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Advances in Mapping the Glaucomatous Visual Field: From Confrontation to Multifocal Visual Evoked Potentials

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Abstract

The visual field is affected in many conditions of the eye, glaucoma being probably the most striking among them, and is hence an essential component of glaucoma diagnosis. Several methods have been developed over time, the simplest of which being the confrontation test. Computer-automated, static threshold perimetry is currently the most common method used to determine the glaucomatous visual field. With the advent of Frequency Doubling Technology (FDT), specific subsets of retinal ganglion cells that project to the magnocellular layer of the lateral geniculate nucleus can be tested resulting in earlier detection of visual field loss. The subjective nature of the above mentioned methods results in many shortcomings which can produce clinically significant errors. The multifocal Visual Evoked Potentials (mfVEP), a technique that evaluates the pathway from the retinal receptors to the occipital cortex, has been proposed to objectively measure the visual field, and may herald a new era in the diagnosis and management of glaucoma.

INTRODUCTION

The simplest eyes in nature function as basic light detectors, whereas the human visual system has evolved into an extremely complex mechanism for processing visual information. The photoreceptors convert incident light energy into electrical signals that are processed by neural elements in the retina, optic nerve and higher visual centers of the brain, involving various subpopulations of neural mechanisms that are responsible for encoding fundamental properties of the visual image such as motion, form, color and depth.

The field of vision is defined as the area that is perceived simultaneously by the fixating eye. The limits of the normal field of vision are 60° into the superior field, 75° into the inferior field, 110° temporally, and 60° nasally.

There are several aspects of visual field testing that are of clinical value. First, it is a means of detecting early functional deficits produced by a wide variety of eye diseases, many of which have their initial effects on peripheral vision while having little or no effect on foveal vision. Glaucoma is perhaps the most notable of these types of disorders. Second, specific features of localized regions of reduced sensitivity can help define the locus of pathology in the visual pathways and the type of disease entity that is likely to be present. Third, patients are often unaware of peripheral vision loss, especially if it has progressed gradually.

With the advent of newer technologies such as the multifocal Visual Evoked Potentials (mfVEP), visual field testing has changed from an art to a more quantitative science. In this article, we have sought to review the recent advances in visual field detection.

METHODS OF DETERMINING THE VISUAL FIELD

Three methods of assessment of the visual field are summarized as follows:

1. Confrontation test
2. Perimetry (Subjective)- Manual static perimetry, Manual kinetic perimetry, Automated static perimetry, Automated kinetic perimetry.
3. Multifocal Visual Evoked Potentials (mf VEP-Objective)

CONFRONTATION

Confrontation visual field exam is a quick and basic evaluation of the visual field done by an examiner sitting

directly in front of the patient. In this test, the patient's right visual field is compared with the left field of the examiner, and hence the test requires that the examiner has a normal visual field. It may be used as a quick screening test in patients to determine obvious visual field defects, but may not be as sensitive as some of the other tests available.

PERIMETRY

Perimetry is a psychophysical test designed to give a quantitative estimate of the function of the visual field.

KINETIC VS STATIC PERIMETRY

In kinetic perimetry, a stimulus of set size and intensity is moved from a nonseeing area of the visual field to a seeing area along a set meridian. The procedure is repeated with the use of the same stimulus along other meridians, usually spaced every 15°. By joining these areas of equal sensitivity, an isopter is defined.

In static perimetry, the size and location of the test target remain constant, but the intensity of a stationary target of constant size is varied to determine the sensitivity of specific locations in the field of vision, i.e. it measures the retinal sensitivity at predetermined locations in the visual field.

MANUAL V/S AUTOMATED PERIMETRY

The Goldmann perimeter is the most widely used instrument for manual perimetry. It is a calibrated bowl projection instrument with a background intensity which is well within the photopic range. The size and intensity of targets can be varied to plot different isopters kinetically and determine local static thresholds.

In cases of suspected functional visual loss, tangent screens have been often used to test patients for tubular visual fields, the demonstration of visual fields of similar size at various testing distances. [1] However, tangent screen testing has several shortcomings, including the inherent subjective nature of manual examinations, difficulty of documentation, and decreasing availability. [1]

The introduction of computers and automation heralded a new era in perimetric testing. [2] The most common test of functional vision used for the clinical diagnosis and evaluation of the stage of glaucoma is computer-automated, static-threshold perimetry, using standard stimulus conditions and psychophysical procedures.

