

Early Diagnosis With Functional Tests: Myth and Reality

Assessing visual function in glaucoma.

BY CHRIS A. JOHNSON, PhD

In recent years, many new test procedures have been developed for the early detection of visual function loss in glaucoma.¹⁻⁶ Several of these procedures have demonstrated (1) an ability to detect glaucomatous loss before conventional clinical tests do, (2) a predictive value for identifying which patients are likely to experience progressive changes and which are likely to remain stable, and (3) an ability to determine progression more readily than conventional clinical tests.¹⁻¹⁴ In particular, Short-Wavelength Automated Perimetry (SWAP), Frequency Doubling Technology (FDT) perimetry, high-pass resolution perimetry, flicker perimetry, motion perimetry, rarebit perimetry, and multifocal visual evoked potentials all provide distinct advantages for detecting early glaucomatous visual function loss.¹⁻²¹ It takes a considerable amount of time, however, to acquire this information through careful, well-controlled clinical investigations. Moreover, for all of the successful procedures are numerous other techniques that have shown promise but were not able to provide a decided clinical benefit.

How does the interested clinician decide whether a new technique for assessing visual function is effective (reality) or not (myth)? This article provides some guidelines for making the determination.

SEPARATING MYTH FROM REALITY FOR VISUAL FUNCTION TESTS

Guidelines

An important factor in evaluating the efficacy of a new clinical test procedure pertains to which techniques can provide useful, important, valid clinical findings and which are limited in their overall performance. This is a difficult issue, but I believe that Harper et al²² have provided some useful guidelines. They cite seven

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standards for the evaluation of diagnostic tests: (1) specification of spectrum composition; (2) analysis of pertinent subgroups; (3) avoidance of work-up or verification bias; (4) avoidance of review bias; (5) presentation of the precision of results for test accuracy; (6) presentation of indeterminate test results; and (7) presentation of test reproducibility. Their article contains details of these criteria and their application to 20 clinical research studies. One of the researchers' rather startling findings was that all 20 clinical studies described in their report demonstrated only limited compliance with the seven aforementioned standards! This revelation clearly indicates that all investigators of clinical diagnostic test procedures should pay closer attention to these issues when conducting future research so that practitioners can receive greater benefit.

I would add several guidelines to those noted earlier. First, I believe that it is important to confirm the findings of a clinical research study, either as part of the initial study or, preferably, by verification from an independent laboratory. The replication of findings usually strengthens their significance, and the robustness of research results enhances their applicability to all clinical situations.

