Visual Function–Specific Perimetry for Indirect Comparison of Different Ganglion Cell Populations in Glaucoma

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Purpose. To compare short-wavelength automated perimetry, frequency-doubling technology perimetry, and motion-automated perimetry, each of which assesses different aspects of visual function, in eyes with glaucomatous optic neuropathy and ocular hypertension.

Methods. One hundred thirty-six eyes from 136 subjects were evaluated with all three tests as well as with standard automated perimetry. Fields were not used in the classification of study groups to prevent bias, because the major purpose of the study was to evaluate each field type relative to the others. Seventy-one of the 136 eyes had glaucomatous optic neuropathy, 37 had ocular hypertension, and 28 served as age-matched normal control eyes. Glaucomatous optic neuropathy was defined by assessment of stereophotographs. Criteria were asymmetrical cupping, the presence of rim thinning, notching, excavation, or nerve fiber layer defect. Ocular hypertensive eyes had intraocular pressure of 23 mm Hg or more on at least two occasions and normal-appearing optic disc stereophotographs. Criteria for abnormality on each visual field test were selected to approximate a specificity of 90% in the normal eyes. Thresholds for each of the four tests were compared, to determine the percentage that were abnormal within each patient group and to assess the agreement among test results for abnormality, location, and extent of visual field deficit.

Results. Each test identified a subset of the eyes with glaucomatous optic neuropathy as abnormal: 46% with standard perimetry, 61% with short-wavelength automated perimetry, 70% with frequency-doubling perimetry, and 52% with motion-automated perimetry. In the ocular hypertensive eyes, standard perimetry was abnormal in 5%, short wavelength in 22%, frequency doubling in 46%, and motion in 30%. Fifty-four percent (38/71) of eyes with glaucomatous optic neuropathy were normal on standard fields. However, 90% were identified by at least one of the specific visual function tests. Combining tests improved sensitivity with slight reductions in specificity. The agreement in at least one quadrant, when a defect was present with more than one test, was very high at 92% to 97%. More extensive deficits were shown by frequency-doubling perimetry followed by short-wavelength automated perimetry, then motion-automated perimetry, and last, standard perimetry. However, there were significant individual differences in which test of any given pairing was more extensively affected. Only 30% (11/37) of the ocular hypertensive eyes showed no deficits at all compared with 71% (20/28) of the control eyes ($P < 0.001$).

Conclusions. For detection of functional loss standard visual field testing is not optimum; a combination of two or more tests may improve detection of functional loss in these eyes; in an individual, the same retinal location is damaged, regardless of visual function under test; glaucomatous optic neuropathy identified on stereophotographs may precede currently measurable function loss in some eyes; conversely, function loss with specific tests may precede detection of abnormality by stereophotograph review; and short-wavelength automated perimetry, frequency-doubling perimetry, and motion-automated perimetry continue to show promise as early indicators of function loss in glaucoma. (*Invest Ophthalmol Vis Sci.* 2000;41:1783–1790)

During the past several years, psychophysical tests of visual function have been used not only as diagnostic methods for measuring a glaucoma patient's current visual performance, but also as tools for understanding the underlying changes in retinal ganglion cell function as a result of the disease. We know that glaucoma damages retinal ganglion cells and that several visual functions are affected early in the disease process.[1]

Some histologic evidence has suggested that damage to larger diameter retinal ganglion cell axons occurs first in the course of glaucoma,[2] but these results have been questioned.[3] Many have used these histologic results to assume that "larger axons" means magnocellular axons are most at risk. This interpretation has also been questioned.[4] Larger diameter optic nerve fibers are not exclusively magnocellular fibers. The size of the fibers is dependent on eccentricity as well as ganglion cell type, so that some eccentric parvocellular retinal ganglion cell axons may be larger than more central magnocellular retinal ganglion cell axons. The axons from the small bistrati-

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fied ganglion cells, which process blue–yellow color vision, are also larger than those from parvocellular cells.[5]

