are plotted with squares and fit with dotted curve. Age matched normals are plotted with hourglasses (and error bars) and fit with dashed curve. Log loss compared to normal are shown in the spatial and temporal visuograms below each contrast sensitivity curve.

Figure 39: Spatial and temporal contrast sensitivity functions for glaucoma patient CN. Data for right eye are plotted with diamonds and fit with solid curve. Data for left eye are plotted with squares and fit with dotted curve. Age matched normals are plotted with hourglasses (and error bars) and fit with dashed curve. Log loss compared to normal are shown in the spatial and temporal visuograms below each contrast sensitivity curve.

Figure 40: Spatial and temporal contrast sensitivity functions for glaucoma patient DM. Data for right eye are plotted with diamonds and fit with solid curve. Data for left eye are plotted with squares and fit with dotted curve. Age matched normals are plotted with hourglasses (and error bars) and fit with dashed curve. Log loss compared to normal are shown in the spatial and temporal visuograms below each contrast sensitivity curve.

Figure 41: Spatial and temporal contrast sensitivity functions for glaucoma patient TK. Data for right eye are plotted with diamonds and fit with solid curve. Data for left eye are plotted with squares and fit with dotted curve. Age matched normals are plotted with hourglasses (and error bars) and fit with dashed curve. Log loss compared to normal are shown in the spatial and temporal visuograms below each contrast sensitivity curve.

Figure 42: Spatial and temporal contrast sensitivity functions for glaucoma patient LO. Data for right eye are plotted with diamonds and fit with solid curve. Data for left eye are plotted with squares and fit with dotted curve. Age matched normals are plotted with hourglasses (and error bars) and fit with dashed curve. Log loss compared to normal are shown in the spatial and temporal visuograms below each contrast sensitivity curve.

Figure 43: Spatial and temporal contrast sensitivity functions for glaucoma patient KD. Data for right eye are plotted with diamonds and fit with solid curve. Data for left eye are plotted with squares and fit with dotted curve. Age matched normals are plotted with hourglasses (and error bars) and fit with dashed curve. Log loss compared to normal are shown in the spatial and temporal visuograms below each contrast sensitivity curve.

Figure 44: Spatial and temporal contrast sensitivity functions for glaucoma patient JM. Data for right eye are plotted with diamonds and fit with solid curve. Data for left eye are plotted with squares and fit with dotted curve. Age matched normals are plotted with hourglasses (and error bars) and fit with dashed curve. Log loss compared to normal are shown in the spatial and temporal visuograms below each contrast sensitivity curve.

Figure 45: Spatial and temporal contrast sensitivity functions for glaucoma patient MS. Data for right eye are plotted with diamonds and fit with solid curve. Data for left eye are not available for this patient. Age matched normals are plotted with hourglasses (and error bars) and fit with dashed curve. Log loss compared to normal are shown in the spatial and temporal visuograms below each contrast sensitivity curve.

Figure 46: Spatial and temporal contrast sensitivity functions for glaucoma patient NJ. Data for right eye are not available for this patient. Data for left eye are plotted with squares and fit with dotted curve. Age matched normals are plotted with hourglasses (and error bars) and fit with dashed curve. Log loss compared to normal are shown in the spatial and temporal visuograms below each contrast sensitivity curve.

Figure 47: Spatial and temporal contrast sensitivity functions for glaucoma patient MS2. Data for right eye are plotted with diamonds and fit with solid curve. Data for left eye are plotted with squares and fit with dotted curve. Age matched normals are plotted with hourglasses (and error bars) and fit with dashed curve. Log loss compared to normal are shown in the spatial and temporal visuograms below each contrast sensitivity curve.

Figure 48: Spatial and temporal contrast sensitivity functions for glaucoma patient KHS. Data for right eye are plotted with diamonds and fit with solid curve. Data for left eye are not available for this patient. Age matched normals are plotted with hourglasses (and error bars) and fit with dashed curve. Log loss compared to normal are shown in the spatial and temporal visuograms below each contrast sensitivity curve.

Figure 49: Spatial and temporal contrast sensitivity functions for glaucoma patient JT. Data for right eye are not available for this patient. Data for left eye are plotted with squares and fit with dotted curve. Age matched normals are plotted with hourglasses (and error bars) and fit with dashed curve. Log loss compared to normal are shown in the spatial and temporal visuograms below each contrast sensitivity curve.