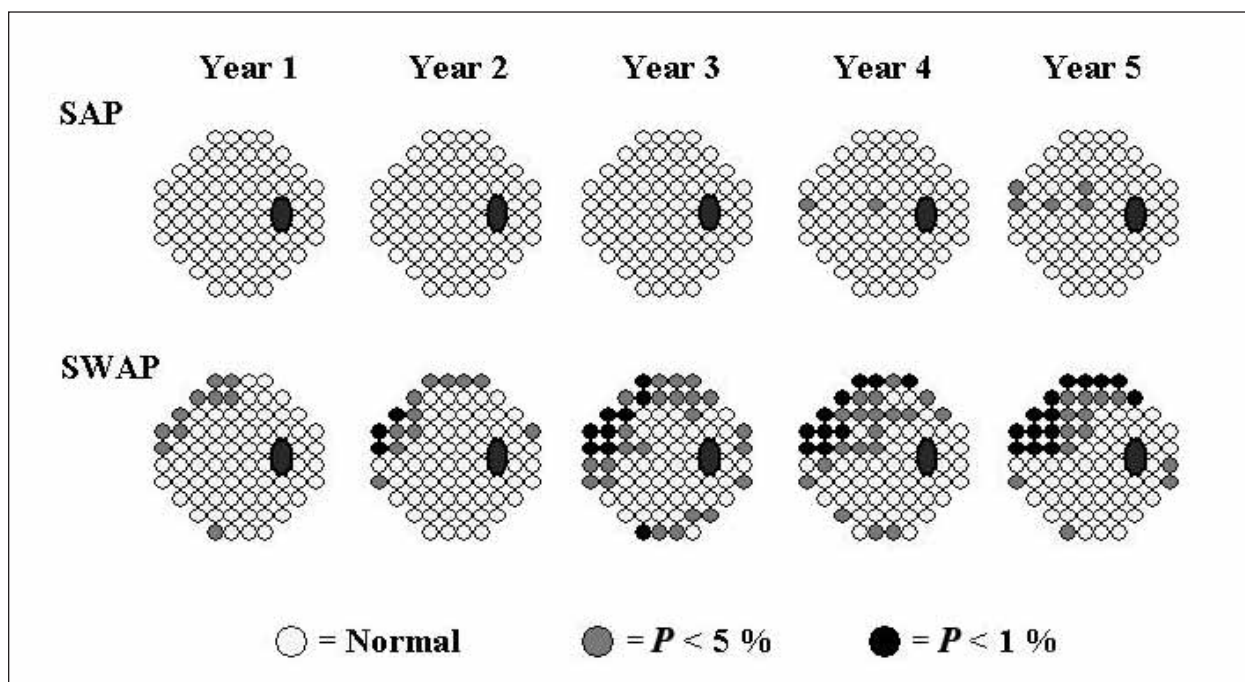


Figure 1. The SWAP results show a superior nasal step deficit during year 1 that progresses to a superior arcuate defect over the next 4 years. Standard automated perimetry (SAP) results are within normal limits for the first 3 years but begin to show a superior nasal step during years 4 and 5. (Reprinted with permission from Demirel S, Johnson CA. Incidence and prevalence of Short Wavelength Automated Perimetry [SWAP] deficits in ocular hypertensive patients. *Am J Ophthalmol.* 2001;131:709-715.)

○ = locations that are within normal limits.

● = locations that are worse than the lower 5% of normal limits.

● = locations that are worse than the lower 1% of normal limits.

Second, it is useful to determine the variation among research results from many different laboratories. For some reason, a test procedure usually performs better in the hands of the investigator who developed it than for other researchers who are evaluating the technique. A procedure that consistently produces accurate results at different laboratories should generate higher enthusiasm than one that yields variable outcomes.

Finally, longitudinal follow-up evaluations can help reveal the clinical value of a new diagnostic test procedure. With a series of test results obtained over a period of time, it becomes possible to determine the clinical sensitivity, specificity, variability, validity, robustness, predictive value, and other important attributes of the test procedure. Three illustrative examples follow.

Example No. 1

Figure 1 presents the results of SAP and SWAP testing in the right eye of a patient with elevated IOP and other risk factors for developing glaucoma. Visual field locations with sensitivity that is within normal limits (normal) as well as those below the normal 5% ($P < .05$) and

1% ($P < .01$) probability limits (abnormal) are given for a 5-year time period for SAP and SWAP. The SWAP results show a superior nasal step in year 1 that progresses to a superior arcuate defect in years 2 through 5. SAP results are within normal limits for the first 3 years of testing, but they begin to show the onset of a superior arcuate defect in years 4 and 5. SWAP deficits occurred several years before the SAP abnormality and were predictive of the development and location of the SAP visual field loss.

Example No. 2

Figure 2 compares FDT perimetry and SAP results for testing performed over a 5-year period on the left eye of a patient with risk factors for developing glaucoma. As in the earlier example, the FDT findings reveal abnormalities approximately 2 years earlier than the SAP results, and they are predictive of the onset and location of subsequent SAP sensitivity losses. FDT results initially show a superior nasal step, which progresses to a superior arcuate defect over 4 years. The deficit remains as a superior nasal step for the 4th year of testing with SAP.