We know that testing vision with standard automated perimetry (SAP) is not selective for a particular ganglion cell type, and that newer tests that attempt to isolate specific subpopulation of ganglion cells by evaluating specific visual functions have shown considerable diagnostic power. For example, short-wavelength automated perimetry (SWAP) necessitates detection by the short-wavelength cones and is then processed through the blue–yellow ganglion cells. Recently, it has been reported that the blue–yellow ganglion cells are separate from the parvocellular ganglion cells.[6,7] It is now thought that these cells project their axons to the interlaminar, koniocellular layers of the lateral geniculate nucleus (LGN) rather than to the primary parvocellular layers.[8] To our knowledge, no study has assessed cell loss at the LGN within the interlaminar layers, but most likely these layers will be included in future studies. Results with SWAP consistently show visual field defects before their appearance on standard visual fields, suggesting that it is not only the magnocellular axons that are affected in the earliest stages.[9–11]

Other visual function tests have been developed in an attempt to evaluate specific retinal ganglion cell populations. We think frequency-doubling technology perimetry (FDT)[12,13] and various forms of motion perimetry[14–18] are most likely to isolate the magnocellular ganglion cells. High-pass resolution perimetry most likely isolates primarily the parvocellular ganglion cells.[19,20] However, we want to point out that the degree of isolation of a particular ganglion cell type with some of these tests is unknown. The question is, when damage to a ganglion cell subtype is present, how severe must the field loss be before another ganglion cell type detects the stimulus? Several studies of SWAP have shown that in normal eyes there is a 15-dB cushion before another system (most likely, the middle wavelength sensitive cells and their connections) can detect the target.[21] Most of this isolation is maintained even in areas of moderate SWAP visual field loss.[22] Although motion automated perimetry (MAP) and FDT were structured to test magnocellular ganglion cells, their designs were based on what is known about normal visual processing and from electrophysiological and lesion studies in cat and monkey.[12,23,24] The amount of isolation is not yet known for either FDT or MAP. Results should therefore be interpreted with this in mind.

These psychophysical tests, which are targeted at specific visual functions, have been shown to be superior to standard visual fields for early detection of vision loss associated with glaucoma.[1,9,10,15,17,18,25–40] Studies comparing results of each of these tests in the same patient should help address three alternate theories of ganglion cell damage due to glaucoma:

1. Early damage is selective for the larger optic nerve fibers of the magnocellular system.[2]
2. All optic nerve fibers are damaged. Tests that favor detection of a stimulus by one visual pathway or processing subsystem reduce the ability of the visual system to use other pathways to compensate for the damaged ganglion cell type under test.[1,3]
3. Not all eyes with primary open-angle glaucoma or those at risk for the disease are affected in the same way. Blue–yellow ganglion cell function may be reduced first in one individual, whereas magnocellular ganglion cell function may be affected first in another.[40,41]

In this study, we compared the results of SWAP, FDT, and MAP in the same individuals. Visual field data were not used to classify patients into study groups to prevent bias, because the main purpose of this analysis was to evaluate the relationships among the different types of field tests.

METHODS

Subjects

One hundred thirty-six eyes from 136 subjects were evaluated on all three tests, as well as on SAP. Fields were not used in classification of study groups. Seventy-one of the 136 eyes had glaucomatous optic neuropathy (GON), 37 eyes had ocular hypertension (OHT), and 28 served as age-matched normal control eyes. Mean age ± SD were 62.46 ± 11.86 years (GON), 60.29 ± 11.26 years (OHT), and 61.80 ± 9.31 years (control).

Each subject underwent a complete ophthalmologic examination that included review of relevant medical history, best corrected visual acuity, slit lamp biomicroscopy (including gonioscopy), applanation tonometry, dilated funduscopy, stereoscopic ophthalmoscopy of the optic disc with a 78-D lens, and stereoscopic fundus photography.

This study was approved by the Human Subjects Committee of the University of California, San Diego, and adhered to the Declaration of Helsinki, with informed written consent obtained from the participants.

