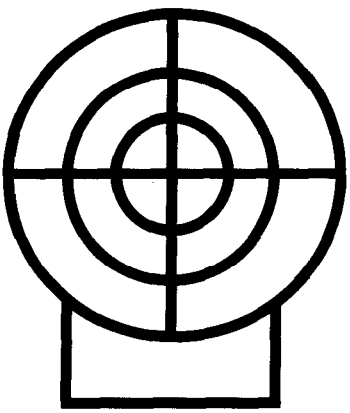
PERIMETRY

Update 1988/89



Proceedings of the VIIIth International Perimetric Society Meeting

Vancouver (Canada), May 9–12, 1988

Edited By

A.Heijl

kugler & ghedini

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INTRODUCTION

The current volume contains a selection of papers and posters presented at the Eighth International Visual Field Symposium. The symposium, organized by the International Perimetric Society, was held in Vancouver, Canada, May 9-12, 1988.

The perimetric meeting was held at the same time as a large Neuro-ophthalmic congress, which included meetings of the International Neuro-Ophthalmology Society, the Frank B. Walsh Society, the Clinical Eye Movement Society, the Japanese Society of Neuro-Ophthalmology, the North American Neuro-Ophthalmological Society and the Pupil Colloquium. This arrangement was of mutual benefit, giving the members of the neuro-ophthalmological societies the opportunity to participate at the sessions of the International Perimetric Society, and making it possible for the IPS members to attend the neuro-ophthalmic meetings.

This joint format was one of the reasons why, again, the Perimetric Society meeting was larger than ever before with approximately 250 participants. The main reason for the increasing interest in our meetings and the Society, however, is the growing interest in perimetric research. This is reflected in the increasing number of members, and of abstracts submitted to our symposia. The growing research activity has been obvious since the advent of computerized perimetry and the founding of the Society. Among a record number of abstracts submitted, in excess of 130, 86 were selected for presentation at the meeting. Thirty-eight read papers were presented during six sessions. Presented papers covered a wide spectrum of subjects in neuro-ophthalmology, with particular emphasis on statokinetic dissociation, color and contrast testing, but there were also numerous presentations on glaucoma, computer-assisted interpretation and newer non-standard tests.

Forty-eight posters were displayed during the entire congress giving participants and authors ample opportunity to discuss the findings. Two sessions were entirely devoted to posters, guaranteeing that all these contributions could be discussed in public.

Perimetry in neuro-ophthalmology was particularly emphasized during the meeting. Several new and exciting observations were reported. One paper compared confrontation visual fields and automated threshold perimetry. Several comparative evaluations of different functional tests for identification of optic neuropathy were presented. The appearance of post-concussive functional field defects in automated perimetry was compared with the more well-known findings of conventional manual kinetic perimetry. A new functional perimetric sign was described, the 'inverted isopter'. Other presentations described new and interesting visual defects in patients with Gilles de la Tourette syndrome, water-shed visual field loss after circulatory arrest and visual field defects in patients with pituitary tumors and the regression of these defects after surgery.

Several contributions were presented on two selected, quite specific topics:

1. What does contrast sensitivity testing and/or color vision add to the detection and diagnosis of optic nerve disease beyond quantitative perimetry and visual acuity?
2. The importance of the dissociation of static and kinetic perimetry in neuro-ophthalmology.

This volume contains numerous articles on these subjects. Two papers dealing with the usage of color perimetry in glaucoma indicated that blue stimuli on a yellow background do not produce results which are dramatically different from those obtained with conventional white stimuli. Contrast sensitivity had been compared with other modalities of testing in several ambitious presentations.

The Society has witnessed computerized perimetry become a standard method. New developments have often first been presented at the IPS symposia. All impor-

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tant research groups in this field have been active participants at our meetings. For a number of years we have seen a similar development take place within the field of computer-assisted visual field interpretation. At this meeting several groups and individual researchers reported progress within this area, or areas which are important for further development of these new tools. Presented papers dealt with new methods like cluster analysis, new visual field indices and regression techniques. Some older methods were tested with positive, as well as with negative, results. In one study mathematical analysis of the actual staircases produced by the computerized thresholding algorithm was used to estimate the frequencies of false positive and false negative responses.

Computer-assisted visual field interpretation often depends on thorough knowledge of normal, and abnormal, visual field variability. Several papers and posters reported new and valuable information in this area. Threshold variability was reported to be lower in multiple-stimulus semi-automated perimetry than with standard fully automatic single stimulus techniques. The patient's general health was shown to be important for threshold fluctuations. Three papers indicated, in various ways, that deviations from age-corrected normal values are positively correlated in neighboring points, and that therefore depressed points tend to occur in clusters also in normal subjects. Several papers dealt with inter-test threshold variability in patients with glaucoma. One contribution studied this variation in sector-shaped areas following the normal retinal nerve fiber layer. Another investigation demonstrated that inter-test fluctuations depend on the degree of abnormality, generally increasing with defect depth.

As always a large proportion of the presentations dealt with glaucoma. Two studies showed no improvement of the differential light threshold after pharmacologically induced acute IOP reduction. In one study acetazolamide had been given to patients with glaucoma, in another study glycerol had been administered to normal subjects. One might conclude that visual field improvement after acute pressure reduction still has not been established beyond doubt. One interesting paper reported results from a long term prospective study comparing the influence of timolol-induced pressure reduction versus no treatment on the visual fields of eyes with ocular hypertension.

Again there were indications that traditional measurements of the differential light threshold may not be the most sensitive technique to detect early glaucomatous damage in the paramacular area. A histological study of a glaucomatous eye indicated widespread partial atrophy of the retinal nerve fiber layer, also in areas where earlier perimetric examination had failed to detect localized loss. One prospective study of eyes with ocular hypertension demonstrated a surprising parallelism in the development of changes in optic disc configuration and the appearance of glaucomatous field defects.

No meeting of the International Perimetric Society has taken place without the presentation of a new automated perimeter. This time was no exception. A new device was presented with a built-in eye tracker. A stimulus is regarded as perceived if the patient shifts his gaze towards it. This is a promising technique, where the patient does not have to maintain fixation or to answer by pushing a response button.

There were many reports on results obtained with newer non-standard perimetric techniques. The techniques had usually been described at earlier meetings. Thus ring perimetry had been studied in several papers. Progress was also reported in the areas of pattern discrimination perimetry, multi-flash campimetry, displacement perimetry and flicker perimetry. Astonishing and most promising results were reported using a background of white noise for the detection of field loss. It was reported that pre-geniculate acquired field defects could be readily detected by the patient, just by maintaining steady fixation on a target surrounded by white noise,

like that of a television set. If it is confirmed that this rapid screening technique is just as sensitive as conventional computerized perimetry, this may have very important clinical applications.

It is obvious from this volume that a large number of interesting contributions were presented in addition to those mentioned above.

Our proceedings continue to mirror, in an excellent way, most of the important perimetric research which is being done all over the world. It is our hope that these books will remain an important and convenient source of reference for researchers and others who seek up-to-date information in this field.

The meeting was excellently organized, not only scientifically, but also socially. Our gratitude for this goes to the host Dr Stephen M. Drance and his co-workers.

On behalf of the editorial committee, I want to thank all authors of manuscripts for their excellent cooperation, which considerably facilitated the work of the editorial committee, and made the editing a pleasant experience.

We all look forward to the next meeting.

Welcome to Sweden in 1990!

Anders Heijl
Editor

OBITUARY

ANDRÉ DUBOIS-POULSEN (1907-1988)

Professor André Dubois-Poulsen died on August 14 1988 in Paris, at the age of 81. He was born in Calais in the north of France in January 1907. He graduated from the Paris School of Medicine and headed the Ophthalmology Department at the Quinze-Vingts Hospital in Paris from 1943 until his retirement in 1975. He taught optic physiology at the Sorbonne and at the Orsay University of Sciences. During his 50-year career, he was very active as president of more than ten major clinical, physiological, and ergological societies. He was an advisor to the French Health Ministry, Vice President of the French branch of the CIE, and a member of the International Ophthalmology Academy. He published nearly 300 papers on pathology, histology, surgery, and new therapeutics between 1932 and 1986 In 1952, he wrote a book with Magis, François and Tibi on the visual field, entitled *Topography of Visual Field Sensitivity,* which gave him international renown as a master of perimetry. According to Traquair, Harrington and Lauber, this book met the expectations of clinicians with its pathological visual fields in each clinical case. Later, a remarkable work on spatial summation called *Photometric Harmony* was discussed at the Liège Symposium on Glaucoma.

He studied the Rönne Step and Bjerrum scotoma in man. In 1960, he and Magis built a prototype automatic perimeter with elementary computerization. He received many foreign visitors at his Quinze-Vingts Laboratory, some of whom, such as Professor Matsuo, worked with him. He carefully studied static and kinetic perimetry and concluded that static perimetry was better in the central field and kinetic perimetry in the periphery. His opposition to color perimetry with pigmentary tests was so strong that it has taken 50 years for the rebirth of a new color perimetry with spectral tests. Professor Dubois-Poulsen also carried out prominent work on the 'visual results after occipital lobectomy'. He discussed the subject at a meeting in Mexico in 1970 and showed that macular sparing is the result of the overshot of the medial field line which has a special pathology, as double hemianopsias respect it completely. A localized agnosia syndrome was described.

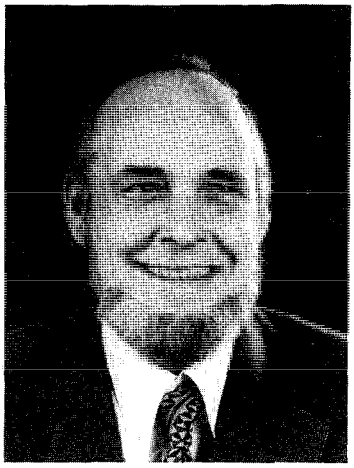
During the First International Visual Field Symposium organized by G.E. Jayle in Marseille in 1974, the International Perimetric Society was founded by Jayle, Greve and Dubois-Poulsen. Professor Dubois-Poulsen was made Honorary President.

In his private life, Professor Dubois-Poulsen liked painting and he was a good amateur painter. He was very interested in color physiology and published numerous papers on congenital and acquired color defects. He was President and Founder of the IRGCVD, together with Guy Verriest who died in October 1988.

His courtesy and scientific integrity made all discussions easier.

The death of Professor Dubois-Poulsen is a loss for international ophthalmology. His contributions to physiological and pathological perimetry have greatly increased our knowledge of visual science, and all of us owe a debt of gratitude to this great scientist.

J. Vola



OBITUARY

GUY VERRIEST

Guy Verriest died on October 20, 1988. He was one of the founders of the International Perimetric Society in the early seventies. In the fifties and sixties he worked extensively on many psychophysical aspects of vision. He was widely known for his knowledge on color vision and was the driving force behind the Research Group for Color Vision Deficiencies.

Guy was a member of the Executive Committee of the International Perimetric Society since its foundation in 1974. He was also interested in ergo–ophthalmology.

Guy has written many papers, reviews and several books. He was a scientist in the pure sense of the word.

Not distracted by the obligations of an overwhelming load of clinical work, Guy could and did devote himself to science. He had a profound knowledge of many aspects of vision.

It would be unfair to write about Guy only in terms of his ophthalmological achievements. Guy was an expert on belcanto and many other musical expressions. He knew a great deal about antiques. His house was almost a museum. He shared his interest in music and antiques with his wife, Jeanne. In fact, the two were almost inseparable.

Guy was not an ordinary person. Apart from being a scientist, he was a wise and a learned man. He was also pleasant company. I have learned a lot from him. Cooperating with him was a pleasure.

The International Perimetric Society has lost not only one of its founding members, but also a friend and a character.

The loss is by far the greatest for his wife Jeanne and son Didier.

Our feelings are with them.

Erik L. Greve

STATOKINETIC DISSOCIATION

COMPARISON OF AUTOMATED KINETIC AND STATIC VISUAL FIELDS IN NEURO-OPHTHALMOLOGY PATIENTS

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Eighty-three patients with various neuro-ophthalmic diseases were submitted to a standard automated protocol including kinetic and static perimetry The kinetic protocol included one peripheral, one intermediate and one central isopter and a blind spot contour determination The static protocol included fast thresholding of 80 points within the pericentral field and a 4-2-2-2 foveolar threshold determination. Discrepancies between the results of the two protocols were found in 24 out of 83 patients. Part of these discrepancies were related to methodological problems: static stimuli provide a more quantitative evaluation of the paracentral scotoma, whereas the kinetic tests appear to be more sensitive for eccentricities exceeding 15 degrees. Statokinetic dissociations were found in 12 subjects with compressive and cortical lesions

Introduction

The development of automated perimetry has mainly been concerned with static perimetry. Considering the number of manual kinetic perimeters still in use in ophthalmology departments equipped with automated static perimeters, it still remains unclear whether this apparent abandonment of kinetic perimetry is due to more stringent requirements in hardware and software or to a definite advance in testing efficiency. The purpose of this study was to compare the performances of the static and kinetic procedures available on the Vision Monitor computer assisted perimeter in the detection, identification and follow-up of deficits.

Methodology

Eighty-three patients with various neuro-ophthalmological disorders were submitted to a standard protocol including kinetic and static perimetry. All examinations were performed on two Vision Monitor computer assisted perimeters manufactured by the METROVISION company. For both examinations, the background luminance was 10 cd/m^2 and the stimulus size 20 minutes of arc. For the kinetic examination, the test luminance of the peripheral isopter was 310 cd/m^2. The test luminances of the intermediate and central isopter are adjusted automatically in order to obtain responses at 30 and 15 degrees of eccentricity. Eight additional measurements are used to determine the blind spot contour (Fig. 1A). The stimulus is displaced at a constant velocity of 10 degrees per second for the peripheral isopter, 5 degrees for the intermediate and 2 degrees for the central isopter and blind spot contour. The static protocol includes the fast thresholding of 80 points within the pericentral field and a 4-2-2-2 foveolar threshold determination (Fig. 1B). Fixation is monitored throughout the examination with a near infrared camera.

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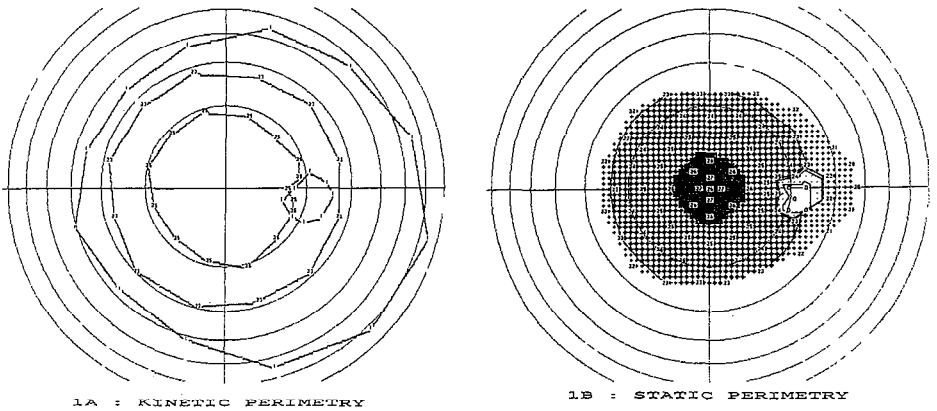


Fig 1 Examination procedures used in this study 1A: kinetic perimetry; 1B: static perimetry. The locations of the responses are shown by figures. The non-linear scale is indicated by reference circles located at every 15 degrees of eccentricity. The gray scale map is obtained by linear interpolation between the measurements All the data in this study are presented as a map of sensitivity so that areas with a total loss of sensitivity like the blind spot appear as white.

Duration of the examination

Fig. 2 shows the histogram of the duration of the examinations for each eye and for kinetic and static examinations. The average duration for the examination of one eye was 7.1 min for kinetic perimetry and 9.7 min for static perimetry. There is no significant influence as to the order in which the examinations are performed (kinetic OD, static OD, kinetic OS, static OS). The 35% shorter testing time is a definite advantage for kinetic perimetry, considering that a shorter duration is better for patient reliability and that automated perimetry is now a bottleneck in many ophthalmology departments.

Deficit detection and evaluation

Out of 83 patients, 59 or 71% showed complete agreement between kinetic and static examinations. The deficits were detected in both cases and their depth and shape were similar. Twenty-four patients or 29% presented noticeable field differences.

Figs. 3A to 3F show the results from six examination sessions performed over two months on the same patient with pituitary adenoma. Both kinetic and static fields show a progressive reduction of deficits, from extensive bitemporal alterations in Fig. 3A to normal fields in Fig. 3F. Fig. 3E shows small relative static defects which might easily be disregarded, whereas the bitemporal kinetic deficits are definitely present.

Kinetic perimetry appears generally more sensitive in detecting small scotomas located over 15 degrees of eccentricity. These differences are related to the threshold measuring technique. The static perimetry protocol uses a fast thresholding technique derived from the one initially proposed by Heijl and Krakau[1]. The threshold is only measured if the deficit is larger than 4 dB with respect to a reference map in the computer memory.

Any relative deficit of less than 4 dB is not taken into account. Even with a full

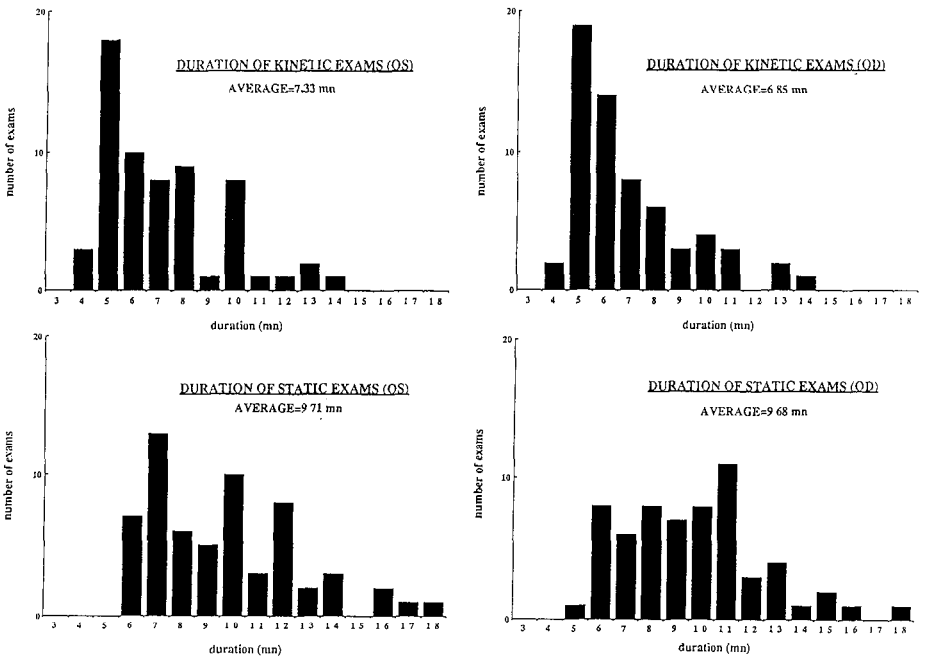


Fig 2 Histograms of duration of kinetic and static examinations.

thresholding procedure which is also available on the Vision Monitor but is also more time consuming, one might miss deficits of 2 dB or less due to the 2 dB steps used in the staircase procedure. The kinetic technique is more sensitive as it approaches the threshold in a continuous manner.

The delay in the patient's response causes an absolute error proportional to the stimulus velocity and response time of the patient[2]. However, the sensitivity for detecting relative defects is limited by relative errors, not absolute errors. This includes the response time fluctuation and the threshold fluctuation. The error due to the response time fluctuation can be estimated to be less than half a degree of eccentricity for a stimulus velocity of 2 degrees per second and a response time variation of 200 ms.

The next example shows deep paracentral scotoma in one patient with optical neuropathy (Fig. 4A) and a second patient with a sellar meningioma (Fig. 4B). The central isopters of kinetic perimetry do not give any information about the depth of scotoma. Such under-estimation of the depth of paracentral scotoma occurred in nine of the 83 patients included in this study. This is really nothing new[3] and it just reminds us that, in perimetry, one only finds what he is looking for.

In some patients, the spread of the central scotoma is greatly under-estimated by the kinetic protocol. Fig. 4C shows the worst cases encountered in this study. However, in all patients, there were small but still noticeable signs of kinetic deficits.

Statokinetic dissociations

Twelve out of the 83 patients presented noticeable differences between the kinetic and static fields which could not be related to the testing procedure. This

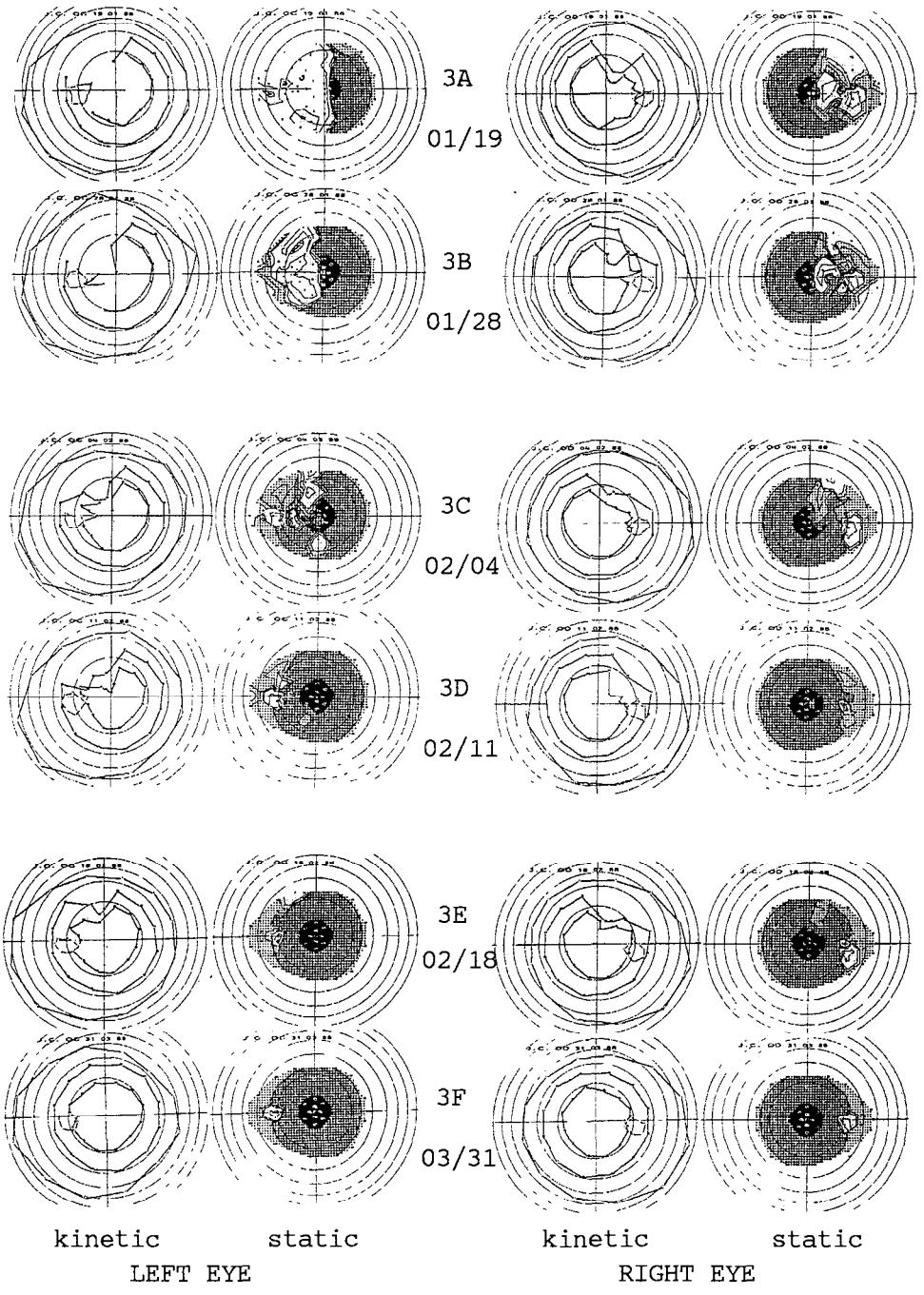
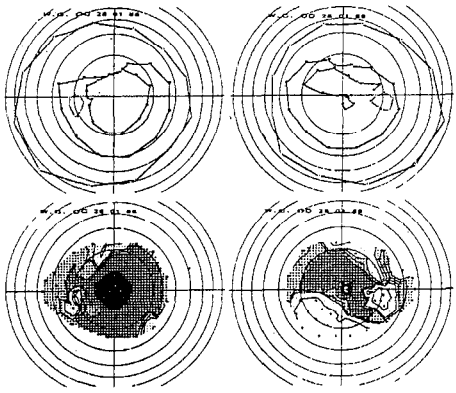
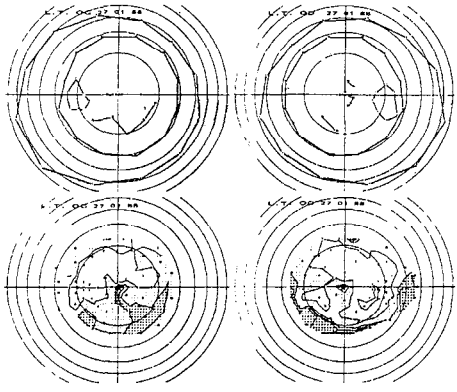


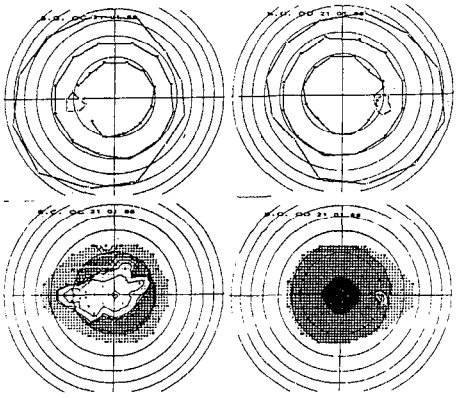
Fig 3 Follow-up of patient with pituitary adenoma



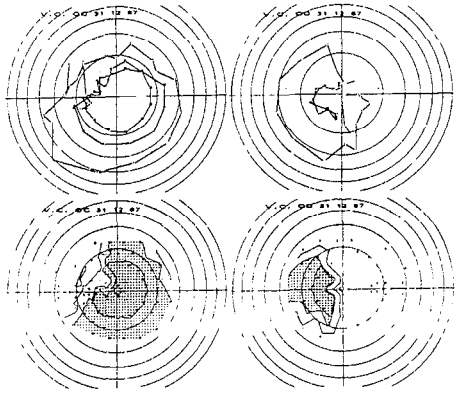
4A : OPTICAL NEUROPATHY



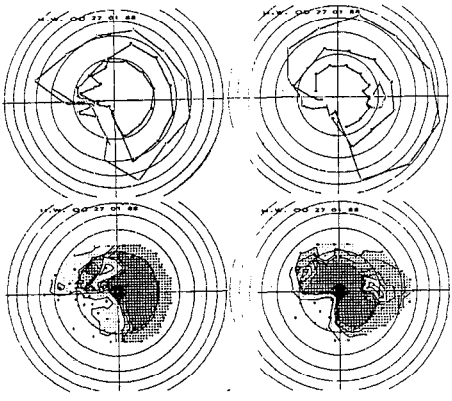
4B : SELLAR MENINGIOMA



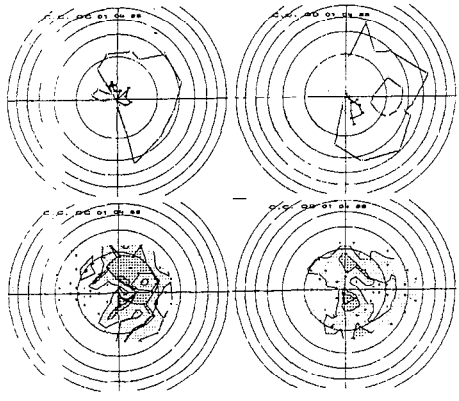
4C : OPTICAL NEUROPATHY



4D : PITUIRY ADENOMA



4E : CRANIOPHARYNGIOMA



4F : PARIETAL CYST

Fig 4 Examples of discrepancies between static and kinetic visual fields in neuro-ophthalmological diseases

group included seven out of 40 patients with pituitary adenoma, one out of four patients with craniopharyngioma, four out of ten patients with cortical lesions. These differences seem to be related to a phenomenon Riddoch described in 1917[4] for cortical lesions. Similar effects have been reported for other lobe lesions[5] and for lesions of the anterior pathways[6].

The results of this study support the existence of different pathways for the information involved in static and kinetic fields. One piece of evidence is that visual acuity is in agreement with the static field when the dissociation occurs over the macular regions (Fig. 4D). Temporal summations at the retina are not likely to cause such dissociations due to the use of 300 ms presentations in static perimetry. The effect of spatial summation would hardly explain that a large number of patients do not present dissociations (Fig. 4E). Furthermore, one of the patients in this study presents less deficit in the static field than in the kinetic field (Fig. 4F). Further interpretation of these dissociations can only be made by speculation. Statokinetic dissociations might be related to mechanisms of selective attention described by Singer[7]. According to this author, such mechanisms involve the control of the geniculate pathway by subcortical circuits and might alter the threshold levels by 5 to 10 dB.

Conclusions

The results of this study indicate that the ideal evaluation of neuro-ophthalmology patients should include complete kinetic and static fields. Both examinations present significant advantages, namely, the static examination assesses more precisely the volume of large paracentral scotomas and the kinetic examination is more sensitive and reliable for the detection of relative scotomas at eccentricities of over 15 degrees. Both examinations provide correlative and complementary information and their confrontation is extremely valuable for the establishment of a diagnosis.

However, if time limitations are taken into account, compromises have to be made, such as combining kinetic and static perimetry within the same protocol. For neuro-ophthalmology patients, a preliminary assessment of the field with kinetic perimetry and a control of the central field with static perimetry seems to be the ideal compromise.

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STATOKINETIC DISSOCIATION IN OPTIC NERVE DISEASE**

LINDA WEDEMEYER, CHRIS A. JOHNSON and JOHN L. KELTNER*

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Abstract

Statokinetic dissociation refers to a greater impairment of detection sensitivity for stationary targets (static perimetry) relative to detection sensitivity for moving targets (kinetic perimetry) Although statokinetic dissociation was originally reported by Riddoch to be associated with post-chiasmal lesions in some patients, subsequent investigations have demonstrated that it is prevalent in optic neuritis and other optic neuropathies In the present study, we evaluated velocity-dependent properties of statokinetic dissociation in five normal subjects and six patients with a history of optic neuritis No meaningful or consistent differences in stimulus detection were found for stimulus velocities between 1 and 8 degrees per second for either patients or normal observers However, both groups demonstrated higher sensitivity for moving targets as compared to stationary ones (statokinetic dissociation) Normal observers showed a relatively small amount of statokinetic dissociation, whereas the effect in optic neuritis patients was approximately 3 5 times larger than in normals Our findings are consistent with the hypothesis that there is a selectively greater loss for tonic (sustained, X-type) mechanisms in optic neuritis

Introduction

In 1917, Riddoch[1] observed that patients with post-chiasmal lesions sometimes demonstrated a dissociation of visual functions, with sensitivity to stationary targets being reduced or absent in certain visual field regions in which a similar *moving* target could be readily detected. Subsequent studies[2,3] have established that this phenomenon can occur in chiasmal disorders and optic neuropathies as well, and it has been given the term 'statokinetic dissociation'.

Riddoch's[1] initial report was mainly descriptive, providing a detailed account of the qualitative manifestations of statokinetic dissociation and its clinical prognostic value. He attributed the existence of statokinetic dissociation to the fact that movement was a more 'primitive' visual function, and therefore was more readily spared in cases of traumatic injury to the occipital lobe. Zappia *et al.*[2] suggested that statokinetic dissociation may reflect a visual adaptation anomaly or 'fatigue-like' effect. Recently, Safran and Glaser[3] have proposed that statokinetic dissociation may reflect a selectively greater loss to tonic (X-type, sustained) neural mechanisms than to phasic (Y-type, transient) neural mechanisms, particularly in optic neuropathies and chiasmal disorders. Additional support for this hypothesis (selective loss of tonic or X-type nerve fibers) has been provided by several studies[4,5] that have evaluated chromatic and flicker responses in patients with optic neuritis and other optic nerve disorders.

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The purpose of the present study was to provide a more thorough evaluation of the velocity characteristics of statokinetic dissociation and to examine the selective tonic system loss hypothesis by measuring sensitivity to stationary targets and those moving at different velocities (between 1 and 8 degrees per second) in normal subjects and patients with a clinical history of optic neuritis and statokinetic dissociation.

Methods

Static and kinetic visual field testing was performed on five normal observers (ages 23 to 45 years), and six patients (ages 29 to 68 years) with a previous history of optic neuritis and clinical evidence of statokinetic dissociation (subjective evaluation of significantly better visual fields with kinetic perimetry on the Goldmann perimeter than with automated static perimetry on the Humphrey Field Analyzer).

Both static and kinetic visual field testing were performed using the SQUID automated perimeter, whose operating characteristics have been previously described in detail[6-8]. The background adaptation level was adjusted to 31.5 asb, and fixation was monitored subjectively and objectively throughout the test sessions by means of an infrared video camera system. A size I target was used for all examinations, since preliminary studies revealed that a small stimulus was most effective in demonstrating differences between the detection of stationary and moving targets. Normal observers and patients were tested without a refractive correction in place, because all participants had low refractive errors, most kinetic responses occurred outside of the central 30 degrees, and we wanted to maintain equivalent test conditions for static and kinetic visual field testing.

Static perimetric testing consisted of threshold measurements performed at 5 degree intervals from 5 to 55 degrees radius along the 45, 135, 225 and 315 degree meridians. The stimulus duration was 1.0 seconds with a variable interstimulus interval of 0.5 to 0.75 seconds. The selection of target locations for each presentation was randomized, and thresholds were obtained by means of an 8-4-2 staircase procedure (8 dB initial step size, 2 dB final step size). A 0.25 degree diameter red stimulus was employed as a fixation target.

Kinetic perimetry was conducted along the 45, 135, 225 and 315 degree meridians using the Size I target at 0 dB (1000 asb) or -6 dB (4000 asb) at a rate of 1, 2, 4 or 8 degrees per second. Each trial began at 75 degrees eccentricity, with the stimulus visible and stationary for 1.5 seconds, followed by movement at the pre-defined rate. If a response occurred within the first 1.5 seconds of no movement, or the first 0.5 seconds of the moving stimulus, the trial was repeated. Trials during which eye movements occurred were also discarded. For each condition, a total of seven kinetic scans were performed, and the mean of the seven scans was selected as the kinetic threshold measure. Other details of the kinetic visual field test procedure may be found in Johnson and Keltner[6].

To perform direct comparisons of static and kinetic test results, it was necessary to determine the location along the static profiles corresponding to detection of the 0 dB or -6 dB target by interpolating between the 5 degree target intervals. Because of the limited time available for evaluation of patients, only one or two of the oblique meridians were evaluated with static and kinetic perimetry. They were chosen on the basis of previous static and kinetic visual field records and the regions demonstrating the greatest amount of statokinetic dissociation.