Figure 50: Spatial and temporal contrast sensitivity functions for glaucoma patient JN. Data for right eye are not available for this patient. Data for left eye are plotted with squares and fit with dotted curve. Age matched normals are plotted with hourglasses (and error bars) and fit with dashed curve. Log loss compared to normal are shown in the spatial and temporal visuograms below each contrast sensitivity curve.

Figure 51: Spatial and temporal contrast sensitivity functions for glaucoma patient PR. Data for right eye are plotted with diamonds and fit with solid curve. Data for left eye are plotted with squares and fit with dotted curve. Age matched normals are plotted with hourglasses (and error bars) and fit with dashed curve. Log loss compared to normal are shown in the spatial and temporal visuograms below each contrast sensitivity curve.

Figure 52: Spatial and temporal contrast sensitivity functions for glaucoma patient SM. Data for right eye are plotted with diamonds and fit with solid curve. Data for left eye are plotted with squares and fit with dotted curve. Age matched normals are plotted with hourglasses (and error bars) and fit with dashed curve. Log loss compared to normal are shown in the spatial and temporal visuograms below each contrast sensitivity curve.

Figure 53: Spatial and temporal contrast sensitivity functions for glaucoma patient VJ. Data for right eye are plotted with diamonds and fit with solid curve. Data for left eye are plotted with squares and fit with dotted curve. Age matched normals are plotted with hourglasses (and error bars) and fit with dashed curve. Log loss compared to normal are shown in the spatial and temporal visuograms below each contrast sensitivity curve.

Figure 54: Spatial and temporal contrast sensitivity functions for glaucoma patient JG. Data for right eye are plotted with diamonds and fit with solid curve. Data for left eye are not available for this patient. Age matched normals are plotted with hourglasses (and error bars) and fit with dashed curve. Log loss compared to normal are shown in the spatial and temporal visuograms below each contrast sensitivity curve.

Figure 55: Spatial and temporal contrast sensitivity functions for glaucoma patient LH. Data for right eye are plotted with diamonds and fit with solid curve. Data for left eye are not available for this patient. Age matched normals are plotted with hourglasses (and error bars) and fit with dashed curve. Log loss compared to normal are shown in the spatial and temporal visuograms below each contrast sensitivity curve.

Figure 56: Spatial and temporal contrast sensitivity functions for glaucoma patient DK. Data for right eye are plotted with diamonds and fit with solid curve. Data for left eye are not available for this patient. Age matched normals are plotted with hourglasses (and error bars) and fit with dashed curve. Log loss compared to normal are shown in the spatial and temporal visuograms below each contrast sensitivity curve.

Figure 57: Spatial and temporal contrast sensitivity functions for glaucoma patient JO. Data for right eye are plotted with diamonds and fit with solid curve. Data for left eye are not available for this patient. Age matched normals are plotted with hourglasses (and error bars) and fit with dashed curve. Log loss compared to normal are shown in the spatial and temporal visuograms below each contrast sensitivity curve.

Figure 58: Spatial and temporal contrast sensitivity functions for glaucoma patient AS. Data for right eye are plotted with diamonds and fit with solid curve. Data for left eye are plotted with squares and fit with dotted curve. Age matched normals are plotted with hourglasses (and error bars) and fit with dashed curve. Log loss compared to normal are shown in the spatial and temporal visuograms below each contrast sensitivity curve.

An indicator of which type of loss is most common in early glaucoma is the number of eyes that demonstrate each type of significant loss. Figure 59 demonstrates significant losses graphically. Chi-square analysis was performed on this data. It showed that red-green color losses are significantly more common than achromatic losses (either luminance measure, red-green or blue-yellow), ($X^2 = 4.713$, $P < 0.05$). It also suggests that red-green selective losses (C/L) are more common than blue-yellow selective losses ($X^2 = 4.013$, $P < 0.05$).

Figure 59: Histogram of number of eyes with significant loss of each type of measurement.

Spearman rank-order correlations were performed on all the data. For the purposes of calculating correlation coefficients, only one eye from each subject was used. If data for both eyes were available, data for the eye with the highest mean spatial loss were chosen. This was done because it was felt that as mean spatial contrast sensitivity probably has similar inputs from small, medium, and large retinal ganglion cells, it would not bias the data toward any specific type of loss. All Spearman rank-order correlation coefficients are shown in Tables 3 and 4. Scatter plots with correlation coefficients for these data are shown in figures 60-67.