Inclusion Criteria. Simultaneous stereoscopic photographs were obtained for all subjects and were of adequate quality for the subjects to be included. All subjects had open angles, best corrected acuity of 20/40 or better, spherical refraction within ±5.0 D, and cylinder correction within ±3.0 D. All subjects had reliable visual fields results on all four tests. For SAP, SWAP, and FDT this was defined as 25% or fewer false-positive results, false-negative results, and fixation losses. For MAP, which is a forced-choice test, trials with fixation losses were aborted, and if more than three of these occurred, the test was judged unreliable and not used. One eye was selected randomly from each subject, except in participants in which only one eye met study criteria, and that eye was included. Candidates with a family history of glaucoma were included.

Exclusion Criteria. Normal and ocular hypertensive subjects were excluded if they had a history of intraocular surgery (except for uncomplicated cataract surgery). We also excluded all subjects with nonglaucomatous secondary causes of elevated intraocular pressure (IOP; e.g., iridocyclitis, trauma), other intraocular eye disease, other diseases affecting visual field (e.g., pituitary lesions, demyelinating diseases, HIV positivity or AIDS, or diabetes) or problems affecting color vision other than glaucoma.

Classification of Study Groups

There has also been a change in our understanding of the best way to evaluate new techniques for measuring visual function in glaucoma. Earlier, each new method was evaluated relative to the clinical gold standard, SAP. However, our research and that of many other laboratories[9–11,28,39,42] has shown that new psychophysical procedures are more sensitive and specific than SAP for identifying eyes with glaucomatous optic neuropathy, evident by both qualitative and quantitative analysis of the optic nerve. To more objectively compare these new func-

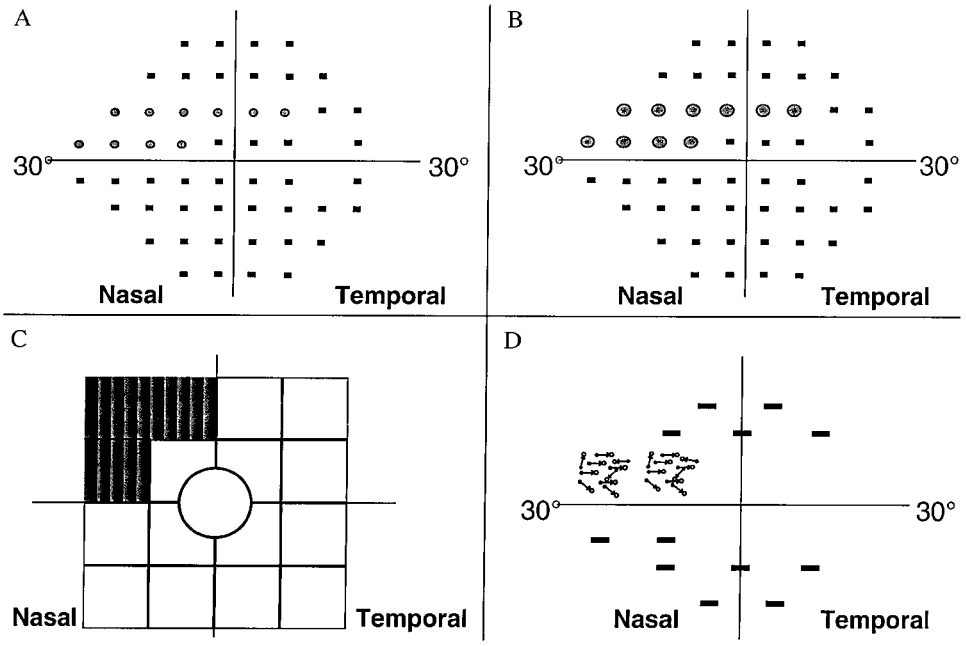

FIGURE 1. An example of test results for the same GON-affected eye on all four visual field tests. Normal locations are depicted by *filled squares* in each field. (**A**) The 52 test locations for Humphrey program 24-2, with the defective SAP locations shown as *circles*. (**B**) The same information for SWAP. (**C**) The 17 test locations for FDT (C-20). The sectors filled with the FDT grating pattern are the defective locations. (**D**) The 14 test locations for MAP. Two defective MAP locations are shown in the superior nasal area of the field (*upper left*) with sample MAP targets. Only 10 of the 20 stimulus dots are shown at time one (●), with *arrows* showing direction of motion to time two (○). These targets suggest 50% coherent motion.