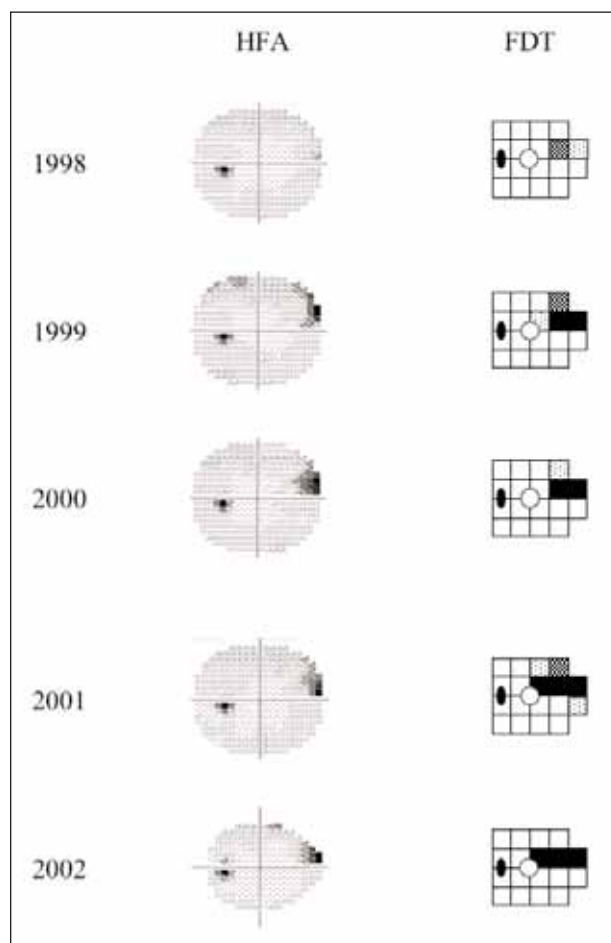


Figure 2. A gray-scale representation compares SAP (left) and FDT perimetry (right) over 5 years. The shaded regions indicate locations with progressively lower sensitivity. SAP results are within normal limits during the first year, with a superior nasal step developing during the next 4 years. FDT results indicate a superior nasal step in the first year that progresses to a partial superior arcuate defect over the next 4 years.

Example No. 3

Figure 3 presents results obtained with rarebit perimetry for several patterns of visual field loss. Briefly, rarebit perimetry incorporates short presentations of very small stimuli consisting of one or two bright spots on a dark background shown on an LCD computer display. The arrangement of the dots accords with a predetermined pattern that is designed to detect early visual field losses in glaucoma and other ocular and neurologic diseases. The patient's task is to indicate whether he detects one or two dots for each presentation. Although the technique is relatively new, the current results for a variety of visual pathway disorders have been clinically useful.²⁰

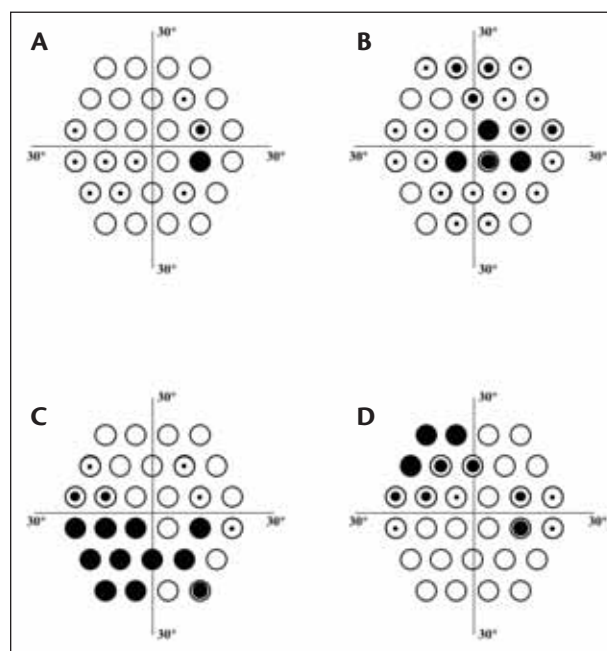


Figure 3. Rarebit perimetry testing reveals an inferior defect produced by chronic papilledema (A), a central scotoma produced by an acute demyelinating optic neuropathy (B), an inferior altitudinal defect produced by a nonarteritic anterior ischemic optic neuropathy (C), and a superior visual field deficit that is part of a homonymous congruent deficit from an initial attack of multiple sclerosis (D). (Reprinted with permission from Frisén L. New, sensitive window on abnormal spatial vision: rarebit probing. *Vision Res.* 2002;42:1931-1939.)

SUMMARY

Evaluating the clinical impact and significance of a test procedure for visual function assessment in glaucoma remains both a challenge and an enigma. Careful, well-controlled, longitudinal investigations of a large cohort of patients and control subjects are required, but these studies are costly and time-consuming. Following the guidelines set forth herein may help individuals determine which new procedures have distinct clinical benefits and which are of limited value. □

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