Results

Results for five normal observers are presented in Fig. 1 for (a) the 45 degree meridian, (b) the 135 degree meridian, (c) the 225 degree meridian, and (d) the 315 degree meridian. The visual field location corresponding to target detection is plotted as a function of stimulus velocity. In general, there are minimal differences

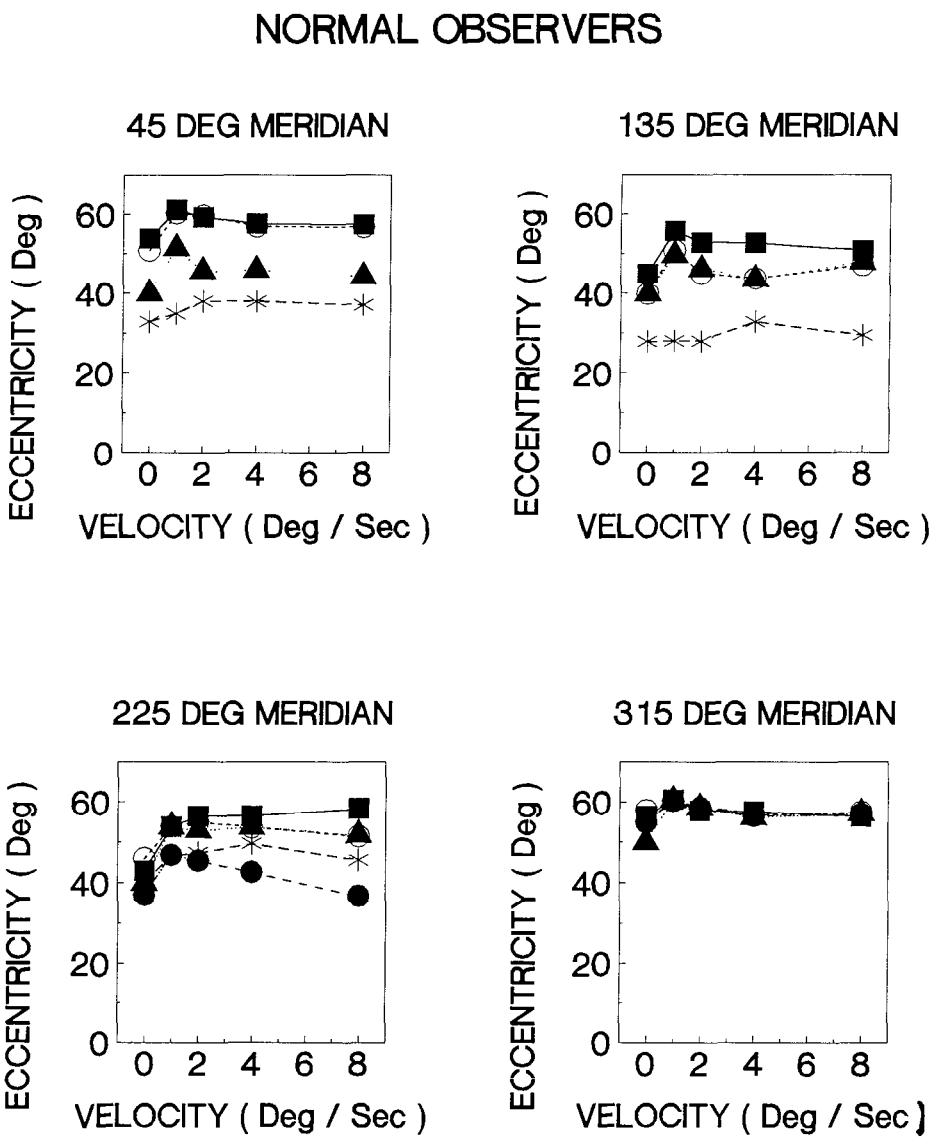

Fig 1 Visual field location of responses to kinetically moving targets (Size I target, 1000 asb) plotted as a function of stimulus velocity The results for four normal observers are presented for (a) the 45 degree and (b) the 135 degree meridian, and the results for five observers are presented for (c) the 225 degree meridian and (d) the 315 degree meridian

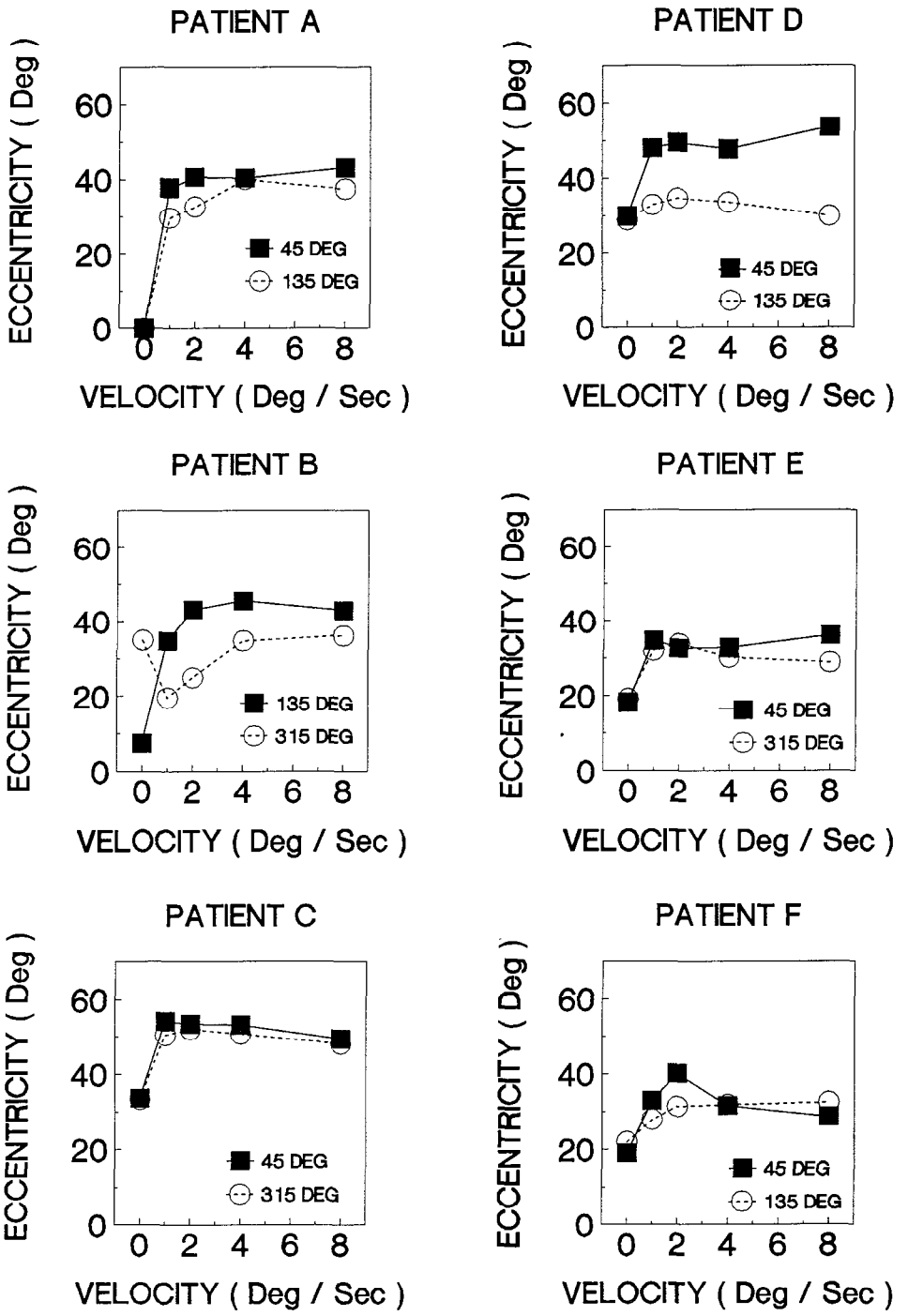

Fig 2 Visual field location of responses to kinetically moving targets (Size I target, 1000 asb unless otherwise specified) for six observers (a-f) with a history of optic neuritis and statokinetic dissociation.

in the visual field location corresponding to target detection for stimulus velocities between 1 and 8 degrees per second. Some of the subjects at some meridians showed a difference between the target location for moving and stationary targets, with moving targets being detected at more peripheral locations. In a few instances, the magnitude of these differences was up to 13 degrees. This type of statokinetic dissociation in some normal observers has been previously reported by Safran and Glaser[3].

The results for the patients with a previous history of optic neuritis are presented in Fig. 2. All of the patients demonstrated some amount of statokinetic dissociation, ranging in magnitude from approximately 9 degrees to about 42 degrees. In most instances, the responses from patients were similar for stimulus velocities between 1 and 8 degrees per second, with an abrupt decline in sensitivity occurring for the stationary target. Two of the patients exhibiting the greatest amount of statokinetic dissociation (Fig. 2a,b) demonstrated a slight decline in sensitivity for the 1 degree per second moving target. Although most of the patients exhibited a similar amount of statokinetic dissociation for all visual field locations examined, one patient (Fig. 2d) showed a distinct difference in responses for the 135 degree meridian (about 4 degrees) and the 45 degree meridian (about 20 degrees), indicating that statokinetic dissociation can be present in localized regions as well as diffusely distributed throughout the visual field.

The mean and standard deviation of statokinetic dissociation magnitude in the normal subjects and patients with a previous history of optic neuritis is presented in Fig. 3. The average difference in sensitivity between stationary and moving targets is larger in the patients than in the normal group, although there is considerable variation among the six optic neuritis patients.

Discussion

Our findings confirm the results of several previous studies that have reported statokinetic dissociation in patients with optic neuritis and other optic neuropathies[2,3,9,10]. The magnitude of statokinetic dissociation exhibited considerable variation from one patient to another, ranging from approximately 9 degrees to 42 degrees difference in visual field location for detection of stationary vs moving targets. Results from one patient also indicate that statokinetic dissociation

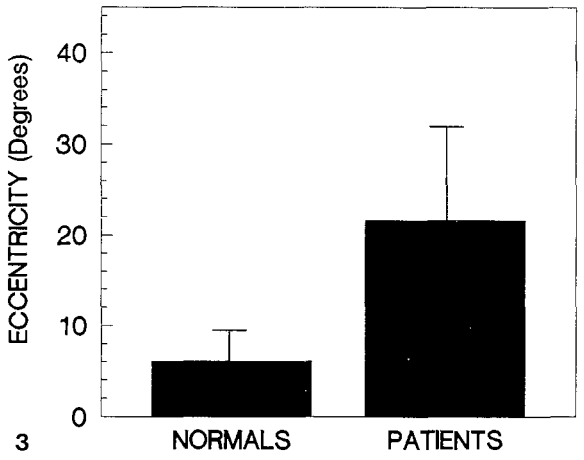

Fig 3 The average amount of statokinetic dissociation for the five normal observers and the six patients with a previous history of optic neuritis. Error bars indicate 1 standard deviation.

can vary from one visual field location to another, reflecting local as well as diffuse deficits in detecting stationary targets.

In accordance with previous investigations[3,11], we found that some normal subjects also exhibited a small amount of statokinetic dissociation. On the average, sensitivity to moving targets in the periphery was slightly better than sensitivity to stationary targets. Neither the normal subjects nor the optic neuritis patients displayed any meaningful or consistent differences in sensitivity as a function of stimulus velocity, with the possible exception of a slight reduction at higher rates of movement. It is likely that reaction time delays were responsible for these minor reductions in higher velocities[6]. The magnitude of statokinetic dissociation was three to four times greater, on the average, for the optic neuritis patients than for the normal subjects. Thus, differences in response properties to stationary and moving targets in optic neuritis patients and normal subjects appear to be mainly quantitative rather than qualitative.

Several investigators[3-5] have attributed statokinetic dissociation and other visual anomalies in optic neuritis to a selectively greater loss of function in tonic (X-type, sustained) ganglion cells. Our results support this hypothesis, since there was a dramatic reduction in sensitivity for stationary targets, with little or no sensitivity differences for targets moving at different velocities. In this view, the small amount of statokinetic dissociation that was observed in some normal observers may reflect a general difference in sensitivity for tonic and phasic mechanisms in the periphery. Kulikowski and his colleagues[12,13] have shown that psychophysical evidence of sustained and transient channels can be demonstrated by appropriate selection of spatial and temporal stimulus parameters. Thus, a parsimonious interpretation of these findings is that phasic (Y-type, transient) mechanisms are slightly more sensitive than tonic (X-type, sustained) mechanisms in the normal peripheral visual field, under the conditions typically employed for perimetry and visual field testing. With optic neuritis and some other types of optic neuropathies, this sensitivity difference becomes significantly exacerbated due to a selectively greater functional loss of tonic mechanisms.

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A COMPARISON OF KINETIC AND STATIC PERIMETRY FOR LESIONS IN THE VISUAL PATHWAY

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Abstract

The authors compared results of kinetic and static perimetry of lesions in the visual pathway, optic nerve lesions (65 eyes), chiasmal lesions (bitemporal hemianopsia group, 53 eyes) and post-chiasmal lesions (homonymous hemianopsia group, 44 eyes). The results were classified into: those in which visual field abnormality was demonstrated to a similar extent by the two methods of examination; those in which visual field abnormality was more pronounced by static perimetry than by kinetic perimetry (Riddoch phenomenon); and those in which visual field defect was more severe when examined by kinetic perimetry than by static perimetry.

The Riddoch phenomenon was observed in approximately 20%, regardless of the region of the lesion in the visual pathway There was no evidence of a difference in the prognosis for lesions with or without a positive Riddoch phenomenon.

Introduction

It is known that in lesions in the visual pathways different results can be obtained using kinetic and static perimetry. The Riddoch phenomenon is one typical pattern which has remained unexplained for a considerable time.

The authors retrospectively analyzed the visual fields of lesions in the visual pathway, including optic nerve disease, to compare kinetic and static perimetry. A detailed assessment was made of the cases in which dissociation of results was observed.

Material and methods

The material consisted of 162 eyes of 102 cases measured during the 20-month period from April 1986 to November 1987 (Table 1).

Kinetic visual fields were measured by the Goldmann perimeter and static visual fields were measured by the Octopus, Humphrey, and Friedmann (FA) instruments. Results were compared by five perimetry experts.

Results

The cases were classified into two types:

I. Cases in which the results of the two field tests showed similar visual field abnormality.

II. Cases in which the results of the two field tests were evidently different.

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Table 1 Type of visual pathway lesions and number of subjects

Type	Number of patients	Number of eyes
Optic nerve lesion	48	65
Retrobulbar neuritis	29	37
Optic nerve injuries	2	2
Ischemic neuropathy	7	8
Papillary edema, unknown etiology	4	7
Optic nerve atrophy, unknown etiology	6	11
Chiasmal lesion	31	53
Post-chiasmal lesion	22	44
Total	102	162

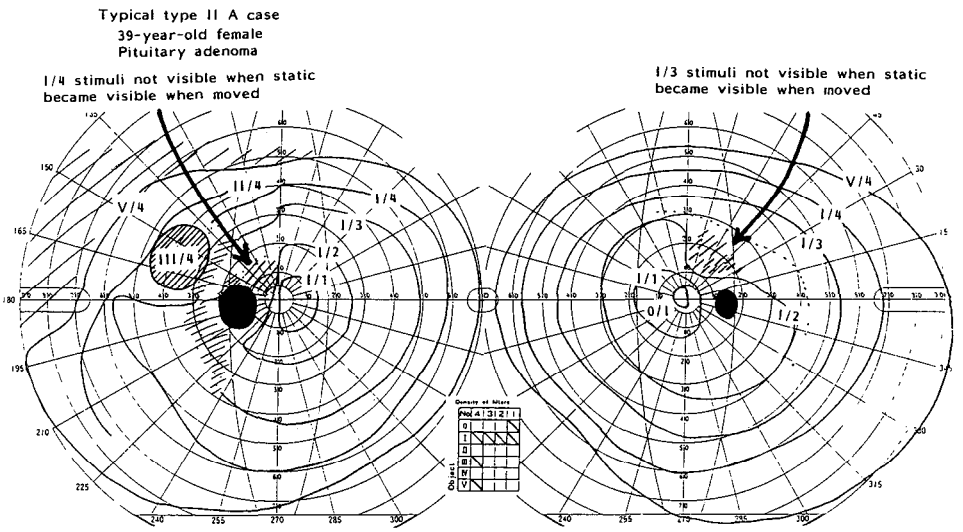

Fig 1 A case with dissociation when changing between static and kinetic targets with the Goldmann perimeter

Group A:Perception of the target was only possible when the targets were moving (Fig. 1).

Group B:Static perimetry demonstrated more severe visual field abnormality than kinetic Goldmann perimetry (Fig. 2).

Group C:Kinetic perimetry exhibited more severe visual field abnormality than static perimetry (Fig. 3).

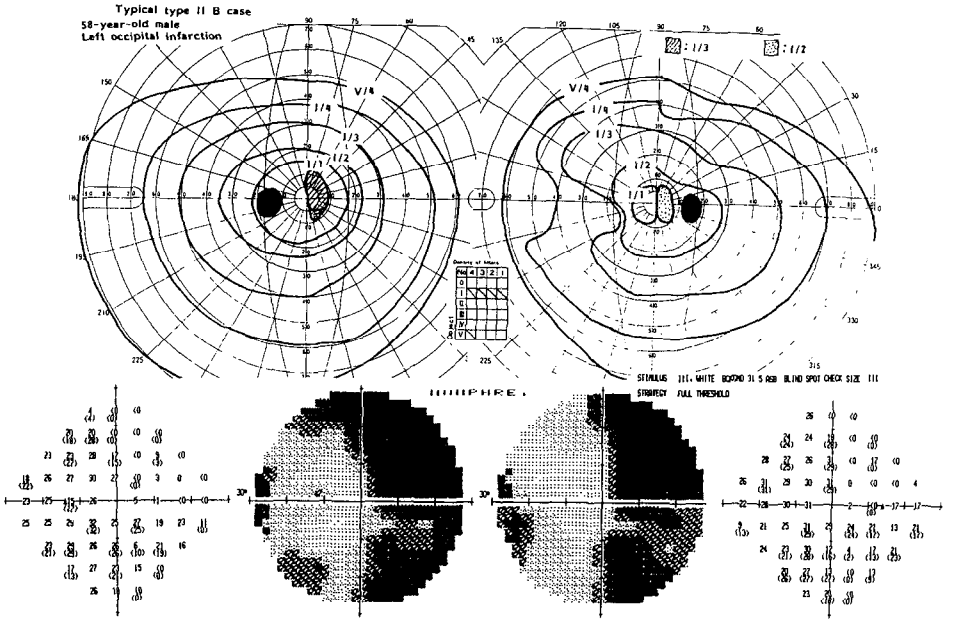

Fig 2 A case in which the Humphrey perimeter detected more extensive field defects than the Goldmann kinetic perimeter.

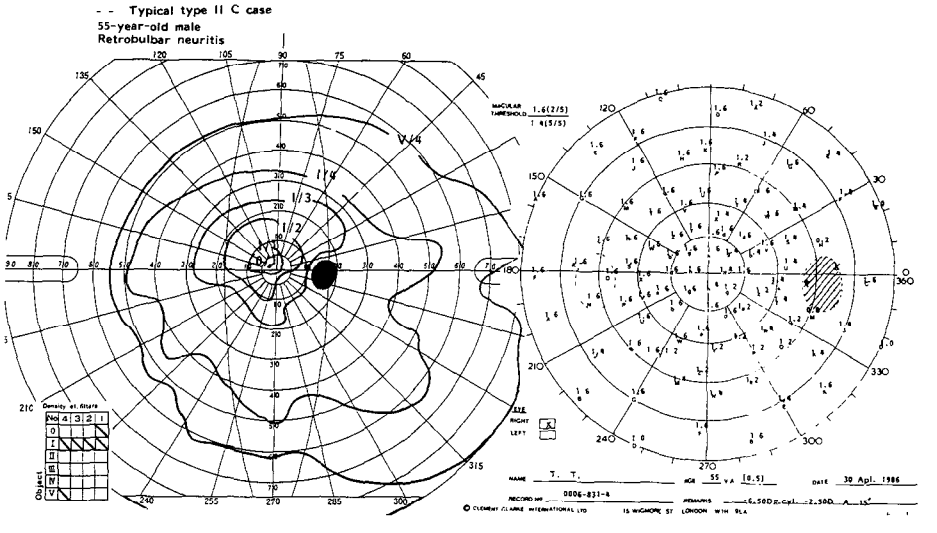

Fig 3 A case in which visual field abnormality was detected more sensitively by Goldmann kinetic perimetry than by static perimetry by FA.

Table 2 Comparison of visual fields measured by kinetic and static perimetry

Type	Optic nerve lesion	Chiasmal lesion	Post-chiasmal lesion
I	50 (76 9%)	42 (79.2%)	35 (79.5%)
II	15 (23 1%)	11 (20.8%)	9 (20.5%)
A	9 (13.8%)	9 (17.0%)	5 (11 4%)
B	4 (6 2%)	2 (3 8%)	4 (9.1%)
C	2 (3.1%)	0	0
Total	65 eyes	53 eyes	44 eyes

The course and prognosis were evaluated among those cases in Group II in which we had a follow-up of at least a couple of years.

Analysis of the results of the perimetric methods is shown in Table 2.

I. The results of the kinetic and static methods were in agreement in most cases of optic nerve injuries, ischemic neuropathy and papillary edema.

II. All cases in which static perimetry detected more extensive visual field abnormality are as described above (Table 2). In optic nerve lesions, A and B pattern dissociation was observed in 11 eyes of retrobulbar neuritis and in two eyes of optic atrophy. In chiasmal lesions, A pattern dissociation was detected in seven eyes of pituitary adenomas and in one eye of tuberculum sella meningioma and in one eye of aneurysm of the internal carotid artery. B pattern dissociation was detected in two eyes of pituitary adenomas. In post-chiasmal lesions, A and B pattern dissociation was detected in nine eyes of cerebral infarction of the parietal and occipital lobes and in two eyes of idiopathic intracerebral hematoma.

The cases which showed different results with each method and in which the visual field abnormality was more extensive at static testing, were approximately 20% in each group of lesions, showing no trend for the frequency to be higher in any particular disease.

Cases in which kinetic perimetry showed more severe visual field abnormalities (Group II C) were seen in only two eyes in cases with retrobulbar neuritis.

There was no recognizable tendency to suggest that recovery of the visual field disorder was different in cases in which the Riddoch phenomenon was observed.

Discussion

Riddoch reported on the dissociation between the results of kinetic and static perimetry in cases of injury to the occipital cortex in 1917[1]. Zappia *et al.* reported a similar dissociation in 1971 in cases of chiasmal tumor and aneurysm of the internal carotid artery[2]. It is well known that the Riddoch phenomenon is generally observed in lesions of the visual pathway[3-5]. We retrospectively analyzed the visual fields in cases of lesions of the visual pathway to assess the incidence of a stato-kinetic dissociation, to relate this to disease entity and to assess any possible relationship between such a dissociation and the prognosis.

We presume that the Riddoch phenomenon can be explained as follows: When the visual field abnormality consists of sieve-like scotomas, as observed in optic neuritis, or the area of depression is very small or there is a portion where slight retinal sensitivity remains in the region of visual field defect, summation is activated by moving the target slowly, thereby making perception possible.

The phenomenon of visual field disorder shown to be more severe by kinetic perimetry than by static perimetry was observed in two eyes with optic nerve lesion. The phenomenon was observed only once each in the course of two cases of retrobulbar neuritis. These opposite results might be due to intra-subject variability. Therefore, far more correct observation should be done to ascertain this phenomenon.

We were not able to confirm the possible relationship reported elsewhere[1] that the Riddoch phenomenon suggests some degree of recovery, thereby indicating a better prognosis.

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COLOR TESTING

BLUE/YELLOW COLOR CONTRAST PERIMETRY COMPARED TO CONVENTIONAL KINETIC PERIMETRY IN PATIENTS WITH ESTABLISHED GLAUCOMATOUS VISUAL FIELD DEFECTS*

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Patients with ocular hypertension and glaucoma are known to have a high incidence of type III acquired dyschromatopsia (a tritan-like confusion of blue/yellow hues), suggesting that blue/yellow hue discrimination in the visual field may be preferentially impaired by the glaucomatous process To test this possibility, I examined 19 eyes of 15 patients with the established diagnosis of primary open angle glaucoma, and compared the results of conventional, manual kinetic perimetry with the Goldmann instrument to those obtained by manual kinetic color contrast (blue/yellow) perimetry with a modified color video tangent screen Eyes were intentionally selected for having typical glaucomatous visual field defects (nerve fiber bundle defecs, including combinations of arcuate scotomas, paracentral scotomas and nasal steps) The color video screen had a yellow adapting background (red and green phosphors with combined luminance of 15 foot lamberts) and test objects were generated by addition of a blue phosphor component with simultaneous, equiluminant subtraction of yellow component Maximum blueness of test objects was 10% of the available range in the yellow-to-blue shift through color space, and equiluminance was individually determined for each patient by heterochromatic flicker photometry In all but one eye, all defects detected by conventional perimetry were similarly demonstrable by the color contrast method In no case was there a color contrast defect that could not be simultaneously detected by the conventional method Defects had more distinct topographic features when mapped by conventional perimetry than when studied by the color contrast method The acquired blue/yellow dyschromatopsia of glaucoma, found by tests of foveal and parafoveal color vision, may have no specificity for the detection of glaucomatous damage

Introduction

As part of a long-term prospective study of ocularly hypertensive patients known to have a high risk for future development of glaucomatous damage, we are employing multiple tests of foveal and extrafoveal color perception. In the work reported here, a separate group of patients with established glaucomatous visual field defects was studied to determine the relative sensitivities of conventional luminance increment kinetic perimetry and blue/yellow color contrast kinetic perimetry for the detection of glaucomatous visual field defects.

Methods

Patients included in this study carried the established diagnosis of primary open angle glaucoma. They had gonioscopically open angles, visual acuities of 20/70 or better, intraocular pressures of greater than or equal to 24 mm Hg on three or more occasions, pathologic cupping of the optic disc and glaucomatous visual field changes. Patients underwent visual field testing with the Humphrey automated perimeter, using program 30-2. 'Statpac' single field analysis was used to categorize the visual field defects. All patients had glaucomatous defects that were at least one log unit (10 dB) in depth. Nineteen eyes of 15 patients were included in the study.

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Conventional kinetic perimetry with the Goldmann perimeter was performed, using an adapting background of 31.5 asb. Corrective lenses of appropriate strength were used for all testing in the central 30 degrees of the visual field. For color contrast perimetry, a previously described instrument was used[1]. The color contrast perimeter was modified for this study so as to produce a yellow adapting background (illuminating solely the red and green phosphors of the video screen) with

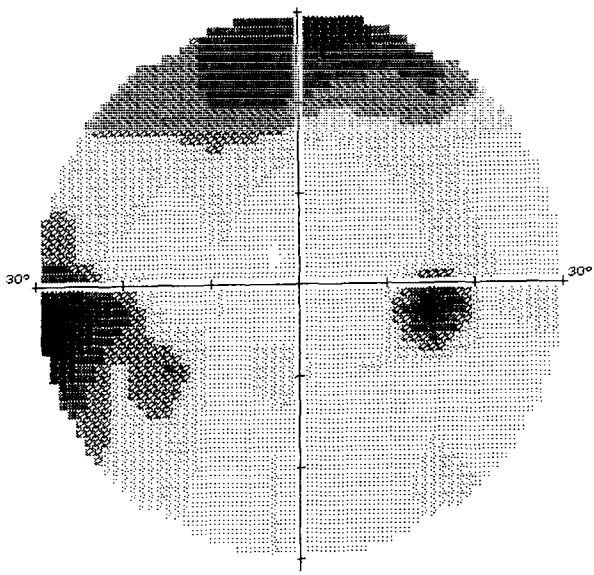

Fig 1a Case 1. Threshold static perimetry showing inferior nasal step at 20-30 degrees eccentricity and 1 5 log units deep

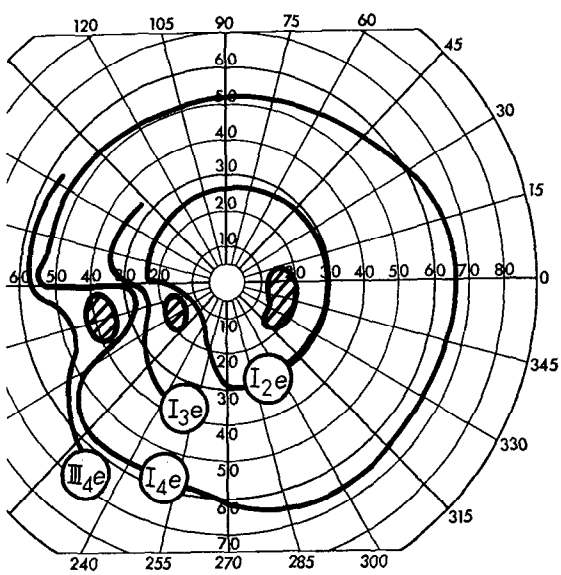

Fig 1b Case 1 Conventional kinetic perimetry, showing inferior nasal step.

a luminance of 15 ft lamberts. Test objects were generated by addition of blue phosphor illumination in the test object with simultaneous, equiluminant subtraction of the yellow component.

As previously described, equiluminance between the test object and surround components was obtained by heterochromatic flicker photometry at 15 Hz. The maximum degree of 'blueness' of any test object was 10% of the available range in the yellow to blue shift through chromaticity space. Test objects for the color contrast technique were fixed at an angular size of 3 degrees, and color contrast was varied at 1% increments for values from 1 to 10%. Glaucomatous defects were classified as moderate, advanced or profound, based upon the depth of the defect. A defect less than or equal to 1 log unit was defined as moderate, defects between 1 and 2 log units in depth as advanced, and those in excess of 2 log units as profound.

Results

Blue/yellow color contrast visual field defects were detectable in all but one of the eyes that had defects demonstrable by conventional luminance increment testing. In no case, however, was a blue/yellow color contrast defect detected where a luminance increment defect could not also be demonstrated.

However, the sensitivity for detection of defects with the blue/yellow technique appeared to be somewhat less than that obtained with conventional perimetric testing. This was especially true for defects that were only moderate in depth. Nasal steps of approximately 1 log unit in depth provided clearly defined topographic characteristics by both conventional Goldmann as well as automated static perimetry, whereas the same defects mapped by blue/yellow color contrast perimetry showed only subtle isopter depression. This finding was confirmed even when the test object size was reduced to 1 degree.

These differences are illustrated by the first case, depicted in Fig. 1 (a,b and c). Static perimetry (Fig. 1a) demonstrated an inferior nasal step located between 20 and 30 degrees away from fixation, having a maximum depth of approximately 1.5 log units. Kinetic perimetry (Fig. 1b) showed this nasal step extending from between 10 and 20 degrees of eccentricity all the way out to the nasal periphery of the visual field. This defect was classified as advanced. Kinetic perimetry with the blue/yellow color contrast instrument (Fig. 1c) demonstrated only an area of subtle wedge-shaped depression involving color contrast isopters lying between 10 and 20 degrees of eccentricity. It was not possible to find any color contrast scotomas located within the margins of this depression.

An even more advanced visual field defect is illustrated in Fig. 2 (a,b and c). This defect had a depth approaching 2 log units, producing a superior nasal step and including a small parafoveal scotoma of approximately 1 log unit in depth (Fig. 2a). Conventional Goldmann kinetic perimetry (Fig. 2b) demonstrated a nerve fiber bundle defect with nasal steps in four adjacent isopters, including a scotoma just outside the I4e isopter. In addition, the paracentral scotoma seen on static perimetry was confirmed within the I2e isopter. Blue/yellow color contrast kinetic perimetry (Fig. 2c) also demonstrated superior nasal steps in all isopters between 10 and 30 degrees of eccentricity, but failed to locate the paracentral scotoma.

A profound visual field defect is illustrated in Fig. 3. Static perimetry (Fig. 3a) demonstrated a very dense nasal nerve fiber bundle defect with a depth greater than 2 log units, and another superior arcuate scotoma with a depth of between 1.5 and 2 log units. Goldmann perimetry (Fig. 3b) detected these same features with a scotoma to the I4e test object lying between 20 and 30 degrees of eccentricity within the inferior nasal step and nearly baring of the blind spot to the I4e test object in the superior Bjerrum region of the defect. For this profound defect, color contrast

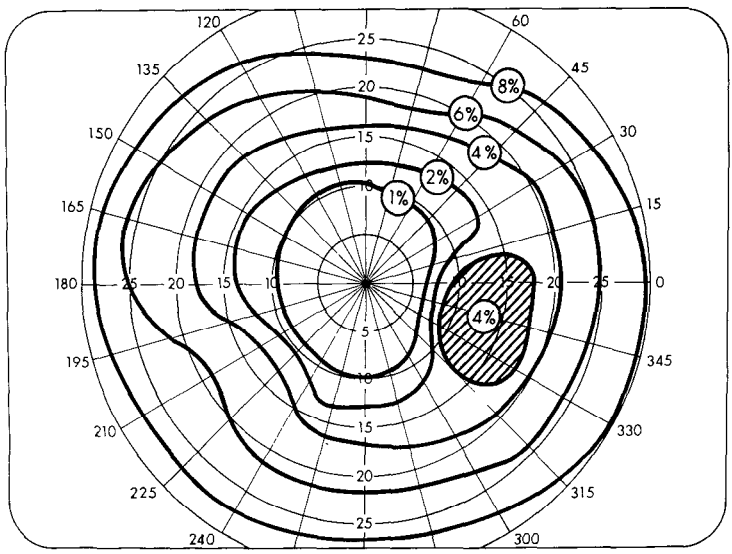

Fig 1c Case 1 Blue/yellow color contrast kinetic perimetry. Nasal step not clearly seen, only subtle wedge-shaped depression found

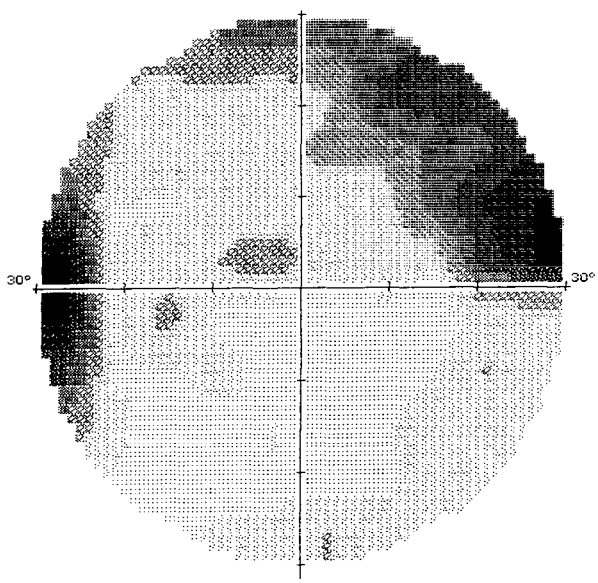

Fig 2a Case 2 Threshold static perimetry detected dense superior nasal step and paracentral scotoma

perimetry (Fig. 3c) demonstrated dense nasal loss located between 10 and 30 degrees of eccentricity, where the maximum color contrast target was not visible. Additionally, in the superior Bjerrum region, a localized scotoma to the 10% color contrast test object was detected.

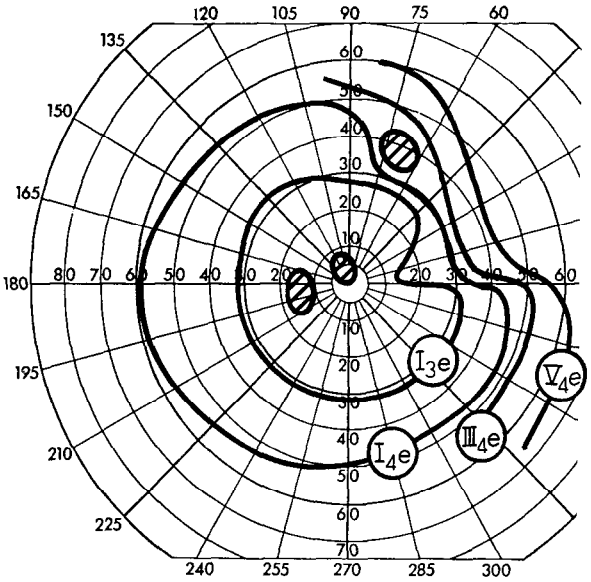

Fig 2b Case 2. Conventional kinetic perimetry also detected dense nasal step and associated paracentral scotoma.

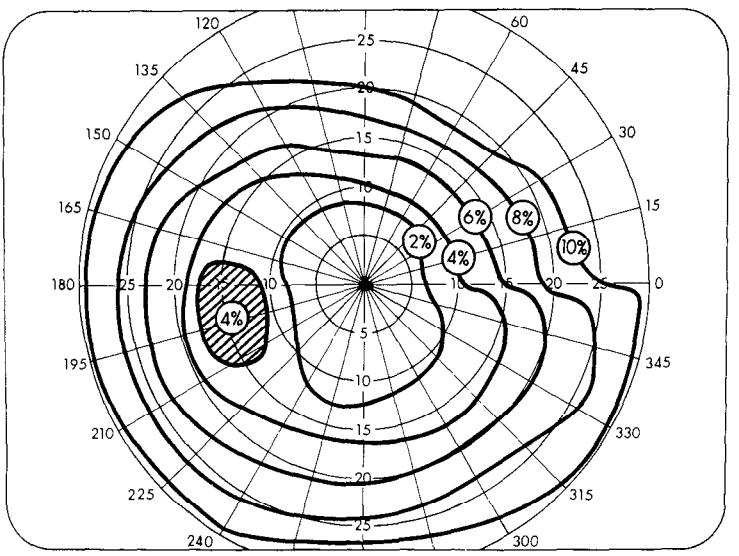

Fig 2c Case 2 Blue/yellow color contrast kinetic perimetry. Clear definition of nasal step, but failure to detect small paracentral scotoma

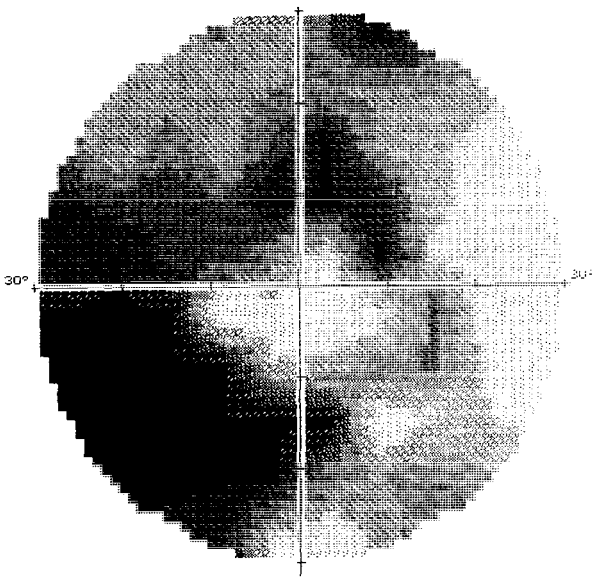

Fig 3a Case 3. Threshold static perimetry showed profound arcuate defects

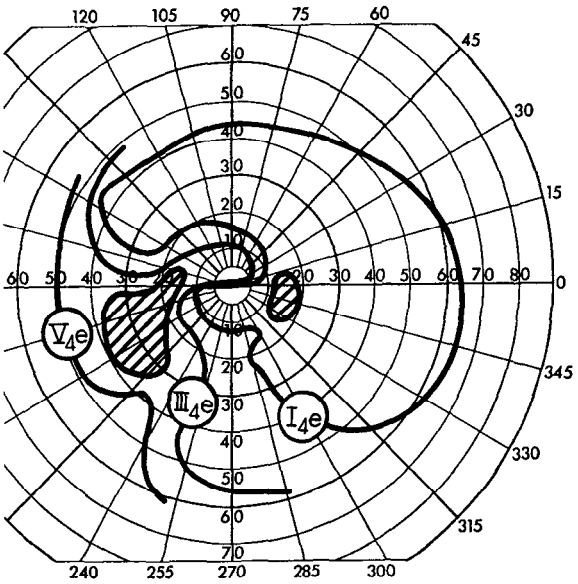

Fig 3b Case 3 Conventional kinetic perimetry. Dense defects in superior and inferior Bjerrum regions

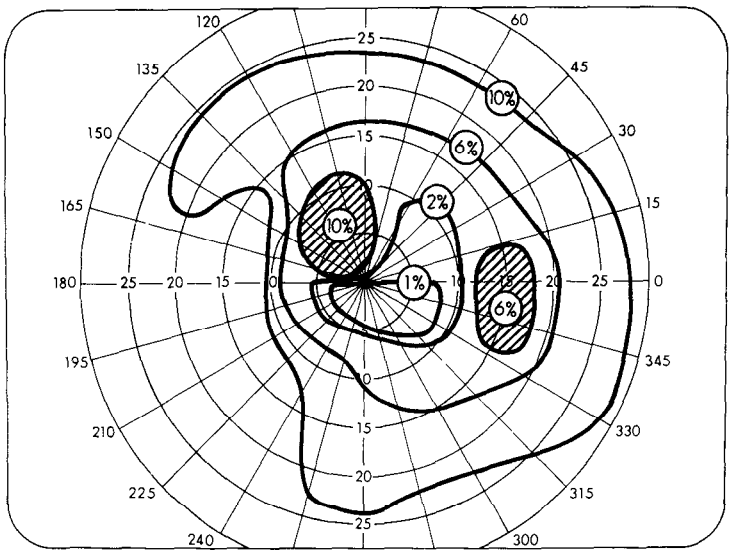

Fig 3c Case 3. Blue/yellow color contrast kinetic perimetry found same features: dense inferior nasal and superior Bjerrum region defects

Discussion

Moderate to profound visual field defects, as defined by conventional perimetry, are likewise detectable by blue/yellow color contrast testing. However, the color contrast method does not appear to provide greater sensitivity or better definition of the topography of these glaucomatous visual field defects. For defects of moderate depth, topography can be clearly delineated with conventional kinetic methods. Sharply defined nasal steps and small, localizable scotomas located within the sloping margins of nerve fiber bundle depressions are readily demonstrable. The color contrast method on the other hand shows only poorly defined isopter depressions in these same regions. Part of this effect may be attributable to the relatively large (3 degrees) test object size used for kinetic perimetry with the color contrast method. However, attempts at using smaller test object sizes were not found to improve the detectability of localized depressions by color contrast testing in this group of patients.