tion tests with SAP, we have shifted the emphasis in the clinical research of our laboratory to select a structural measure of glaucomatous optic disc damage as our gold standard when evaluating results of psychophysical tests of vision. In this study we used evaluation of stereoscopic optic disc photographs, because this is the current clinical standard.

Stereoscopic Optic Disc Photographs. Subjective evaluation of structural damage to the optic nerve was based on clinical assessment of stereoscopic optic disc photographs. Two experienced graders, each of whom was certified after grading standardized photographs satisfactorily, evaluated all photographs. Each grader was masked to the subject's identity, study group classification, results from the other grader, and other test results. In cases of disagreement, the two graders re-evaluated to reach consensus. The diagnosis of GON was based on cup-to-disc asymmetry between two eyes of 0.2 or more, rim-thinning, hemorrhage, notching, excavation, or nerve fiber layer defect.

Normal Control Eyes. Normal eyes had intraocular pressures of 22 mm Hg or less with no history of increased IOP and normal optic discs when judged by the study criteria. Subjects classified as normal also had normal visual field results on the standard visual field program 24-2 of the Humphrey Field Analyzer (Humphrey, San Leandro, CA), as analyzed by the statistical package included with the instrument, which shows a mean defect (MD) and corrected pattern SD (CPSD) within confidence limits of 95%, and a glaucoma hemifield test (GHT) result within confidence limits of 99% of age-specific norms.

Ocular Hypertensives. Ocular hypertensive eyes had normal optic discs and IOP of 23 mm Hg or more on at least two separate occasions. For this study, field results for SAP were not part of the definition of this patient group.

Glaucomatous Optic Neuropathy. The more traditional classification of primary open-angle glaucoma (POAG), required a triad of signs: abnormal visual field, abnormal optic nerve, and increased IOP. For this study, we use only evidence of glaucomatous-appearing optic discs, reflecting a change in thinking that IOP is a risk factor for glaucoma but not a necessary sign. We also did not include standard visual fields in the GON classification to prevent bias, because the major purpose is to evaluate each of the visual fields types against one another.

Psychophysical Tests of Function

Four perimetric procedures were used to test visual function. Each subject underwent all four tests. The three function-specific tests were all measured on the same day. All SAP tests were conducted within 1 month of the other function tests. Photographs were obtained within ±6 months of the date of the three field tests. All procedures tested within the central 30° of visual field and required fixation by the patient. Proper refraction was provided for each device. All required a 3-mm or larger pupil. Patients with mitotic medications underwent a 24-hour washout before testing, and dilation was used, if necessary.

Standard Achromatic Automated Perimetry. This achromatic test uses a small (0.47°) 200-msec flash of white light as the target presented on a dim background (10 candelas[cd]/m^2 or 31.5 apostilb). The target was randomly presented to 54 locations within the central 24° of visual field using the field analyzer (program 24-2; Humphrey). The two locations just above and below the blind spot were not included in the analysis. The test is nonspecific for ganglion cell type, and detection can be mediated through many types of retinal ganglion cells. Figure 1 shows all target locations for all four tests. Also shown are the abnormal locations for each test in the same sample eye with glaucomatous optic neuropathy.