Static testing can be performed in a standardized fashion with minimal perimetrist bias. A quantitative representation of the visual field can be obtained more rapidly than with manual testing. The computer allows stimuli to be presented in a pseudorandom, unpredictable fashion. Patients do not know where the next stimulus will appear, so fixation is improved, thereby increasing the reliability of the test. Random presentations also increase the speed with which perimetry can be performed by bypassing the problem of local retinal adaptation, which requires a 2-second interval between stimuli if adjacent locations are tested.

Computerized static perimetry provides an estimate of the reliability and variability of the test. Data storage is possible, and computer-assisted statistical analysis is available.

The most widely used automated perimeters are the Humphrey visual field analyzer (HFA) and the Octopus perimeter. Both perimeters perform a wide variety of programs so that examinations can be tailored to the needs of individual patients. Computerized perimetry can be used as an alternative to tangent screen testing for tubular visual fields. [1] Another advantage is that patients apparently do not easily recognize the visual field expansion, making it an ideal test to “fool” patients with functional visual loss.

Computerized Automated Perimetry uses a small fixed-size stimulus, and light intensity is varied. Although these stimuli easily attract attention near fixation, they are less efficiently seen with increasing eccentricity. [3,4] Lower visual acuity of peripheral vision could be compensated for by increasing stimulus size, and because large stimuli in the periphery are more salient, it is possible that these larger stimuli would be more resistant to the effects of divided attention.

A number of testing strategies and screening programs have been used. Screening tests can quickly identify abnormal visual fields and provide information about the location of defects. Multiple-level tests also provide some data about the depth of defects. Shallow, subtle defects and early generalized depression may be missed by screening tests.

On the Octopus perimeter, the intensity of the suprathreshold stimulus is based on data from age-matched normal subjects. On the Humphrey perimeter, age-matched data can be used (age referenced screening) or the central reference level can be measured by thresholding at one location in each quadrant and adjusting the height of the hill of vision accordingly. Alternatively, the central reference level can be set manually at a level appropriate for a patient's age.

Automated suprathreshold perimetry has been used as the

test of choice for glaucoma screening in population-based epidemiologic studies. In suprathreshold perimetry, stimuli are presented above the estimated detection threshold of a normal visual field location. If the patient responds, it is assumed that the corresponding test location does not have significant loss. In normal observers and those with early glaucoma, most stimulus presentations occur well above threshold, and the observer may be less uncertain of how to respond. Suprathreshold tests may therefore be easier tasks to perform with these patients, who often have little or no experience with perimetry. Although it is widely accepted that suprathreshold tests may be less sensitive to shallow visual field loss than threshold tests, they have often been used in epidemiologic screening [5,6,7] and are routinely used in primary eye care. As with threshold perimetry, the results of conventional suprathreshold tests exhibit large test–retest variability in patients with glaucoma. [8]

Two main screening strategies are used:

1. Single-Level Suprathreshold Test: A stimulus that is 2 to 6 db brighter (suprathreshold) than the expected hill of vision is used to test multiple locations in the visual field. Results are recorded simply as seen (normal) or not seen (defect). On the Humphrey perimeter, this is called the threshold-related strategy.

2. Two-Level Suprathreshold Test: These tests often are referred to as three-zone tests because the visual field is classified into three categories: normal, relative defect, and absolute defect. As in the single-level test, testing is performed initially with a mildly suprathreshold stimuli approximately 2 to 6 db brighter than the expected threshold. Seen spots are recorded as normal. If a spot is not seen, the brightest stimulus available for the apparatus is presented. If the brightest target is seen, a relative defect is recorded. If the brightest target is not seen, an absolute defect is recorded.

The full-threshold visual field test is currently regarded as a quasi-standard in perimetry. It is time consuming, and, particularly at damaged field locations, its threshold estimates are highly variable. [9] The Swedish interactive test algorithm (SITA) standard (a more efficient threshold strategy based on maximum-likelihood estimation) has much shorter test times, but its variability is similar to that of the full-threshold strategy. [10,11,12] Threshold tests are demanding procedures, and many patients produce consistent results only after some training. [13] Many clinical applications, however, call for fast, simple, and reliable visual field tests that can be performed by patients with no training.