Foveal tests of blue/yellow hue discrimination clearly demonstrate defective function in patients with ocular hypertension and early glaucoma, even when visual acuity is normal and the visual field shows no defects[2]. (This subject has recently been reviewed[3].) However, the use of blue/yellow color contrast perimetry did not in this group of patients appear to increase the sensitivity for detection of glaucomatous visual field defects. The sensitivity and specificity of blue/yellow color contrast for detecting glaucomatous damage was no greater than that of luminance contrast testing in the peripheral visual field, and for defects of about 1 log unit in depth, the sensitivity of the color contrast method appeared to be less than that of conventional perimetry.

These results might be explained by differences in the density and overlap of ganglion cell receptive fields for luminance contrast and simultaneous color contrast neurons. Near the foveal representation of the visual field, where there is a physiological scotoma for perception of blue light, the number of receptive fields

is probably small relative to those subserving luminance contrast functions. Only a small proportion of blue/yellow sensitive receptive fields would need to be damaged at this location in order to produce a detectable dyschromatopsia. Farther away from fixation, blue/yellow receptive fields are greater in number. Although they are still less numerous than luminance contrast receptive fields, they have larger receptive fields[4], and may have greater overlap with one another, producing a functional redundancy and a resistance to damage greater than that for the luminance contrast detectors.

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AUTOMATED PERIMETRY OF SHORT-WAVELENGTH MECHANISMS IN GLAUCOMA AND OCULAR HYPERTENSION
Preliminary findings**

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Abstract

Many recent studies have reported deficits for short-wavelength stimuli as an early indicator of glaucomatous damage, often preceding the presence of visual field defects Frequently, these measures have been restricted to the foveal region, have not been corrected for absorption of short wavelength light by the ocular media, and have not been compared to the most recent automated perimetric test procedures. In the present study, we used a modified Humphrey Field Analyzer to test the central 30 degrees Visual field examinations included standard automated perimetry (Program 30-2), automated perimetry of short-wavelength-sensitive mechanisms (standard Humphrey 30-2 test with a size V blue target and a 635 asb yellow background), and a high luminance background control condition (standard Humphrey 30-2 test with a size V yellow target and a 635 asb yellow background) Ocular media attenuation of short wavelength light was determined by measuring scotopic thresholds for long and short wavelength targets at 15 degrees eccentricity, and an appropriate correction was applied to the blue on yellow perimetry values Both eyes of 38 patients with ocular hypertension, 22 patients with early glaucomatous visual field loss and 62 normal control subjects, were tested Our findings indicate that more abnormalities were obtained for the blue on yellow test condition in 5 to 10% of the ocular hypertension patients and approximately 15% of the early glaucoma patients than for the standard white on white or the yellow on yellow tests (No differences were found between the standard and yellow on yellow visual field tests) These data suggest that short-wavelength-sensitive pathways may be more susceptible to early glaucomatous damage The short wavelength sensitivity loss appears to be primarily diffuse across the central 30 degrees, with the exception of a somewhat greater loss in the inferior nasal visual field for some patients.

Introduction

A number of recent studies[1-6] have reported that foveal blue and blue-yellow color vision deficits occur in ocular hypertensive and glaucoma patients, and that these deficits may be the earliest indicators of glaucomatous damage (see Sample *et al.*[1] for a review). Drance and his colleagues[5] found that ocular hypertensive patients with color vision deficiencies had a much higher incidence of the onset of glaucomatous visual field loss five years after the initial color vision testing than those ocular hypertensive patients with normal color vision responses. This suggests that blue or blue-yellow color vision deficits may have predictive value as a precursor to glaucomatous visual field defects. In this view, Airaksinen and his co-workers[6] found that the blue and blue-yellow deficits were correlated with diffuse nerve fiber layer loss in patients with early glaucoma. Recently, Heron *et*

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al.[4] have measured both foveal and peripheral sensitivity to short wavelength stimuli, using techniques designed to isolate the activity of short-wavelength-sensitive pathways. Their findings indicate both diffuse and localized sensitivity losses present in short-wavelength-sensitive pathways in some ocular hypertensive and glaucoma patients.

The present investigation represents an extension of previous studies in several respects. First, chromatic adaptation techniques for isolation of short-wavelength-sensitive mechanisms were adapted to a commercially-available automated perimeter (Humphrey Field Analyzer). Second, by using the central 30-2 test pattern of the Humphrey Field Analyzer, a larger number of visual field locations (76) were evaluated than for the previous investigation by Heron *et al.*[4]. Third, it was possible to make direct comparisons of standard automated perimetric test procedures and short wavelength sensitivity of the visual field, since the same test strategies and procedures were used for all visual field evaluations. Fourth, variations in the attenuation of short wavelength light by the ocular media, which are known to occur both within and between age groups[7-9], were accounted for by measuring relative lens density in each eye. Finally, a control group of normal subjects, equally distributed across a large age span (20 to 72) was examined with all test procedures to provide a basis for defining early deficits that were beyond age-related sensitivity losses. Our purpose was to conduct a preliminary examination of short wavelength sensitivity loss in ocular hypertension and early glaucoma and to assess its feasibility as a precursor to the development of glaucomatous visual field defects.

Methods

Both eyes of 62 normal control subjects (33 males, 29 females; 20 between the ages of 20 and 39, 22 between the ages of 40 and 59, and 20 between the ages of 60 and 72), 38 ocular hypertensives with normal visual fields and 22 patients with early glaucomatous visual field loss in one or both eyes, were evaluated in this study. Normal subjects were included if they had visual acuities of 20/40 or better OU, intraocular pressures of less than 20 mm Hg OU, refractive errors of less than 5 diopters spherical equivalent and 3 diopters cylinder, no history of ocular or neurologic disease or surgery, no history of diabetes or other systemic disease, and were not taking medications known to significantly affect visual field sensitivity. Patients were included if they had visual acuities of 20/40 or better OU, intraocular pressures of greater than 21 mm Hg, refractive errors of less than 5 diopters spherical equivalent and 3 diopters cylinder, no other ocular or neurologic disease, no history of diabetes or other systemic disease, no medications being taken that are known to significantly affect visual field sensitivity, and a clinical diagnosis of ocular hypertension or primary open angle glaucoma.

All visual field examinations were performed with a modified Humphrey Field Analyzer, using Program 30-2. Details of the test strategy employed by the Humphrey Field Analyzer have been described in previous publications[10,11]. Three modifications were made to the Humphrey Field Analyzer. First, a custom ROM chip set was provided by the manufacturer to allow background illumination to be turned off while maintaining independent control of stimulus illumination. Second, an auxiliary background illumination system was installed. The lighting system consisted of two boxes, each containing a fan to dissipate heat, an 80 watt Kodak carousel projector bulb (ELS) mounted behind heat-absorbing glass, opal diffusing glass and a yellow Schott OG530 filter (530 nm cutoff filter). Each lighting box was installed as near as possible to the original background lights on each side of the Humphrey Field Analyzer. The output of the lighting boxes was balanced to

provide a uniform background (within 0.1 log unit or 1 dB) over the central 40 degrees radius of the visual field. A separate calibration system was used to monitor and adjust the auxiliary lighting system. The third modification consisted of a filter holder attached to the projection arm of the Humphrey Field Analyzer to accommodate the 50 mm diameter yellow (Schott OG530) and blue (OCLI 500 nm cutoff filter) stimulus filters.

Three test conditions were employed: (a) a standard Humphrey Field Analyzer Program 30-2 examination (Size III target, 31.5 asb background) herein referred to as the 'White on White' test condition; (b) a 'Yellow on Yellow' test condition that was identical to the White on White condition, except that a Size V yellow target was presented on a 635 asb yellow background; and (c) a 'Blue on Yellow' condition designed to isolate the sensitivity of short-wavelength-sensitive mechanisms. The Blue on Yellow test was identical to the other tests, except that a Size V blue target was superimposed on a 635 asb yellow background. Preliminary studies in normal observers[9,12] revealed that these conditions were able to provide excellent isolation of short-wavelength-sensitive mechanisms.

Pre-retinal media absorption was determined for each eye on a Tubinger perimeter by measuring dark-adapted scotopic thresholds (0.001 asb background) at 15 degrees eccentricity in the superior visual field for both short wavelength (450 nm) and long wavelength (656 nm) stimuli. In the event that this stimulus location fell within an area of visual field loss for patients, an alternatep site at the same eccentricity was selected. Three interleaved threshold measures were obtained for short and long wavelength stimuli after dark adaptation. Our calculations of media transmission loss utilized the procedure of Van Norren and Vos[7], which assumes that the shape of the rhodopsin absorption spectrum is invariant, and that differences in dark-adapted spectral sensitivity can be attributed entirely to pre-retinal media absorption. Also, we assumed that the amount of light loss through the unit path-length remains constant during life while the lens continues to thicken[13]. All media correction values were referred to the Van Norren and Vos 'proposed standard observer', for which ocular media transmission at 656 nm was assumed to be 100%[7,8].

Results

The mean and 95% confidence limits were determined for the full central 30 degree visual field, 0 to 10 degrees, 10 to 20 degrees, 20 to 30 degrees and each of the four quadrants (superior temporal, superior nasal, inferior temporal, inferior nasal) in each of the three normal subject age groups (20 to 39 years, 40 to 59 years, 60 and over). Visual field results from ocular hypertensive and early glaucoma patients were then compared to the normal confidence limits for their particular age group. Fig. 1 presents the percentage of ocular hypertension and early glaucoma eyes that had sensitivity values below the normal 95% confidence limits for the full central 30 degrees (upper left), 0 to 10 degrees (upper right), 10 to 20 degrees (lower left) and 20 to 30 degrees (lower right). For each of these regions, approximately 5% of the ocular hypertensive eyes and 30 to 35% of the eyes from early glaucoma patients had average sensitivity values that were below the normal 95% confidence limits for the standard white on white and high background luminance yellow on yellow visual field tests.

The blue on yellow test condition that isolated the activity of short-wavelength-sensitive mechanisms revealed more than twice as many ocular hypertensive eyes (approximately 12%) that were beyond normal limits for the full central 30 degrees and the 0 to 10 degree and 10 to 20 degree regions. No differences were found for the 20 to 30 degree region, which may in part be due to the greater individual

variation in short wavelength sensitivity of the normal population in this region. A similar pattern can be noted for the eyes of early glaucoma patients, where approximately 15% more eyes are beyond the normal confidence limits for the blue on yellow test than for the other two conditions for the full central 30 degrees, 0 to 10 degrees and 10 to 20 degrees.

For all tests, the percentage of eyes from early glaucoma patients that exceeded normal limits was between 25 and 50%. This low amount can be attributed to the fact that most of these patients had small localized deficits in only one eye and our

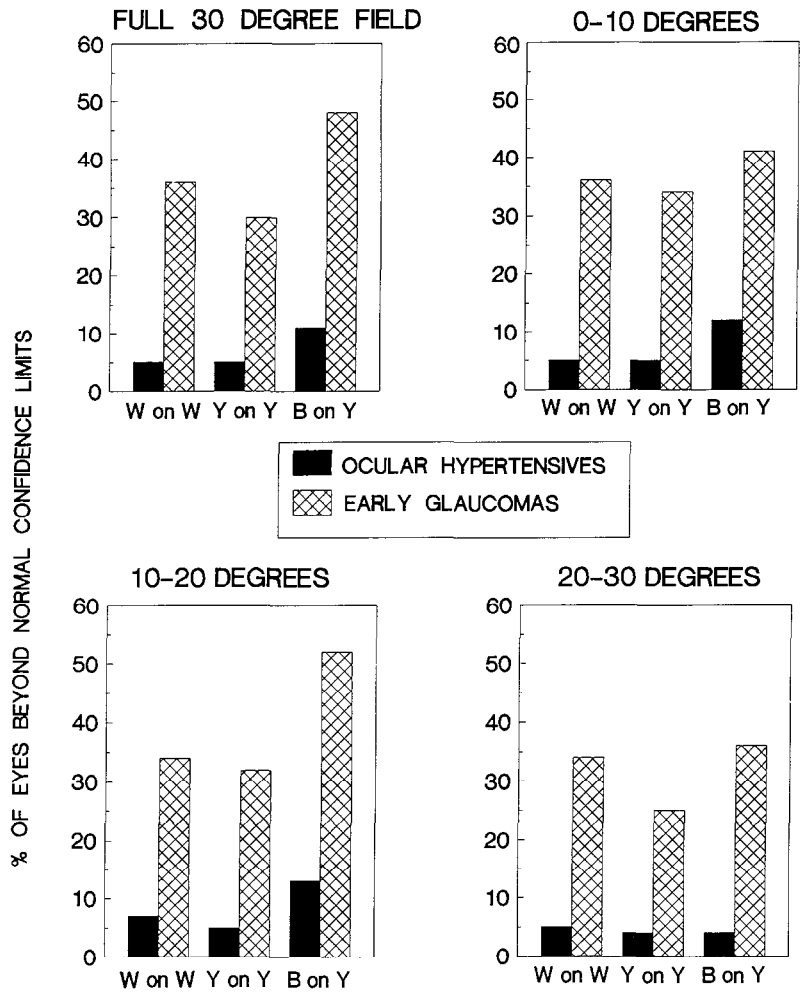

Fig 1 Percentage of eyes from ocular hypertensive patients (solid bars) and early glaucoma patients (crosshatched bars) that were beyond the normal age-related 95% confidence limits for the white on white (W on W), yellow on yellow (Y on Y) and blue on yellow (B on Y) test conditions Results are shown for the full central 30 degree visual field (upper left), 0 to 10 degrees (upper right), 10 to 20 degrees (lower left) and 20 to 30 degrees (lower right) See text for an explanation of the three test conditions

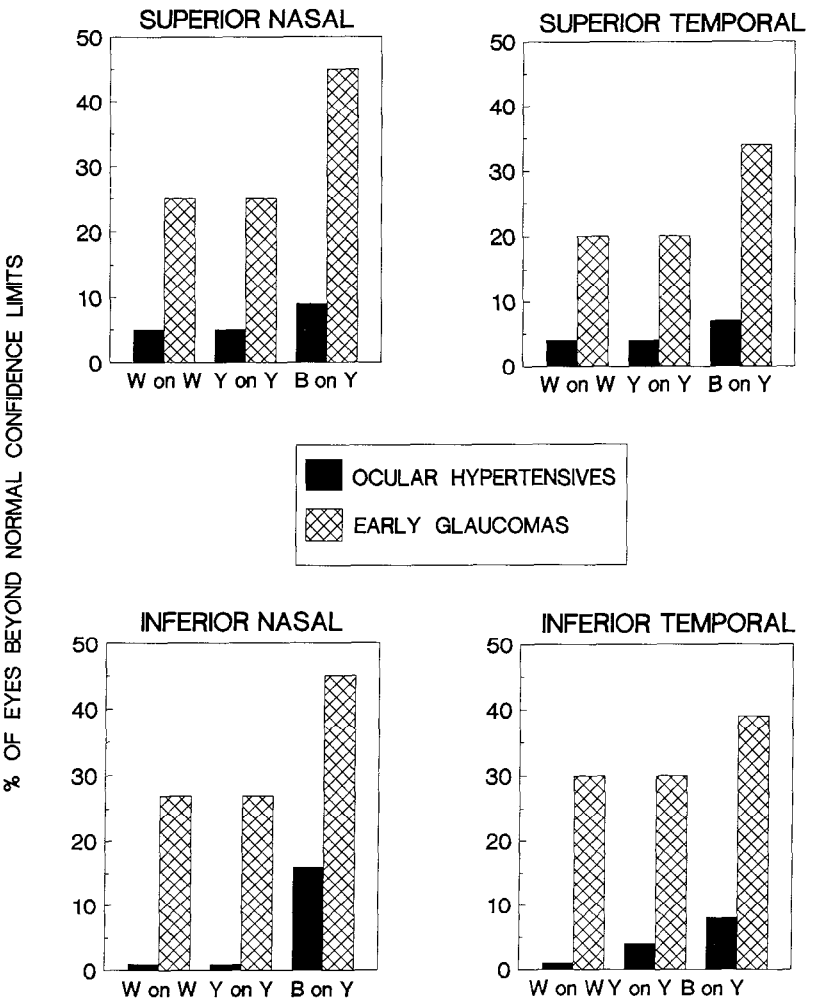

Fig 2 Percentage of eyes from ocular hypertensive patients (solid bars) and early glaucoma patients (crosshatched bars) that were beyond the normal age-related 95% confidence limits for the white on white (W on W), yellow on yellow (Y on Y) and blue on yellow (B on Y) test conditions Results are shown for the superior nasal (upper left), superior temporal (upper right) inferior nasal (lower left) and inferior temporal (lower right) visual field quadrants See text for an explanation of the three test conditions

analyses were conducted for rather large areas of the central visual field. Our primary intent for this study was to examine diffuse short wavelength sensitivity loss in early stages of disease.

Similar results are presented in Fig. 2 for the superior nasal (upper left), superior temporal (upper right), inferior nasal (lower left) and inferior temporal (lower right) visual field quadrants. For all quadrants, there is a greater percentage of abnormalities for the blue on yellow test condition than for the other two test conditions. However, there is an especially high number of short wavelength sensitivity losses in the inferior nasal quadrant for both the ocular hypertensive and

early glaucoma groups. These findings suggest that selective short wavelength sensitivity losses in ocular hypertension and early glaucoma may reflect both diffuse and localized deficits.

Discussion

In accordance with the results of Heron *et al.*[4], our findings indicate both diffuse and localized short wavelength sensitivity losses in some patients with ocular hypertension and early glaucoma. Approximately 7% more ocular hypertension patients and 15% more early glaucoma patients showed selective short wavelength sensitivity deficits in the central 30 degree visual field, as compared to standard Humphrey Field Analyzer testing or automated perimetry of middle- and/or long-wavelength-sensitive mechanisms (yellow on yellow condition). These results indicate that short wavelength sensitivity losses represent an early deficit from glaucomatous damage.

When assessing the sensitivity of short-wavelength-sensitive pathways, several test considerations are crucial to its success. First, it is important to have an appropriate background illumination and spectral distribution combined with an appropriate stimulus size, duration and spectral distribution to ensure that short-wavelength-sensitive mechanisms have been sufficiently isolated from middle- and long-wavelength-sensitive mechanisms. Second, there is an average reduction in short wavelength light transmission by the ocular media, especially for individuals over 60. In addition, there are large individual differences in the amount of short wavelength light attenuation by the ocular media, making it necessary to measure the lens density of each eye in order to distinguish between short wavelength sensitivity losses due to the normal aging of the lens from those that are related to early pathologic glaucomatous losses. Third, it is important to have an age-matched normal control group for comparison of results for short wavelength sensitivity measurements of the central 30 degree visual field, since their normal age-related changes are different from those of middle- and/or long-wavelength-sensitive mechanisms[12].

The present study demonstrates that chromatic adaptation techniques for isolating the sensitivity of individual cone pathways can be readily adapted to automated perimetry. Preliminary results indicate that after age-related changes in lens density are taken into account, some ocular hypertensive and early glaucoma patients demonstrate diffuse and/or localized short wavelength sensitivity losses in spite of normal results with conventional automated perimetric testing. These findings indicate that short wavelength sensitivity losses represent early glaucomatous damage, and suggest that this may be a precursor to the development of visual field loss as measured by conventional procedures. The subjects in this study (both normal controls and patients) are currently being followed prospectively on an annual basis, which will help to identify the temporal sequence of glaucomatous losses. Further evaluations must be conducted to establish the relationship between perimetry of short-wavelength-sensitive mechanisms and conventional automated perimetry, the clinical prognostic value of evaluating short-wavelength-sensitive mechanisms, and related questions.

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THE USEFULNESS OF SENSITIVITY MEASUREMENTS ON A WHITE BACKGROUND FOR DETECTING MINOR CHANGES IN VISUAL DISTURBANCES IN OPTIC NERVE DISEASES

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Abstract

In this study we investigated whether or not the spectral sensitivity measurements on a white background could be useful in detecting early stages or minor visual disturbances in optic nerve diseases. The spectral sensitivity was measured using a Maxwellian view optical system for 1°, 200-ms test flashes on a 1000 photopic troland white background on three patients with optic neuritis in one eye. A slight decrease in sensitivity, mainly of the blue cone system, was found in all three patients even though visual acuity and Goldmann perimetry had returned to almost normal

As a result, it was felt that the sensitivity measurements on a white background might be useful not only to investigate the characteristics of the opponent channel damage but also to detect minor visual disturbances in optic nerve diseases.

Introduction

It has been found that the spectral sensitivity curve for a low temporal frequency test flash on an intense white background shows three peaks which are at about 440 nm, 530 nm and 610 nm. The peak near 440 nm can be accounted for by the action of blue cones, while the narrowed peaks about 500 nm have been attributed to linear subtractive interaction between the green and the red cones[1-3]. Therefore, this technique has been applied to demonstrate a selective loss of opponent system in clinical cases.

In this study, we investigated whether or not the spectral sensitivity measurements on a white background could be useful in detecting early stages or minor visual disturbances in optic nerve diseases.

Methods

A two-channel Maxwellian view optical system with a 150 watt xenon arc as a light source was used in this study. A 1° diameter circular test light was superimposed in the center of an 8° circular xenon white background field of 1000 photopic trolands. Interference filters with dominant wavelengths of between 400 and 700 nm with 6 to 10 nm half-band widths were used for the test light which was exposed for 200 ms every two seconds.

Measurements were made on three patients with optic neuritis in one eye whose visual acuity and visual field had returned to almost normal with steroid treatment. Their pupils were dilated with 1% tropicamide. Prior to the measurements, the patients were adapted to the background for 3 min and the detection threshold for the test flash was measured at least three times for each test wavelength.

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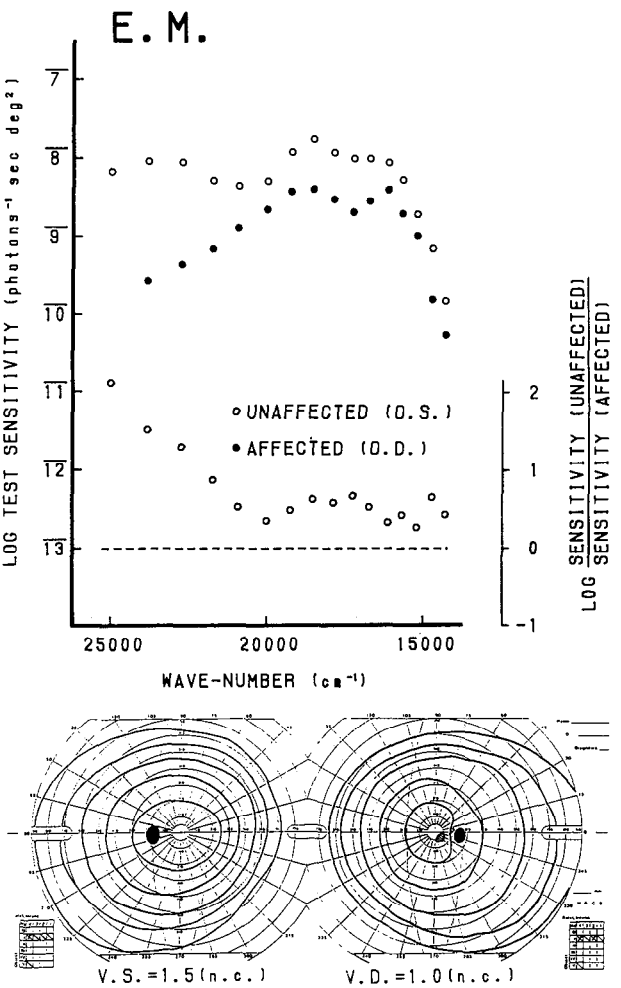

Fig 1 Case EM. The upper panel represents the results of the spectral sensitivity on a white background. The test sensitivities for the unaffected eye (open circles) and the affected eye (closed circles) were plotted as a function of the wave number. The lower portion of the upper panel shows the log sensitivity for the unaffected eye minus log sensitivity for the affected eye (ordinate scale to the right). The lower panel shows the Goldmann visual field.

Results

The results of the test sensitivities (photons^{-1} sec deg^2) were plotted as a function of the wave number (cm^{-1}). The sensitivities for the unaffected and the affected eye are shown as open and closed circles, respectively. Each circle represents the mean value of three measurements. The log sensitivity for the unaffected eye minus log sensitivity for the affected eye was plotted below each test sensitivity curve (ordinate scale to the right).

Case 1 (EM): A 29-year-old female had sudden onset of retrobulbar optic neuritis in her right eye. Visual acuity was 0.01 (n.c.) in her right eye and 1.5 (n.c.) in her left eye. Visual acuity recovered following steroid treatment. The spectral sensitivities were measured when visual acuity improved to a level of 1.0 (n.c.) but the kinetic visual field using the Goldmann perimeter revealed a small paracentral scotoma (lower panel of Fig. 1). The results of the test sensitivities are illustrated in Fig. 1. The log sensitivity for the unaffected eye minus log sensitivity for the affected eye is shown in the lower part of Fig. 1. Although there was a loss in sensitivity for both the blue cone system and the red and green cone system, there was a definite lack of a peak in the short wavelength region. The spectral sensitivities were measured again when visual acuity recovered to 1.5 (n.c.) and the paracentral scotoma disappeared (Fig. 2). The sensitivity for the affected eye still showed a slight decrease in sensitivity, mainly in the short wavelength region. The mean difference in sensitivity between the affected eye and the unaffected eye from 400 nm to 480 nm was 0.252 log units, but in the range from 490 nm to 700 nm, it was 0.081 log units.

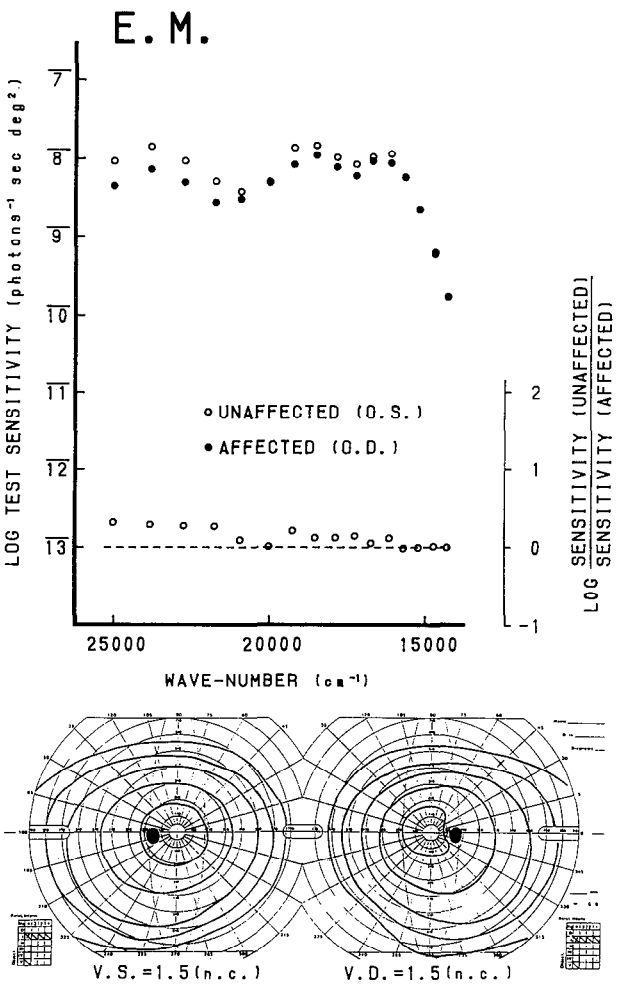

Fig 2 Case EM. Upper panel: spectral sensitivity; lower panel: Goldmann visual field.

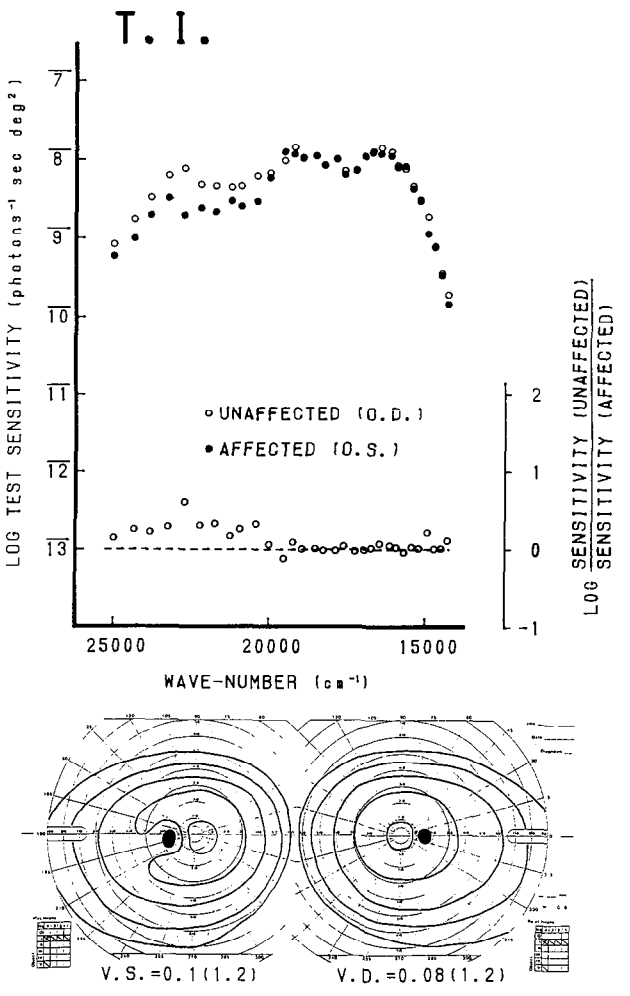

Fig. 3 Case TI. Upper panel: spectral sensitivity; lower panel: Goldmann visual field.

Case 2 (TI): A 38-year-old male had retrobulbar optic neuritis in his left eye. Visual acuity was 0.08 (1.2) in his right eye and 0.01 (n.c.) in his left eye. Goldmann perimetry revealed a large central scotoma in his left eye. When visual acuity in his left eye recovered to 0.1 (1.2) and the central scotoma disappeared (lower panel of Fig. 3) following steroid therapy, the spectral sensitivities were measured (upper panel of Fig. 3). The sensitivity for the affected eye (closed circles) showed a slight reduction in sensitivity in the region from 400 nm to 490 nm. However, there were no significant differences between the affected eye and the unaffected eye in the middle- and long-wavelength regions. The mean difference in sensitivity from 400 nm to 490 nm was 0.286 log units and in the region from 500 nm to 700 nm was 0.030 log units.

Case 3 (KK): A 58-year-old female had optic neuritis in her right eye. Visual acuity was 0.03 (n.c.) in her right eye and 1.0 (1.2) in her left eye. The visual field demonstrated a large centrocecal scotoma with superior temporal depression in her right eye. When visual acuity in her right eye recovered to a level of 0.9 (1.0) and the centrocecal scotoma disappeared (lower panel of Fig. 4), the sensitivities were measured (upper panel of Fig. 4). The spectral sensitivity for the affected eye showed a loss in sensitivity for both the blue cone system and the red and green cone system. The mean difference in sensitivity in the region from 400 nm to 480 nm was 0.423 log units and in the region from 500 nm to 700 nm it was 0.298.

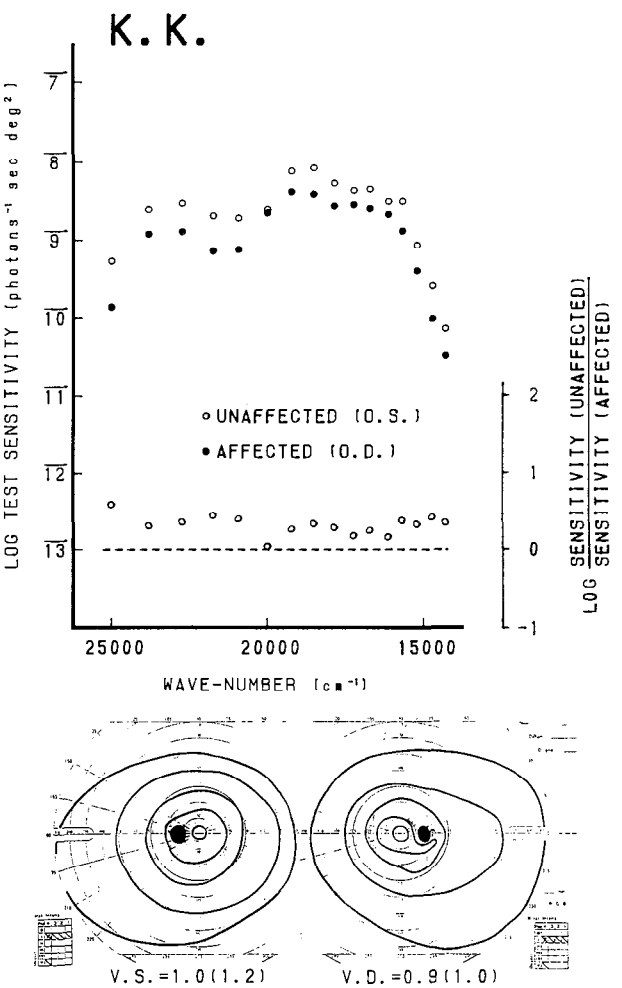

Fig. 4 Case KK. Upper panel: spectral sensitivity; lower panel: Goldmann visual field.

Discussion

Applying the spectral sensitivity measurements on a white background, we have found that although there was a loss in sensitivity for both the blue cone system and the red and green cone system, there was a definite lack of a peak in the short wavelength region in most optic nerve diseases. Consequently, it was felt that the blue cone system was much more vulnerable in most optic nerve diseases as well as retinal diseases.

In this experiment, the spectral sensitivities for a 1°, 200-ms test flash on a 1000 photopic troland white background were measured on patients with optic neuritis in one eye. Then, the sensitivities for the affected eye were compared to the unaffected eye in each case to avoid inter-observer variability. The results showed a slight decrease in sensitivity of the affected eye, mainly in the blue cone system, even though visual acuity and Goldmann perimetry had returned almost to normal.

As a result, it was felt that the sensitivity measurements on a white background might be useful not only to investigate the characteristics of the opponent channel damage but also to detect minor visual disturbances in optic nerve diseases. Previously, we reported on a case of blue-yellow defect in one eye, which was induced by intense blue light[4]. The spectral sensitivity on a white background showed a reduction only in the region from 400 nm to 480 nm. In this case the static perimetry using a 430 nm test light showed a marked decline in sensitivity while the static perimetry for white, 650 nm, 580 nm, 550 nm and 480 nm test light showed no significant differences between the unaffected eye and the affected eye. Furthermore, in a related paper[5], we found that the peak at about 440 nm, which was attributed to the blue cone system, remained prominent for normal observers even outside the fovea. Therefore, color perimetry for a blue test light (say λ max = shorter than 450 nm) on an intense white background might be useful for assessing minor visual field defects in optic nerve diseases.

Acknowledgement

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CHROMATIC FLICKER DEFICITS IN GLAUCOMA PATIENTS AND SUSPECTS

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Chromatic and luminance flicker sensitivity was assessed in glaucoma patients and suspects, as well as in a group of control observers. In spite of the fact that all subjects scored within the normal range on the FM-100 hue test, both patients and suspects exhibited deficits in detecting yellow-blue and luminance flicker, whereas only the suspects showed a mild attenuation of sensitivity to red-green flicker These data attest to the sensitivity of dynamic color discrimination tasks as well as to the sensitivity of flicker techniques in general

1. Introduction

There is now little doubt that automated static perimetry is a clinical, psychophysical technique that is quite sensitive to the visual consequences of glaucoma. The extent of its sensitivity, however, depends upon how central visual field losses are explained, that may not be reflected in conventional perimetric data. These deficits are usually measured along a single perceptual dimension such as color, spatial sensitivity, and temporal sensitivity. Perimetry contrasts to the techniques that reveal these deficits in that static increments in luminance can be detected along a number of perceptual dimensions. Detection, for example, could be based upon edge information, the luminous inner region of a target, or upon seeing a patternless flash.

The conventional way of accounting for central visual field deficits has been to assume that perimetry measured localized defects, whereas single dimensional tests reflect a generalized, diffuse loss of optic nerve fibers. Another possibility is that impairment along a single perceptual dimension may be masked in perimetric data due to detection occurring at a normal level along another dimension. This line of reasoning implies that single dimensional losses, rather than reflecting a generalized depression in sensitivity, may represent damage to neurons that specialize in processing certain types of visual information. It is in this latter context that we have studied the attenuation of chromatic sensitivity to flickering stimuli in glaucoma.