Correlations were also performed between visual field loss (mean deviation) and the psychophysical tests performed in our laboratory. Visual field data were only available for ten patients, so only ten eyes are were used for these analyses. Figure 68 shows the only data that had a significant correlation with visual field loss, which was achromatic (blue-yellow luminance) loss.

TABLE 3

Spearman rank-order correlation coefficients for all losses. Significant ($P < 0.05$) correlations are marked with an asterisk (*).

	MD	CPSD	RGC	RGL	BYC	BYL	SPM	TEM
MD	1							
CPSD	-.855*	1						
RGC	-.333	.164	1					
RGL	-.527	.358	.763*	1				
BYC	-.164	.152	.916*	.813*	1			
BYL	-.648*	.503	.795*	.941*	.798*	1		
SPM	-.394	.079	.639*	.824*	.720*	.803*	1	
TEM	-.430	.285	.505*	.703*	.553*	.692*	.685*	1

TABLE 4

Spearman rank order correlation coefficients for selectivity of losses. Significant correlations ($P < 0.05$) are marked with an asterisk (*)

	RGC/L	BYC/L	SPS	TES
RGC/L	1			
BYC/L	.808*	1		
SPS	.211	.251	1	
TES	.123	.418*	.200	1

Figure 60: Scatter plot for red-green color loss vs. red-green luminance loss. ($R=0.763$, $P<.001$)

Figure 61: Scatter plot of blue-yellow color loss vs. blue-yellow luminance loss. ($R=0.798$, $P<.001$)

Figure 62: Scatter plot of red-green color loss vs. mean spatial contrast sensitivity loss. ($R=.639$, $P<.01$)

Figure 63: Scatter plot of blue-yellow color loss vs. mean spatial contrast sensitivity loss. ($R=.720$, $P<.001$)

Figure 64: Scatter plot of achromatic (red-green luminance) loss vs. mean spatial contrast sensitivity loss. ($R=.824$, $P<.001$)

Figure 65: Scatter plot of achromatic (red-green luminance) loss vs. mean temporal contrast sensitivity loss. ($R=.703$, $P<.001$)

Figure 66: Scatter plot of red-green color loss vs. mean temporal contrast sensitivity loss. ($R=.505$, $P<.05$)

Figure 67: Scatter plot of blue-yellow color loss vs. mean temporal contrast sensitivity loss. ($R=.553$, $P<.01$)

Figure 68: Scatter plot of achromatic (blue-yellow luminance) loss vs. mean deviation of the visual field. ($R=-.648$, $P<.05$)

Figure 69: Scatter plot of temporal mean loss vs. spatial mean loss. ($R=.685$, $P<.001$)

Figure 70: Scatter plot of Log RG C/L loss (red-green selectivity) vs. Slope of the spatial visuogram. ($R=.211$, NS)

DISCUSSION

The patients involved in this study show a variety of foveal visual losses that are associated with optic nerve damage due to glaucoma. In fact, all possible types of losses measured by our psychophysical tests are demonstrated by at least one patient. It may appear at first glance that this variety of losses suggests a non-selective loss of all types of nerve fibers. However, there are several results that indicate otherwise.

A greater number of eyes were found to have red-green color losses than had achromatic losses. This may suggest a relatively selective loss of cells signaling red-green color vision. These are primarily thought to be Type I cells (Wiesel and Hubel, 1966). However, it has been suggested (Sterling et al, 1994) that red-green color information may be carried mainly by Type II cells, previously thought to be more common in the blue-yellow pathway than in the red-green. Whether they are Type I or II cells, these cells are a part of the parvocellular pathway.

Second, there are 15 eyes which show significantly elongated red-green ellipses (C/L ratios), and only 2 eyes which show significantly widened red-green ellipses (C/L ratios significantly <0). An elongated ellipse suggests a relatively selective loss of chromatic signaling mechanisms (P cells), while a widened ellipse suggests a relatively selective loss of achromatic signaling mechanisms (which may be either M or P cells

(Ingling and Grigsby, 1990)). Thus, the large number of elongated ellipses compared to the relative paucity of ellipses which are significantly widened along the achromatic axis, again suggests that losses of P ganglion cells are more common than losses of M ganglion cells.