FREQUENCY DOUBLING TECHNOLOGY (FDT)

Visual field testing with standard automated perimetry (SAP) is not selective for a particular ganglion cell type. As there is a considerable overlap in the receptive fields of retinal ganglion cells, a nonselective test may not be sensitive for the earliest loss of retinal ganglion cells due to a considerable redundancy in the coverage of a given location in the retina. Therefore, attention has been directed at developing functional tests that can target selective retinal ganglion cell types.

Frequency doubling technology [14,15] (Welch Allyn, Skaneateles, NY, and Carl Zeiss Meditec, Dublin, CA) is a recent development in automated perimetry that attempts to functionally isolate a subset of retinal ganglion cells that project to the magnocellular layer of the lateral geniculate nucleus and sub-serve visual functions such as motion detection and scotopic vision. The frequency doubling phenomenon, or “frequency doubling illusion,” as described by Kelly [16,17] is a phenomenon where alternating light and dark bars appear to have twice the actual number of bars created by a low spatial frequency sinusoidal grating undergoing high temporal frequency counterphase flicker. This effect is thought to be mediated by magnocellular retinal ganglion cells with nonlinear response properties (My-cells). [15] However, there is evidence to show that at contrast threshold, all magnocellular cells are likely to be responsive to this type of stimuli. [18,19] Studies have shown that the screening-mode of the FDT demonstrates good sensitivity and specificity in detection of glaucomatous visual field loss. [20,21]

Given the relatively large size and low density of this FDT stimulus array, changes in the instrument design—specifically increases in the target spatial resolution—may improve visual field defect profile description. Prototype instrumentation using more test locations and a smaller stimulus size has been described, attaining a stimulus resolution increase. With this instrumentation FDT testing using a stimulus pattern equivalent to the Humphrey field analyzer 24-2 test pattern resulted in a positive impact on discriminatory power for

detection of initial glaucomatous visual field loss. A second generation instrument using similar small FDT stimuli, the Humphrey Matrix, became available for clinical use in 2003. To date, however, scant clinical data are available describing this instrument's performance.

With high sensitivity and specificity, FDT perimetry is increasingly employed as a diagnostic tool for glaucoma. [9] Frequency doubling technology perimetry offers the potential advantage of reduced testing time and less variability compared with SAP. [22,23] Several cross-sectional studies have suggested that FDT may be able to detect visual field loss before SAP. Paczka and associates [24] found that FDT perimetry had better overall performance for detection of glaucomatous damage than the assessment of retinal nerve fiber layer photographs, suggesting that FDT may be sensitive to early glaucoma damage. A recent longitudinal study by Bayer and Erb [25] showed that progressive defects on FDT were detected 12 to 24 months before SAP visual field progression; however, all patients in their study already had SAP visual field defects at baseline. Frequency doubling technology has also been shown to detect abnormalities in the other hemifield of patients with SAP visual field defects restricted to one hemifield. [26,27]

Longitudinal studies evaluating the ability of the FDT perimetry to predict the development of SAP visual field defects in glaucoma suspects with normal SAP visual fields at baseline are lacking. [28]

PERISTAT AND BINOCULAR VISUAL FIELD TEST

Peristat is a computer-based reliable self-test perimetry system that demonstrates high clinical utility for the detection of visual-field defects from glaucoma. [29] Peristat could be a valuable public health tool for cost-effective screening of glaucoma. [29]

Binocular visual field testing gives the best indication of a subject's visual field in terms of functioning and visual disability. [30,31] For example, the availability in various automated perimeters of the binocular Esterman visual field test has meant this has become the standard to implement the guidelines recommended by the Driving and Vehicle Licensing Authority (DVLA) in assessing patient's legal fitness to drive in the UK. Moreover, the binocular Esterman test has been widely used in many studies that have examined the link between visual function and visual disability. [32] However; the binocular visual field testing is not routinely performed because monocular visual fields are clinically more relevant in both detection and follow-up of degenerative retinal disease such as glaucoma.

FLICKER PERIMETRY

There are two twpes of flicker perimetry: temporal modulation perimetry (TMP), which measures contrast thresholds for a fixed temporal frequency, and critical flicker frequency (CFF), which measures the highest frequency for which flicker is detected at a fixed contrast. Both methods of flicker perimetry testing provide acceptable test-retest reliability, and both can distinguish normal subjects from glaucoma patients. However, Yoshiyama, et al suggested that TMP is more effective in separating normal subjects from glaucoma patients than CFF, suggesting that TMP is the method of choice for detecting glaucomatous damage using flicker perimetry. Lachenmayr, et al suggested that automated flicker perimetry might represent a specific functional test of the retinal Y-ganglion cells. Flicker fusion frequency (FFF), the threshold criterion of flicker perimetry, is a functional parameter of the temporal transfer properties of the visual system.