There is a growing body of evidence indicating that impaired temporal sensitivity represents an early symptom of chronic open angle glaucoma[1-4]. However, the methodologies typically employed favor detection within the achromatic system. There is also an established body of evidence that color discrimination is sacrificed early in the course of glaucoma[5-8]. The purpose of this study was to address two related questions. The first concerned whether temporal sensitivity losses in the chromatic system are also typical of glaucoma. An assumption underlying the second question is that, if only the chromatic characteristics of a light are temporal-

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ly modulated, then the basis of flicker detection must be the ability to discriminate the chromaticities. The second question then was whether deficits in dynamic color discrimination are also a characteristic symptom of glaucoma.

The initial strategy that was adopted entailed testing pure glaucoma patients and suspects who scored within the normal range on both the H-R-R Pseudo-isochromatic Plates, and the Farnsworth-Munsell 100 Hue Test. In this way, we could also clearly assess the value of measuring temporal chromatic sensitivity as compared to the use of color discrimination tests conducted under steady-state luminance conditions.

2. Methods

2.1. Subjects

Due to the restrictive screening criteria (no other ophthalmological disorders, and no conventionally measured color defects), only six early glaucomatous eyes have been tested at the time of writing. All of these eyes had reproducible glaucomatous visual field defects as assessed by the Octopus G1 program and/or disc cup abnormalities. The age of the glaucomatous eyes ranged from 52 to 72 years, with a mean of 61.5 years and a standard deviation of 9.1 years. Nine suspect eyes were tested that exhibited no visual field defects or optic disc abnormalities. All patient and suspect eyes consistently exhibited intraocular pressures of 22 mm Hg or greater. Suspect eyes ranged in age from 27 to 75 years with a mean of 49.9 years and a standard deviation of 16.2 years. Fifteen control eyes (no known ophthalmological disorders) were also tested. Ages in this group ranged from 22 to 70 years with a mean of 48.3 years and a standard deviation of 16.2 years. All eyes that were tested were measured to have 20/25 (6/7.5) corrected or uncorrected far acuity.

2.2. Apparatus and stimuli

All stimuli were generated on a 20 inch RGB video monitor (Gigatek-1931CC) interfaced with an LSI11/23+ computer system (Digital Equipment Corporation) through a set of graphics boards (Matrox QVAF-512 and QRGB-Graph boards). The monitor was equipped with an industry standard 'medium persistence P22 phosphor' whose longest duration to full decay (red) was measured to be 4 ms. Through software control over the timing of the vertical sync pulse, frames could be generated at a rate of 120 Hz (non-interlaced) that contained 128 lines with 512 pixels per line.

The available colors were constrained by the chromaticities of the three phosphors that could be described by a triangular region within the CIE u′v′ chromaticity diagram (see Fig. 1). Within this region, chromatic modulation was generated along a tritan confusion line (yellow-blue flicker), and along a deutan confusion line (red-green flicker). These lines also defined cardinal directions that presumably reflect functioning within the red-green and yellow-blue opponent systems[9]. The deutan and tritan confusion lines intersected at D65, a white with coordinates : u′ =0 .198; v′ =0 .468. All temporal modulation was sinusoidal, and was centered around the midpoint of either confusion line. Given the timing constraints imposed by the 120 Hz frame rate, temporal frequencies were chosen (1, 2, 5, 10 and 15 Hz) so that: (a) a minimum of eight points could be sampled on the sine wave, and (b) the same points on the sine wave could be sampled on successive flicker cycles.

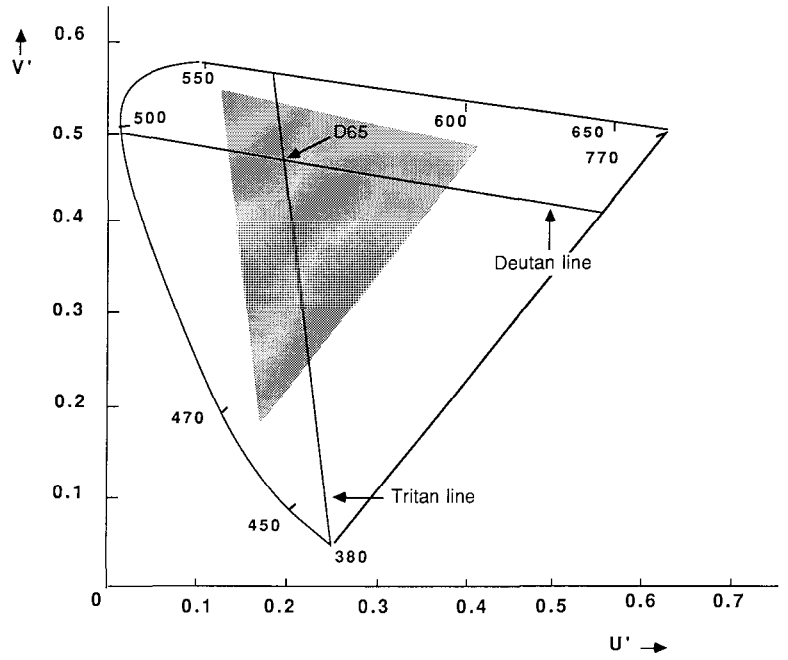

Fig 1 The CIE u′v′ chromaticity diagram. The triangular region specifies the chromaticities available on the video monitor, and the two lines represent the range of chromaticities that could be modulated in a red-green condition (the deutan line), and a yellow-blue condition (the tritan line)

Chromaticities were sampled along a given confusion line so that they were equidistant from each other in u′v′ space, and were produced by mixing appropriate amounts of those chromaticities defining the end points of each line. The reference luminance levels of the end points were determined for each individual tested through conventional heterochromatic flicker photometry. The luminance levels of all end points were equated to that of the white background which was fixed at 5.65 cd/m^2. A relatively low level was chosen because of recent evidence that the equation of luminance levels with flicker photometry is only independent of temporal frequency at retinal illuminance levels less than about 50 trolands[10]. Since the stimulus display was always viewed monocularly through a 3 mm artificial pupil, the effective retinal illuminance was always maintained at 40 trolands. An achromatic flicker condition was also implemented with a 40 troland time-average retinal illuminance level. The artificial pupil was contained in a phoropter that was also used, if a participant normally wore glasses, to obtain a best correction for far acuity.

2.3. Display and procedure

At a viewing distance of 1 meter, the display consisted of a 2 deg diameter test field centered within a 15 x 9 deg white (D65) background field (see Fig. 2). Four six min points were painted 1.5 deg away from the edge of the test field along the vertical and horizontal meridians. These points served to guide fixation in the event that an individual found it difficult to distinguish the test field from the background.

Before a testing session began the luminance levels of the end points of each confusion line were equated with that of the white background. This was ac-

complished within the test field by alternating the D65 white with one of the colors in the counterphase, square wave flicker at 20 Hz. A subject adjusted the luminance of the chromatic portion that was initially set to be noticeably higher or lower than the fixed level of the white until, under the conditions of this experiment, there was no detectable flicker. This was done four times, with the mean of the four settings taken to be the point of equated luminance. The color whose luminance was just established was then alternated with the color existing at the other end of its confusion line. This procedure was then repeated for the two end points of the other confusion line. With this conventional heterochromatic flicker photometry procedure, the luminances of all four end points were equated with each other, and with that of the D65 white.

During a test session, flicker detection thresholds were assessed with a five-reversal staircase procedure. The two eyes of an observer were tested separately and in a random order, but within an eye, all staircases for the five frequencies x 3 chromatic conditions were randomly interspersed. Fifteen catch trials were included in each block. Data from only one eye per observer were included in subsequent analyses.

3. Results

Figs. 3-5 present the data for chromatic modulation along the deutan (red-green) and tritan (yellow-blue) lines, and luminance flicker, respectively. Chromatic flicker thresholds were defined as the distance in u′v′ space between the midpoint of a confusion line and the peak or trough of the sine wave required to first detect

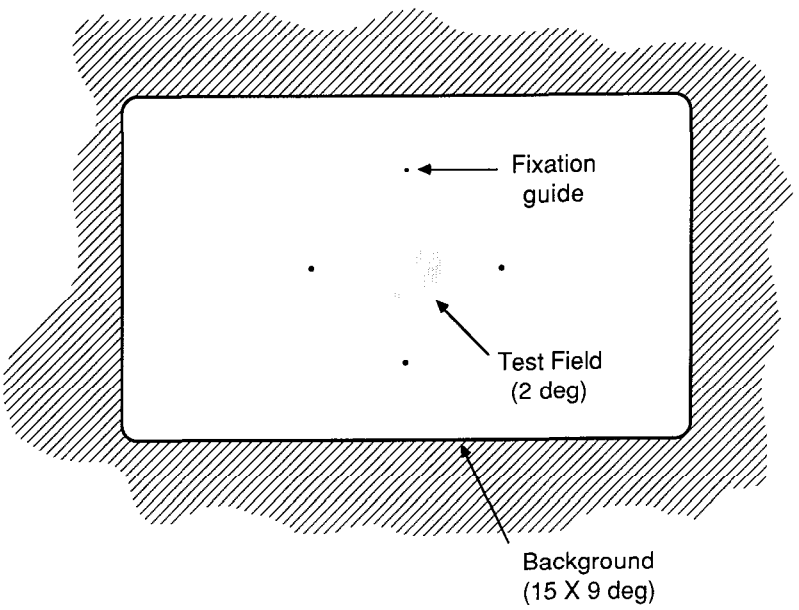

Fig 2. The display viewed by all individuals tested.

flicker. Achromatic sensitivity was defined as the reciprocal of the depth of modulation threshold. In all three figures, sensitivity increases as one moves up the Y-axis.

When exposed to pure red-green flicker, glaucoma patients and control observers produced almost identical data. Although an inspection of Fig. 3 seems to indicate that the performance of the suspects was consistently worse than that of the other groups, a 5 x 3 split-plot ANOVA revealed a significant group by frequency interaction, $F(8,104) = 4.542, p < 0.01$. The source of this interaction was the lower sensitivity of the suspects above 4 Hz only. A significant interaction was also observed in the yellow-blue flicker condition, $F(8,108) = 2.099, p < 0.05$. However, in this case, it indicated that the performance of *both* the glaucoma and suspect groups was worse than that of the controls above a temporal frequency of 2 Hz. For the luminance flicker condition, the performance of the glaucoma patients and suspects was attenuated relative to that of the controls at all frequencies. However, the significant group by frequency interaction, $F(8,108) = 2.223, p < 0.05$, indicated that the difference was exacerbated at 10 and 15 Hz. This finding is consistent with reports in the literature that the middle range of temporal frequencies may be most affected in glaucoma[4,11-13]. When considered together, these data indicate that for the eyes that were tested, the predominant deficits were in the yellow-blue and achromatic domains.

4. Discussion

Confidence in interpreting these results depends upon the successful equation of luminance levels in the deutan and tritan line conditions, the influence of differences in the average age among the groups, and consideration given to the presently small patient and suspect sample sizes. Successful flicker photometry is suggested

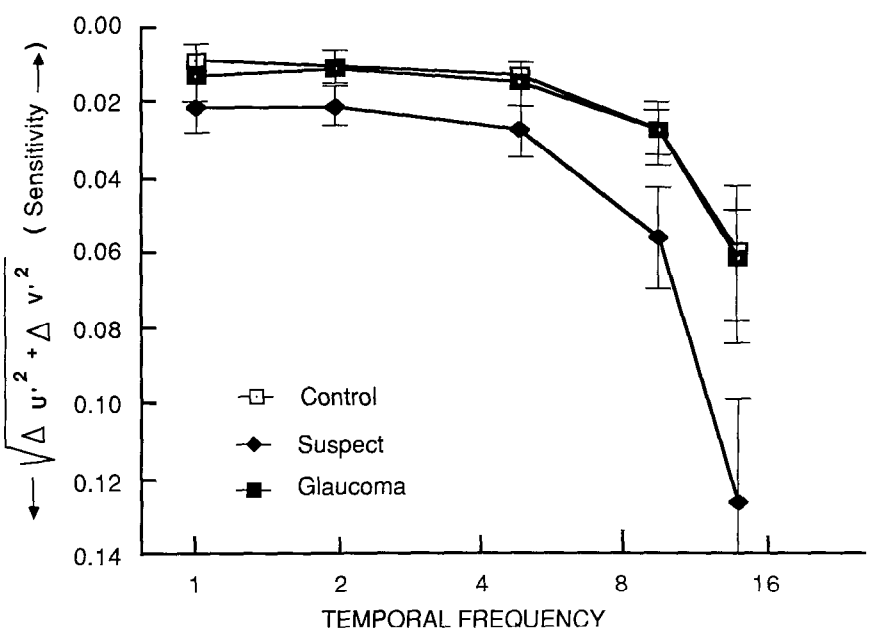

Fig 3 Chromatic sensitivity as a function of temporal frequency for control, patient and suspect eyes in the red-green flicker condition Bars around data points represent 1 standard error

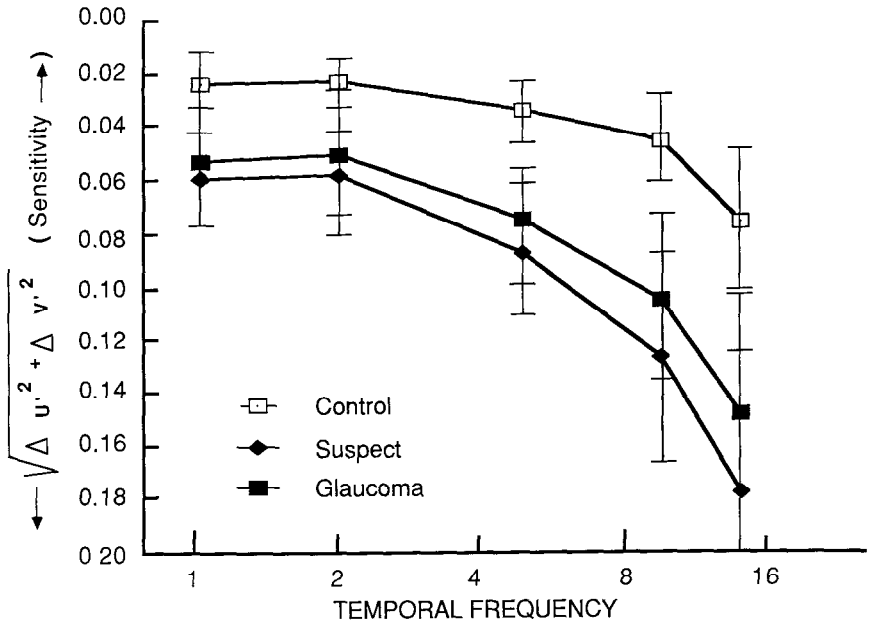

Fig 4. Chromatic sensitivity as a function of temporal frequency for control, patient and suspect eyes in the yellow-blue flicker condition. Bars around data points represent 1 standard error.

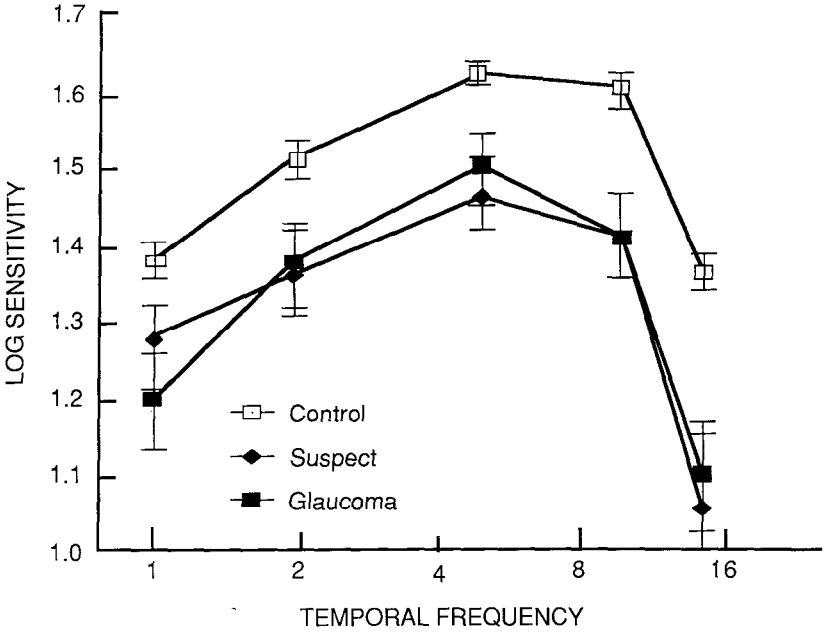

Fig 5 Achromatic sensitivity as a function of temporal frequency for control, patient and suspect eyes in the luminance flicker condition. Bars around data points represent 1 standard error

by the typical low-pass characteristics of the deutan and tritan line functions[14], compared to the band-pass characteristic of the achromatic functions[15]. Furthermore, lack of patient deficits in the deutan condition, combined with significant but somewhat different sensitivity losses in the tritan and achromatic conditions, also imply that different mechanisms were mediating flicker detection in these three conditions. Age differences between the glaucoma *vs* suspect and control groups, may not be problematical. Although yellowing of the lens with age could explain why patient deficits were observed with yellow-blue but not red-green flickering stimuli, it cannot be easily reconciled with the finding that patient and suspect data were the same in the tritan condition, in spite of the fact that the average age difference between the two groups was almost 12 years. One would expect any combined effects of age and glaucoma to cause patient sensitivity to be worse than that exhibited by suspects.

The currently small patient and suspect sample sizes would usually preclude the possibility of making strong interpretations. However, in this case it lends credence to at least one important conclusion. It is impressive that in spite of the small sample sizes and lack of color deficiency measured with conventional means, yellow-blue as well as achromatic deficits were revealed in both patients and suspects, and were more severe than the red-green deficit exhibited by the suspects only. This result is consistent with the literature suggesting the predominance of yellow-blue deficiencies in glaucoma under steady state conditions[5-8], and additionally attests to the sensitivity of flicker techniques in both the chromatic and achromatic domains.

Two obvious questions remain to be addressed: why do chromatic flicker techniques seem to be more sensitive than static color discrimination tasks, and why in either case are yellow-blue deficits more common in glaucoma than red-green deficits. A possible answer to the first question lies in the psychophysical domain. In general, any technique that is associated with greater variability will be less sensitive. One factor that influences variability is the difficulty of the task. There is little question that deciding upon an order in which chips of similar chromaticity should be placed is more difficult than deciding whether flicker is present or absent. A second source of variability that exists in the conventional color discrimination tasks, but that is absent in a chromatic flicker detection technique, is the fact that colored chips are equated in luminance on the basis of an average spectral sensitivity function. This means that for any individual, there may be brightness as well as hue differences among chips. Since the perceptual dimensions of hue, saturation and brightness are not as discrete as they are made out to be in textbooks, the confounding of these two response criteria could cause chips to be improperly ordered even by individuals with normal color discrimination abilities. In a chromatic flicker task, the two chromaticities defining the peak and trough of the flicker can be equated in luminance for every individual tested.

A reason as to why yellow-blue flicker losses are more characteristic of glaucoma than red-green losses has been suggested recently by Heron *et al*[8]. They cited studies in which it was demonstrated that large optic nerve fibers are sacrificed early in the course of glaucoma[16,17], as well as evidence that optic nerve fibers carrying yellow-blue information in the primate visual system are larger than those carrying red-green information[18,19]. It follows that yellow-blue fibers should be more susceptible to glaucomatous damage than red-green fibers.

Although this type of theoretical speculation, based upon associating selective fiber size loss with function, is not incompatible with the idea of diffuse fiber loss, it takes some of the meaning away from the concept. Diffuse loss must now be qualified to include a preference for large fiber damage. It might be more meaningful to explore other functions that are associated with large optic nerve fibers in an attempt to predict the type of visual loss that might be expected to occur early in

glaucoma. It might also be useful to develop clinical techniques that focus upon revealing deficits in these specific domains, and recognize that automated static perimetry measures impairment that exists along a number of unspecified perceptual dimensions.

Acknowledgements

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COMPARATIVE EVALUATION OF VARIOUS FUNCTIONAL TESTS FOR THE EARLY DIAGNOSIS OF OPTIC NEUROPATHY

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Abstract

A group of 30 subjects with multiple sclerosis and normal visual acuity underwent a series of functional tests in order to detect the first signs of optic neuropathy: visual field examination (Goldmann kinetic quantitative perimetry, Humphrey 630: program 30.1 with STATPAC analysis), chromatic sense examination (Farnsworth 100 Hue test, Lanthony New Color Test), contrast sensitivity evaluation (with a particular octotype in which letters are presented at contrasts varying from 4 3 to 85 6%) and VEP assessment (pattern reversal 2/s)

Chromatic sense (red/green and blue/yellow axis) and contrast sensitivity (medium and high frequencies) abnormalities were found to be well related with mild visual field defects (paracentral scotomata or SF increase) and VEP alterations (latency increase) All of the functional tests utilized revealed a good reliability in detecting early optic nerve involvement, when performed by sufficiently refined and precise methodologies, but the automatic static visual field examination showed a higher percentage of pathological results

1. Introduction

The perimetric[1-5], contrast sensitivity[6-8], color sense[9-13] and visual evoked potential (VEP)[1,11,14] alterations in patients with multiple sclerosis (MS) during and after recovery from optic neuropathy are reported.

The goal of the present study was to contribute to the early diagnosis of clinically silent optic neuropathy in definite multiple sclerosis, by studying the visual field, chromatic sense, contrast sensitivity and VEPs.

2. Material and methods

Thirty subjects (18 females and 12 males; average age 35 years, range 19-49 years) affected by clinically definite multiple sclerosis, according to McAlpine's classification[15], for an average of five years (range two to ten years) were examined.

All patients presented typical cerebrospinal fluid alterations. None had previous optic neuritis or a history of visual disturbance and all had a visual acuity greater than or equal to 20/25, uncorrected or corrected, with a refraction error of less than or equal to 3 diopters.

Optic disc examination was performed by direct ophthalmoscopy, but was not taken into consideration because of the difficulty of objectively quantifying the optic disc pallor.

The control group consisted of 28 subjects (15 females and 13 males, average age

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36 years, range 20-50 years) free from systemic and ophthalmologic disorders.

The following tests were performed:
- Standard kinetic perimetry (Goldmann)
- Automatic static perimetry (Humphrey)
- Classification chromatic tests (Farnsworth 100 Hue, New Color Test)
- Contrast sensitivity (Paliaga-Gracis Visugram)
- VEPs (pattern reversal)

Standard kinetic perimetry, according to Goldmann, was performed manually, at the photopic (31.4 asb) luminance level, with four targets (I.4, I.3, I.2, I.1); particular attention was paid to the search for scotomata in Bjerrum's area and in the central visual field. The visual fields were evaluated by means of traditional criteria and judged abnormal if scotomata or isopteric alterations were present.

Automatic static perimetry was carried out by means of the Allergan-Humphrey 630 Field Analyser, which performs threshold static perimetry. We used program 30-1, which tests 76 points equally distributed within the central 30 degrees of the visual field. Evaluation of the visual field was carried out by means of the automatic statistical program 'STATPAC' of the Humphrey perimeter. This program takes into consideration some 'visual field indices' (*i.e.*, MD = mean defect, SF = short-term fluctuation, PSD = pattern standard deviation, CPSD = corrected pattern standard deviation) that are above physiological levels if perimetry alterations are present.

We considered pathological all visual fields with one or more altered indices.

Color vision was tested with both the Farnsworth 100 Hue and the Lanthony Munsell New Color Test, which were administered by a technician who followed the directions supplied with each test. The MacBeth lamp was used to provide an illumination level of 1750 lux for the tests.

Age-specific upper normal limits were established to evaluate the Farnsworth 100 Hue results, according to Pinckers and Verriest[10] (total score: age 15-29 years = 110; 30-39 years = 130; 40-49 years = 150).

The New Color Test was evaluated by means of correct or incorrect separation between achromatic and chromatic targets and classification of the 15 targets in each of the four boxes (8/4, 6/4, 4/4, 2/4 saturation levels). Minimal errors in separation between the grays and the desaturated 15 Panel and inversion in classification were considered normal findings[16].

Contrast sensitivity was examined by means of Paliaga and Gracis'[17] visugram, which graphically expressed the contrast sensitivity threshold in relation to the angular resolution power: a special octotype presents ten vertical lines which have different contrasts varying from 4.3 to 85.6%. On the visugram the visual acuity value is given in relation to a normal sensitivity curve. On the basis of personal experience acquired in previous studies[18], we fixed the normal values of contrast sensitivity at a score of 0.8 or higher.

VEPs were evoked by stimulation with a checkerboard subtending 10 degrees of the visual angle at a distance of 170 mm from the observer's eye, with single checks of 55′ aperture and generated by a standard system MPS LACE 0.1 on a TV screen. Pattern reversals were presented at a frequency of 2/s, and for each stimulus condition no less than 256 reversals were performed. The P 100, *i.e.*, the major positive VEPs component, was identified by two independent observers. The mean latency measured by them at the peak of P 100 was used for further computation. We found the maximal normal value was 112 ms, and considered pathological all values greater than this[19].

3. Results

Fifty-four of the 60 patients with multiple sclerosis showed abnormal findings in one or more of the examinations.

The alterations encountered with the different tests are listed in Table 1. Table 2 reports the number of cases that were found to have anomalies with each single test.

With Goldmann kinetic perimetry, small paracentral scotomata were found in 15 eyes (25%) in the MS group; in the control group only three defects (5.3%) were found.

With Humphrey automatic perimetry, scotomata or depressed central sensitivity were found in 51 of the MS patients' eyes (85%); the rate of visual field alterations in the normal subjects was 14.3% (eight eyes).

The Farnsworth 100 Hue test revealed abnormalities in total score and in partial score in the third box and axis errors were found in 32 eyes of MS patients (53.3%): the axis errors were tritan (40%), deutan (20%) and mixed (40%). In the control group, a pathological total score was present in three eyes (5.3%) and no axis error was found.

New Color Test examination showed the separation of colored and gray targets to be normal in all cases in both the controls and the MS patients. Color discrimination was abnormal and axis errors (mainly tritan) were present in 28 eyes (46.7%). In the control group, classification was abnormal in six eyes (10.7%).

Among the MS subjects, a pathological level of contrast sensitivity was found in 38 eyes (63.3%). The medium and high frequencies were the most affected. In the control group, an alteration of contrast sensitivity was present in nine eyes (16.1%).

VEPs findings were pathological in 40 eyes (66.7%) in the MS group and in four eyes (7.1%) of the control group.

Table 1 Total alteration of psychophysical tests and VEPs in MS patients and in the control group

Test	MS patients	Normal subjects
Goldmann perimetry	15 eyes (25%)	3 eyes (5 3%)
Humphrey perimetry	51 eyes (85%)	8 eyes (14 3%)
Farnsworth 100 Hue	32 eyes (53.3%)	3 eyes (5 3%)
New Color Test	28 eyes (46 7%)	6 eyes (10 7%)
Contrast sensitivity	38 eyes (63.3%)	9 eyes (16.1%)
VEPs	40 eyes (66.7%)	4 eyes (7 1%)

Table 2 Single alteration of psychophysical tests and VEPs in MS patients and in the control group

Test	MS patients	Normal subjects
No alterations	9 eyes (15%)	48 eyes (67 8%)
Visual field	15 eyes (25%)	18 eyes (19 6%)
Chromatic sense	4 eyes (6 7%)	3 eyes (5 3%)
Contrast sensitivity	11 eyes (18 8%)	6 eyes (10 8%)
VEPs	12 eyes (20%)	3 eyes (5.3%)

4. Discussion and conclusions

The above results show that an involvement of the optic nerve is fairly common in MS patients with normal visual acuity.

On the basis of our experience, we maintain that when visual disturbances are not clinically evident, a perimetric examination, performed with threshold static strategy in a sufficient number of points in the centro-paracentral area, permits the detection of alterations in a large percentage of definite multiple sclerosis patients.

The good performance of the other psychophysical tests suggests their routine utilization in the ophthalmological examination of subjects at risk of developing an optic neuritis in the course of multiple sclerosis.

Humphrey perimetry appeared to be the most sensitive test in detecting optic nerve involvement, but contrast sensitivity testing, color examination and VEPs analysis yielded similar, if slightly inferior, results (Table 1).

A striking feature of our work is the relatively high number of cases that showed alterations in only one of the tests performed (Table 2). It is not possible, on the basis of present knowledge, to state whether this finding is related to different forms of optic nerve damage, or is merely the product of statistical variation in the results. The latter hypothesis, however, appears more likely because a similar finding was encountered even in the normal subjects.

The rather high number of alterations encountered in the normal subjects suggests, therefore, that a complete examination by means of visual field, contrast sensitivity, color discrimination and VEPs is needed to detect optic nerve involvement in MS patients and that true optic nerve damage can be confirmed only when alterations are found in several tests.

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CONTRAST SENSITIVITY, COLOR VISION AND PERIMETRY IN 100 EXAMINATIONS OF PATIENTS WITH OPTIC NEUROPATHIES AND NORMAL SNELLEN ACUITY

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Abstract

The results of sensory visual testing of 100 examinations performed on patients with optic neuropathies were analyzed to determine the importance of contrast sensitivity and color vision testing in patients with normal Snellen visual acuity Patients were included who had objective evidence of an optic neuropathy. The most sensitive tests for detecting visual loss were: color comparison test was abnormal in 68%, perimetry demonstrated defects in 66%, 64% had contrast sensitivity loss and 63% had an abnormal Lanthony desaturated 15 hue test. Of those with normal perimetry, 38% had contrast sensitivity loss and 24% had an abnormal Lanthony color test Contrast sensitivity and Lanthony color testing are useful for diagnosis and following selected patients with optic neuropathies and normal Snellen visual acuity

Introduction

It has been established that there can be considerable damage to the optic nerve while measures of Snellen acuity or kinetic perimetry remain normal[1,2]. Many investigators have developed more sensitive methods of sensory visual testing to detect this 'hidden' visual loss. Others propose that these tests are not necessary and that Snellen acuity and perimetry are sufficient for diagnostic purposes. The clinician is faced with the decision of which, if any, of a large number of subjective afferent visual tests to use in various circumstances.

To determine the usefulness of contrast sensitivity and color vision testing in patients with normal Snellen acuity, we have reviewed the results of 100 examinations of patients with optic neuropathies and Snellen acuity of 20/20 or better.

Methods

Entrance into the study required (1) presence of an optic neuropathy (non-pseudotumor cerebri), (2) 20/20 vision or better, (3) manual (Goldmann) or automated perimetry performed, (4) presence of an objective clinical neuro-ophthalmologic deficit, neuro-imaging abnormality or laboratory finding diagnostic of an optic neuropathy.

We retrospectively reviewed four years of our records to retrieve 100 eye examinations from a total of 43 patients. Some patients were tested at multiple visits. Only examinations of eyes fulfilling the criteria were entered into the study (fellow eyes were ignored if the entrance criteria were not met). Of the objective deficits of the inclusion criteria, an abnormal ophthalmoscopic examination was present in 73% and a relative afferent pupillary defect in 58%. The patients' diagnoses are listed in Table 1. Forty-one examinations were of patients with a diagnosis of optic neuritis.

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Table 1 Diagnoses of patients with involved eyes in the study

Diagnosis	Number of patients
Optic neuritis	41
Thyroid ophthalmopathy	11
Optic disc drusen	9
Ischemic optic neuropathy	8
Sarcoidosis	7
Big blind spot syndrome	6
Low tension glaucoma	4
Undetermined	4
Other	10

A neuro-ophthalmologic examination was performed at each visit which included testing of Snellen visual acuity, confrontation visual fields, careful testing for a relative afferent pupillary defect and ophthalmoscopic examination.

Contrast sensitivity was tested with the Vistech Contrast Test Chart. It was used in the recommended fashion [3]. Subjects viewed the test chart from a distance of three meters for spatial frequencies of 1.5, 3.0, 6.0, 12.0 and 18.0 cycles per degree.

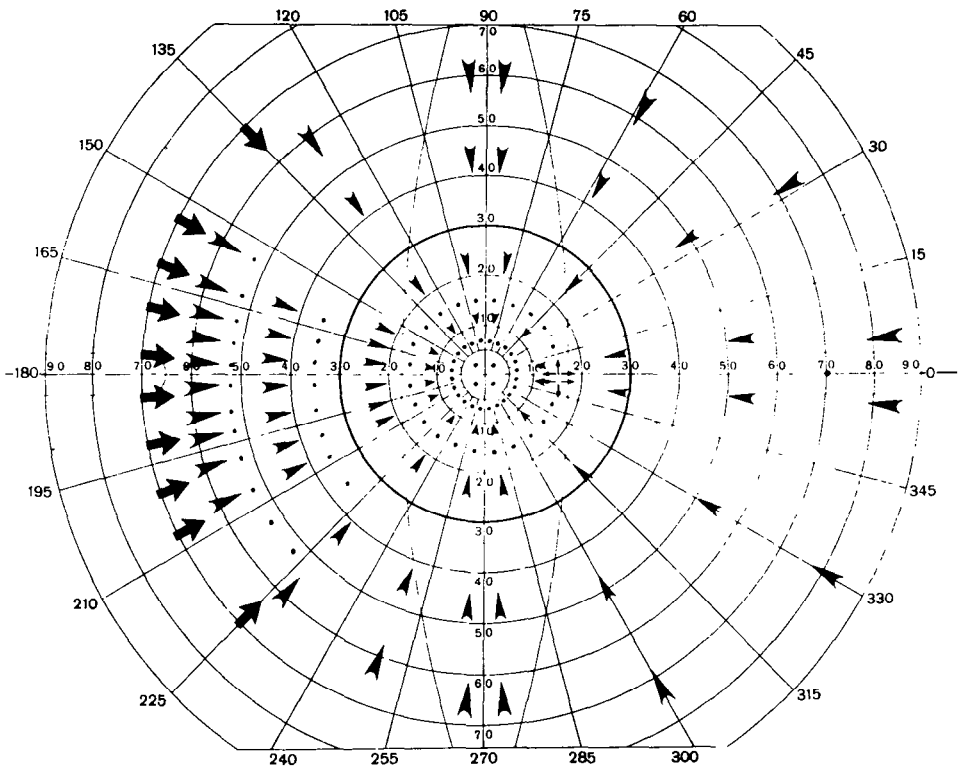

Fig 1 A modification of the Armaly-Drance strategy used for Goldmann perimetry on this study

Subjects were required to indicate the grating orientation for each of a succession of photos of progressively less contrast. If the subject stated that he could not tell the orientation of the grating, he was asked to guess. This was performed one time for each spatial frequency.

Color vision testing was performed under fluorescent room illumination with a color comparison test and the American Optical pseudoisochromatic plates at all visits. The Lanthony desaturated 15 hue test and Farnsworth 15 hue test were used in the recommended fashion to test 52 and 39 of the eyes, respectively. The lighting used was a Verilux lamp which produced an illumination of 400 lux.

The central 10 of the visual field was tested with white and polarized Amsler grid testing in the suggested way[4,5]. Goldmann perimetry was performed on 60 eyes with the strategy shown in Fig. 1. Automated perimetry was performed with the Humphrey Visual Field Analyzer or an Octopus 201 on 40 eyes. A program offset from the meridians thresholding test points in the central 30 of the visual field was used.

The results of the study are shown in Table 2 and Figs. 2 and 3. The most sensitive tests performed (Table 2) were color comparison, perimetry, contrast sensitivity and the Lanthony desaturated 15 hue test. The cumulative rate of detecting abnormalities on afferent visual testing is shown in Table 3. Use of perimetry and a color comparison test had a sensitivity of detecting 79 of the 100 involved eyes. Adding contrast sensitivity increased the yield to 88 and adding the Lanthony desaturated 15 hue test raised the sensitivity to 95 of 100. It did not matter whether the order of adding the Lanthony and contrast testing were reversed, each added approximately an additional 10%.

A comparison of results of contrast sensitivity and perimetry in these eyes shows that 38% of eyes with abnormal contrast sensitivity had a normal visual field examination (Fig. 2). Thirty percent of eyes examined had visual field loss with normal contrast sensitivity testing. A comparison of the Lanthony desaturated 15

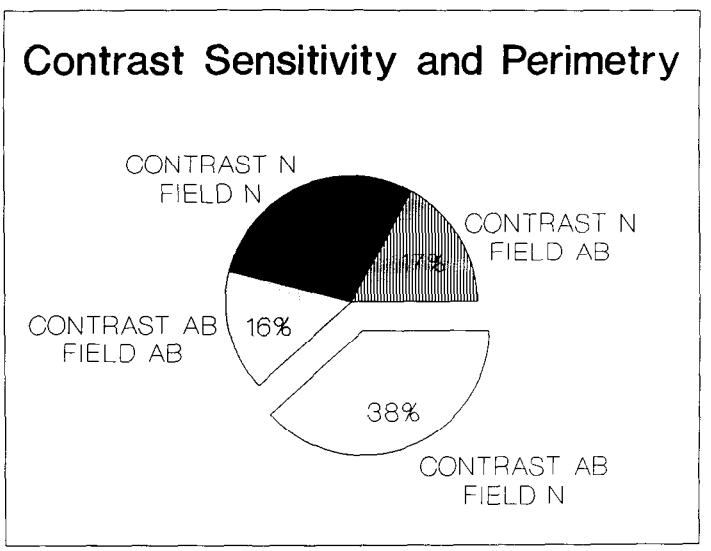

Fig 2. Results of perimetry and contrast sensitivity testing. (N= normal, ABN= abnormal)

Table 2. Results of sensory visual testing

Test	Number tested	% Abnormal
Color comparison test	50/ 74	68%
Automated perimetry	27/ 40	67%
Goldmann perimetry	39/ 60	65%
Contrast sensitivity loss	49/ 76	64%
Lanthony 15 hue test	33/ 52	63%
Polarized Amsler grid	19/ 42	45%
Confrontation visual fields	38/ 93	41%
White Amsler grid	19/ 68	28%
A/O color plate loss	22/100	22%
Farnsworth 15 hue test	8/ 39	20%

hue test and perimetry show 24% with abnormal color with normal perimetry (Fig. 3). Twenty-four percent also had visual field loss with normal Lanthony color testing.