In the correlation analyses, it may be noted that red-green chromatic loss correlates strongly with achromatic loss (see Figure 60). This may seem counter-intuitive, as color sensitivity is commonly attributed to the parvocellular pathway, while luminance information is commonly attributed to the magnocellular pathway. There are two possible explanations for this strong correlation. The first possibility is that color and luminance information are primarily carried by the same cell type, and that this type of cell is affected by glaucomatous damage. As mentioned previously, Ingling and Martinez (1983) and Ingling and Grigsby (1990) have shown that Type I cells are capable of carrying both color and luminance information, which are later “de-multiplexed” in visual cortex. If Type I cells are damaged in glaucoma, then we may expect both color and luminance sensitivities to be affected. This may also explain why color losses are more common, or may precede, luminance losses. It may be that to get a reduction in chromatic sensitivity, one has to lose only one cell type (Type I P-cell), while to get a reduction in luminance sensitivity, two cell types are potentially involved (Type I P-cell, and Type III M-cell).

Another possible explanation for this strong correlation between color and luminance losses is that these attributes are indeed primarily signaled by two different cell types, and that these cells are nearly equally affected in

glaucoma. The relatively similar amounts of spatial and temporal sensitivity losses (see figure 59) may also support a nearly equal loss of two different types of cells. It is well known that the magno pathway is the main pathway responsible for signaling motion and flicker sensitivity. Thus a loss of M-cells would cause a reduction in temporal contrast sensitivity, especially at high temporal frequencies (demonstrated by a significant positive slope of the temporal visuogram). The parvo pathway is believed to have the greatest contribution to the spatial contrast sensitivity function. Thus a loss of P-cells would cause a reduction in spatial contrast sensitivity, especially at high spatial frequencies (demonstrated by a significant positive slope of the spatial visuogram). As the number of spatial mean losses and temporal mean losses are similar (14 eyes vs. 16 eyes), it may be inferred that both P- and M- cells are being damaged in glaucoma, and to nearly equal extents. It should also be noted that the correlation between spatial mean loss and temporal mean loss is strong in these patients ($R=.685$, $P<.001$, see figure 69).

In addition to the strong correlation between red-green color losses and achromatic losses, there is also a strong correlation between blue-yellow chromatic and achromatic losses ($R=.798$, $P<.001$, see figure 61). Again this suggests either that blue-yellow color and achromatic information are carried on the same channel, or that they are carried on different channels, both of which are affected in glaucoma. This second explanation seems much more plausible in this case, as it is widely believed that blue-yellow information is

primarily conveyed by Type II cells, which are not likely to carry much luminance information.

In figure 62, it is seen that red-green color loss correlates strongly with mean spatial contrast sensitivity loss ($R=.639$, $P<.01$). This is not surprising as both red-green color, and spatial contrast sensitivity are properties primarily attributable to Type I cells. Figure 63 shows that blue-yellow color losses also correlate strongly with mean spatial contrast sensitivity losses. This is slightly more surprising as blue-yellow color sensitivity is attributed primarily to Type II rather than Type I cells.

Figure 64 is a scatter plot of achromatic sensitivity loss vs. mean spatial contrast sensitivity loss. Again, the correlation is strong ($R=.824$, $P<.001$). This may be because damage to Type I cells causes reductions in both achromatic sensitivity and in spatial contrast sensitivity. Alternatively, it may be because Type III cells (of the magno pathway) are damaged, causing losses in luminance sensitivity, and that Type I cells are nearly equally damaged, causing a loss in contrast sensitivity.

The correlation between achromatic losses and mean temporal contrast sensitivity losses is displayed in figure 65. The correlation here is also strong ($R=.703$, $P<.001$). This may be because both luminance and flicker information are carried by Type III cells, which are being damaged, or because damage to Type I cells, carrying some of the luminance information, are damaged nearly equally to Type III cells carrying the flicker information.

Figure 66 shows that red-green color losses also correlated strongly with mean temporal contrast sensitivity losses ($R=.505$, $P<.05$). It is not likely that color information and flicker information can be carried by the same type of neuron. The Type I red-green cells have small axon diameters and correspondingly slow conduction velocities, and thus are not able to respond quickly enough to signal flicker sensitivity. Thus, this result suggests that both the M- and P-ganglion cells are being affected, and that eyes as the amount of M-cell loss increases in a given eye, so does the amount of P-cell loss (or vice-versa). A similar interpretation may be made of the strong correlation between blue-yellow color loss and mean temporal contrast sensitivity loss shown in figure 67 ($R=.553$, $P<.01$).