HIGH PASS RESOLUTION PERIMETRY (HPR)

High-pass resolution perimetry, or the “ring test,” is a recently developed type of acuity perimetry. It introduces a new principle for visual field examination, made possible by recent advances in the physiology of vision and computer technology. The method utilizes spatially high-pass filtered “vanishing” targets to measure resolution rather than differential light sensitivity, as do all other perimetric systems. Chauhan, et al suggested that high-pass resolution perimetry detects glaucomatous visual field progression earlier than conventional perimetry in most patients with progression.

RAREBIT PERIMETRY

The Rarebit perimetry test depends on minute stimuli (“rare” bits or “microdots”) and it replaces the conventional thresholding approach (“How well do you see here?”) with simple checks for the presence of function (“Is there a receptive field here? And here? And here?”). Hence, rather than gauging the level of function, the test probes the integrity of the neural matrix. Rarebit Perimetry uses a set number (24) of rectangular test areas and probes repeatedly for the presence of vision within each area, in ever-new locations. Because the retina normally is seamlessly tiled by receptive fields, the expected outcome is that all rarebits

should be seen (100% “hit rate”, or nearly so: provision has to be made for the blindspot and angioscotomas, and for lapses of attention).

SHORT WAVELENGTH AUTOMATED PERIMETRY (SWAP)

The principle of this method is selective testing of the short-wavelength sensitive (SWS) cone-mediated mechanisms. This method is established in early detection of glaucoma, where its use is to detect changes predominantly at the retinal ganglion cell level and loss of retinal nerve fibers. SWS mechanisms also are reported to be susceptible to damage in a variety of retinal diseases, where changes are less specific for retinal nerve fibers and more confined to alterations of the inner retina. Animal experiments have shown a more selective loss of SWS cones to phototoxic or ischemic stimuli.

FREQUENCY OF PERIMETRIC TESTING

There are no set criteria for the frequency of perimetric testing. In glaucoma it has been found that perimetry can be optimised by postponing the next test in the case of an apparently stable field and accelerating the next test in the case of a suspected progression. [33] This results in an earlier diagnosis, a lower perimetric frequency and a shorter period of uncertainty for the patient. Several authors have assessed the optimal frequency of visual field testing by investigating the effect of increasing the frequency to more than one test per year. [34,35,36] Doubling the frequency to two tests per year slightly reduced the time required for diagnosing progression, but failed to halve this time. A frequency higher than four tests per year did not yield any significant additional information [343536] .

VARIABLES AFFECTING ACCURACY AND RELIABILITY OF PERIMETRIC TESTING

Visual field defects may reflect glaucomatous abnormalities or manifest an artifact of the testing process. To distinguish artifact from true defect, it is important to consider the variables involved in perimetric testing and the way that these variables affect visual physiology. Standardization of the various equipment and patient variables is essential to produce accurate and consistent fields.

Instrument variables:

1. Background Luminance: The background luminance of the perimeter determines the level of retinal adaptation and, therefore, the contour (shape) of the hill of vision. 37
2. Stimulus Size: In automated perimetry, the stimulus size usually is held constant while the intensity is varied. Most automated perimeters use the Goldmann size III target (4 mm 2 area) as a standard but allow the stimulus size to be altered. Because of spatial summation, larger targets are seen more easily than smaller targets.
3. Stimulus Duration: Targets that are projected for longer periods are seen more easily than targets that are projected for briefer periods. This process is called temporal summation. Temporal summation continues to improve sensitivity up to maximum exposure duration of 0.5 to 1 second; however, the major effect is complete by 0.1 to 0.2 second. [80]
4. Fixation Control: Steady fixation is crucial to the production of accurate visual fields. Fixation is improved by minimizing stimulus duration and testing at random sites throughout the visual field.
5. Interstimulus Time: The interval between stimulus presentations is adapted to the speed of the patient's response.
6. Cupola Diameter: The diameter of the cupola varies between models from 30 to 51 cm. The perimetrist must be aware of the diameter of the bowl to determine the proper correction to be used for the near add refraction.