Of the tests of perimetry, automated perimetry was abnormal in 27/40 eyes (67%) and Goldmann perimetry in 39/60 eyes (65%). The polarized Amsler grid test showed abnormalities in 45% and the standard white Amsler grid in 28%. Confrontation fields were abnormal in 41%.

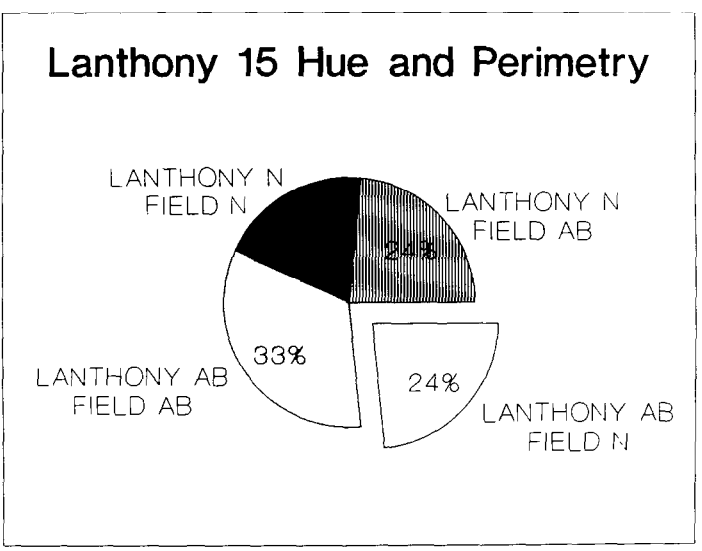

Fig 3 Results of the Lanthony 15 hue desaturated test and perimetry (N = normal, ABN = abnormal)

Table 3 Cumulative sensitivity of defect detection with addition of color and contrast sensitivity testing to perimetry

Test	Cumulative % abnormal
Formal perimetry	66%
Color comparison test	79%
Contrast sensitivity loss	88%
Lanthony 15 hue test	95%

Discussion

Of the subjective sensory visual tests performed, we have found perimetry, contrast sensitivity, Lanthony desaturated 15 hue test and the color comparison test to be the most sensitive in patients with optic neuropathies. Others have reported brightness sense[6], critical flicker fusion[7], Farnsworth Munsell 100 hue test[8], and the visual evoked response[9] to be sensitive tests in patients with optic neuropathies.

In the clinical setting, when a patient with a presumed optic neuropathy has a relative afferent pupillary defect or an ophthalmoscopic abnormality, most clinicians would agree that perimetry and Snellen acuity are usually the only sensory tests needed. The utility of these other tests lies in the detection of visual loss in patients without a clear objective deficit. In this study we have shown that the addition of contrast sensitivity and the Lanthony desaturated 15 hue test to perimetry and a color comparison test each add about a 10% increase in visual defect yield. When coupled with perimetry and a color comparison test, 95 of the 100 examinations of eyes of patients with normal Snellen acuity had at least one demonstrated deficit. In selected patients, addition of these tests may be helpful to increase one's confidence that an optic neuropathy is or is not present.

In addition to defect detection and quantitation, these tests may have utility in following patients with optic neuropathies to determine if change has occurred. We have studied patients with pseudotumor cerebri and have found that contrast sensitivity scores change significantly with change in papilledema grade ($p = 0.002$) while Snellen acuity does not ($p = 0.50$) [10]. These tests may be potentially most useful for patients with optic neuropathies that require intervention, e.g., thyroid ophthalmopathy and pseudotumor cerebri.

Many investigators have reported contrast sensitivity loss in patients with normal Snellen acuity. Kupersmith and colleagues noted that 94% of patients with compressive lesions of the anterior visual pathways had contrast sensitivity loss in patients with normal acuity[11]. In another study, Kupersmith reported contrast sensitivity loss in 78% of eyes of patients with multiple sclerosis and 20/20 vision in eyes that had no associated history of optic neuritis[12]. Beck also noted that 93% of patients had abnormal contrast sensitivity in acute optic neuritis and 78% were abnormal with resolved optic neuritis[13].

The Lanthony desaturated 15 hue test was first studied in 1973[14]. Lanthony reported a detection rate of 88% in patients with known acquired dyschromatopsias. The Farnsworth 15 hue test was abnormal 57% of the time[14]. We have found rates of 63% (Lanthony) and 20% (Farnsworth 15), respectively. The Farnsworth Munsell 100 hue test has been more widely studied in optic neuropathies. The reported yields in optic neuropathies are similar to our Lanthony desaturated 15 hue test results[8,15]. Our preliminary results from an ongoing comparison study are that the 100 hue is a slightly more sensitive test. However, it takes at least four times as

long to administer and score the 100 hue test.

Fleishman and associates have studied patients with resolved optic neuritis[15]. They noted that 26% of eyes of their patients had field loss, compared to 66% of our patients. The difference in the sensitivity of perimetry is probably due to their criteria for abnormality. They used mean loss and did not comment on whether scotomas were detected. Hills and Johnson have shown how mean sensitivity score can be insensitive to the presence of deep scotomas[16]. Our other measures of visual loss (color and contrast sensitivity) are comparable. For example, 72% of patients with resolved optic neuritis had contrast sensitivity loss using the Vistech system compared to our 64%[15].

Burde and Gallin have reported nine patients with resolved optic neuritis all of whom had a depressed field with static visual field examination. Three of the nine had an abnormal Farnsworth Munsell 100 hue test[17].

The question arises as to whether contrast sensitivity and color vision are necessary for neuro-ophthalmologic diagnosis. When we integrate the patient's history with the results of the standard neuro-ophthalmologic examination, we seldom need these tests for diagnosis. On the other hand, no one subjective sensory visual test, including Snellen acuity, is very helpful in isolation. A group of these rapidly performed and sensitive subjective tests should be chosen for the patient who complains of visual loss and has normal Snellen acuity and perimetry. These tests may find greater utility when used by those not highly trained in the diagnosis of optic neuropathies or when used for large scale screening, e.g., examination for drivers' licensing.

A weakness of this study is that we included patients with known optic neuropathies with objective findings. Our test result numbers may not be applicable to the situation where the tests are most needed - when no objective deficit is present. This latter group of patients with optic neuropathies would be an important group to study.

The Vistech contrast sensitivity test and the Lanthony desaturated 15 hue test are sensitive tests in patients with optic neuropathies and normal Snellen acuity and may give useful information in selected patients. We suggest that a series of sensitive visual tests be used in patients in whom there is a question of whether an optic neuropathy is present. In addition, these tests may be useful when a sensitive quantitative marker is needed to follow patients, especially when the results of perimetric examination are normal.

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COLORED TARGETS IN THE ASSESSMENT OF DIFFERENTIAL LIGHT SENSITIVITY

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The Humphrey Field Analyzer offers the opportunity to perform color perimetry, but the manufacturer warns that the results are invalid, because the instrument assumes that the luminances of the colored targets are equal to the luminance of the white target. As a consequence, 'sensitivity losses' for the red, green and blue targets may be due to lower target luminances rather than genuine visual field loss Differential sensitivities of normal observers were measured for all four colored targets at points between fixation and 30 eccentricity. Results showed that, after luminance calibration, the differential sensitivities of the red, green and white targets were equal; however, differential sensitivities of the blue target were slightly higher, thus indicating that the standard observer V_λ function adequately calibrates the green and red targets but not the blue. When corrected for lack of macula pigmentation absorption, the differential sensitivities for all four targets were within ± 2 dB

Introduction

Projection automated perimeters have renewed interest in color perimetry. In an extensive review for the International Perimetric Society, Hedin and Verriest[1] concluded that 'color perimetry demands careful consideration of the test conditions in order to be meaningful'. One of the most basic considerations is equating the luminances of the various colored targets. Failure to properly calibrate has led to severe criticism of color perimetry[2]. Nevertheless, it has been proposed that if colored perimetry is performed properly, it can be a useful diagnostic tool[1,3].

The Humphrey Field Analyzer (HFA), a popular projection automated perimeter, offers the opportunity to perform color perimetry. Unfortunately, the instrument assumes that the luminances of the colored targets and the white target are equal, and the manufacturer *clearly* warns that the results for the colored targets are invalid. The aim of this study was to investigate the relative sensitivities of the luminance-corrected red, green, blue and white targets on the HFA 620 in order to establish calibration factors for the colored targets.

Methods

Differential sensitivities for white, blue, red and green size III targets were determined for 20 subjects using the Macula Threshold program. A second group of 20 subjects was used to investigate the differential sensitivities for the same targets along the 15°-195° meridian from 0° to 30°. In the third part of the study, the effects of spatial summation for the red and white target sizes I through V were determined for ten subjects using the Macula Threshold program.

In all three experiments, the HFA 620's background luminance was 31.5 asb and the subjects were trained, normal observers between the ages of 20 and 30 years. (In order to expand the dynamic range for the red size V target, the red filter had to be placed at the last aperture stop of the projection system.) A portable LEC spectrophotometer was used to measure the luminance and spectral power distribu-

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Table 1 The maximum luminance for each target

Target color	Maximum target luminance (asb)
White	10,000
Red	1,316
Blue	889
Green	457

Table 2 The relationship between the grid position and the Macula Threshold program coordinates of the Humphrey Field Analyzer

Grid position	x,y coordinate	Grid position	x,y coordinate
1	0	10	−1 −3
2	1 1	11	−3 −1
3	1 −1	12	−3 1
4	−1 −1	13	−1 3
5	−1 1	14	3 3
6	1 3	15	3 −3
7	3 1	16	−3 −3
8	3 −1	17	−3 3
9	1 −3		

tion of each of the four targets. The relative sensitivity of each target was referenced to its maximum luminance given in Table 1.

The criterion used to define a difference in sensitivity between any two targets at a given location is that the difference in the means is greater than ±2 dB. This value represents the average standard deviation of the data and is more conservative than most criteria for normality. In displaying the Macula Threshold data, the test point coordinates are specified by grid position numbers. Table 2 lists the coordinates and corresponding grid position numbers.

Results

Figs. 1 and 2 show that, relative to white, the red, green and blue sensitivities appear reduced for both the central 4° and the central 30° prior to luminance calibration. These data are the actual values printed by the perimeter. Figs. 3 and 4 demonstrate that, after luminance calibration, the red, green and white targets have virtually identical sensitivities. However, the sensitivities for the blue target are higher at all points other than fixation. These results indicate that the standard observer $V\lambda$ function adequately calibrates the red and green targets, but not the blue target.

The higher sensitivities for the blue target may result from variations in macula pigmentation within and across individuals, rod interaction, or chromatic adaptation to the yellowish-white background. To test the variations in macula pigmen-

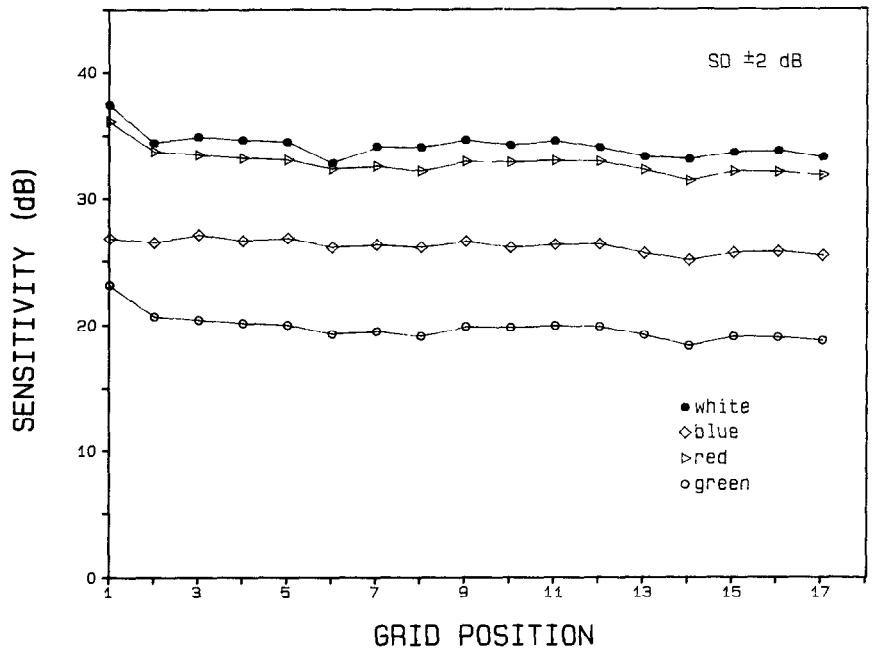

Fig 1. Differential sensitivities for white, blue, red and green size III targets for the Macula Threshold program prior to luminance calibration.

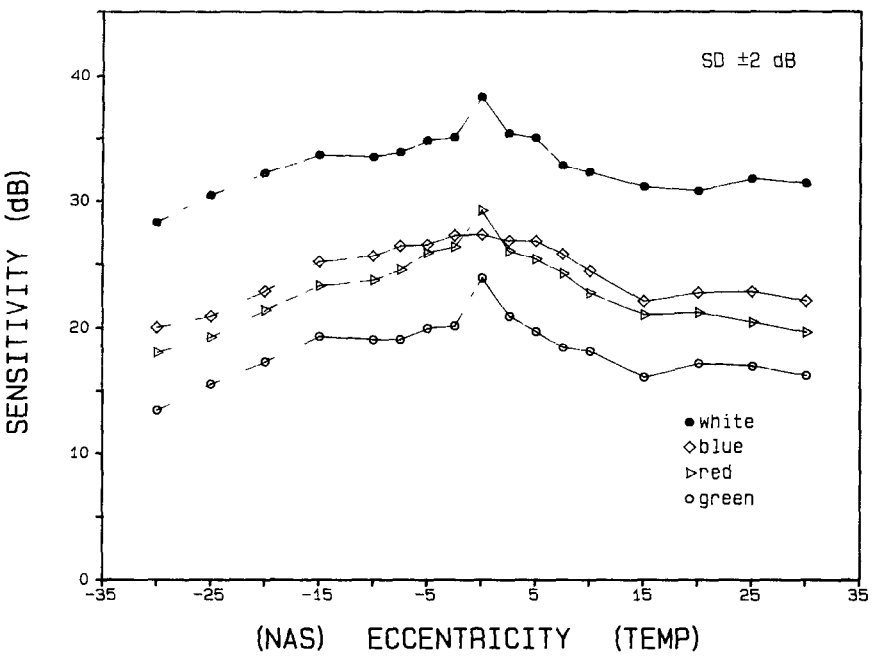

Fig 2. Differential sensitivities for white, blue, red and green size III targets along the 15°–195° meridian, prior to luminance calibration.

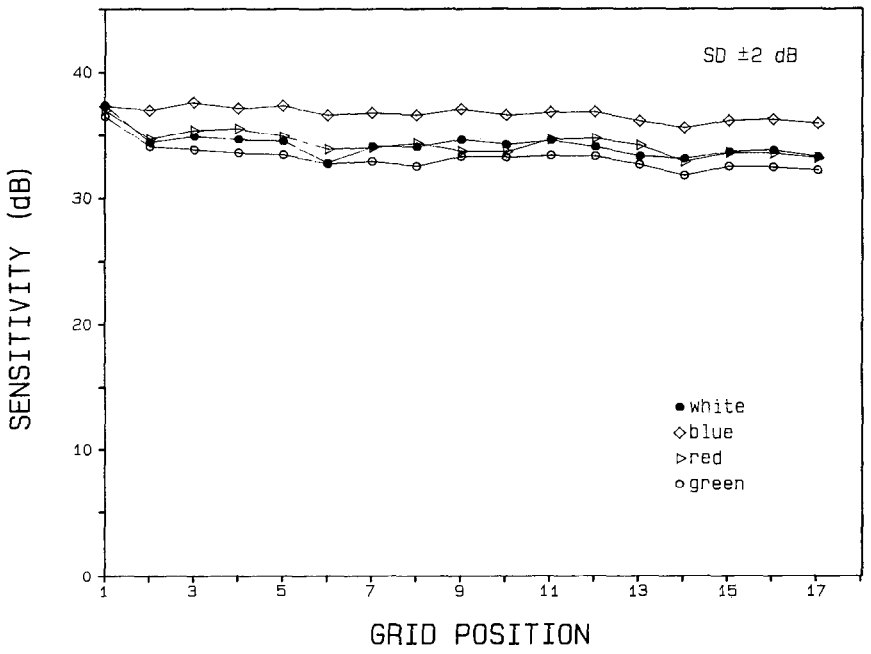

Fig 3 Differential sensitivities for white, blue, red and green size III targets for the Macula Threshold program following calibration for luminance.

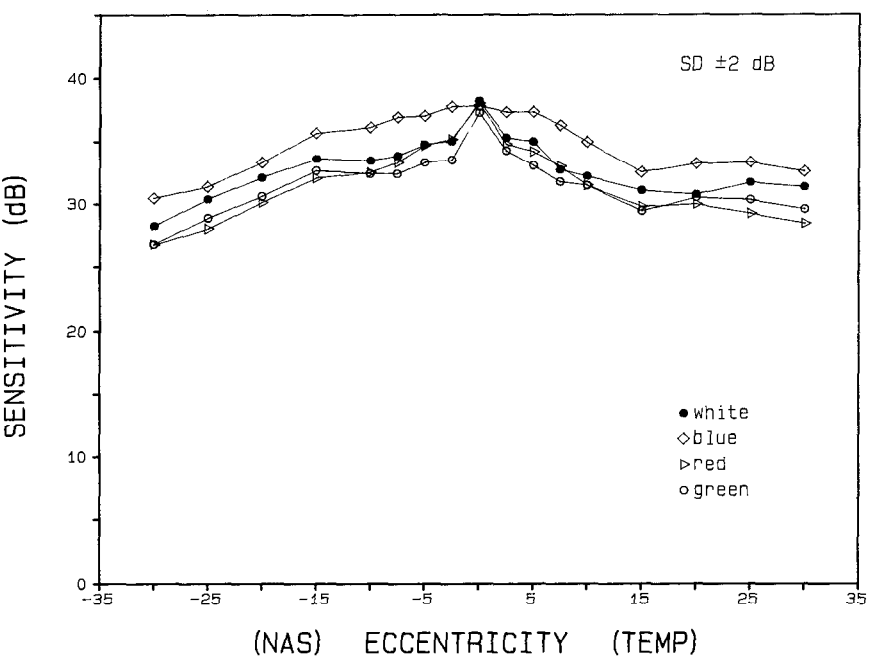

Fig 4 Differential sensitivities for white, blue, red and green size III targets along the 15°–195° meridian, following calibration for luminance.

tation hypothesis, target luminances were adjusted using data from Wyszecki and Stiles[4] to correct for the lack of absorption by the macula pigmentation at all eccentric locations. Figs. 5 and 6 illustrate that this adjustment eliminates any remaining differences in target sensitivities. Although this adjustment eliminates differences in sensitivities between the blue and the other three targets, rod interaction and chromatic adaptation may still occur, but their effects appear to be negligible under the present experimental conditions.

In the third part of this study investigating the effects of spatial summation, the results showed that, although both the red and white targets demonstrated an increase in sensitivity with an increase in target size up to target size IV, the red targets' sensitivities were all lower than the corresponding white targets prior to luminance calibration. Following luminance calibration, spatial summation effects were identical as shown by the representative data in Fig. 7.

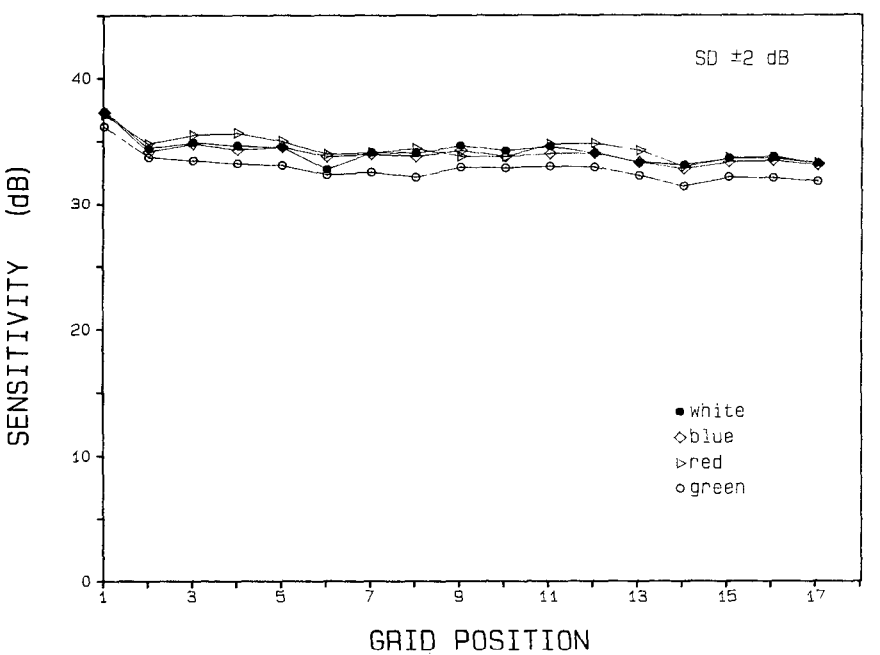

Fig 5 Differential sensitivities for white, blue, red and green size III targets for the Macula Threshold program following re-calibration to correct for the lack of macula pigmentation for all eccentric target locations.

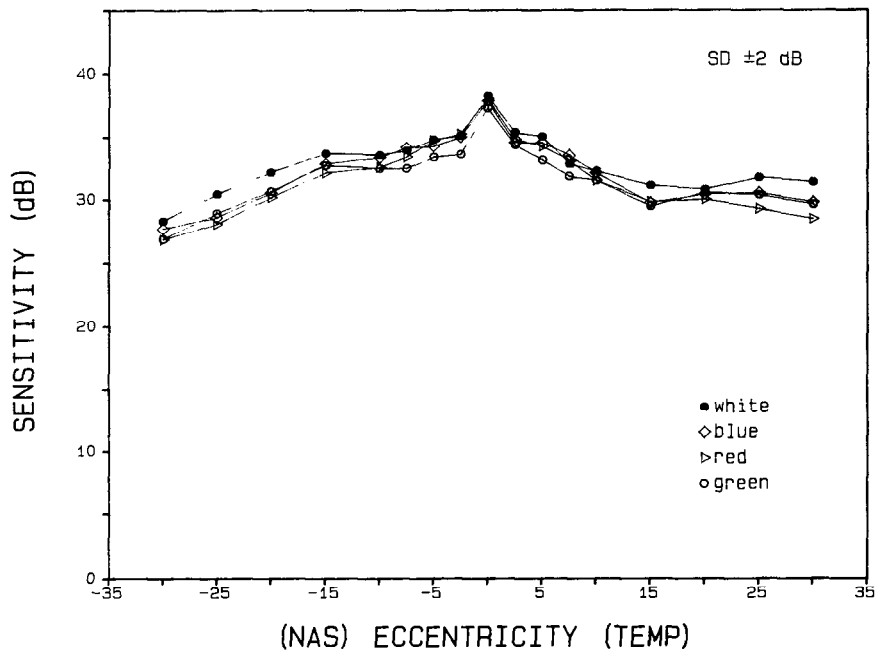

Fig 6 Differential sensitivities for the white, blue, red and green size III targets along the 15°–195° meridian, following re-calibration to correct for the lack of macula pigmentation absorption for all eccentric target locations

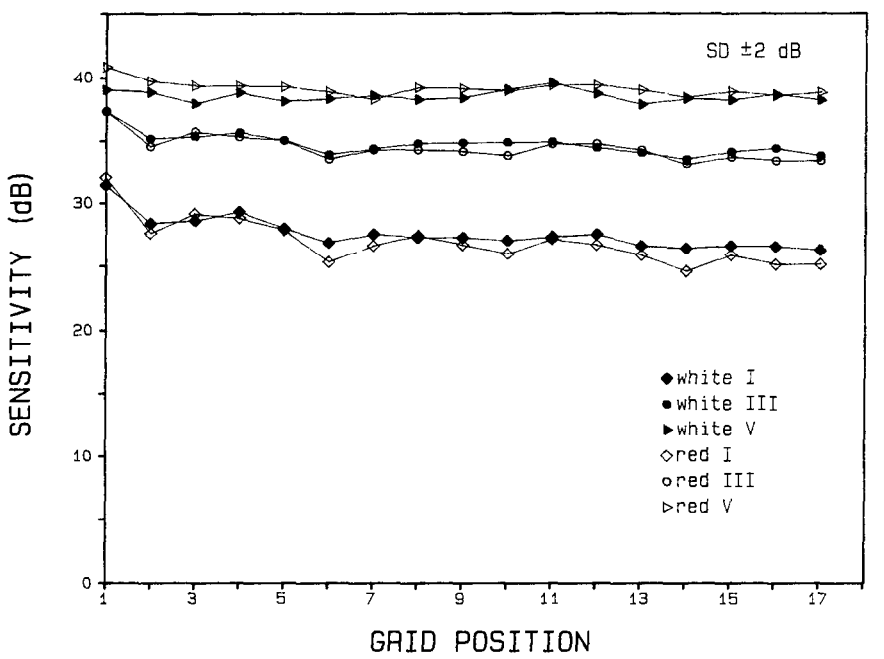

Fig 7 Differential sensitivities for white and red targets I, III and V following calibration for luminance

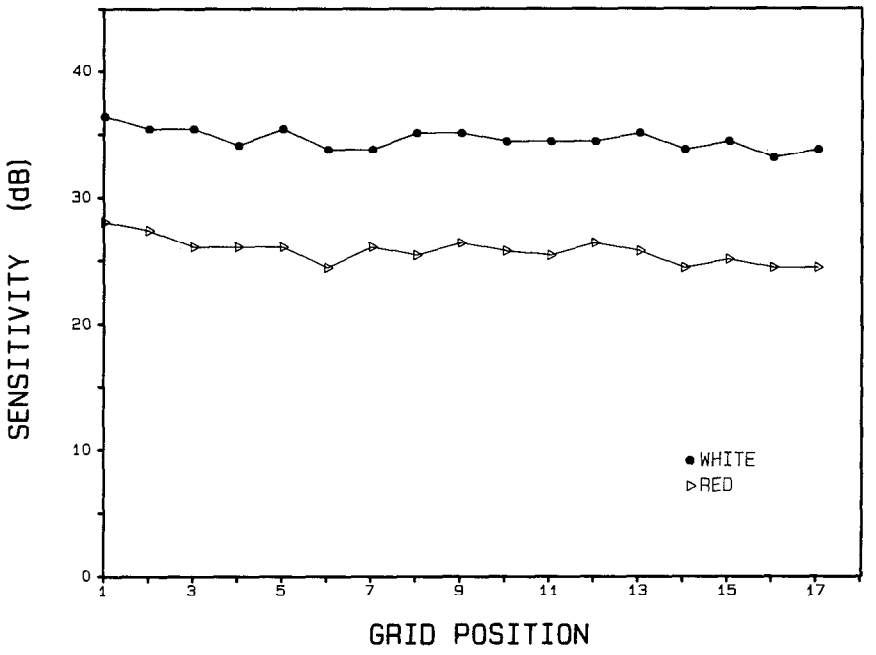

Fig 8 Differential sensitivity for red and white size III targets for the Macula Threshold program of a patient undergoing chloroquine therapy prior to calibration.

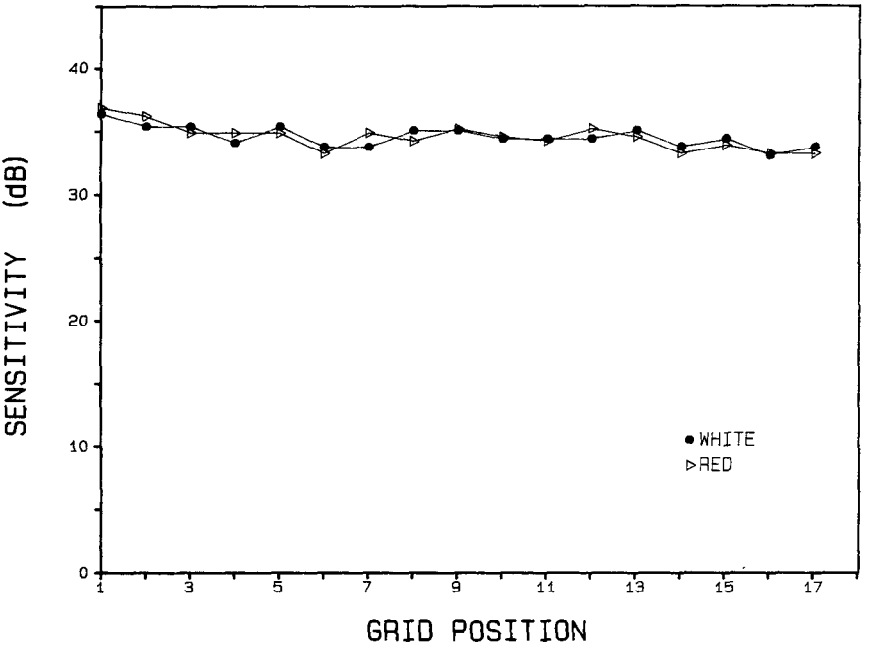

Fig 9 Same as Fig. 8 following luminance calibration

Discussion

Color perimetry performed with the HFA may indicate a selective sensitivity loss that is actually due to the lower luminance of the uncalibrated colored targets. The sensitivities of the red and green targets are identical to the white target for normal subjects once their luminance has been calibrated with the standard $V\lambda$ function. The blue target requires an additional correction for the lack of pigment absorption at all eccentric locations. A consequence of not using calibrated targets is illustrated in the Macula Threshold data of a patient undergoing chloroquine therapy in Figs. 8 and 9. Fig. 8 shows an apparent sensitivity reduction for the red target prior to luminance calibration. Fig. 9 demonstrates that this reduction is a result of the improper calibration, and that, with proper luminance calibration, the macula sensitivities were identical. Conversely, such apparent reductions in sensitivity for uncalibrated targets could mask actual focal colored-field losses.

An important application of proper calibration is that colored target data can be compared with white target normative results. This will enable early detection of genuine selective losses for colored targets.

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NEURO-OPHTHALMIC PERIMETRY

ANOMALOUS KINETIC VISUAL FIELDS IN GILLES DE LA TOURETTE SYNDROME PATIENTS AND FAMILY MEMBERS**

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Anomalous kinetic paracentral visual fields have been found in all individuals tested to date with a confirmed diagnosis of Gilles de la Tourette syndrome (TS), a neuropsychiatric disorder characterized by motor and vocal tics, and behavioral disorders. These pre-chiasmal, generally non-symmetric visual field defects include arcuate anomalies, nasal and temporal steps, enlargement and/or baring of the blind spot About half of these patients show loss in sensitivity with time ('fatigue' effect). None of these individuals manifest glaucoma Automated perimetry is not recommended for this set of complex patients. Extensive parallel studies on families of TS patients show that all fathers and a majority of mothers of probands show comparable characteristic visual field determinations It will be important to determine whether these might serve as a genetic marker for this complex of traits.

Introduction

Gilles de la Tourette syndrome (TS)[1,2] comprises a complex of muscular tics, vocalizations, and certain patterns of behavior, such as obsessive compulsive traits, problems with attentiveness, sleep disorders and dyslexia. This condition generally appears in the latter half of the first decade of life and is generally regarded as a complex inherited condition. In this brief article, we report data on patients having a confirmed diagnosis of Tourette syndrome[3]. Ocular signs such as blinking, eye related facial tics, spastic blinking, eye rubbing, ocular gaze anomalies, etc., are often among the first signs reported by these patients (or by their parents).

In this article, we report summary data on anomalies of the visual field occurring in TS. A more complete discussion reporting our first results has been submitted for publication[4]. Visual field anomalies have not previously been associated with Tourette syndrome. The visual field anomalies reported separately and in this paper have been tested multiply for reliability. In every case, additional trained observers (practitioners, research workers, etc.) commented during examinations. None of the TS patients were diagnosed as manifesting glaucoma. Because TS is a commonly inherited disorder, it is important to evaluate parents, siblings and children of the probands to determine if manifestations of these non-invasive determinations are also present among these individuals. If so, then it is useful to ask if such visual field anomalies serve as a genetic marker.

We have reported separately results on families of probands with diagnosed Tourette syndrome[5] and here we report summary data on families studied to date. These studies are important because, in addition to obvious genetic questions defining the nature of the transmission of the disorder, it would be useful to ask if

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these tests, *i.e.*, kinetic perimetry, can also reveal those who might exhibit Tourette syndrome later in life, and to distinguish those who partially express this condition and/or carry the gene for this condition without an otherwise detectable manifestation. TS is thought to be either an autosomal dominant trait or a complex dominant trait[6-8]. The fathers are said to transmit at a ratio of 4 (3:5): 1 to sons over daughters. The findings we reported previously[5] and here (if in fact they are indicative of a genetic marker) suggest that more than one inheritance pattern may exist and/or that assortative mating may occur. It is difficult to draw definitive conclusions at this stage of the research.

Experimental

All visual fields were obtained using a calibrated Haag-Streit Goldmann perimeter. Complete eye examinations were obtained on all patients. Refrac-tion was corrected carefully to the plane of the cupola.

Tourette syndrome patients are difficult persons to test for several reasons. Many and often lengthy rest periods during testing are necessary and constant monitoring of fixation is crucial. They exhibit associated motor abnormalities (facial, ocular, or trunk). Occasionally, fine nystagmus or accommodative spasming (revealed by pupil contraction) was observed. Their attention may often wander. Also in about half of these individuals there is loss of sensitivity in time which we have termed a 'fatigue' effect.

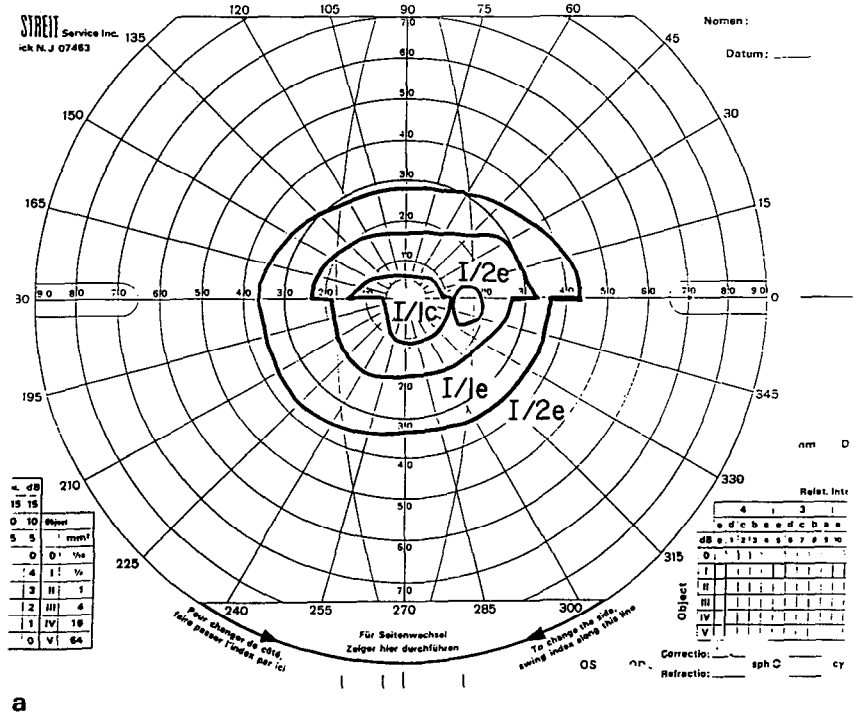
Many TS patients are able to suppress their symptoms for periods of time with surprising effectiveness. When doing so they often experience general and ocular 'fatigue'. The fatigue effects may or may not be like those reported in the literature in patients with optic nerve and central anomalies[9,10]. These effects are not like those seen in studies of glaucoma as reported by Heijl and Drance[11].

Visual field changes reported here occur most commonly in the paracentral visual field and are revealed by using small targets (*e.g.*, Goldmann targets I/2e to I/1b). In every examination the entrance pupil was at least 3 mm in diameter. Multiple data points are obtained if anomalous performance was observed at any test locus. If a step anomaly was noted, the test target was moved in two dimensions, that is, it was moved radially relative to the isopter boundary and perpendicular to the step. Nearby points, away from the horizontal meridian, were tested carefully as well, that is, the approach to the raphe represents a third test of a step.

Automated perimetry is not the proper technique for measuring these visual field anomalies because patient position, attention and fixation are variable and fatigue effects are common. Automated perimetric programs generally utilize essentially uninterrupted random presentation of stimuli. This strategy assumes relatively stable visual response during the test period. Since the onset of disturbing effects of fatigue and the need for rests is unpredictable, random target presentation presents an added complication rather than a control asset in the TS population.