The only parameter measured in our lab that correlated significantly with visual field loss was achromatic (blue-yellow luminance) loss. This is shown in figure 68 ($R=.648$, $P<.05$). It is not surprising that luminance loss measured on our apparatus is related to an over-all reduction in visual field sensitivity, as this is also a measurement of achromatic sensitivity, but measured in peripheral retina rather than foveally.

One other interesting point to mention is that red-green selective losses were significantly more common than blue-yellow selective losses. This seems surprising, in that the bulk of the literature would suggest that when color vision is affected in glaucoma, it is normally in the form of damage to the short wavelength sensitive (blue) pathway (Johnson et al, 1989, 1993 a and b, Flanagan et al, 1990, Sample et al 1993, etc.)

Interestingly, red-green selectivity did not correlate strongly with the slope of the spatial visuogram (see figure 70). One would expect a strong correlation if there were a selective loss of Type I cells, as they are believed to be responsible for both red-green color vision, and for high spatial frequency contrast sensitivity. However, if the data for patient KHS are removed, the correlation becomes much stronger (Spearman $R=0.350$, Pearson $r=0.506$). This patient has a very high red-green color-luminance ratio, but a very small slope of the spatial visuogram. When further assessing his test results, it was determined that this patient may have a deuteranomalous color vision defect, which would explain the elongation of the ellipse, while sparing high spatial frequency contrast sensitivity.

When considering all of our results, then, it appears that retinal ganglion cell losses in glaucoma are fairly non-selective. However, there is evidence that chromatic losses may lead achromatic losses, suggesting that perhaps P-cells are affected slightly before M-cells in foveal retina.

How does one reconcile this finding, then, with the large number of studies that have shown selective loss of large ganglion cells? There are a number of possible explanations.

It may be that the effects on foveal and peripheral retina are different in glaucoma. As the fovea is rich in P-cells, but not M-cells (Bassi and Lehmkuhle, 1989) it is likely that foveal thresholds may reflect this difference. In other words, because there are significantly more P-cells than M-cells at the fovea, it is easier to affect P-cells. However, Glovinsky et al (1993) found that, even at the fovea, large ganglion cells were lost more

readily than were small cells. They admit, though, that the larger cells at the fovea may be Type II P-cells rather than M-cells. Still, this does not seem consistent with our finding that red-green losses are at least as common as blue-yellow losses in our sample.

A reasonable explanation for our findings is that the properties of M- and P-cells at the fovea are altered, even if they are not destroyed (Alvarez et al, 1994). It may be that Type I cells lose some of their ability to signal color, but retain most of their luminance signaling properties. Similarly, Type III cells may lose some of their conduction velocity, resulting in reduced flicker sensitivity, while maintaining much of their achromatic luminance signaling abilities. Also, Gouras and Zrenner (1981) have suggested that there are two types of small (P) cells in the retina: strongly opponent, and weakly opponent. It may be that glaucoma, in its early stages, affects the strongly opponent P-cells, reducing the patient's color sensitivity, but leaves the weakly opponent P-cells relatively unaffected, leaving luminance sensitivity nearly uncompromised. If this is the case, then flicker sensitivity losses could be explained by a loss of M-cells, and color losses may be explained by a relative loss of the weakly opponent P-cells (Alvarez et al, 1994).

Whatever the reason, it is apparent that red-green color vision may be affected as early, if not earlier, in the disease process than are blue-yellow color vision and luminance sensitivity. This may lead to additional use of red-green color testing in screening for glaucoma, either foveally, or in peripheral vision, as is now becoming common with the SWAP visual field

methods (Johnson et al, 1993 a and b). An inherent advantage is that blue-yellow color vision may be affected by absorption of short wavelengths by the lens and macular pigment, both of which may be high in the elderly population- the population most at risk for glaucoma. Currently, measurements of lens density are often performed to rule out absorption by the crystalline lens as a factor in the reduction of short-wavelength sensitivity. As the crystalline lens and macular pigment absorb relatively little light in the medium and long wavelength portions of the spectrum, it may be more convenient to screen for red-green color vision losses than for blue-yellow losses.