Patient variables:

1. Refractive Errors: Uncorrected refractive errors cause defocusing of the test target and apparent depression of retinal sensitivity. Media opacities, such as cataracts, can cause generalized depression of the visual field. As cataracts become denser, visual field defects may appear to worsen. It is important to check for changing acuity, worsening of cataracts, and other media opacities when analyzing visual fields for progression.
2. Pupil Diameter: The amount of light that enters the eye is proportional to the pupillary area. Testing with pupillary diameters of less than 2.5 mm may result in generalized depression of the visual field

by decreasing the light incident on the retina and by increasing diffraction at the pupillary margin. These factors may artifactually simulate the development or progression of glaucomatous visual field defects.

3. Age: A linear decrease in retinal sensitivity occurs with increasing age. 38 On the Octopus perimeter, sensitivity decreases by 0.5 db/decade in the central visual field and by 1 db/decade in the peripheral visual field. 39
4. Facial Structure: Ptosis of the upper lid is a common cause of depression of the superior visual field.
5. Perimetric Experience: There is a clear learning curve for perimetry. The learning effect is greatest between the first and second tests.
6. Fatigue: Patient fatigue from prolonged testing may lead to decreased retinal sensitivity. Often, fatigue is the limiting factor when an attempt is made to increase accuracy by increasing test time. 40,41
7. Psychological Factors: Patient comfort, cooperation, and level of motivation strongly influence the differential light threshold. Stress, fear, and poor concentration can impair the accuracy and reliability of the examination.

Substantial ganglion cell damage can take place before SAP detects functional deficits. [42,43] Further, some patients have difficulty performing this test in a reliable and reproducible fashion. Because of these problems and the importance of assessing early glaucomatous damage, alternative tests of visual function have been proposed.

THE MULTIFOCAL VISUAL EVOKED POTENTIALS (MF VEP) - AN OBJECTIVE METHOD OF VISUAL FIELD ASSESSMENT

INTRODUCTION

The multifocal VEP (mfVEP), introduced by Baseler et al. [43] is a more recent entry into the field of objective field-testing. [44,45] The visual evoked potential (VEP) is a gross electrical potential generated by the cells in the occipital cortex. It is easily recorded with scalp electrodes and provides an objective and reproducible measure of the function of the visual pathways up to and including the visual cortex. For over 40 years, the VEP has been used to diagnose and study diseases of the visual system. However, it has been of limited use in the study of glaucoma. The reason is simple. The VEP does not provide a topographical measure and glaucomatous damage often involves localized regions of the retina. In principle, this limitation could be overcome by obtaining VEPs at different retinal locations but this would be too time consuming. A new VEP method, based upon multifocal technology circumvents this problem. With the multifocal VEP (mfVEP) technique, many (typically 60) spatially local VEP responses can be recorded simultaneously allowing spatially localized damage to be identified.

Over the last 40 years, the pattern VEP has been used as an "objective" assay of many psychophysically elicited responses, including visual acuity, contrast sensitivity, and color vision. "Objective" is defined as (1) requiring no motor or verbal response from the subject, and (2) relatively uninfluenced by "higher" cognitive activity. [46]

A number of studies have demonstrated that the mfVEP can detect glaucomatous damage. [46,47,48,49,50,51] Based on the findings of reliable amplitudes in some patients who had unreliable Humphrey results, the mfVEP has been proposed as an objective measure of visual fields by Hood and his associates.

TECHNIQUE

The technique evaluates the pathway from the retinal receptors to the occipital cortex and assesses the visual field out to 30° using a multifocal pattern VEP stimulus, with multichannel recording. The rapidly alternating checkerboard pattern derives which signal response in the brain came from which location in the field by cross-correlating the signal recorded with the pattern reversal on the screen.

One or more (usually 4) gold surface electrodes are placed with electrode paste on the subject's scalp over the occipital lobes after cleaning the scalp with one of the available detergents or ethanol. Improper skin preparation or drying of the conducting paste results in resistances above 10 kohms and decreases the amplitude of the VEP. Needle electrodes tend to have higher resistances and should probably not be used on more than one subject given the emergence of AIDS. Even surface electrodes must be properly sterilized before reusing. In most labs bipolar recordings are obtained

using a common reference electrode placed on one or both ears (using ear clips) or the forehead. A ground that is electrically zero cannot be found on the body, but for practical purposes the jaw, ear or nose is acceptable.