Results

All 24 patients tested to date with a confirmed diagnosis of Tourette syndrome show anomalous kinetic visual fields. As an example, we present data from an arbitrarily selected 15-year-old white male TS patient (Fig. 1). In this patient, the ocular media were essentially clear, the retinas were normal. There were no microhemorrhages, pits, or blurred borders noted on the discs. Intraocular tension measurements were within normal limits. All anterior chamber angles were open. The discs appeared healthy, with normal cup to disc ratio and coloration. Some mild



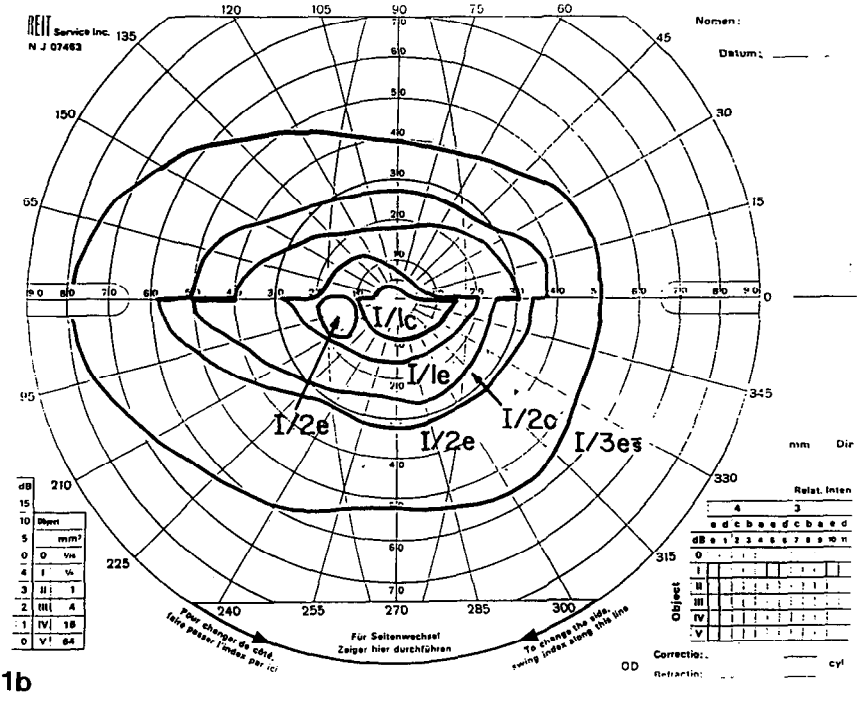
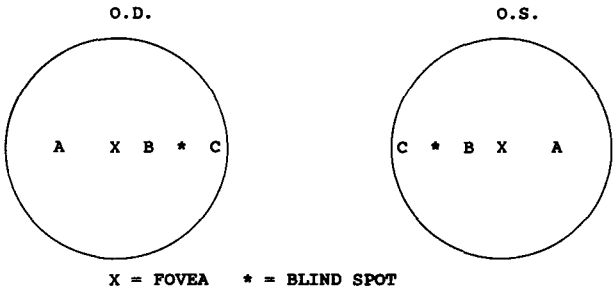


Fig 1 Kinetic visual fields of patient with confirmed diagnosis of Tourette syndrome: (a) right eye, (b) left eye.

Table 1 Summary data on location of visual field anomalies



Total number of patients tested	Number of patients who show visual field steps					
	NASAL STEPS		TEMPORAL STEPS			
	Location A		Location B		Location C	
	OD	OS	OD	OS	OD	OS
24	22	22	15	15	15	16

tortuosity of vessels was seen. His visual acuity was OD: 20/15- and OS: 20/25+. This patient exhibits some of the classic signs of TS: coprolalia and some echolalia. He used to exhibit upper body tics, but at the time of testing had only arm and hand tics. The patients takes 1 mg of clonidine per day, and is on no other medication. It is important to note the presence of both nasal and temporal steps in his visual fields.

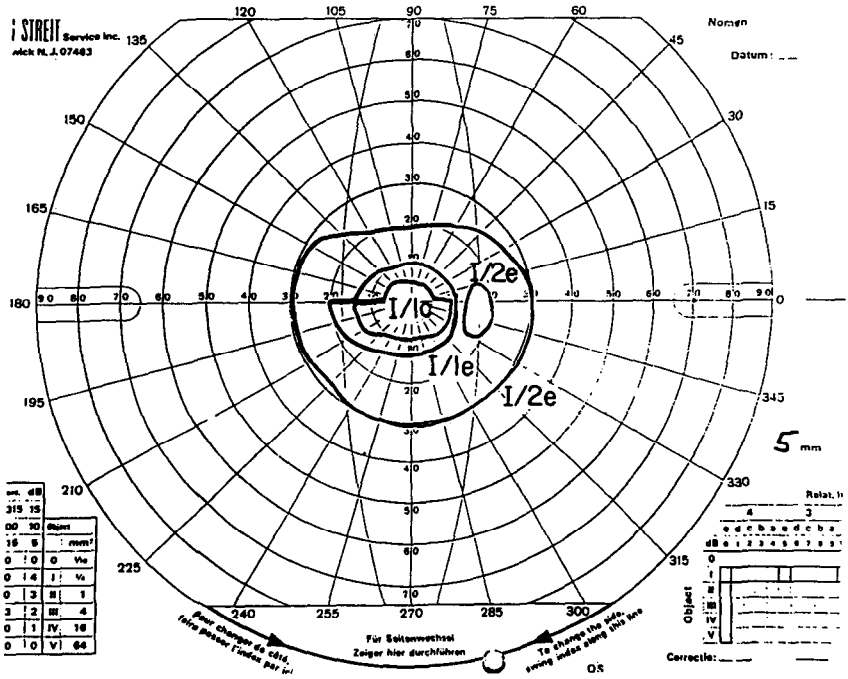
Results summarizing our data on all TS subjects studied to date in this laboratory are presented in Table 1. These kinetic visual field findings are important because they provide additional non-invasive organic evidence for Tourette syndrome. Not only do visual fields need to be assessed but also the transient-like function which has been reported previously at IPS and elsewhere[12,13].

Arcuate, step and blind spot anomalies have been found in all 24 cases tested with a confirmed diagnosis of TS. Steps and step-like anomalies are found in affected field areas both nasal and temporal to the point of fixation and/or the blind spot. Fatigue-like effects were found in 11 out of 24 patients examined. These visual field and fatigue effects are apparently not medication dependent (haloperidol, pimozide, clonidine, etc.).

No TS patient has been diagnosed as glaucomatous by ophthalmological consultants. Field changes are pre-chiasmal nerve fiber bundle anomalies. These steps are unusual and might be an important indicator of the physiological/anatomical mechanisms underlying these defects.

The fatigue effects tend to be either present or not present and are commonly associated with inhibition of TS tic and vocal behavior anomalies, but this is not always true. Fatigue effects are independent of the arcuate, step and blind spot anomalies, although the fatigue may affect and alter specific measurements.

A large percentage of family members of patients with confirmed diagnosis of Tourette syndrome also exhibit visual field defects. As an example, we show the visual fields of the parents of the patient discussed above (Figs. 2 and 3). Both parents have clear media, healthy and normal retinas, and cup to disc ratios are within normal limits. They exhibit normal intraocular pressures, open angles and no glaucomas. The example family tree is shown in Fig. 4. Table 2 provides the summary data from several families which were tested (through early 1988) in this



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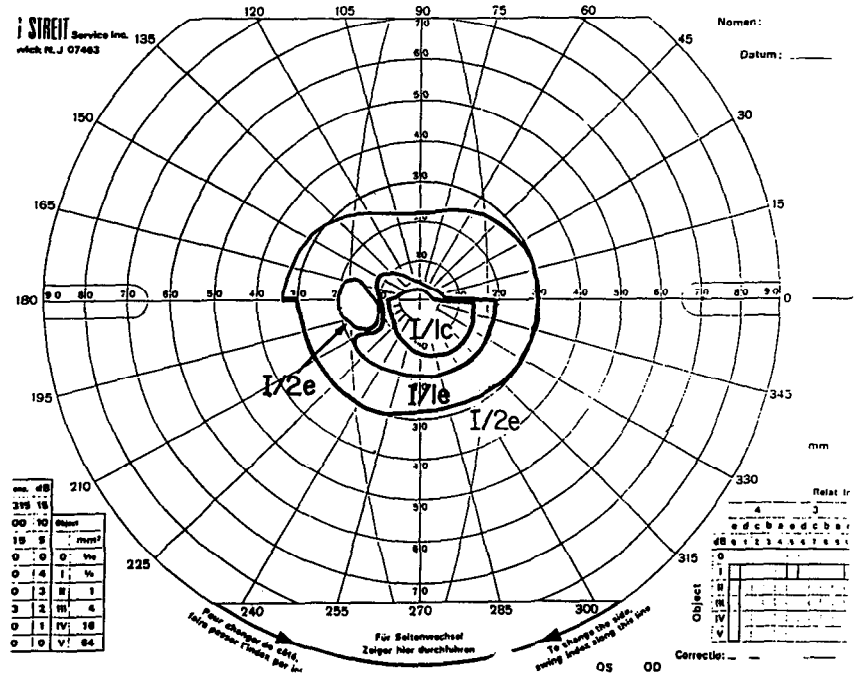
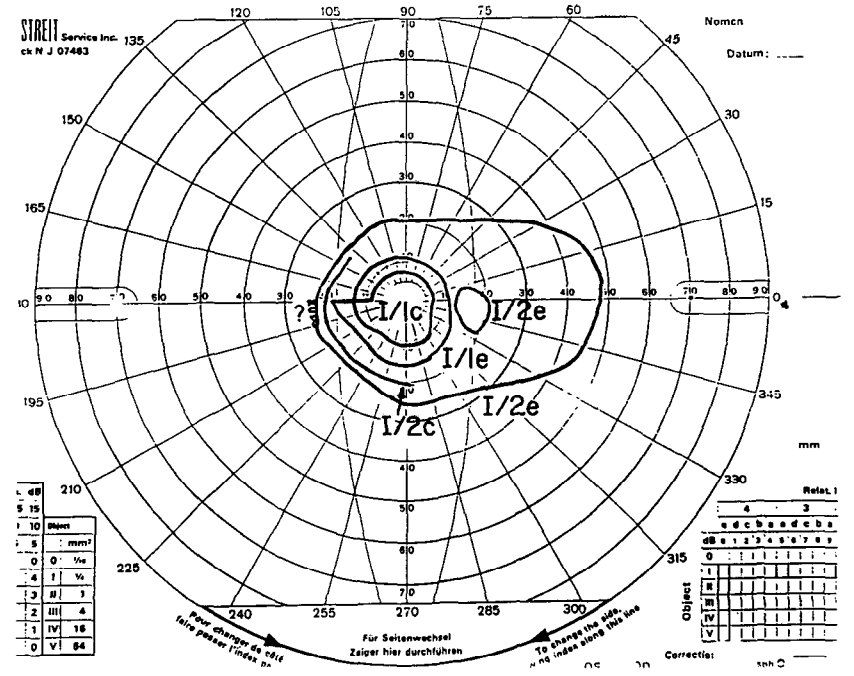


2b

Fig 2 Kinetic visual fields of father of TS patient: (a) right eye, (b) left eye.



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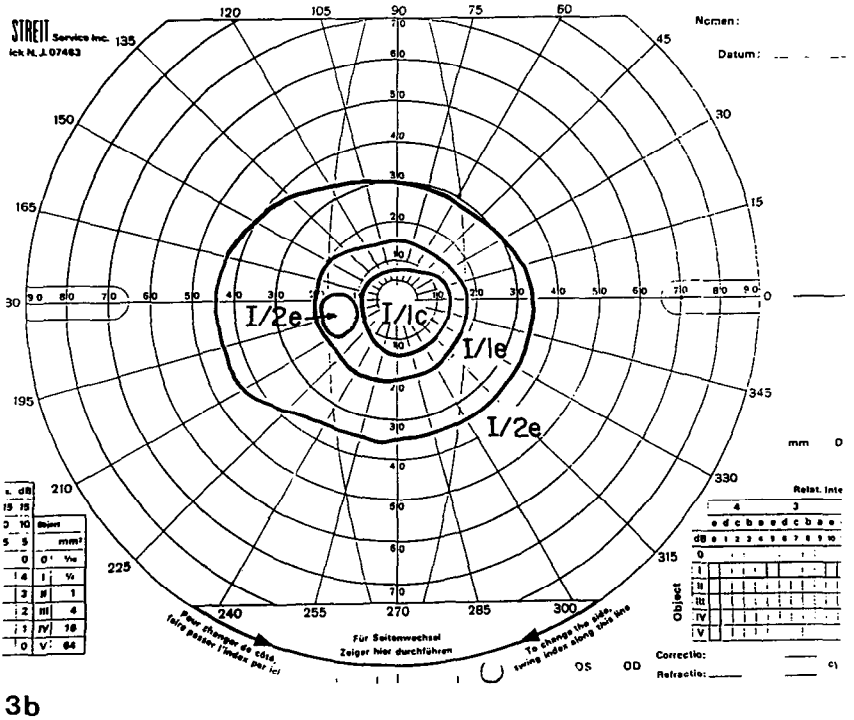

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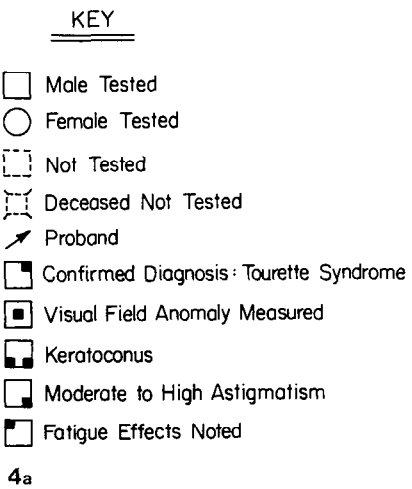
Fig 3 Kinetic visual fields of mother of TS patient: (a) right eye, (b) left eye.

Table 2 Summary data on all families studied to date

	Visual field defects		Fatigue	
TS patients	24/24	100%	11/24	46%
Father	16/16	100%	4/16	25%
Mother	12/15	80%	1/15	7%
Brothers	4/7	57%	1/7	14%
Sisters	5/8	63%	4/8	50%



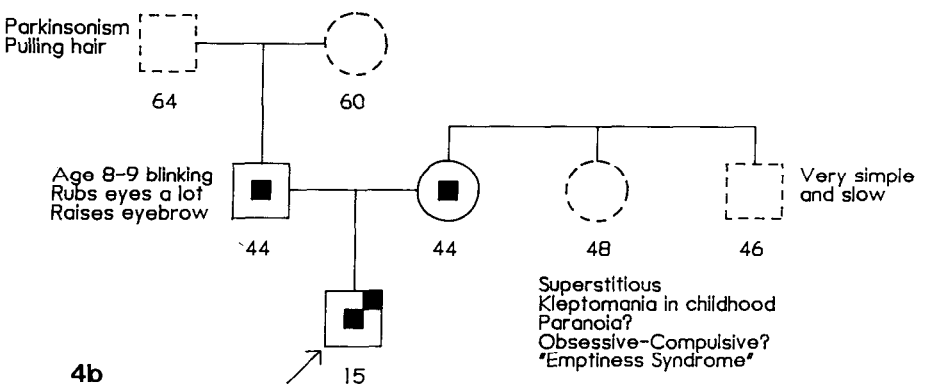


Fig 4 (a) Symbols used in genealogical chart, (b) family genealogical chart

laboratory. It should also be pointed out that several uncles/aunts and grandparents have also been tested, but numbers of individuals are still too limited to provide proper numeric assessment.

In a majority of families studied, both parents show visual field anomalies rather than the father alone. However, in no case examined to date have we recorded a visual field anomaly only in the mother of a Tourette syndrome child.

If the visual field anomalies described are a marker for Tourette syndrome, then the collective data presented suggests that there may be more than one form of genetic transmission of Tourette syndrome and/or assortative mating. It is important to determine if the measured visual field changes may be regarded as a genetic marker for TS. TS probands, their families, and a control population must be studied in far greater depth.

Separately, we are alert to the presence of keratoconus and/or high astigmatism because in our modest size TS population we have found two individuals with keratoconus and two with high astigmatism (greater than two diopters). To date no apparent familial evidence of covariance has emerged. Further work is needed to resolve these complicated questions.

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CONFRONTATION VISUAL FIELD TEST IN COMPARISON WITH AUTOMATED PERIMETRY

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Abstract

The accuracy of confrontation visual field test has previously been compared with Goldmann kinetic perimetry, but to our knowledge no comparison has been made with static automated perimetry, a more sensitive test. This study assessed the accuracy of confrontation test in comparison with static automated perimetry in 412 visual fields. The sensitivity to anterior visual field defects was only 32.3%. With the exclusion of non-specific patchy defects, the sensitivity of detecting anterior visual field defects increased to 42 9%. Arcuate scotomas from compressive optic neuropathy and glaucoma had a very low sensitivity of 22.2%. In contrast, anterior lesions producing altitudinal defects and central scotomas had high sensitivities (100%). The overall sensitivity for detection of posterior visual field defects was 64.9%. The sensitivity was highest for junctional scotomas and homonymous hemianopsias at approximately 75%, but low (40%) for parasellar lesions producing bitemporal hemanopsias. Confrontation test under-estimated the size of the visual field defect in 62% of cases. The overall sensitivity increased to 51.0% when non-specific patchy defects were excluded. The high specificity (92.3%) and positive predictive value (70.7%) obtained with confrontation test indicated that defects identified on confrontation test were often real. Confrontation test is useful, but an understanding of its shortcomings should be remembered.

Introduction

Visual field evaluation by confrontation methods is a useful screening technique for identifying visual field defects[1]. Comparison of confrontation test has been made with Goldmann kinetic perimetry[2]. Automated static perimetry, however, is felt to be a more sensitive test than Goldmann kinetic perimetry, at least within the central 30 degrees[3–8]. As such, we were interested in comparing the accuracy of confrontation technique with automated static perimetry.

Material and methods

The records of 262 consecutive patients seen in 1987, for whom confrontation and automated static perimetry were available, were reviewed. All subjects underwent full threshold visual field examination for the first time with Humphrey automated perimetry (Program 30-1), using a Goldmann size III stimulus. Program 30-1 tests the central 30 degrees of vision utilizing 72 test points spaced six degrees apart. Right eye visual field examination was always performed before the left eye examination. A five to ten minute rest period was provided between each eye examination and as needed. Test results were compared with age-matched normal controls stored on the perimeter's statistical program. The visual field obtained on

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automated perimetry was considered abnormal if three or more clustered points, with greater than 6 dB difference in sensitivity in comparison with the normal controls, were present.

Generalized constriction, arcuate scotomas, central scotomas, paracentral scotomas, and altitudinal visual field loss were classified as anterior visual field defects. Three or more clustered points of depressed sensitivities that did not fit any specific visual field defect pattern were classified as patchy anterior defects. Posterior visual field defects included junctional scotomas, bitemporal hemianopsias, and homonymous hemianopsias. The visual field defects in each eye were considered to be separate visual fields, with the exception of posterior visual field defects (junctional scotomas and hemianopsias) which were considered as single visual field defects.

Monocular confrontation visual field examination was performed by an experienced perimetrist (LNJ), located approximately 66 cm in front of the patient. The examiner held one finger from each of his hands equidistant between himself and the patient, and off axis with respect to the vertical and horizontal meridians. Either one or both fingers were wiggled (oscillation less than 5 degrees) and the patient identified the finger(s) that moved. This provided an assessment of the peripheral visual field. The patient then monocularly looked at the examiner's nose while detailing any facial distortion noted. This latter test was performed at a distance of approximately 30 cm from the patient and promoted the detection of central scotomas, paracentral scotomas and subtle visual field defects. An estimate of the visual field defect size was made by noting the number of quadrants in which a visual field defect was identified. The above confrontation visual field method utilized both kinetic and static techniques.

Patients were excluded from the study if there was significant blepharoptosis or functional visual loss, as these would produce inaccurate assessment of the true visual field. Thirty of the 262 patients were excluded based on this criterion. Additionally, visual fields were excluded from the study if two or more of the following criteria were met on automated perimetry: fixation loss, false-positive or false-negative errors greater than 30%, or short-term fluctuation greater than 3 dB. Fifteen visual fields were excluded based on the above perimetric criteria. Thus, a total of 232 patients (412 visual fields) were selected for the study. Ninety patients were men and 142 patients were women. Their ages ranged from 8 to 90 years (mean 45 years, median 49 years).

The sensitivity, specificity, false-positive error, and positive predictive value were calculated. The sensitivity of confrontation visual field testing was defined as the ratio of visual field defects identified by confrontation test to the defects present on automated perimetry. False-positive errors represented defects noted on confrontation test that were not present on automated perimetry. Specificity was defined as the ratio of normal visual fields on confrontation test to the number of normal visual fields on automated perimetry. The predictive value of a positive confrontation test was defined as the ratio of true positive confrontation visual field to the total positive confrontation test identified.

Results

Of the 412 visual fields entered in the study, 285 had no defects, 90 had anterior visual field defects, and 37 represented posterior visual field defects. Table 1 lists the etiology of the visual field defects present in the study. Optic neuropathy (ischemic or traumatic optic neuropathy, optic neuritis, or optic nerve drusen) comprised the majority (30) of disorders producing anterior visual field defects. In 27 cases, patchy visual field defects were present, but were associated with a

Table 1 The etiology of the visual field defects noted in the study Patchy defects in 13 cases could not be attributed to a specific disease entity

Visual field defect	Orbital disease	Glaucoma	Retinal	Optic neuro-pathy	Stroke	Cranial
Altitudinal	0	0	2	5	0	0
Central/centrocecal	1	1	1	2	0	0
Monocular hemianopsia	0	0	3	0	0	0
Constriction	3	1	5	1	0	0
Paracentral scotoma	2	1	0	0	0	0
Arcuate scotoma	8	7	6	15	0	0
Patchy defects	2	0	5	7	0	0
Junctional scotoma	0	0	0	0	1	3
Homonymous hemianopsi a	0	0	0	0	11	12
Bitemporal hemianopsia	0	0	0	0	0	10
Total	15	10	22	30	12	25

Table 2 Sensitivity of confrontation visual field test in the detection of anterior visual field defects

Defect type	Number (% total)	Sensitivity
Altitudinal	7 (7 8%)	100 0%
Central/centrocecal	5 (5.6%)	100 0%
Monocular hemianopsia	3 (3 3%)	66 7%
Constriction	9 (10 0%)	44 4%
Paracentral scotoma	3 (3 3%)	33 3%
Arcuate scotoma	36 (40 0%)	22 2%
Patch defects	27 (30.0%)	7 4%
Total	90	32.2% [42 9%]*

*Sensitivity in brackets excludes patchy defects

discernible lesion in only 14 (51.9%) cases. Retinal disorders[22], orbital diseases such as dysthyroid orbitopathy or orbital pseudotumor[15], and glaucoma[10], accounted for the remaining anterior visual field defects. The primary causes of posterior visual field defects were strokes[12] and tumors[25].

Tables 2 and 3 provide comprehensive information on the visual field defects encountered during the study. Thirty-six (40.0%) arcuate scotomas and 27 (30.0%) patchy defects comprised the majority of anterior visual field defects. Nine subjects had visual field constriction, seven had altitudinal visual field loss, and five had

Table 3 Sensitivity of confrontation visual field test in the detection of posterior visual field defects

Defect type	Number (% total)	Sensitivity
Junctional scotoma	4 (10.8%)	75.0%
Homonymous hemianopsia	23 (62.2%)	73.9%
Bitemporal hemianopsia	10 (27 0%)	40.0%
Total	37	64.9%

central or centrocecal scotomas. Twenty-three (62.1%) homonymous hemianopsias accounted for the majority of posterior visual field defects. There were ten bitemporal hemianopsias and four junctional scotomas.

The false-positive error for confrontation test was 7.7%, resulting in a specificity of 92.3%. The positive predictive value was 70.7%, indicating that defects identified on confrontation test were most often real. The sensitivity of confrontation test for anterior visual defects was 32.2%, while posterior defects had a sensitivity of 64.9%. Confrontation visual field test was fairly sensitive at detecting anterior defects such as altitudinal field loss (100%), central and centrocecal scotomas (100%), and monocular hemianopsias from retinal degeneration (67%). Confrontation visual field was relatively insensitive at detecting arcuate scotomas (20.0%) and patch defects (8.7%). The sensitivity of detecting anterior visual field defects increased to 42.9% when patchy defects were excluded. Junctional scotomas and homonymous hemianopsias had the highest sensitivities among posterior visual field defects, being 75.0% and 73.9%, respectively. Bitemporal hemianopsias were detected with only 40% sensitivity. The overall sensitivity of confrontation visual field test was 41.7%. When patchy defects were excluded, the overall sensitivity of confrontation test increased to 51.0%.

Confrontation test underestimated the size of the visual field defect in 62% of the cases. The size of the visual field defect identified by confrontation test was equivalent to that of automated perimetry in 30% of cases. In 8% of cases the visual field defect on confrontation test was larger than that identified by automated perimetry.

Discussion

Confrontation visual field test provides a rapid and inexpensive method of detecting visual field defects. Our study indicated that confrontation visual field examination was quite sensitive in detecting posterior visual field defects (64.9%), but less sensitive (33.2%) in detecting anterior visual field defects. This difference may result from anterior lesions producing smaller areas of visual loss, in contrast to posterior lesions which may produce larger and denser scotomas. Although anterior visual field defects as a group were often not identified, certain defects such as altitudinal and central scotomas had high sensitivities. Despite the high sensitivity of detecting homonymous hemianopsia, confrontation test was not always accurate. In one particular case, automated static perimetry identified a homonymous hemianopsia that was not discovered even on repeat confrontation test, despite knowing that a defect was present on automated perimetry. Goldmann

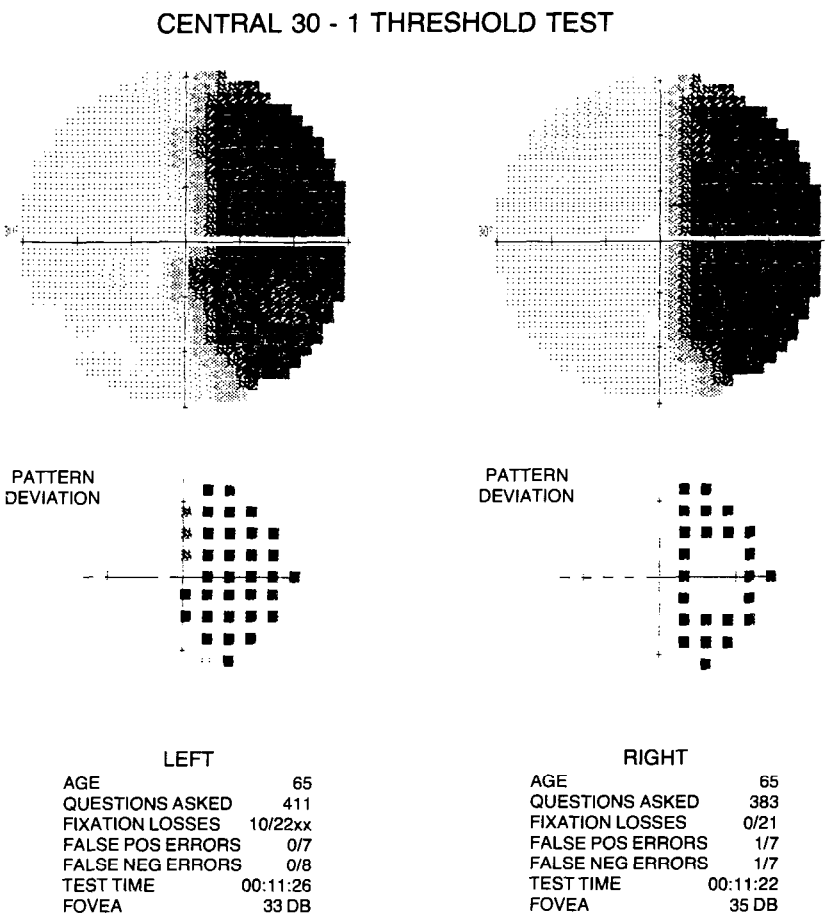

Fig 1a. Static automated perimetry showing right homonymous hemianopsia that was not identified on confrontation test.

kinetic perimetry also failed to detect this hemianopsia until the I4e stimulus was utilized (Fig. 1).

Trobe and colleagues noted that static confrontation test was superior to kinetic confrontation test[2]. The confrontation test used in our study was a combination of static and kinetic techniques. It is difficult to compare our confrontation technique with that of Trobe and colleagues who used Goldmann perimetry as a standard, in addition to the differing techniques. Further studies are required to determine whether our confrontation technique is superior.

The high specificity (92.3%) and positive predictive value (70.7%) of confrontation test combined with the high sensitivity (73.9-100%) of detecting visual field defects such as altitudinal, central, junctional, and homonymous hemianopsias is helpful in the identification of lesions which produce these visual field defects. Thus, lesions such as strokes or tumors producing homonymous hemianopsias, and ischemic optic neuropathy producing altitudinal defects may be easily identified with confrontation test. However, even with experience, confrontation test is not sensitive enough to detect visual field defects such as arcuate scotomas (22.2%)

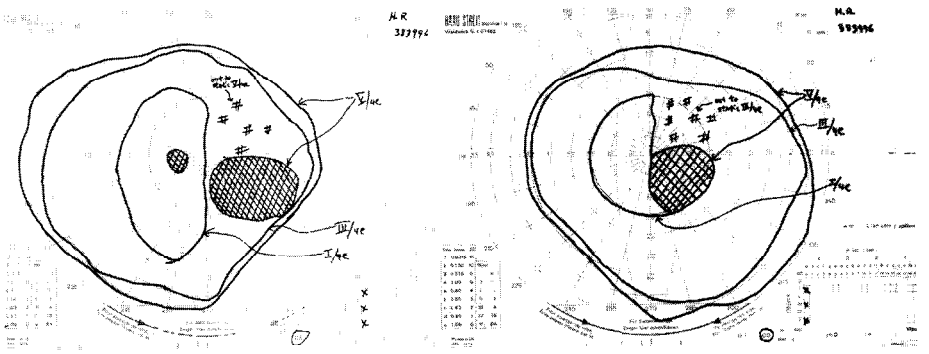

Fig 1b The corresponding Goldmann kinetic perimetry identifying the right homonymous hemianopsia only on the I4e isopter, but not on the V4e or III4e isopters. Static testing using Goldmann perimetry identified the defect with the III4e isopter

and bitemporal hemianopsias (40.0%). Thus, many serious eye diseases such as glaucoma and compressive optic neuropathy, which produce these low sensitivity visual field defects, may often go undiagnosed if one relies on confrontation test. If the examiner suspects the presence of visual loss despite a normal confrontation test, an alternative visual field test should be performed. Additionally, the examiner should always consider additional visual field tests whenever defects are identified on confrontation test, as the size of the defects is often underestimated. In summary, visual field examination by confrontation technique is useful, but an understanding of its shortcomings should be remembered.

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TRAQUAIR'S MONOCULAR HEMIANOPIC JUNCTION SCOTOMA
A sign of compressive optic neuropathy

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Eight patients with monocular hemianopic visual field defects had optic nerve compression close to the anterior chiasm Each defect, whether complete or incomplete, respected the vertical meridian and was associated with either acute or subacute visual loss and an ipsilateral relative afferent pupillary defect Each compressive lesion (three craniopharyngiomas; three meningiomas; one anaplastic suprasellar astrocytoma; one aneurysm) was managed surgically with improvement in vision in seven of the eight patients Visual loss associated with a monocular hemianopic field defect, Traquair's Junction Scotoma, should direct attention to the anterior chiasmal region in a search for a remediable lesion These findings support the hypothesis that the crossed and uncrossed fibers in the posterior optic nerve must separate before reaching the chiasm, indeed before reaching Von Wilbrand's anterior knee

Introduction

Sir Isaac Newton (1704) postulated the existence of a structure allowing a proportion of the afferent visual fibers from each retina to project to the contralateral visual cortex so that each hemisphere may have binocular representation[1]. In lower species all afferent visual fibers in the optic nerve cross to the contralateral side, but with higher species more fibers remain uncrossed and project to the ipsilateral visual cortex. In man, approximately 47% of axons from the retinal ganglion cells remain uncrossed, while 53% cross in the chiasm[2]. Axons from nasal retinal ganglion cells, subserving the superotemporal visual field, are kinked forward in the contralateral optic nerve near its junction with the chiasm. This kink in chiasmal anatomy is said to result from the progressive shift of the fetal eyes toward the frontal plane during development[3]. Wilbrand and Saenger (1906) drew attention to the typical pattern of visual loss caused by damage to the anterior angle of the optic chiasm as a result of this peculiar anatomy[3]; the symptomatic eye has a central scotoma, while the asymptomatic eye has a superotemporal defect respecting the vertical meridian[4] and the pattern is popularly known to clinicians as a *junctional scotoma*. In 1925 Traquair reported a small transient paracentral temporal hemianopic defect in a patient with acute retrobulbar neuritis; he attributed it to a lesion involving the crossed nasal fibers in the terminal optic nerve and called it a junction scotoma[5]. He later suggested this defect was typical of multiple sclerosis[6]. Subsequent reports have described predominantly monocular nasal hemianopic defects caused by internal carotid artery aneurysms[7-15]; many of these reports include patients with either binocular defects or monocular defects which do not respect the vertical. Isolated nasal visual loss may also be caused by a number of ocular disorders such as glaucoma, chronic papilledema, optic nerve ischemia, drusen, optic nerve pits, sectoral retinitis pigmentosa and retinoschisis; however, these defects do not respect the vertical. Others have reported unilateral hemianopic field defects caused by optic neuritis, chiasmal arachnoiditis, migraine, tumors of the sellar region, and functional visual loss[16-19]. In one series of 1000 patients with pituitary adenomas, about 5% of those with visual field loss had monocular superotemporal defects[21].

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Table 1. Clinical findings in eight patients with monocular hemianopic scotomata

Name	*Age*	*Gender*	*Presentation*	*Acuity*	*Visual field*	*OA*	*Rapid*	*Color*	*Other*	*Cause*
1. BB	29	M	HA Blurring OS	20/20; 20/400	Nasal hemianopia	-	+	↓	Felt pop in head	Aneurysm
2. JA	46	F	Blurring OD One week	20/25; 20/20	Temp. hemianopia	-	+	↓	Pain on EOM	Craniopharyngioma
3. RH	21	F	Blurring OS	20/20; 20/25	Sup. temp. quadrantanopia	-	+	-	Mild HA	Craniopharyngioma
4. CC	8	M	Headache	20/20; 20/20	Sup. Temp. quadrantanopia	-	+	-	-	Craniopharyngioma
5. CB	15	F	Thirst, DI	20/30; 20/40	Temp. hemianopia	-	+	-	HA, ET	Suprasellar astrocytoma
6. BB	44	F	Progressive blurring OD	20/70; 20/20	Inf. nasal	+	+	↓	Aneurysm	ONS meningioma
7. LG	61	F	Blurring OS 4 weeks	20/50; 20/100	Temp. hemianopia	+	+	↓	Blepharitis	Pl. S. meningioma
8. EK	32	F	↓ VA OD	20/50; 20/20	Temp.Hemianopia	+	+	↓	Known meningioma	Pl. S. meningioma

OD = right eye; OS = left eye; HA = headache; ET = esotropia; EOM = extraocular movements; ONS = optic nerve sheath; Pl. S. = planum sphenoidale; OA = optic atrophy

Patients and methods

Patients with monocular hemianopic visual field defects, referred to our respective institutions over a period of six years, were included in the study. Patients with monocular defects which did not respect the vertical, or with binocular defects, were excluded. All patients were referred because of visual loss, either as the presenting complaint or associated with other symptoms, most commonly headache. The clinical details are contained in Table 1.

Case report

Patient 2: A 46-year-old woman developed bilateral retro-ocular pain, worse on the right, aggravated by eye movement and blurring with distorted vision in her right eye, as if 'looking at a photographic negative'. Optic neuritis was diagnosed and treatment with corticosteroids was implemented. Two weeks earlier she had had a severe upper respiratory tract infection associated with sinusitis and frontal headache.

Upon referral, her best corrected visual acuity was 20/25 +1 and 20/20 with impaired color vision and a right relevant afferent pupillary defect. Fundoscopic examination was normal. With the exception of impaired ability to appreciate smell on the left side, attributed to sinusitis, neurological examination was normal. Goldmann perimetry demonstrated a small monocular temporal hemianopic defect in the right field (Fig. 1). Magnetic resonance imaging of the head (MRI) demon-

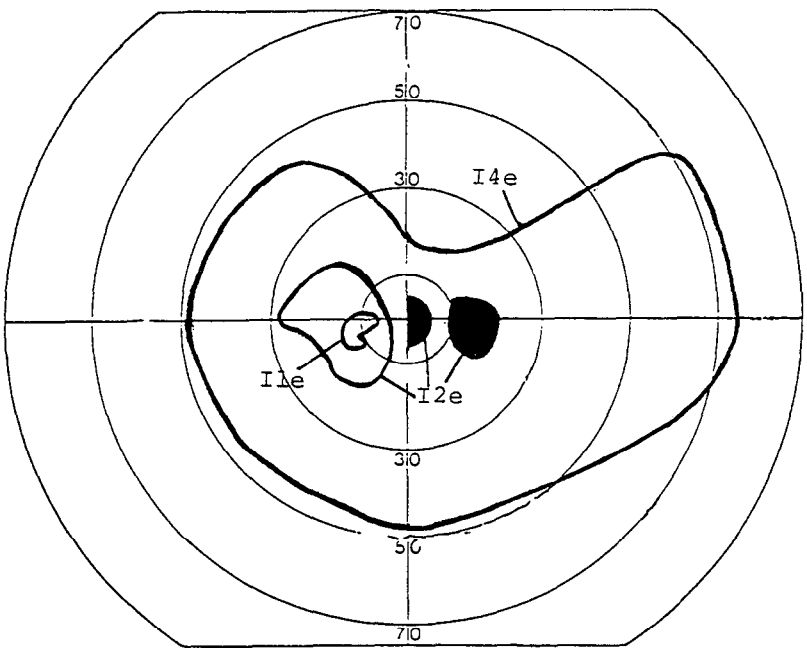

Fig 1 Patient 2: Goldmann perimetry of the right eye showing a small paracentral temporal hemianopic defect. The left visual field was normal.

strated a large suprasellar mass with a high T2 weighted signal suggesting a craniopharyngioma.

The craniopharyngioma was subtotally removed at craniotomy and subsequently irradiated. Postoperatively, acuity and color vision returned to normal despite an incomplete bitemporal hemianopia. One year later her visual fields were almost completely full.

Discussion

All eight patients had monocular hemianopic visual loss caused by compression of the ipsilateral optic nerve near the chiasm. None had multiple sclerosis or other non-compressive disease. In each patient the hemianopic defect respected the vertical meridian, splitting fixation, a finding implicating the crossed or uncrossed fibers before they reach the chiasm.