Short-Wavelength Automated Perimetry. A modification of SAP using the same perimeter and programs,[21] SWAP uses a 440-nm, narrow band, 1.8° target at 200 msec duration on a bright 100 cd/m^2 yellow background to selectively test the short-wavelength–sensitive cones and their connections. At the ganglion cell level, the patient's response to this test is most likely mediated by the small bistratified blue–yellow ganglion cells, which comprise approximately 9% of the total population of retinal ganglion cells.[7] The test provides a dynamic range of

approximately 35 dB and 15 dB of isolation before the next most sensitive mechanism can detect the target, most likely the middle-wavelength–sensitive pathway.[21,33]

Frequency-Doubling Technology Perimetry. This test[12,43] is based on the frequency-doubling illusion[44,45] that occurs when the subject views a counterphased grating with a low spatial frequency and a high temporal rate. The percept is double the spatial frequency of the actual physical grating.[45] This illusion has been attributed to a subset of the magnocellular ganglion cells, which are nonlinear in their response properties.[46] There is some debate about whether FDT at threshold measures this small subset (estimated at approximately 3% of the ganglion cells), or whether the target is more likely to be detectable, because of its flicker component,[24,47,48] by the full complement of magnocellular cells (still only approximately 10% of the population). At threshold, the percept is not always of a grating, either perceptually doubled or veridical, but sometimes is described as a "shimmering" or "flickering."[49,50] Either way, early evidence has shown the test to be sensitive to early glaucomatous defect and to correlate well with SAP for determining MD.[43,51–54]

Frequency-doubling perimetry was measured with the Humphrey FDT Visual Field Instrument using Welch–Allyn Frequency-Doubling Technology (Skaneateles Falls, NY). This is a new instrument and is not a test that can be conducted with the Humphrey Visual Field Analyzer. The targets consist of a 0.25 cycle/deg sinusoidal grating that undergoes 25-Hz counterphase flicker. The test uses a modified binary search staircase threshold procedure with stimuli presented for a maximum of 720 msec and measures the contrast needed for detection of the stimulus. During the first 160 msec, stimulus contrast is increased gradually from zero to the contrast selected for that presentation. If the stimulus is not seen, it remains at this contrast for up to 400 msec and then is gradually decreased to zero during the final 160 msec. The interstimulus interval varies randomly up to 500 msec. Each grating target is a square subtending approximately 10° in diameter (Fig. 1). Targets are presented in one of 17 test areas located within the central 20° radius of visual field (program C-20). With a shift in fixation point location, the range can be extended to 30° in the nasal step area (program N-30).

Motion Automated Perimetry. This test also is designed to test the magnocellular ganglion cells.[17,55] The test presents a localized random-dot kinematogram with varying degrees of coherent motion on a uniform gray background. It is a perimetric procedure testing 14 separate locations where nerve fiber bundle–like defects are likely to occur in glaucoma (Fig. 1). The stimulus is produced on a computer-controlled imaging display (Barco CCID color calibrating monitor; Kennesaw, GA) with 1024 × 768 lines of resolution and a refresh rate of 75 Hz. Each pixel subtends 0.31 mm (7.35 minutes of arc at a viewing distance of 16.5 cm). This allows the full 30° of visual field to be tested. Seven frames are shown in rapid succession to create the apparent motion stimulus, which lasts for 420 msec. With each of these frames, 20 dots are randomly placed within a circular test region of 7.3° of visual angle. These dots move at a constant velocity of 8.3° per second in random directions. A new direction of motion is chosen after each spatial displacement. A subset of the dots, chosen at random, moves together in one of four cardinal directions (up, down, left, right) to create the coherent motion signal the subjects are to detect. The signal ranges in strength from 0% to 100% coherence. Signal dots remain the same for all seven frames and have the same spatial displacement as the noise. Thresholds are determined by a staircase procedure, which begins with a coherence value of 80% and a step size of 20% coherence. Each staircase reversal results in a halving of the step size down to a minimum of 5% coherence. Threshold is taken as the mean of the last three reversals at 5%.