TYPES

1. Flash VEPs: The earliest VEP studies, originating from existing EEG facilities, used photostimulators to generate the spatially unstructured or diffuse flash VEP (FVEP). Discrepancies on the exact form of the wave components and their latencies are probably related in no small part to electrode location, luminance (brightness) of the flashes, and temporal frequency of the flashes between laboratories. The FVEP amplitude is dependent on temporal frequency, with the largest amplitude seen at approximately 10 Hz. Variability is present among subjects and even within the same subject comparing responses from electrodes over each hemisphere.

2. Pattern Visual Evoked Potentials: The second major methodological advancement, using a uniform repetitive checkerboard or bar grating pattern as the visual stimulus made the PVEP clinically useful. (Figure 1) This approach takes advantage of the functional organization of the visual cortex, which responds best to spatial pattern stimuli. The luminance for the whole display and the contrast between the black and white checks remain constant for a given PVEP. The checks or gratings are reversed or the pattern is turned on and off (with constant screen luminance). A PVEP can be generated with check displacement of less than the width of one square. 52,53,54 Refractive errors must be corrected so the pattern is not degraded at the retina, especially with checks less than 30 minutes of visual angle.

Figure 1

Figure 1: The Pattern multifocal Visual Evoked Potentials (mfVEP test): The patient is seated in front of the screen having a dartboard array with a changing checkerboard pattern. The patient concentrates at the center of the screen while electrical impulses transmitted from the eye to the brain are picked up by the electrodes placed on the scalp in the occipital region.

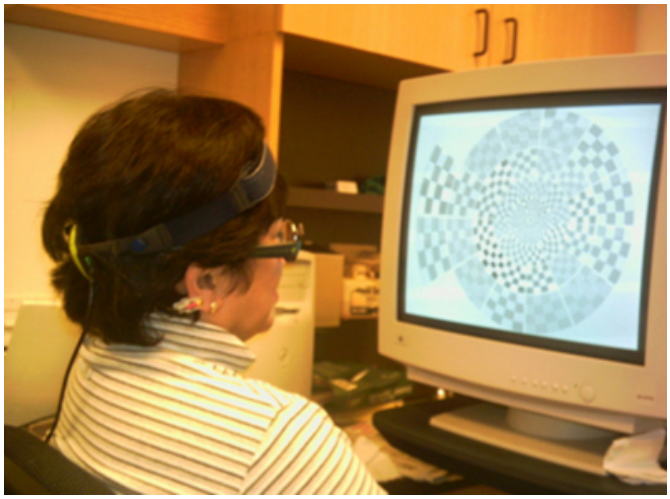
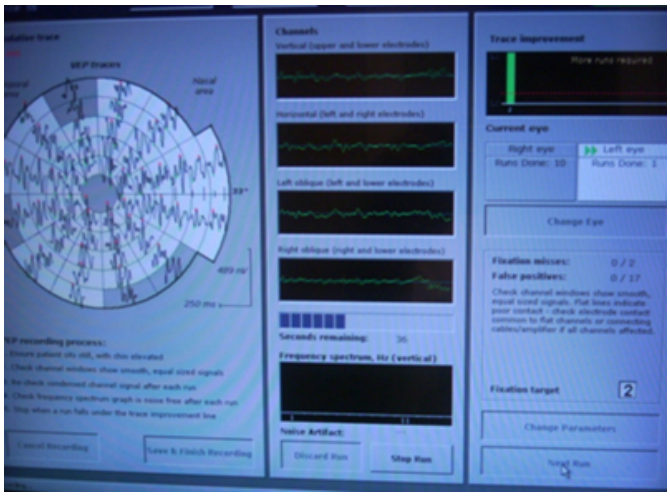


Figure 2

Figure 2:The multifocal VEP trace: The figure shows the screen in front of the operator. The four electrodes record the signal in four axes- right oblique, left oblique, horizontal and vertical.



Decreases in PVEP amplitude and wave shape perturbation are the usual findings in patients with glaucoma when large, high-contrast, bright checks are the stimuli. [54,55] Prolonged P100 latencies are found with a low luminance pattern, particularly if the field loss involves the macula field. [56] VEPs elicited by sinusoidal gratings may be prolonged in patients with elevated intraocular pressure without field loss.

[57] Ocular hypertensives who develop glaucoma do not consistently have VEP abnormalities.