Hemianopic visual field loss, whether homonymous or bitemporal, is indicative of disease involving the chiasm or retrochiasmal pathways. Chiasmal visual field defects are typically bitemporal but may sometimes be junctional, of the type described by Wilbrand and Saenger[4]. Both types are most frequently caused by compressive lesions. Monocular hemianopic visual field defects, whether complete or incomplete, are less well recognized but equally important because, in our experience, they are also caused by compressive lesions.

Demyelinating disease rarely causes chiasmal syndromes, despite occasional reports[5,6,21], and despite the more frequent pathological finding of chiasmal plaques[22]. Because chiasmal plaques are usually found in the context of widespread disease, it is likely that simultaneous involvement of the optic nerves masks chiasmal syndromes. Furthermore, those patients with isolated demyelinating chiasmal syndromes may have monophasic, parainfectious, disorders[23].

Visual loss associated with a monocular hemianopic field defect *(Traquair's Junction Scotoma)*, particularly if associated with an afferent pupillary defect or disc changes, should lead to a thorough evaluation of the chiasmal region in search of a remediable cause. The very existence of such hemianopic scotomata confirms the hypothesis that the crossed nasal fibers in the posterior optic nerve separate from the uncrossed fibers before the chiasm, indeed before Wilbrand's anterior knee.

Acknowledgements

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THE INVERTED, OR REVERSED, ISOPTER

A sign of functional visual loss

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Eight out of 28 patients with functional visual loss had unusual responses to kinetic visual field testing (Goldmann perimeter) Typically the patients, who each had constricted visual fields, responded to a weak kinetic target moving along a meridian, only after it had crossed the fixation point, sometimes by as much as 5 to 10 degrees; such a response was obtained consistently around the points of the compass, despite good fixation. This phenomenon could not be explained by any known anatomical or physiological defect, any direction specific perceptual deficit (pursuit), slow reaction time, or poor fixation. This phenomenon, The Inverted Isopter, is added to the armamentarium of the clinician faced with the task of documenting positive features of functional visual loss

Introduction

Patients with functional visual loss, a common problem in neuro-ophthalmological practice, may present with reduced visual acuity, visual field defects, or both; less commonly, patients may have pharmacological pupils or motility disturbances[1-6]. Constricted (tunnel/tubular) and spiral visual fields are common findings in these patients, hemianopic and quadrantanopic defects are less common[2], and very occasionally bitemporal or binasal defects are found[1]. One must distinguish between a tunnel pattern of constricted field and a funnel pattern which is invariably organic[1]. Spiral fields may occasionally result from some forms of optic neuropathy, in which case they are attributed to 'visual fatigue'[7]. Functional monocular hemianopic defects may persist even when the patient is 'confronted' binocularly[1]. Other perimetric findings include star shaped fields, and crossed isopters. Inconsistent and variable responses are helpful clues to functional visual field defects.

Patients and methods

After first observing this phenomenon, *The Inverted Isopter*, while checking a 'difficult visual field', I prospectively studied patients with functional visual loss. I have found *Inverted Isopters* in eight patients now with documented functional visual loss, based on the criteria of Kathol *et al.*[7], in a consecutive prospective series of 28 patients. Because a similar phenomenon was detected in a severely depressed patient, those with dementia, severe depression, or other reasons for psychomotor retardation, were excluded. Five patients were male and three were female, ages 19-53 years (mean 28 years).

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Case reports

Patient 1 · A 33-year-old man developed progressive impairment of vision on his left side, after a minor head injury at work. His best corrected visual acuity was 20/30; 20/70 and J1; J5. He could see only the nasal figures with the left eye. He had impaired color vision with the left eye. He was able to discern 40 seconds of arc using the Titmus stereo-acuity test. With the fogging technique, he was coaxed to read 20/20 OU. Confrontation visual fields were constricted on the left, in a tunnel pattern, even when tested binocularly. Pupillary responses and funduscopic examination were normal. Formal visual fields (Goldmann perimetry) initially demonstrated marked constriction to the IV4e and the I4e target. When the examination was repeated by the author, the isopters were increased in size, and the I4e and I3e isopters were crossed. During the visual field examination with the I3e target, the patient responded only after it had crossed the fixation point, by approximately 5 degrees despite good fixation. He continued to give similar responses as each meridian was tested around the points of the compass. After he recovered from the glare of a dilated funduscopic examination, he was coaxed to read 20/25 OU.

An MRI scan of the head, performed before referral, was normal.

Patient 2: A 19-year-old female college student with purpura attributed to an undiagnosed 'qualitative platelet defect' and a family history of lupus, complained of progressive visual loss for three years

Examination demonstrated her best corrected visual acuity to be 20/80 OU, and J 10 OU. Color vision (Ishihara plates) was normal. Pupil responses were brisk, no afferent defect was detected. Stereo-acuity demonstrated the ability to detect 100 seconds of arc. Goldmann perimetry demonstrated enlarged blind spots and bilateral central scotomata. Funduscopic examination was normal. Investigations included magnetic resonance imaging of the head, visual evoked responses, and

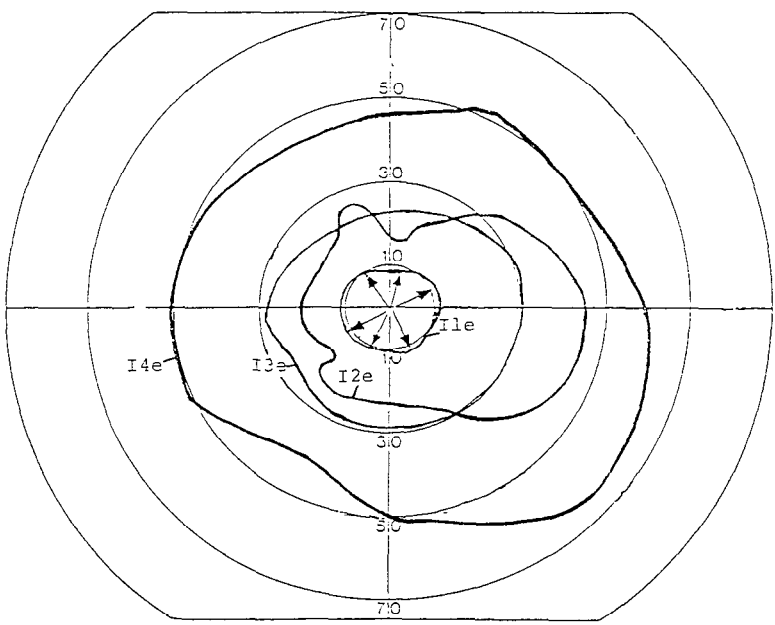

Fig 1 Patient 2: Right visual field showing crossing of the I3e and I2e isopters and 'inversion' of the I1e isopter. The left visual field was similar

serology for collagen vascular disease and syphilis were normal.

A further examination, a couple of months later, demonstrated visual acuity of 20/80 OU; and J6 OU. Repeated visual field testing demonstrated 'inverted isopters' bilaterally (Fig. 1). With coaxing she read 20/30 binocularly.

The 'qualitative platelet defect' and prolonged bleeding time could have been caused by medication such as aspirin. Further evaluation of her social history, in depth, revealed significant stress factors including divorced parents, a difficult step-father and significant peer pressure.

The purpura, like the visual loss, was 'psychogenic' in origin (the Gardner-Diamond syndrome).

Discussion

Eight of the 28 patients with documented functional visual loss studied prospectively, had unusual responses during formal visual field testing.

Typically, during kinetic perimetry, the patient responded to the target only after it had passed fixation by as much as 5-10°, despite alertness, good fixation and normal pursuit direction analysis; this response was repeated when the target was moved in the opposite direction and along the other meridians tested during perimetry. Thus, each patient produced an isopter which was reversed, or turned inside-out; I have termed this *The Inverted Isopter*. One must be sure that the patient is alert, with good reaction time, and normal pursuit eye movements, because psychomotor retardation as a result of dementia, drugs, depression, etc., could mimic this phenomenon. One patient, who was severely depressed, gave responses consistent with the inverted isopter; however, by encouraging alertness and moving the target a little slower, a constricted rather than an inverted isopter was obtained.

While it is possible to diagnose functional visual loss on the basis of anatomic and physiologic knowledge of the visual system, the patient's behavior, the criteria of Kathol *et al.*[4], and common sense, such patients still present a considerable challenge to the clinician, particularly when congenital or previously sustained neurological deficits are present. To this end, the physician must be able to make a positive diagnosis of functional illness rather than just by excluding organic disorders.

The finding of an 'inverted isopter' in patients with functional visual loss is added to the armamentarium of the clinician.

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RESULTS OF MANUAL AND AUTOMATED PERIMETRY IN THE POSTCONCUSSIVE SYNDROME

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Abstract

Forty-four patients with postconcussive syndrome after minor closed head injury were tested using kinetic Goldmann perimetry and using the neurological 20 threshold test and the macular threshold test of the Humphrey Visual Field Analyzer. The same computerized perimetry tests were recorded in 34 normal age-matched subjects Typical functional changes including concentric constriction, inward spiralling, oscillation and enlargement of the blind spot, could be demonstrated in patients' kinetic fields Analysis of the automated neurological 20 threshold test showed significantly higher fluctuation rates, more false negative errors, more fixation losses, and more localized sensitivity losses among patients than among normals The macular threshold test showed only significantly higher fluctuation rates and more localized sensitivity losses. No correlation between abnormalities of the Goldmann field and any of the evaluation parameters of the automated field was found. Manual kinetic and automated static perimetry examine different field disturbances in the postconcussive syndrome.

Introduction

It is well known that blunt head injury is often followed by a complex of mainly subjective or functional symptoms. This persistence of symptoms after cerebral concussion is known as the postconcussive or postconcussional syndrome[1] or 'le syndrome post-commotionnel' in the French literature[2]. The general symptoms are all very vague and include fronto-occipital headache, vertigo, loss of memory, insomnia, irritability and fatigue. Neurovegetative and endocrinological symptoms have been noted as well[2]. The postconcussive syndrome, an ubiquitous and ill-understood condition, has particular relevance to the practicing ophthalmologist because of the unusually high incidence of visual symptomatology. A number of sequelae including asthenopia, decompensation ametropia, heterophoria, accommodation and convergence insufficiency, are of oculomotor origin. Other subjective and objective problems are sensorial. Patients complain of blurred vision and photophobia. With manual perimetry, concentric constriction[3], inward spiralling[4], inversion of the limits[5], oscillation[6], star shaped deformation[7], and enlargement of the blind spot[8,9], are the most typical findings[2].

Several opposing opinions exist regarding the origin of the syndrome; most authors believe that the syndrome has an organic origin[1,10]. Cerebral edema and hemorrhages are frequently found in pathology specimens[2]. Alterations of the electroencephalogram[2], decrease of the tensio arteriae centralis[2] and delayed conduction times of the brainstem evoked responses[11], have been found in the syndrome. The constriction of the visual fields has been ascribed to organic changes

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after contusion, to increased pressure of the cerebrospinal fluid in the vaginal space[3] or to disturbances of the higher visual functions above the calcarine level[12].

Other authors are convinced that the syndrome is merely a functional problem; Miller[13] describes it as a compensation neurosis. An important argument is that the routine physical examination and laboratory testing are invariably normal[1]. Also, some of the ophthalmological signs, *e.g.*, the incongruity of the fields as measured with varying test objects at varying distances suggest a functional origin[14]. Bregeat and Juge and Dubois-Poulsen demonstrated the reversibility of the concentric constriction after injection of Maxiton, an amphetamine[2]. Kluyskens and Titeca[15] demonstrated a discrepancy between the subjects' answers and the objective electro-encephalographic registrations.

We are also convinced that such defects are or can be purely functional, *e.g.*, due to an unconscious narrowing of the 'functional' field of useful perception[4]. As in hysteria, the functional visual field constriction is not conscious as opposed to cases of malingering and aggravation where the visual field is intentionally constricted[7]. Of course there are transitional cases[16,17]. Some other perimetric signs encountered in the postconcussional syndrome, for example inversion of the limits, are found in malingering as well[18].

There is disagreement in the medical community as to the validity of the diagnosis and the credibility of the patient. Neurologists and insurance physicians often ask to be informed about the perimetric symptoms as a part of the objective assessment of the postconcussive syndrome. As manual perimetry tends to be replaced by automated perimetry and since kinetic automated perimetry is not yet readily available, we were interested in comparing the results of the two techniques.

Material and methods

Forty-four patients and 34 normal subjects were included in the study. All patients and normal subjects were examined between January and September 1987. Patients and normals were given a baseline examination, including history, refraction, best corrected acuity at distance and at near, slitlamp and fundus examination.

The patients, 19 men and 25 women, mean age 32.3 years (SD 12.7), were referred for a routine ophthalmological examination by an insurance company physician. On the average, the examination took place 14.5 months (SD 9.3 months) after the injury. The patients presented with a number of symptoms of varied severity. One patient had no complaints at the time of the examination, 32 had varying ocular complaints (blurred vision, asthenopia, photophobia) and the other 11 only had headaches. Four eyes with amblyopia were ruled out, reducing the total to 84 eyes.

The 34 normal volunteers, 12 men and 22 women, were all employees of the hospital and all were inexperienced subjects. Their mean age was 33.1 years (SD 9.3). After ruling out three eyes with amblyopia or incomplete tests, 65 eyes were included.

To minimize the variability, ophthalmological examination and manual perimetry were performed by the same ophthalmologist (GV). It was ensured that all patients were tested under similar conditions.

A standard Goldmann perimeter from Haag-Streit with background luminance of 10 cd/m^2 was used. The right eye was always tested first, the starting point was inferior.

The three tested stimuli were I4e, I2e, and I1e. For each of them, centripetal perception eccentricity was examined along eight meridians distributed about 10 degrees from the four principal meridians (Figs. 1 and 2). We examined the meridians in a counterclockwise order. The starting meridian was tested a second

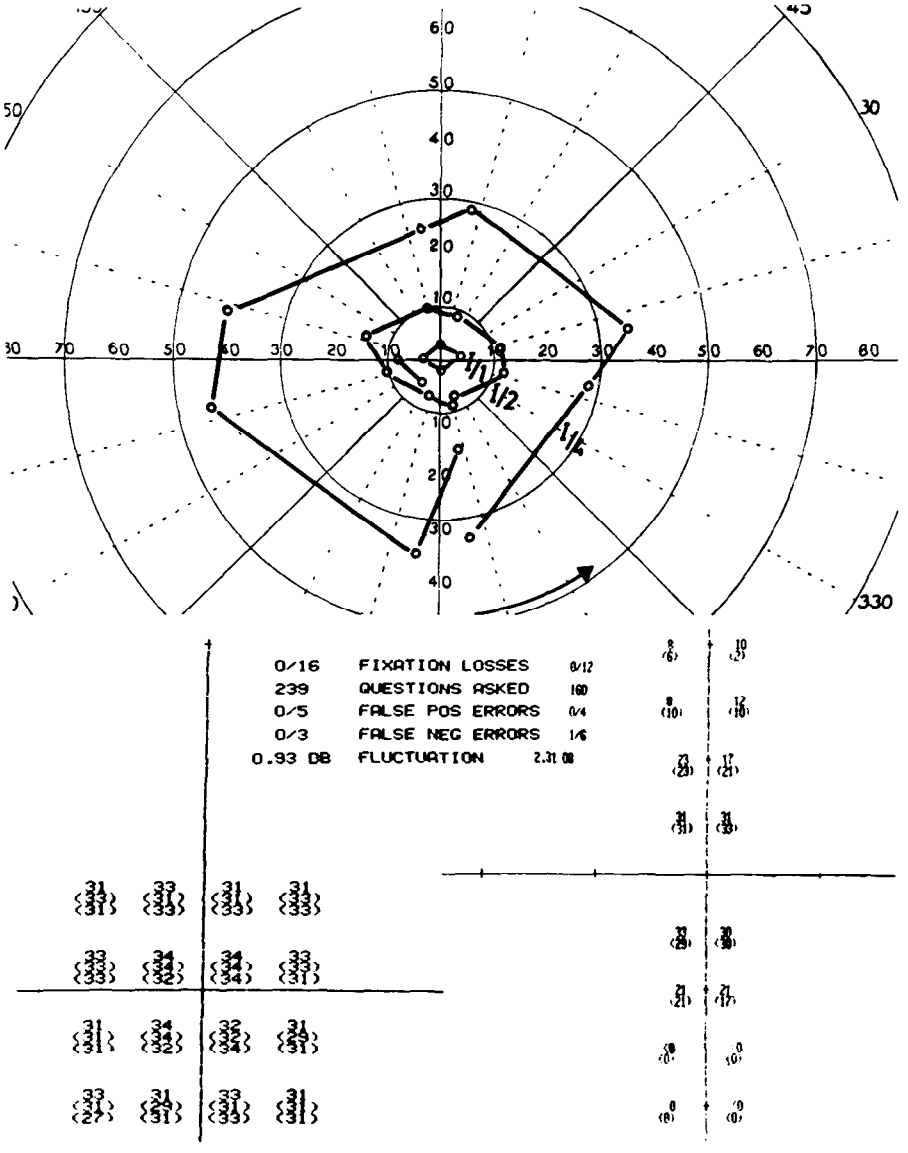

Fig 1 Visual fields of a 24-year-old woman struck in a car accident 14 months prior to the test. Her chief complaint was frontoparietal headache The Goldmann field is constricted and inward spiralling is present. The automated macular test is unremarkable The neurological test has one false negative error and an elevated fluctuation of 2 31 There is a loss of sensitivity in the inferior part.

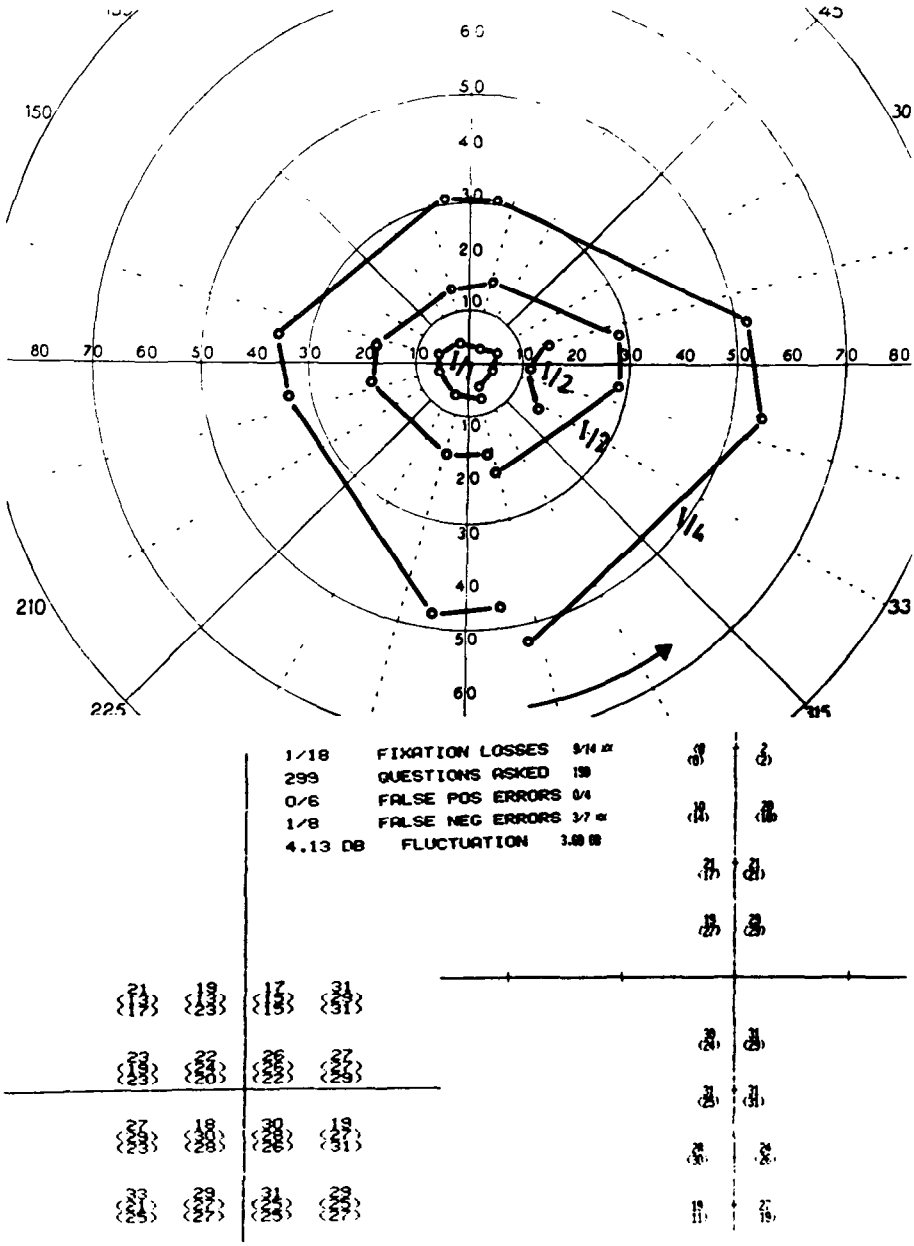

Fig 2 Goldmann and Humphrey field of a 32-year-old man who fell from a ladder 15 months prior to examination. He complained of photophobia. He has spiral fields for isopters I/4 and I/2. The blind spot could not be delineated. The automated field shows a high fluctuation, high false negative errors, high fixation losses and loss of sensitivity in the superior 10 to 20 degrees of the neurological threshold test

time. The results of kinetic perimetry were compared with age related norms established earlier[20]. Special attention was paid to detection of concentric constriction, inward spiralling, oscillating and enlargement of the blind spot. By concentric constriction we mean that the entirety of the answers is beyond the normal eccentricities. An inward spiral is produced when at successive trials the limits become more restricted. The endpoint is now positioned centrally from the starting point (Fig. 1). By oscillation or fluctuation we mean that two points symmetrically placed from the main meridian are on different eccentricities (Fig. 1). The enlargement of the blind spot was compared with normal data[20].

Sometimes the blind spot could only be delineated inward (Fig. 2). We did not look for inversion of the limits although we were well aware that this is a particularly common sign in this syndrome.

Static computerized perimetry was performed next. Both eyes were tested with the macular program and the neurological 20 degree program of the Humphrey perimeter in a random order. Special attention was paid to the number of fixation losses, the number of questions asked, false positive errors, false negative errors, and the fluctuation as indicated on the printout (Figs. 1 and 2). We also looked for sensitivity loss and local field defects on the gray scale.

Analysis

Goldmann

To allow for statistical evaluation, the four characteristics studied on the Goldmann fields of the patients were scored in three levels: normal (=0), slightly abnormal (=1), and very abnormal (=2) (Table 1). These values were analyzed using the chi-square test.

Table 1 Arbitrarily given scores for the different ordinal values

Goldmann	Normal	Slightly abnormal	Very abnormal
Concentric constriction	0	1	2
Oscillation	0	1	2
Spiralling	0	1	2
Enlargement of blind spot	0	1	2
Humphrey fixation losses	0%	<20%	≥20%, <50%	≥50%
	0	1	2	3
	Absent	Present	
False positives	0	1	
False negatives	0	1	
Sensitivity loss	no	slightly	severely
	0	1	2
Fluctuation	below 2 sd	above 2 sd	
	0	1	

Table 2 Frequency (%) of pathological Goldmann characteristics

	0	1	2
Concentric constriction	56%	26%	18%
Oscillation	72%	26%	2%
Spiralling	61%	33%	6%
Enlargement blind spot	67%	33%	0%

Automated perimetry

The Student *t*-test was used to evaluate the two continuous variables: number of questions and fluctuation. Because the distribution of the fluctuation was very skewed, a square root transformation was used to make the distribution of scores more Gaussian.

Scores were obtained for number of fixation losses (four levels), false positive errors (two levels), false negative errors (two levels), sensitivity loss (three levels), and fluctuation (two levels) as indicated in Table 1. For the macular test, the upper limit of normal fluctuation used was 1.92 (p=.05) and for the neurological test the upper limit used was 2.33 (p=.05). These score values were evaluated with the chi-square test. A total score value of the Humphrey field (the sum of the given scores for either the neurological or the macular test) was also analyzed with the chi-square test.

Finally we determined the correlations between all parameters from Goldmann and automated perimetry using the Prelis SSI 1986 statistical analysis package.

Results

Goldmann perimetry

The frequency with which the four elevated parameters, concentric constriction, inward spiralling, oscillation and enlargement of the blind spot were found are listed in Table 2. The mean size of the visual field was not smaller for the second tested (left) eyes. Consequently we treated both eyes the same way in the statistical analysis. We did not encounter localized visual field defects or angioscotomata[2,7].

Table 3 Frequency (%) of pathological Humphrey characteristics

Patients		MAC	NEUR
Fixation loss	≥50%	4 7%	10.8%
False +	≥20%	9.5%	7.2%
False -	≥20%	5.9%	24 %
Sensitivity loss (2)		3.1%	14.1%
Normal controls		**MAC**	**NEUR**
Fixation loss	≥50%	3.1%	4 7%
False +	≥20%	3 1%	9.4%
False -	≥20%	3.1%	0 %
Sensitivity loss (2)		3.1%	14.1%

Humphrey visual field analyzer

The frequency of the relative disturbance of the four parameters studied (fixation losses, false positive errors, false negative errors, and sensitivity loss) is given in Table 3. The patients did worse than the normal controls. Especially for the neurological program, they have more fixation losses (10.8% versus 4.7%) and a higher rate of false negative errors (24% versus 0%).

The total scores tend to be low for normals and high for patients. Again this is especially true for the neurological program where higher values are found for the patients.

Results of the statistical analysis are summarized in Table 4.

Correlations exist between all parameters of the Goldmann examination. The highest correlation between Goldmann parameters was found for constriction and enlargement of the blind spot (r=0.83, df=1, p<.001), but all other parameters were correlated as well.

Correlations between parameters for the Humphrey test were low, for patients as well as for normals. The highest correlation was found between fluctuation and sensitivity loss (r=0.59, df=1, p<.001) for the neurological program and (r=0.65, df=1, p<.001) for the macular program in patients.

Table 4 Significant results

I Goldmann: significant correlations between parameters				
Fluctuation and sensitivity loss		r=0.23	df=1	p<0.05
Fluctuation and spiralling		r=0.56	df=1	p<0.001
Fluctuation and enlargement blind spot		r=0.21	not significant	
Spiralling and sensitivity loss		r=0 69	df=1	p<0 001
Blind spot enlargement and sensitivity loss		r=0.83	df=1	p<0.001
II. Humphrey: differences between patients and normals				
t-test; continuous variables				
Fluctuation	(M)	t=3.61	df=147	p<0.01
	(N)	t=6.23	df=144	p<0.01
Number of questions:		not significant		
Chi square test ordinal variables				
Fixation losses	(N)	chi square = 7.51	df=2	p<0 05
False +		not significant		
False -	(N)	chi square = 16.93	df=1	p<0.001
Field deficit	(M)	chi square = 7.22	df=1	p<0 01
	(N)	chi square = 23 98	df=1	p<0.001
Total score	(M)	chi square = 10.77	df=4	p<0.05
	(N)	chi square = 23.74	df=4	p<0 01
III Correlation between Goldmann and Humphrey				
For total scores		r=0 49 (M)	df=1	p<0.001
		r=0 33 (N)	df=1	p<0.01

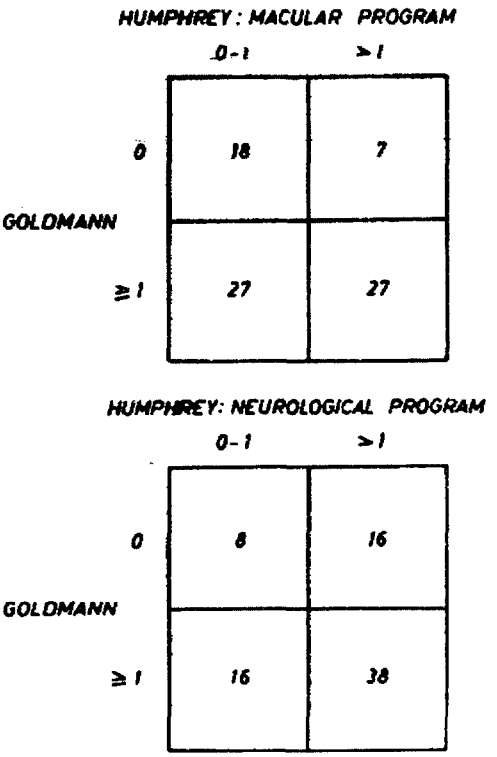

Fig 3 2 x 2 table. 0-1, and 1 above the columns refer to the total score values attributed to the Humphrey fields. The row marks 0 and 1 refer to the score values given to the Goldmann fields.

Significant differences between patients and normals were found for fluctuation, field deficit and total scores for both macular and neurological tests.

The number of questions and number of false positive errors were not significantly different. Significantly different results between patients and normals were found in the number of fixation losses and the false negative errors for the neurological test alone.

Correlations between Goldmann and Humphrey for total scores in patients are low but statistically significant (macular test: r=0.49, df=1, p.<001; and neurological test: r=0.33, df=1, p<.01). The same can be seen in the 2 x 2 table where the existence of pathology on manual perimetry does not necessarily mean disturbance of the automated field (Fig. 3). Of the 24 eyes with a normal kinetic field examination, 16 would have an abnormal neurological threshold test, and of the 24 eyes with a normal neurological threshold test, 16 would show abnormalities on the Goldmann. The Goldmann and macular threshold tests are not correlated (macular test chi-square = 2.54, p>.05). Neither are the Goldmann and neurological tests correlated (chi-square = 0.035, p>.05).

Discussion

We found field disturbances using Goldmann perimetry in patients with postconcussive syndrome. Many patients had concentric constriction, oscillation, inward spiralling and enlargement of the blind spot. Furthermore, all these parameters are well correlated. Our results of kinetic perimetry in the postconcussive syndrome are similar to those reported by others[2,6-8,12,21,22]. We also found that patients with a postconcussive syndrome had field abnormalities when tested with static automated perimetry. In particular the neurological 20 test, a quick test which takes only five minutes per eye, gave some interesting results. Fluctuation, fixation losses, false negative errors, sensitivity loss and arbitrarily given total score values were all statistically different from results of normal subjects.

The fluctuation, fixation losses, false positive and negative errors are all indices of reliability. Smith and Baker[23] tested 15 patients with functional disorders with the Octopus perimeter (program 32) and the Digilab perimeter (C-80 threshold test) and found severe peripheral depression present in 12/15 (80%), false negative errors occurred in 25.4% of the 331 catch trials, false positive errors in 1.9% of the 367 trials, 10.2% fixation errors in fields assessed by the Digilab perimetry. The RMS values used as measures of the short-time fluctuation ranged from 1.2 to 12.

Their study population consisted mainly of malingerers. It is not known whether they included patients with the postconcussive syndrome. They attribute the low percentage of false positive errors to the fact that the patient is trying to convince the examiner of a defect.

They conclude that automated perimetry is not useful in differentiation of organic diseases because none of the reliability tests currently available is capable of characterizing the functional defect. We agree with this, but have to add that the distinction between organic and functional diseases with the Goldmann perimeter is not evident either and depends on the physician's judgment. We feel that automated static perimetry and manual kinetic perimetry provide complementary information.

The field abnormalities found with automated perimetry are certainly not as specific as the classical signs found with Goldmann perimetry and the findings are not correlated. There are signs best detected with Goldmann perimetry (spiral fields, oscillation) and there are signs to be detected with static automated perimetry (fluctuation, false negative errors, sensitivity loss).

However, one advantage is that there are numeric values which can be followed over time. Disregarding the functional or organic origin of the postconcussive syndrome, it has been shown that its sequelae last for years[1] and follow-up is often required.

Another advantage of automated testing is that the examination can be done by a technician while, conversely, the Goldmann examination requires special training and understanding of the special signs and follow-up should be done by the same examiner in this syndrome.

The ophthalmologist who is asked by the neurologist or the insurance company to examine patients with postconcussive syndrome can use automated static perimetry with success. Future automated kinetic programs may yield more success in providing data which are better correlated to the signs found in kinetic manual perimetry.

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SUBCLINICAL CENTRO-CECAL FIELD DEFECTS IN MULTIPLE SCLEROSIS

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Abstract

Centro-cecal light sensitivity of 19 patients with definite or probable multiple sclerosis (MS), but without visual disturbance in 13 cases, was examined by automatic computerized perimetry, using a Humphrey Field Analyzer high-resolution threshold grid custom test. The results were then compared with visual evoked potentials (VEPs) and Farnsworth-Munsell 100 hue test findings

An abnormal centro-cecal mean sensitivity in at least one eye was found in 57.9% of patients. Small non-absolute scotomata could be detected in about three-quarters of tested patients. VEPs showed a higher sensitivity rate in the detection of subclinical damage to the visual pathways, but perimetric defects in the centro-cecal area could also be observed in patients with normal VEPs The Farnsworth-Munsell 100-hue test did not add any further information.

New perimetric programs, specially designed to detect subclinical visual field defects in these patients, could be helpful, together with VEPs, for an early diagnosis of MS

Introduction

The involvement of the anterior visual pathways in multiple sclerosis (MS) is so common that it can be considered essential for the pathological diagnosis of the disease[1]. However, a typical retrobulbar acute optic neuritis can only be observed in about 50% of patients with MS.

Subclinical damage can be detected using various methods, such as visual evoked potentials (VEPs)[2-4], color vision tests[5,6], contrast sensitivity[7-9], evaluation of retinal nerve fiber layer[10,11] and profile static perimetry[12-14]. Computerized automatic perimetry seems to be helpful in several cases as well[15,16].

The aim of this study was to evaluate the frequency of centro-cecal visual field defects in MS patients (no visual disturbance in the majority of cases), using threshold automatic static perimetry. The patients were also examined with VEPs and with the Farnsworth-Munsell 100–hue test. The results were then compared.

Material and methods

Nineteen patients (16 females and 3 males) aged 18-54 years (mean 37.5 ±10) were examined (37 eyes). Fifteen had clinically definite MS and four probable MS, according to the classification of Poser *et al.*[17].

Nine patients had previously suffered from acute optic neuritis, bilateral in two cases. One eye with optic subatrophy was disregarded in this study. At the time of examination, 13 patients (68.4%) were found to be free of visual symptoms. Visual acuity was 20/20 in 35 eyes (94.6%).

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A complete ocular examination, including standard manual or automatic perimetry, was carried out to exclude other possible ocular disorders.

Automatic centro-cecal field examination was performed with the Humphrey Field Analyzer (HFA) Model 620 (Allergan-Humphrey), using a 50-point threshold grid custom test, previously described[18]. Mean sensitivity in this area was calculated for every test. Those results which exceeded previously established limits (mean +2 SD from 50 age-matched controls) were considered to be abnormal.

Disturbed points (all points with a sensitivity at least 5 dB lower than the expected value based on the threshold of the neighboring points) not connected to the blind spot were also recorded. In a previous unpublished study, we examined 53 eyes from 46 normal subjects (age 29-67) with the same centro-cecal test; in this group at least one disturbed point was recorded in three eyes (5.7%).

VEPs were recorded using a black-and-white checkerboard pattern, with a check dimension of 5.2 and 2.6 mm, that subtended a visual angle of 22′ and 11′, respectively. The pattern reversal frequency was 1.6 Hz.

The fixation was central and the pupillary size unaltered. Full-field monocular stimulation was used.

We employed a system bandpass from 2 to 500 Hz, a digital filter from 5 to 40 Hz and an analysis time of 500 ms. For each run, 250 responses were averaged. A standard disk EEG electrode was placed over midline occipital region, 5 cm above the inion, with the reference electrode over midline frontal.

We considered as abnormal the values exceeding 2 5 SD from the mean of an

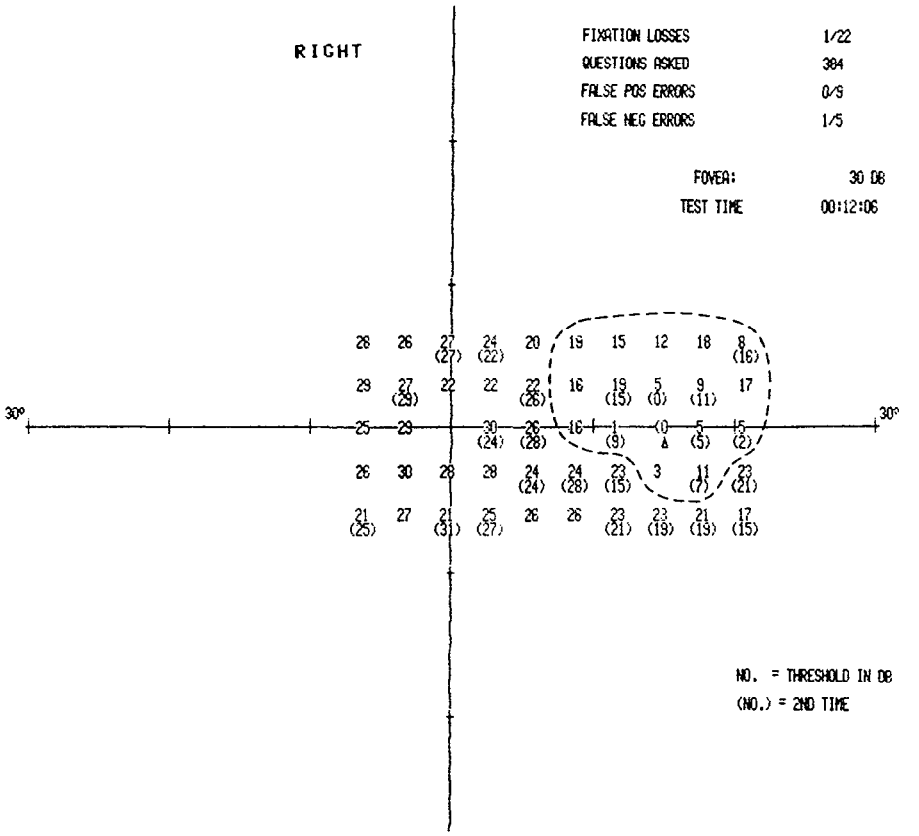

Fig 1 Wide pericecal defect in a patient with definite MS without visual symptoms. VEPs and color vision test were also abnormal.

age-matched control sample of 20 normal subjects ranging between 20 and 50 years.