Abnormality on Visual Field Tests

Abnormality for all tests was determined by comparison with the manufacturer's internal normative database for SAP and FDT and for our laboratory's normative databases for SWAP (n = 214) and MAP (n = 99). Although this is consistent with the way these tests will be used in clinical practice, there may be some bias in this choice. Ideally, there would be a large normative database of the same eyes for all tests, but because each test has been developed at a different time and by different manufacturers or laboratories, there is no such database with a sufficient number of eyes to accurately assess probability limits. The criteria for an abnormal field on SWAP, FDT, and MAP were determined for each to approximate the same specificity for this study's normal control subjects (n = 28), none of whom were part of any of the normative databases. This was intended to equate the test results somewhat for diagnosing abnormality, because each test uses different stimuli and test locations and assesses different visual functions. A variety of different criteria were tried, and those that will be described gave the closest match for specificity.

Visual field results were evaluated to determine whether the defective areas for the tests fell within the same quadrant of the visual field for extent of these defects, based on number of quadrants affected and for the percentage of abnormal eyes identified in the two patient groups, OHT and GON.

Standard and SWAP visual fields were classified as abnormal if the result of the GHT was outside normal limits, the CPSD was triggered at 5% probability or worse, or the MD was triggered at 5% probability or worse, with no generalized depression. Quadrants were identified as abnormal by a cluster of three or more points at 5% probability or worse on the pattern-deviation plot. These criteria produced a specificity for SWAP of 86%.

A problem with this study is that because of the longitudinal study design, the 28 normal controls were all enrolled after it was determined that they had normal SAP fields. To address this as best we could, we used the criteria for a normal SAP developed for the National Eye Institute–sponsored Ocular Hypertension Treatment Study (OHTS).[56] These criteria require a GHT result within the normal limits or a CPSD within the 95% normal limits. It was determined for OHTS that these criteria provided a specificity of approximately 92% for normal eyes (personal communication, Chris Johnson, August 1999).

Table 1. Percentage of Abnormal Test Results for Each Test in Each Patient Group

	GON (n = 71)	OHT (n = 37)	Normal (n = 28)
SAP	46 (33)	5 (2)	
SWAP	61 (43)	22 (8)	14 (4)
FDT	70 (50)	46 (17)	14 (4)
MAP	52 (37)	30 (11)	11 (3)

Data in parentheses are number of eyes.

TABLE 2. Relationships from χ^2 Analysis in GON Eyes for Each Ganglion Cell–Specific Field Test Paired with SAP

	SAP	
	Abnormal	**Normal**
SWAP		
Abnormal	26	17
Normal	7	21
FDT		
Abnormal	29	21
Normal	4	17
MAP		
Abnormal	23	14
Normal	10	24

FDT fields were abnormal when a cluster of two adjacent points reached 5% or worse probability limits. This yielded a specificity for FDT of 86%. A MAP field was considered abnormal if a cluster of three adjacent points 2 SD from normal or two adjacent points 3 SD from normal were found, resulting in a specificity for MAP of 89%.

RESULTS

Abnormal Visual Function

Table 1 shows the percentage of abnormal results for each test in each patient group using the outlined criteria for abnormality. Of the 71 eyes with GON, FDT identified the highest percentage, 70% (50/71), followed by SWAP with 61% (43/71), MAP with 52% (37/71), and SAP with 46% (33/71). FDT also identified a larger percentage of the OHT eyes, 46% (17/37), with SWAP showing 22% (8/37) and MAP showing 30% (11/37). Two OHT eyes were abnormal on SAP (5%). The number of normal eyes shown in Table 1 reflects the attempt to set specificity equally for the three visual function–specific subtests. A χ^2 analysis (JMP software, SAS, Cary, NC) showed that SWAP ($P = 0.003$), FDT ($P = 0.002$), and MAP ($P = 0.005$) all identified significantly more eyes than SAP in the GON group. Because this analysis is dependent on agreement between test results and not just on differences, the breakdowns are summarized in Table 2.

Table 3 gives the percentage of eyes by number of abnormal results for each group. This breakdown indicates that 10% (7/71) of the eyes with GON showed no visual function loss.