REFERENCES

Airaksinen PJ, Lakowski R, Drance SM, and Price M: Color vision and retinal nerve fiber layer in early glaucoma. *Am J Ophthalmol* 1986; 101:208-213.

Alvarez SL, Vingrys AJ, Benes SC, Weber PA, and King-Smith PE: Comparison of red-green, blue-yellow, and achromatic losses in glaucoma. In Press (1994).

Arden GB and Jacobson JJ: A simple grating test for contrast sensitivity: preliminary results indicate value in screening for glaucoma. *Invest Ophthalmol Vis Sci* 1978; 17:23-32.

Bassi CJ and Lehmkuhle S: Clinical implications of parallel visual pathways. *J American Optometric Assoc* 1990; 61:98-110.

Breton ME, Wilson TW, Wilson R, Spaeth GL, and Kuprin T: Temporal contrast sensitivity loss in primary open-angle glaucoma and glaucoma suspects. *Invest Ophthalmol Vis Sci* 1991; 32:2931-2941.

Brussel EM, White CW, Faubert J, Dixon M, Balazsi GA, and Overbury O: Multi-flash campimetry as an indicator of visual field loss in glaucoma. *Am J Optometry and Phys Opt* 1986; 63:32-40.

Brussel EM, Muermans M, White CW, Faubert J, and Balazsi AG: Chromatic flicker deficits in glaucoma patients and suspects. In *Perimetry Update 1988/89*, Heijl A, editor. Amsterdam: Kugler and Ghedini Publications; 1989:45-52.

Casson EJ, Johnson CA, and Shapiro LR: Longitudinal comparison of temporal modulation perimetry with white-on-white and blue-on-yellow perimetry in ocular hypertension and early glaucoma. *J Opt Soc Am A* 1993; 10:1792-1806.

Dandona L, Hendrickson A and Quigley HA: Selective effects of experimental glaucoma on axonal transport by retinal ganglion cells to lateral geniculate nucleus. *Invest Ophthalmol Vis Sci* 1991; 32:1593-1599.

Drance SM, Lakowski R, Schulzer M, and Douglas GR: Acquired color vision changes in glaucoma: Use of 100-Hue and Pickford anomaloscope as predictors of glaucomatous visual field change. *Arch Ophthalmol* 1981; 99:829-831.

Drance SM: The early structural and functional disturbances of chronic open-angle glaucoma. *Ophthalmology* 1985; 92:853-857.

Drance SM: Diffuse visual field loss in open angle glaucoma. *Ophthalmology* 1991; 98:1533-1538.

Flanagan JG, Trope GE, Popick W, and Grover A: Perimetric isolation of the SWS cones in OHT and early POAG. In Perimetry Update 1990/91, Mills RP and Heijl A, editors. Amsterdam: Kugler Publications 1991:331-337.

Fitzke FW, Pooinsawmy D, Nagasubramanian S, and Hitchings RA: Peripheral displacement thresholds in glaucoma and ocular hypertension. In Perimetry Update 1988/89, Heijl A, editor. Amsterdam: Kugler and Ghedini Publications 1989:399-405.

Flammer J, Drance SM, Augustiny L, and Funkhouser A: Quantification of glaucomatous visual field defects with automated perimetry. *Invest Ophthalmol Vis Sci* 1985; 26:176-181.

Glovinsky Y, Quigley HA, and Dunkelberger GR: Retinal ganglion cell loss is size dependent in experimental glaucoma. *Invest Ophthalmol Vis Sci* 1991; 32:484-491.

Glovinsky Y, Quigley HA, and Pease ME: Foveal ganglion cell loss is size dependent in experimental glaucoma. *Invest Ophthalmol Vis Sci* 1993; 34:395-400.

Gouras P and Zrenner E: Color vision: A review from a neurophysiological perspective. In Progress in Sensory Physiology 1, Autrum H, Ottoson D, Perl ER, and Schmidt RF, editors. Berlin: Springer-Verlag; 1981:139-179.

Grigsby SS, Vingrys AJ, Benes SC, and King-Smith PE: Correlation of chromatic, spatial, and temporal sensitivity in optic nerve disease. *Invest Ophthalmol Vis Sci* 1991; 32:3252-3262.

Hammil TR, Post RB, Johnson CA, and Keltner JL: Correlation of color vision deficits and observable changes in the optic disc in a population of ocular hypertensives. *Arch Ophthalmol* 1984; 102:1637-1639.