Damage to the optic nerve and ganglion cells has been reported to affect visual evoked potential (VEP). Thus it was logical to base objective perimetry on VEP techniques. Wide intersubject variability, as described by Baseler et al. 1994, however, strongly limited the clinical use of VEP techniques. Hood et al. (2000) and Graham et al. suggested asymmetry analysis between eyes within subjects to overcome the problem of intersubject variability. Asymmetry analysis has been reported by Hood et al. to work well in early or unilateral cases of glaucoma but it is unable to identify defects when corresponding locations in the retina are damaged. Gender represents one of the factors considered to affect VEP variability. The scaling method was reported by Klistorner and Graham to remove the gender-based difference in VEP amplitude. Further improvements have been made to optimize VEP signals of multifocal stimuli.

Multifocal VEP results can be compared with visual fields obtained with standard SAP, such as the 24-2 Humphrey visual field (HVF; Carl Zeiss Meditec, Dublin, CA). In fact, special procedures have been developed to make such comparisons. [58,59] With these procedures, probability plots like those used to summarize the HVF results are produced. Two kinds of probability plots have been developed based on either local monocular mfVEP amplitudes [45,59,60] or the interocular ratio of the local monocular amplitudes. [45,48,51]

THE IMPORTANCE OF THE LEVEL OF SIGNAL TO NOISE RATIO (SNR):

How well the mfVEP does relative to the HVF in detecting glaucomatous damage depends on the SNR of the mfVEP recordings. [61] If the SNR of the recordings is poor, then the mfVEP will not do as well as the HVF. The SNR depends in turn on the stimulus paradigm and on the quality of the recordings. Shorter recordings, for example, decrease the SNR and decrease the number of abnormal clusters identified. Moreover, lower electrode resistance, additional electrodes, and less contamination from alpha and neck muscles increase the SNR and increase the number of abnormal clusters identified. Similarly, the mfVEP performs better in the regions of the field with good SNRs. As discussed, according to our theoretical framework, [45,62] the interocular test is more likely to pick up a defect in a particular region when the better eye has a large SNR in that region. The data from the present study can be used to test this hypothesis. In particular, the mean SNR for the better eye was calculated for the mfVEP locations corresponding to the clusters in the more affected eye.

ADVANTAGES

1. Compared with most electrophysiological tests of visual function, the mfVEP has the advantage that it produces a topographical measure of damage.

2. It presents objective results, removing the effects of patient indecision. It does not seem to have a learning curve, 63 and it has a high level of patient acceptance. 64

3. It has been shown to be 95% to 97% sensitive for glaucomatous scotoma detection in clinical trials. In contrast with HVF testing, the objective perimetry provided by mfVEP is less affected by patient performance or learning curve. 59

4. There is evidence that glaucomatous changes can be detected by the mfVEP technique before HVF losses occur. For example, Goldberg et al. 59 studied patients with glaucomatous disc changes and abnormal HVF in at least one eye and found that the mfVEP was abnormal in more than 50% of the 29 fellow eyes that had normal fields on HVF. More recently, Thienprasiddhi et al 65 reported that the mfVEP detected deficits in hemifields with apparently normal HVF results in glaucoma patients with unilateral hemifield defects.

5. In addition to evaluating patients with unreliable or questionable HVFs, the mfVEP can be used for ruling out nonorganic visual loss, diagnosing and observing patients with optic neuritis and multiple sclerosis, and observing disease progression. 44,45,66

Hood and Greenstein [45] provided a theoretic framework for judging when the SAP or the mfVEP will be superior in detecting damage. Based on a comparison of mfVEP amplitudes and local visual field losses [62] , they conclude that, although clearly circumstances occur under which the mfVEP will detect damage missed on the SAP, the reverse can be true as well. Assuming that the visual fields obtained on SAP are reliable, theoretic analysis suggests that the two tests will often, but not always, agree. They predict that the mfVEP test will become a powerful tool for the detection,

management, and study of glaucoma, but it will not replace SAP. [45]

CONCLUSIONS

Automated achromatic perimetry is generally accepted as the "gold standard" for detecting glaucomatous damage. However, there are problems with this visual field technique. For some patients it is very difficult, or even impossible, to obtain reliable visual field measures. In addition, significant loss of ganglion cells can occur prior to the development of visual field loss. The mfVEP has been proposed as a solution to these problems. Local damage can be visualized in mfVEP recordings, but it is not yet clear to what extent the mfVEP will either replace or augment the information obtained with static automated perimetry.

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