TABLE 3. Number of Eyes with Number of Abnormal Tests for Each Patient Group

Number of Abnormal Results	GON	OHT	Normal
4	19 (27)	0 (0)	
3	18 (25)	2 (5)	0 (0)
2	8 (11)	7 (19)	1 (4)
1	19 (27)	17 (46)	7 (25)
SAP only	1	0	0
SWAP only	6	1	3
FDT only	8	10	3
MAP only	4	6	1
0	7 (10)	11 (30)	20 (71)

Data in parentheses are percentage of eyes tested.

TABLE 4. Specificity and Sensitivity with Paired Tests

	Specificity	Sensitivity
SWAP or FDT	75% (21)	80% (57)
SWAP or MAP	82% (23)	80% (57)
FDT or MAP	82% (23)	80% (57)
Any of the three tests	75% (21)	90% (64)

Data are percentages with number of tests in parentheses.

An additional 27% (19/71) showed loss on only one test, whereas 63% were abnormal on two or more tests. Of the OHT eyes, 30% (11/37) had abnormal function on two or more tests in spite of normal-appearing optic nerves, whereas only 4% (1/28) of normal eyes showed such a finding. Combining two tests improved the sensitivity, with slight reductions in specificity (Table 4). Table 3 also shows that individual eyes could be abnormal on any one of the tests in both the GON and OHT groups.

Overlap in Location of Field Defect

A percentage of eyes showed at least one defective quadrant in common for various pairings of the three visual function–specific field tests, when both tests in the pair were abnormal. Thirty-eight of 39 GON eyes that were abnormal on both SWAP and FDT had one quadrant in common (97%). MAP and FDT also had a 97% overlap (30/31), with MAP and SWAP showing a 92% overlap (24/26). Although many fewer OHT eyes showed abnormality on two or more tests, when two were abnormal, there was always overlap. Six eyes were abnormal on SWAP and FDT, five on MAP and FDT, and four on SWAP and MAP.

Extent of Field Defect

The relative extent of defect between paired test results (number of quadrants) is given in Table 5. The total number in each case should equal the numbers given in the previous paragraph for eyes shown to be abnormal on both tests. The extent of defect showed individual differences and was not always greatest on the same test in a given pair. However, overall, defects were greatest on FDT, followed by SWAP, followed by MAP.

In all 71 GON fields, regardless of overlap, the mean number of quadrants (from 0 to 4) that were abnormal for each test were 0.59 ± 1.10 (SAP), 1.18 ± 1.38 (SWAP), 1.67 ± 1.62

TABLE 5. Number of Eyes with More Extensive Field Loss for Paired Tests When Results in Both Were Abnormal

	SWAP > FDT	FDT > SWAP	SWAP = FDT
GON	8	20	10
OHT	3	1	2
	MAP > FDT	**FDT > MAP**	**FDT = MAP**
GON	7	19	5
OHT	4	1	0
	SWAP > MAP	**MAP > SWAP**	**MAP = SWAP**
GON	14	6	6
OHT	2	2	0

(FDT), and 0.79 ± 1.34 (MAP). In the 37 OHT eyes, abnormal quadrants were 0.02 ± 0.16 (SAP), 0.47 ± 1.10 (SWAP), 1.00 ± 1.27 (FDT), and 0.95 ± 1.61 (MAP). Normal eyes had an average of 0.25 abnormal quadrants or less for SWAP, FDT, and MAP.

Discussion

Theories

This work shows the presence of significant overlap in the location of visual field deficits for SWAP, MAP, and FDT when more than one function is affected. This overlap may be expected in eyes with known optic nerve damage, but it is present even in OHT eyes with normal-appearing optic discs and normal standard visual fields. This implies that a particular location (quadrant) of the retina is affected first in a given individual regardless of the test used. It does not, however, tell which of the visual functions was first to become reduced at that location.