Hart MM, and Becker B: The onset and evolution of glaucomatous visual field defects. *Ophthalmology* 1982; 89:268-279.

Hart WM, Silverman SE, Trick GL, Nesher R, and Gordon MO: Glaucomatous visual field damage: luminance and color-contrast sensitivities. *Invest Ophthalmol Vis Sci* 1990; 31:359-367.

Heijl A: Lack of diffuse loss of differential light sensitivity in early glaucoma. *Acta Ophthalmologica* 1989; 67:353-360.

Heron G, Adams AJ, and Husted R: Central visual fields for short wavelength sensitive pathways in glaucoma and ocular hypertension. *Invest Ophthalmol Vis Sci* 1988; 29:64-72.

Ingling CR and Grigsby SS: Perceptual correlates of magnocellular and parvocellular channels: seeing form and depth in afterimages. *Vision Res* 1990; 30:823-828.

Ingling CR and Martinez E: The spatiochromatic signal of the r-g channel. In Color Vision. London: Academic Press 1983:433-444.

Johnson CA, Adams AJ, and Lewis RA: Automated perimetry of short-wavelength mechanisms in glaucoma and ocular hypertension: preliminary findings. In Perimetry Update 1988/89. Heijl A, editor. Amsterdam: Kugler and Ghedini Publications, 1989:31-37.

Johnson CA, Adams AJ, Casson EJ, and Brandt JD: Blue-on-yellow perimetry can predict the development of glaucomatous visual field loss. *Arch Ophthalmol* 1993(a); 111:645-650.

Johnson CA, Adams AJ, Casson EJ, and Brandt JD: Progression of early glaucomatous visual field loss as detected by blue-on-yellow and standard white-on-white automated perimetry. *Arch Ophthalmol* 1993(b); 111:651-656.

Kanski JJ: Glaucoma. In Clinical Ophthalmology. London: Butterworth and Co. Publishers, 1987:7.1-7.38

King-Smith PE, Grigsby SS, Vingrys AJ, Benes SC, and Supowit A: Efficient and unbiased modifications of the QUEST threshold method: theory, simulations, experimental evaluation and practical implementation. *Vision Res* 1994; 34:885-912.

King-Smith PE, Vingrys AJ, and Benes SC: Visual thresholds measured with color video monitors. *Color Res and Application* 1987; 12:73-80.

Korth M, Nguyen NX, Junemann A, Martus P, and Jonas JB: VEP test of the blue-sensitive pathway in glaucoma. *Invest Ophthalmol Vis Sci* 1994; 35:2599-2610.

Korth M, Horn F, Storck B, and Jonas JB: Spatial and spatiotemporal contrast sensitivity of normal and glaucoma eyes. *Graefe's Arch Clin Exp Ophthalmol* 1989; 227:428-435.

Lachenmayr BJ, Drance SM, Chauhan BC, House PH, and Lalani S: Diffuse and localized glaucomatous field loss in light-sense, flicker, and resolution perimetry. *Graefe's Arch Clin Exp Ophthalmol* 1991; 229:267-273.

Lakowski R and Drance SM: Acquired dyschromatopsias: the earliest functional losses in glaucoma. *Docum Ophthalmol Proc Series* 1979; 19:159-165.

Livingstone MS and Hubel DH: Segregation of form, color, motion, and depth; anatomy, physiology, and perception. *Science* 1988; 240:740-749.

Motolko M, Drance SM, Douglas GR: The early psychophysical disturbances in chronic open-angle glaucoma: a study of visual functions with asymmetric disc cupping. *Arch Ophthalmol* 1982; 100:1632-1634.

Odom JV, Feghali JG, Jin J, and Weinstein GW: Visual function deficits in glaucoma: electroretinogram pattern and luminance nonlinearities. *Arch Ophthalmol* 1990; 108:222-227.

Pierce GE: An experimental comparison of yes-no and forced choice threshold measurement techniques. Master's thesis 1992.

Pooinsawmy D, Nagasubramanian S, and Gloster J: Colour vision in patients with chronic simple glaucoma and ocular hypertension. *Brit J Ophthalmol* 1980; 64: 852-857.

Quigley HA, Addicks EM, and Green WR: Optic nerve damage in human glaucoma: III. Quantitative correlation of nerve fiber loss and visual field defect in glaucoma, ischemic neuropathy, papilledema, and toxic neuropathy. *Arch Ophthalmol* 1982; 100:135-146.

Quigley HA, Dunkelberger GR, and Green WR: Chronic human glaucoma causing selectively greater loss of large optic nerve fibers. *Ophthalmology* 1988; 95:357-363.

Quigley HA, Dunkelberger GR, and Green WR: Retinal ganglion cell atrophy correlated with automated perimetry in human eyes with glaucoma. *Am J Ophthalmol* 1989; 107:453-464.

Quigley HA, Sanchez RM, Dunkelberger GR, L'Hernault NL, and Baginski TA: Chronic glaucoma selectively damages large optic nerve fibers. *Invest Ophthalmol Vis Sci* 1987; 28:913-920.

Ross E, Bron AJ, and Clarke DD: Contrast sensitivity and visual disability in chronic simple glaucoma. *Brit Ophthalmol* 1984; 68:821-827.

Sample PA, Taylor JDN, Martinez GA, Lusky M, and Weinreb RN: Short wavelength color visual fields in glaucoma suspects at risk. *Am J Ophthalmol* 1993; 115:225-233.

Sample PA, Weinreb RN, and Boynton RM: Acquired dyschromatopsia in glaucoma. *Survey of Ophthalmology* 1986; 31:54-63.

Schmeisser ET and Smith TJ: High frequency flicker visual evoked potential losses in glaucoma. *Ophthalmology* 1989; 96:620-623.

Sellers KL, Chioran GM, Dain SJ, Benes SC, Lubow M, Rammohan K, and King-Smith PE: Red-green mixture thresholds in congenital and acquired color defects. *Vision Res* 1986; 26:1083-1097.

Silverman SE, Trick GL, and Hart WM: Motion perception is abnormal in primary open-angle glaucoma and ocular hypertension. *Invest Ophthalmol Vis Sci* 1990; 31:722-729.

Stedman's Medical Dictionary. Baltimore: Williams & Wilkins Publishing, 1990

Sterling P, Calkins DJ, Kluh KJ, Schein SJ, and Tsukamoto Y: Parallel pathways from primate fovea. *Invest Ophthalmol Vis Sci (ARVO Supplement)* 1994; 35:2001.

Tamaki R, Kitahara K, Kandatsu A, and Nishio Y: The vulnerability of the blue cone system in glaucoma. In Perimetry Update 1990/91, Mills RP and Heijl A, editors. Amsterdam: Kugler Publications 1991:343-345.

Trick GL: Retinal potentials in patients with primary open-angle glaucoma: physiological evidence for temporal frequency tuning deficits. *Invest Ophthalmol Vis Sci* 1985; 26:1750-1758.

Tyler CW: Specific deficits of flicker sensitivity in glaucoma and ocular hypertension. *Invest Ophthalmol Vis Sci* 1981; 20:204-212.

Tyler CW, Ryu, S, and Stamper R: The relation between visual sensitivity and intraocular pressure in normal eyes. *Invest Ophthalmol Vis Sci* 1984; 25:103-105.

Tytila ME, Trope GE, and Buncic JR: Flicker sensitivity in treated ocular hypertension. *Ophthalmology* 1990; 97:36-43.

van Essen DC, Anderson CH, and Fellman DJ: Information processing in the primate visual system: an integrated systems perspective. *Science* 1992; 255:419-423.

Vingrys AJ and King-Smith PE: Factors in using color video monitors in assessment of visual thresholds. *Color Res and Application* 1986 (supp); 11:S57-S62.

Watson AB and Pelli DG: QUEST: A Bayesian adaptive psychophysical method. *Perception and Psychophysics* 1983; 33:113-120.

Wiesel TN and Hubel DH: Spatial and chromatic interactions in the lateral geniculate body of the rhesus monkey. *J Neurophysiol* 1966; 29:1115-1156.
Yamazaki Y, Lakowski R, and Drance SM: A comparison of the blue color mechanism in high- and low-tension glaucoma. *Ophthalmology* 1989; 96:12-15.

Zwas F, Shin DH, and McKinnon P: Early spectral sensitivity changes in unilateral glaucoma. In Color Vision Deficiencies X. Drum B, Moreland JD, and Serra A, editors. Dordrecht: Kluwer Academic Publishers 1991: 551-560.