The high percentage of GON and OHT eyes with abnormal test results only on SWAP, only on FDT, or only on MAP (Table 2) calls into question the theory that the magnocellular optic nerve fibers show the earliest functional loss from glaucoma and lends support to the theory that not all eyes are affected in the same way in the earliest stages of the disease. Follow-up of these eyes is necessary to determine the relative rates and pattern of drop-out for each visual field test.

Which Tests to Use

This study indicates that each of the three visual function–specific tests is more sensitive to early visual field loss in eyes with GON than is SAP. FDT identified 70% of these eyes when specificity for normal control eyes was set to 86%. Standard fields using routine clinical criteria for abnormality identified only 46%. This suggests that FDT may be useful for observing rather than just screening for glaucoma. However, in the OHT group of patients, FDT was abnormal in 46%, a percentage that is much higher than the percentage expected to convert to glaucoma and also much higher than the percentage shown for other function-specific tests. SWAP and MAP have identified between 20% and 25% of the OHT eyes, depending on the study.[9,10,31,40] The reason FDT is abnormal in so many OHT eyes must be evaluated.

Another issue surrounding FDT and requiring further study is the suggestion that FDT is processed by a small subset of the M-ganglion cells, called the M-y ganglion cells.[12,43] This suggestion is based on work by several physiologists who have identified cells at the level of the retina and LGN that respond in a nonlinear way to pooled inputs from different parts of their receptive fields. That is, the cell responds best at twice the fundamental modulation frequency.[57] Others have not found evidence to support the existence of a distinct, nonlinear class of magnocellular unit and propose that the changes in temporal frequency leading to alterations in the spatial frequency contrast response could be found in both M and P units at retina and LGN.[58,59]

Attempts to relate the frequency-doubled percept to M-y or M-type cells using a variety of techniques in human observers are in progress, but results have been inconclusive.[50,60–62] At present, we can say that detection of targets using the combination of high temporal flicker and low spatial frequency comparable to that used in FDT is often attributed to the M-cells.[59,63]

FDT has some advantages over SAP and SWAP. The test time is approximately one half the time required for a full-threshold 24-2 field, primarily because of the smaller number of test locations used. As with MAP, the results are less affected by blur, pupil size differences if always greater than 2 mm in diameter, or bifocal correction,[13] and FDT has lower test–retest variability than SAP.[64] It is similar to SAP and SWAP in that statistical analysis packages can be developed to give global indices, such as MD and PSD, and pattern deviation probability plots can be derived.

Although FDT shows promise for early detection of visual loss due to glaucoma, more work is needed to answer questions that have already been answered in part for SWAP,[21,30,33,34,36] such as: What amount of isolation is necessary before other ganglion cell subtypes can pick up detection of the target? Will FDT work well for advanced cases of glaucoma? How will the test perform for reliable identification of progression?

Although SWAP identified slightly fewer GON eyes (61%) the percentage of OHT eyes (22%) was more in line with the percentage expected to convert to glaucoma. In addition, SWAP has more than 12 years of longitudinal evaluation and has been shown by several independent studies to be a more effective test than SAP for early detection of glaucoma-related field loss. SWAP also identifies progression 1 to 3 years before detection by standard visual fields[30,34,35] and works well in advanced cases that are not complicated by the presence of advanced cataracts.[36] Although, SWAP has slightly higher test–retest variability than SAP—more than is desirable for long-term follow-up for progression of glaucomatous vision loss[65,66]—it has consistently been shown superior to SAP for identifying progression.[30,34]

Motion perimetry has also been shown to be superior to standard visual fields for early detection of glaucomatous vision loss.[17,67] However, it is time consuming and has more variability than the other tests, which makes it less than ideal for observing patients over time. Answers to the same questions posed earlier for FDT also must be found for MAP.

Summary

Each of the three visual function–specific field tests, SWAP, FDT, and MAP, is superior to SAP for identifying eyes with GON. These results suggest that FDT may be useful as more than just a screening test. We also found that loss of function is specific to a given retinal location in each eye. Follow-up of eyes showing defects on only one test should allow better understanding of the rate and pattern of drop-out of various visual functions.

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