Color vision testing was performed with the Farnsworth-Munsell 100–hue test.

We considered as abnormal at the 95% level of confidence the cases with a total score above the age-dependent critical values, according to Verriest *et al.*[19].

Results

Centro-cecal mean sensitivity was abnormal in 15 eyes of 11 patients. Six of them had a history of optic neuritis, which was bilateral in two cases. Among patients without visual symptoms, six gave an abnormal result (46.1%).

Among the 15 patients with definite MS, an abnormal centro-cecal mean sensitivity in at least one eye was found in ten cases (66.7%). Within the centro-cecal field, light sensitivity was most depressed around the blind spot(Fig. 1). Disturbed points, corresponding to small scotomata, were observed in 18 eyes of 14 patients (Fig. 2).

VEP latencies were pathological in 23 eyes of 15 patients. An abnormal centro-cecal mean sensitivity was found in 12 of these eyes (52.2%) and in two of the 14 eyes (14.3%) with normal VEPs.

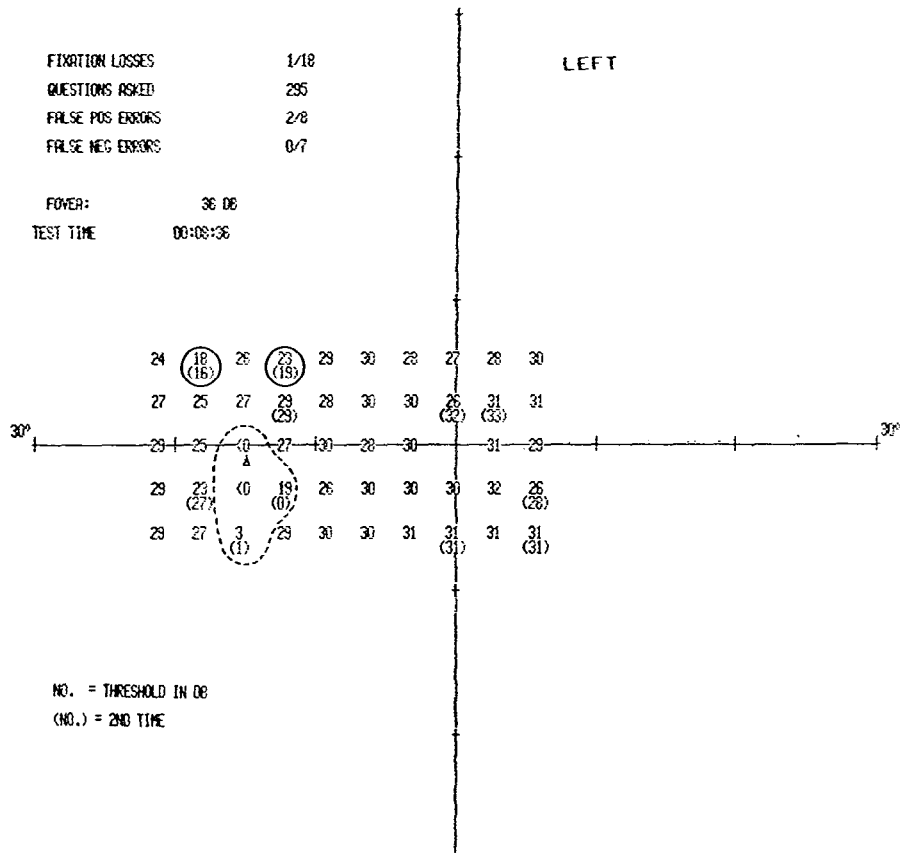

Fig 2 Two disturbed points in a 46-year-old woman with definite MS. The dotted line marks the blind spot limits. Centro-cecal mean sensitivity is within the normal range, as are the VEPs and the Farnsworth-Munsell 100 hue test.

Disturbed points were observed in 14 eyes with abnormal VEPs (60.9%) and in four eyes with normal VEPs (28.6%).

The Farnsworth-Munsell 100–hue test gave abnormal results (defects on red/green axis in particular) in 12 eyes of eight patients. All these patients had defects in the centro-cecal area (depression of mean sensitivity or disturbed points) and abnormal VEP latencies.

Discussion

Subclinical visual field defects can be detected in a high percentage of patients with MS using either manual or automated perimetry. These defects, often subtle and shallow, are usually located in the mid-periphery between 15 and 30° [15,20]. According to Meienberg *et al.*[15], the centro-paracentral area is rarely affected in MS patients without visual disturbance. Little is known as yet about the pericecal area[21].

Using a high-resolution grid, we were able to find a significant sensitivity depression in the centro-cecal area in at least one eye of about 67% of our patients with definite MS. This depression is principally located around the blind spot. Small (one to two points) non-absolute scotomata were observed in about three-quarters of the patients. On the basis of our data, the specificity of this finding seems to be satisfactory (false positive results less than 6%) and leads us to suggest that most of these 'disturbed points' could well be considered as a sign of a genuine visual field defect.

At present VEPs remain the most sensitive method in the detection of subclinical damage in the visual pathways. The presence of centro-cecal field defects in eyes with normal VEPs could be explained remembering that these two techniques probably test different functions.

The Farnsworth-Munsell 100–hue test does not seem to give any further useful information in MS patients.

New perimetric programs, with test points densely distributed in areas more affected in MS (pericecal area and mid-periphery in particular), could increase the still good sensitivity of automatic visual field examination. Together with a VEP recording, which remains fundamental, they could be used for an early and accurate diagnosis of subclinical optic nerve involvement in MS patients.

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AUTOMATED PERIMETRY AND THE VISUAL EVOKED POTENTIALS IN MULTIPLE SCLEROSIS

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In a prospective study of two groups of multiple sclerosis (MS) patients (57 in Vancouver, 78 in Saskatoon) visual evoked potentials (VEP), FM 100-Hue color vision and automated perimetry were performed Retinal nerve fiber layer photography was done in the Vancouver group. Perimetric studies in all patients in the Vancouver group were by Competer and, in 44 patients, also by Octopus (program G1). In the Saskatoon group, all patients were examined by Octopus program 31 The two groups were very similar in age and disease duration, but the Saskatoon group was more disabled by its MS and had a higher incidence of reduced visual acuity A normal Competer 'P' value was determined to be 444 (P 0.05) in 20 normal eyes. Octopus G1 normal parameters were as in the program and Octopus 31 normal mean deviation in 30 normal eyes was found to be 3.2 (P 0 05). In all probable or definite MS patients with a history of optic neuritis, the VEP was abnormal slightly more often than the perimetry: Vancouver VEP = 74%, Competer 'P' = 65%, MD (G1) = 67%; Saskatoon VEP = 88%, Octopus 31 MD = 81%. In definite or probable MS patients with no history of optic neuritis, the VEP was also slightly more sensitive than the perimetry except in the case of MD (G1): Vancouver VEP abnormal in 46%, Competer 'P' in 41%; Saskatoon VEP was abnormal in 52%, Octopus 31 MD in 50%. In general, large or deep scotomata were uncommon The corrected loss variance in the G1 examined eyes is a statistical measure of localized defects and in Vancouver definite and probable eyes, it was abnormal in 39%. Of all eyes with an abnormal VEP, 45% had an abnormal 'P', 52% an abnormal MD (G1) and 73% an abnormal Octopus 31 MD. It is not clear whether the above perimetric abnormalities are the result of demyelination or axonal loss, but they are notably diffuse/multifocal

Introduction

Since the first report of delayed visual evoked potentials (VEP) in optic neuritis in 1972[1], this technique has become the most widely used test of optic nerve function in patients with multiple sclerosis (MS). Although the prolonged VEP latency does not correlate with the severity of the disability in MS, it is sensitive to the presence of demyelinative lesions in the optic nerve, being abnormal in approximately 85% of definite MS, 58% of probable and 37% of possible MS[2]. This sensitivity of the VEP, which changes little in spite of the remitting and exacerbating nature of the disease, makes it an appropriate standard of comparison with other tests of visual function in MS.

Prior to the advent of the VEP technique, the visual fields in MS patients were probably measured more frequently than at present: the methodology being kinetic perimetry or tangent screen. In such a perimetric study of 100 consecutive cases of optic neuritis during the initial attack, Chamlin[3] found only centrocecal defects in 52 cases. Central, paracentral or peripheral field defects occurred in 48 cases and only peripheral defects in four cases. These findings were consistent with the generally accepted principle that acute optic neuritis or MS usually produced

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central or paracentral field defects and that the corresponding maculopapillary bundle was selectively affected by the acute disease. Kinetic perimetry, when compared to flash evoked visual potentials, was found to be less sensitive (97% versus 56%) in detecting previous optic neuritis and also in detecting asymptomatic MS lesions in the visual pathways (56% versus (14%)[4]. In a more recent study of pattern evoked visual potentials and automated perimetry (Octopus programs 33 and 34), the two techniques were found to have equal sensitivity (71%:67%) in MS eyes with no history of optic neuritis. The VEP was somewhat more sensitive than perimetry in MS eyes with a positive history of optic neuritis (86%:67%)[5].

The following report on pattern evoked visual potentials and visual fields as determined by automated perimetry has arisen from a prospective study of the eyes and visual function in two groups of MS patients, the hypothesis being that all eyes in definite MS patients will be abnormal.

Patient selection

Two groups of patients were selected: (1) 57 ambulatory patients from the MS Clinic at the Health Sciences Centre Hospital, Vancouver, half of whom had a positive history of optic neuritis, (2) 106 consecutive patients from the Neurology Service and the MS Clinic of the University Hospital, Saskatoon, Canada. In all patients vision of at least 20/30 in one eye was required. Twenty-eight of the Saskatoon group were excluded because of incorrect diagnosis, incomplete data or congenital color vision deficiency. The remaining 78 patients are the Saskatoon group in this report. Each of the Vancouver and Saskatoon patients was assigned an extended disability status score (EDSS) as a measure of their disease disability[6]. Fifteen Saskatoon subjects with no eye or neurologic disease were similarly studied as controls. The profile of the two patient groups and the Saskatoon controls is outlined in Table 1.

Table 1 Profile of patients, n = 135 & 15 controls

CATEGORY		SEX	+ O.N.	AGE mean	DISEASE DURATION years	EDSS mean
DEFINITE + PROBABLE	Vanc	31F 10M	21	37±11	8±7	2.0±1.5
	Sktn	32F 24M	22	40±12	9±7	3.7±2.2
POSSIBLE	Vanc	12F 4M	6	43±11	4.5±3	1.4±1.8
	Sktn	7F 15M	4	38±10	4±6	1.9±1.9
CONTROLS	Sktn	9F 6M	0	38±14		

Study protocol

Both eyes of all patients and controls were examined as follows:
1. Snellen visual acuity with correction.
2. Direct ophthalmoscopy (SMD, GRD, IAC).
3. Farnsworth-Munsell 100-Hue color vision test[7].
4. Pattern reversal visual evoked potentials: in all subjects these were recorded via a gold cup recording electrode 5 cm above the inion and a reference electrode at FZ. In the Vancouver patients (Saskatoon patients) an alternating checkerboard video screen pattern was used with a field size of 23 (14) degrees, stimulus size 44′ (27′), rate 1.7 (1.9) Hz, analysis time 200 (200) msec - 100 (100) repetitions. Mean luminance 3 inches from the screen was 65.7 candela/m and black-white check contrast was 96%. Mean normal P100 latency = 102±6.0 msec (93±4 msec) with the upper limit of normal = mean latency + 2 SDs = 114 (101) msec.

The remainder of the study differed in Vancouver and Saskatoon patients. The Saskatoon patients had perimetry of their visual fields on an Octopus 2000R using program 31. The mean sensitivities and mean deviations (MD) of the fields were calculated manually. In the 30 Saskatoon control eyes, these were 26.2±1.5 and 0.8±1.2 respectively (Table 2). A mean of over 0.8 + 2 SDs (3.2) was considered abnormal.

The Vancouver patients had their intraocular pressure measured (all were normal: 21 mm Hg or less). Retinal photography with red free light for semi-quantitative assessment of retinal nerve fiber layer defects[8] and stereoscopic optic disc photography for measurement of optic disc and neuroretinal rim areas[9] was carried out and the results are to be published separately[10].

Table 2 Test scores eyes, $n = 270$ & 50 controls

VANCOUVER PATIENTS								SASKATOON PATIENTS			
CATEGORY	"n"	VEP lat. msec	COMP-ETER "P"	OCTOPUS PROGRAM G1 "n"	MS	MD	CLV	"n"	VEP lat. msec	OCTOPUS PROGRAM 31 MS	MD
DEFINITE + PROBABLE	82	124 ±25 (25)*	421 ±95 (37)*	67	25.3 ±3.1	3.2 ±3.1 (44)*	9.6 ±20.2 (26)*	112	117 ±26 (31)*	21.9 ±5.3	5.0 ±5.4 (66)*
POSSIBLE	32	113 ±16 (5)	403 ±102 (16)	22	24.8 ±3.5	3.8 ±3.9 (12)	11.2 ±13.8 (11)	44	101 ±20 (6)	23.5 ±4.6	3.4 ±4.6 (6)
All WITH + OA or + ON	42	130 ±26 (28)	390 ±120 (21)	33	24.8 ±4.0	4.1 ±4.0 (22)	15.1 ±27.1 (17)	56	126 ±28 (39)	20.3 ±6.8	6.9 ±6.7 (43)
CONTROLS	20		524 ±40					30	93 ±4	26.2 ±1.5	0.8 ±1.2

* (n)= number of abnormal scores.

Perimetric examination of the visual fields of the Vancouver patients was done by two techniques:

1. Competer with 64 static light emitting diode test points in the visual field at 5, 10, 15 and 20 degrees of eccentricity11,12. The 'P' value in this test is the sum of the 62 threshold values (the blind spot = 2 points) and stands for performance or 'total ability'. A 'normal' P value will vary from instrument to instrument. Ten control subjects (20 eyes) were examined and had a mean 'P' = 524±40. A minimum normal 'P' was considered to be 524 - 2 SDs = 444.

2. Octopus 201 (Program G1): 45 of the 57 Vancouver MS patients (89 eyes) were examined. Normal values were as outlined in the instrument printout with mean deviation (MD) and corrected loss variance (CLV) being primarily considered as measures of (ab)normality.

Table 3. Percent abnormal scores patients, $n = 135$

CATEGORY		+ OA	VEP	PERIMETRY			
				COMP "P"	OCTOPUS G1		OCT. 31
					MD	MD or CLV	MD
DEFINITE	Vanc n=21	57	67	57	n=16 75	75	
	Sktn n=29	72	79				76
PROBABLE	Vanc n=20	40	70	65	n=17 82	94	
	Sktn n=27	37	59				52
POSSIBLE	Vanc n=16	25	50	62.5	n=11 64	73	
	Sktn n=22	36	32				41

Results

Table 1 outlines the characteristics of the Vancouver and Saskatoon patient groups. The two groups are very similar in age and disease duration but the Saskatoon group is more disabled. An EDSS of 2 is a 'minimal disability' whereas an EDSS of 4.0 means 'fully ambulatory without aid; up and about some 12 hours a day despite relatively severe disability'[6]. Half of the Vancouver patients were chosen to have a positive history of optic neuritis and 47% did so. Thirty-three percent of the Saskatoon group had a history of optic neuritis. Visual acuity was worse than 20/30 in 16% of Saskatoon and 7% of Vancouver eyes.

Table 2 lists the mean test scores for the VEP latencies and the respective automated perimetry fields (Competer 'P' and Program G1 for Vancouver eyes and Program 31 for Saskatoon eyes).

Table 4 Percent abnormality by test results. VEP - Perimetry

CATEGORY	VANCOUVER n=57							SASKATOON n=78		
	n	VEP	COMP. "P"	n	OCTOPUS G1			n	VEP	OCT. 31 MD
					MD	CLV	MD or CLV			
All with + ON	27	78	67	19	84	74	84	26	92	77
All with + OA	24	75	58	19	68	63	79	39	77	79
All with abn. VEP	36		58	26	69	50	73	46		76
All with abn. CVT	24	67	75	16	87	75	94	32	94	84
All with abn. MD	33	58	64	33		73		45	78	
All with abn. CLV	26	50	65	26	92					
All with abn. "P"	35	60		24	87	71	92			
All with abn. RNFL	31	71	61	23	78	65	87			
All with abn. NRR	17	65	76	14	79	64	86			

ON = optic neuritis; OA = optic atrophy; CVT = FM 100-Hue color vision total error score; RNFL = retinal nerve fiber layer; NRR = neuroretinal rim area.

Table 3 outlines the percentage of VEP or perimetry scores which were abnormal in the MS disease categories (definite, probable or possible) of the two patient groups. Competer 'P' is less frequently abnormal than the VEP latency in Vancouver MS patients except in possible MS. The G1 program MD is marginally but consistently more often abnormal than VEP latency in all MS categories. Program 31 MD and the VEP latency are abnormal to a similar degree in the Saskatoon MS categories.

Stepwise discriminant analysis (BMDP) in the Vancouver patients of the VEP latency scores, the Competer 'P' values or Program G1 MD/CLV does not separate the patients in the three disease categories. Similarly, a chi-square test of the null hypothesis that the variables (optic atrophy, positive history of optic neuritis, VEP latency, color vision score, retinal nerve fiber layer abnormalities, and the neuroretinal rim area) are independent of the MD of the Octopus G1 program in Vancouver definite and probable MS eyes proves it to be correct. In Saskatoon definite and probable MS eyes, where the VEP and MD of program 31 were more equally abnormal than in the same Vancouver eyes, chi-square analysis reveals a

Table 5 VEP & perimetric scores vs RNFL defects Vancouver definite & probable MS eyes

	VEP LATENCY msec	PERIMETRY	
		COMPETER "p"	PROGRAM G1 M.D.
10 eyes with diffuse RNFL loss throughout retina	136±35 (70%)	376±116 (50%)	6.1±5.4 (87%)
Definite & Probable MS eyes with no RNFL loss n=51	119±22 (41%)	439±75 (43%)	2.7±2.6 (57%)

(%) percent of scores which are abnormal.

significant correlation between these two variables ($X^2 = 20.4$, $p = 0.001$).

Table 4 lists the percentages of VEP, Competer or Octopus scores which were abnormal in various patient groups each with a specific eye or visual function abnormality. To the extent that retinal nerve fiber layer defects are a semi-quantitative measure of a specific anatomic defect, *i.e.*, the ganglion cell axon, it is worth noting that in the 10 Vancouver MS eyes with diffuse RNFL defects throughout the entire retina, the VEP latency and perimetric findings are consistently more abnormal (but not to a statistically significant degree) than in MS eyes with no RNFL defects (Table 5).

Figs. 1, 2 and 3 are facsimiles of the visual field printouts in the Competer, the central 52% of the Octopus G1 program and the Octopus Program 31, respectively. On each figure is superimposed the percentage of abnormal stimulus points in the four visual field quadrants, in 'central' vision and the percentage of defects which are absolute. In Vancouver definite and probable MS eyes (Figs. 1 and 2), the Competer and Program G1 figures are very similar and indicate that visual field defects are evenly distributed between
'central' vision and mid-periphery and among the four field quadrants. A considerably higher percentage of abnormal stimulus points was found in the Program 31 examination of Saskatoon definite MS eyes, but the distribution is the same, *i.e.*, uniform within the central 60 degrees of vision. In both Vancouver and Saskatoon visual fields, the percentage of stimulus point defects which are 'absolute' is very small, *i.e.*, less than 4%.

Discussion

The results of automated perimetry in our two groups of MS patients indicate that this method of testing reveals abnormalities in visual function with a frequency equal to or slightly better than the VEP. Even with contradictory statistical evidence about the relationship of the VEP and field defects detected by automated perimetry, it seems very likely that these two measures of visual function are not the result of identical pathophysiological processes. It has been widely accepted that a prolonged VEP latency is primarily the result of demyelination within the anterior visual pathway, although other mechanisms such as synaptic delay may

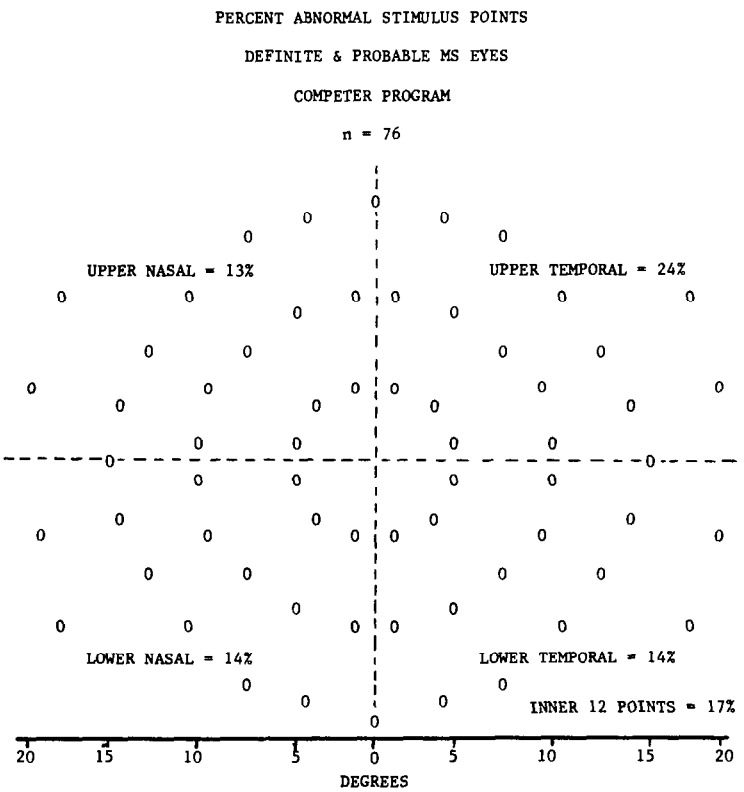

Fig 1 Facsimile of the Competer visual field printout with added quadrantic borders

also play a part[13]. The extent to which demyelination and conduction delay within the optic nerve is the cause of the visual field changes in our MS eyes is not clear.

We have shown in a study of the retinal nerve fiber layer in our Vancouver MS patients that 38% of definite and probable MS eyes have RNFL loss[10]. When detectable, this loss represents at least a 50% loss of the underlying axons[14]. Diffuse RNFL loss was more common than localized loss (32%/12%). A high degree of correlation between RNFL loss and visual field changes in glaucomatous eyes has been documented[15], but no such correlation occurred in the MS eyes we have studied: for example, 57% of 51 definite and probable MS eyes with no RNFL loss have an abnormal MD in program G1.

In peripheral nerve conduction studies as well as in VEP studies it has been generally assumed that temporal dispersion of the VEP and, in some circumstances, a diminished VEP amplitude are characteristic of delayed conduction when axons are also damaged[13,16]. This, too, seems not to be the case in our study. The coefficient of correlation in our definite and probable MS eyes between RNFL loss (local plus diffuse) and VEP amplitude shows no significant correlation ($r = -0.2458$).

This VEP and visual field study at a moment in time in the disease process provides no unique information as to the underlying pathophysiology of MS as it affects the optic nerve. It provides no definite clues as to which of demyelination

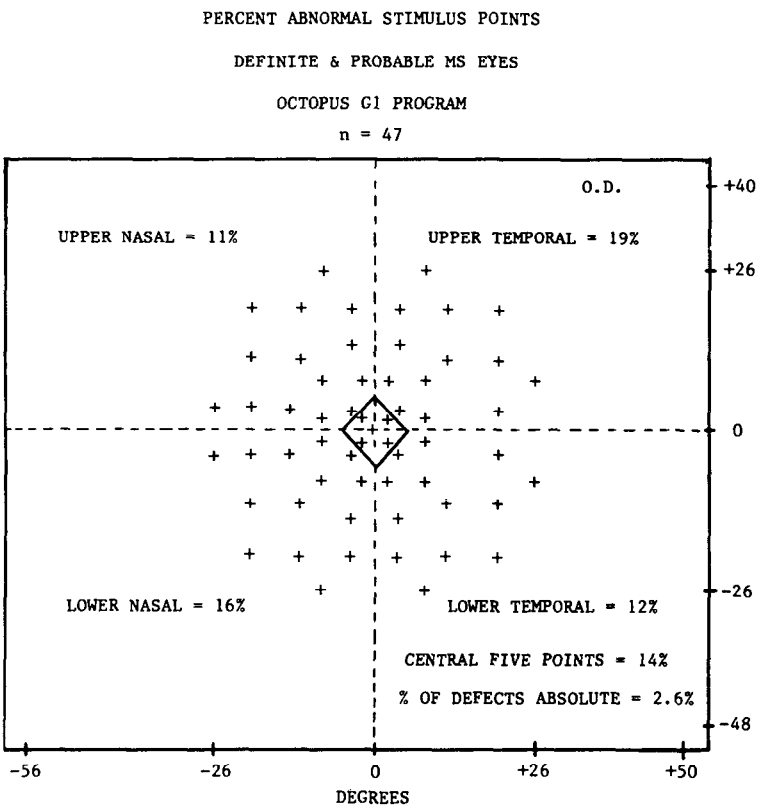

Fig 2 Facsimile of the central 52 degrees of the Octopus G1 program with added quadrantic and 'central' borders.

and/or axonal loss account for the frequent and widespread visual field losses. It does indicate that automated perimetry is at least as sensitive as the VEP to optic nerve dysfunction in MS. It also shows that automated perimetry will significantly detect optic nerve dysfunction in MS eyes where the VEP is normal, *e.g.*, with Competer in 44% of such eyes, with the MD of Program G1 in 46% of eyes and with the MD of Program 31 in 44% of Saskatoon MS eyes with a normal VEP. Our findings also indicate that in established, symptomatically static MS, visual field defects are almost universal in symptomatic eyes, are common in asymptomatic eyes and, in both, are diffuse, multifocal, subtle and evenly distributed throughout central and mid-peripheral vision.

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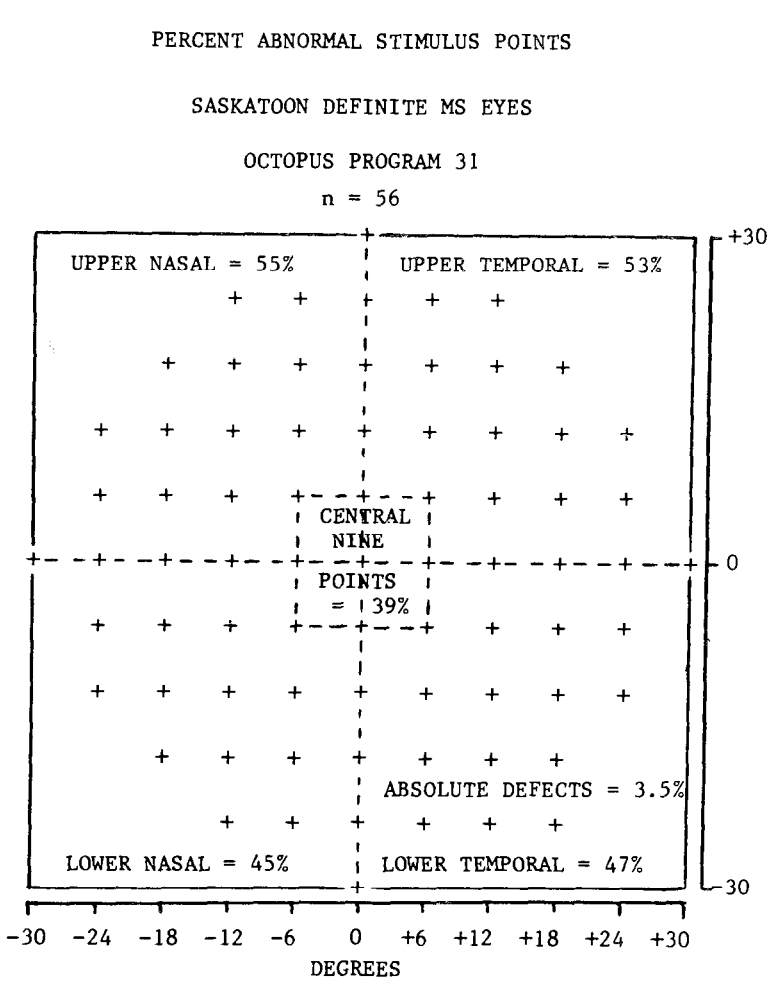

Fig. 3 Facsimile of Octopus Program 31 visual field printout with added quadrantic and 'central' borders.

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VISUAL FIELDS IN PATIENTS WITH PITUITARY TUMORS

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Abstract

Forty patients with a pituitary tumor were examined on the Octopus automated perimeter before, and most of them also after, they underwent surgery. A quantitative program (32) was used which examined the visual field out to 30 degrees of eccentricity. The age corrected mean loss of each quadrant and the whole visual field as well as an overall average were calculated by computer Thirty-four patients had a pituitary tumor with suprasellar extension, compressing the chiasm from below Most of them showed rather symmetric visual field damage which was most pronounced in the upper temporal quadrant, less in the lower temporal quadrant and even less in the nasal upper and lower quadrants. This sequence of damage could be observed in all the patients A statistically significant correlation between age and mean loss could be observed Six patients had no suprasellar extension of the tumor They also showed slight visual field defects, mainly in the temporal upper quadrants, although the sequence could not be seen as clearly as in the other group with suprasellar extension. The reason for this slight visual field damage with purely intrasellar pituitary tumors is not clear All patients were operated on using a trans-sphenoidal approach. Their visual fields were re-examined one week after the operation ($n = 22$), and if still abnormal, again after three months ($n = 13$). Recovery one week after the operation was most pronounced in the center In the two temporal quadrants, it was less Three months after the operation, the largest recovery was observed in the temporal lower quadrant, less in the temporal upper and even less in the nasal lower quadrant The nasal upper quadrant exhibited only minimal recovery, although still statistically significant Seven patients had a visual field examination one year postoperatively They showed no further recovery Patients without suprasellar extension of the tumor showed no statistically significant recovery. There was no correlation between recovery and age. The data show that nerve fibers affected last by compression recover most and first. The recovery takes place within three months of the operation. Later on, there is no further recovery. The better recovery of the central part of the visual field might be due to less convergence of retinal neurons in the center as compared with those in the periphery

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OBJECTIVE AND SUBJECTIVE ASSESSMENT OF THE VISUAL FIELD IN COMPRESSIVE LESIONS OF THE CHIASM

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Objective and subjective visual field assessment was performed on nine patients with well documented compressive lesions of the chiasm. An attempt was made to correlate the extent of the visual field loss with the diagnostic capabilities of topographically recorded Visual Evoked Potentials (VEPs) Full and half field stimulus presentations were compared for a variety of field and check sizes Differential light thresholds were measured using projection automated perimetry and quantified according to Drasdo's graticule for the neural representation of visual space Results showed a strong correlation between the degree of information loss and the diagnostic value of the VEP The objective assessment was, however, capable of detecting abnormality in the absence of recordable subjective field loss when large field and check sizes were used

Introduction

Objective assessment of the visual field using electrodiagnostic techniques has always proven somewhat controversial in the literature. There have been claims that multi-channel, pattern reversal, transient Visual Evoked Potentials (VEPs) are capable of detecting early compressive lesions of the chiasm in the absence of demonstrable visual field loss[1-4]. Contradictory findings have also been reported claiming that VEPs were not clinically reliable even when a bitemporal hemianopsia was clearly recordable[5].

In an attempt to correlate the perimetric and electrodiagnostic data, the visual field was quantified according to Drasdo's graticule[6]. Ten Doesschate[7] first proposed the idea of a chart for visual field quantification which he based on integrated visual acuity. Crick[8] suggested a projection based on cortical area. Drasdo and Peaston[6] based their chart on the visual system's information channel capacity calculated from the cortical magnification equations of Drasdo[9]. The visual field was divided into areas of equal weighting for neural representation, superimposed on a conventional perimetric projection.

The visual field may thus be quantified by calculating the defect depth at each point in the field representing 1% of the total information channel capacity. This can be demonstrated graphically as a Depression Profile, in which the spatial coordinates are scanned spirally from fixation to 30° eccentricity, and numerically as the integral of the area under the curve expressed as a percentage of the total information channel capacity (% Information Loss)[10].

The aims of this study were firstly to establish whether there was a correlation between the degree of Information Loss, measured subjectively, and the diagnostic value of the VEP, a largely objective measurement. Secondly, to establish whether the VEP was capable of detecting early compressive lesions of the chiasm before perimetric results were noticeably affected. Finally, to determine the optimal stimulus parameters for the detection of compressive chiasmal lesions.

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Method

The sample consisted of eight subjects with diagnosed pituitary adenoma and one with a meningioma which had compressed the chiasm. VEPs were recorded using the Nicolet Pathfinder II and a seven electrode transverse montage (T_5, O_3, O_1, O_z, O_2, O_4, T_6) referenced to Fz. Perimetric examination was performed using Program 31 of the Octopus 201. Three patients had 16-channel VEPs recorded by the Biological Brain Atlas III (see Fig. 3 for montage) and visual fields were assessed using Program 30-2 of the Humphrey 620 Field Analyzer.

Three field and check sizes were presented to produce full field, right half field and left half field stimulation (30° field; 72 min check: 10° field; 24 min check: 3 field; 7.5 min check). The pattern stimulus was an optically produced, twice per second reversing, black and white checkerboard, with a contrast of 74%. One

Table 1 Summary of Information Loss and the diagnostic value of the different stimulus parameters used to elicit the VEP

Subject	VA	Information loss	Peripheral isopter	VEP			
				30 FF	30 HF	10 FF	3 FF
9 (R)	6/24	High	~	.	.	~	~
9 (L)	6/9–2	High	~		.	~	~
8 (R)	6/6–2	39 53%	~	.			X
8 (L)	6/9+2	40.71%	~	.	.		X
4 (R)	6/9+1	29 34%	~	.	.	.	X
1 (L)	6/24	23 04%	~			X	X
4 (L)	6/6-2	12.83%	~	.	.	X	X
2 (R)	6/9+2	11 32%	~	X	.	X	X
3 (L)	6/6	2 05%	~	X	X	X	X
5 (L)	6/6	0%	N	X	.	.HF	.HF
6 (R)	6/5–1	0%	N	X	.	X	X
6 (L)	6/5–2	0%	N	X	.	X	X
7 (R)	6/6+2	0%	N	.	.	.HF	X
7 (L)	6/6+1	0%	N	X		.HF	X

Diagnostically conclusive; ~ not examined; X not conclusive; N normal

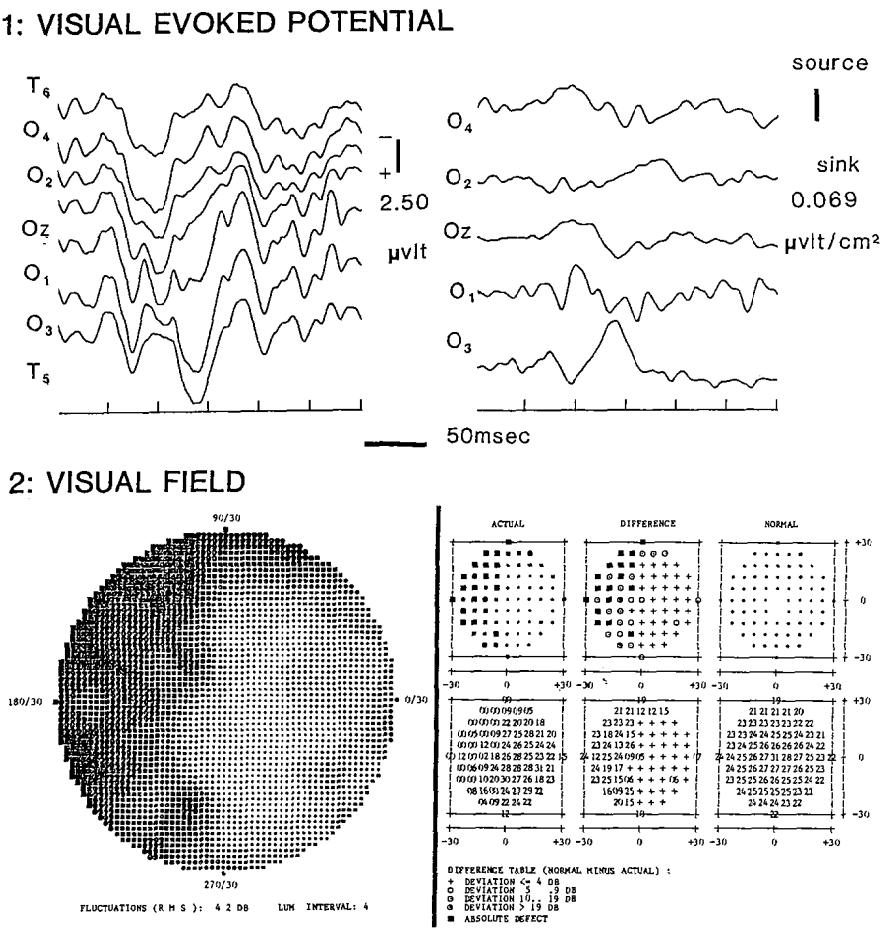

Fig 1 Typical result of subject with pituitary adenoma (left eye of subject 1) 1. The VEP following 30° full field stimulation recorded on the Nicolet Pathfinder II. The result is normal over the right occiput (O_2-T_6) but abnormal over the left occiput (O_1-T_5) The 5-channel result shows the source derivation of the scalp potential (11) 2 The visual field recorded by the Octopus 201, Program 31. 3. The Depression Profile illustrating an Information Loss of 23 04%.

hundred sweeps were averaged and bandpass filters with a low frequency cut-off of 0.5 Hz and a high frequency cut-off of 70 Hz were used.

When no visual field abnormality was detected in the central 30° peripheral Goldmann isopters were measured. A more detailed outline of the methodology and the normative data related to this study have been published elsewhere[11,12]. The established criterion for VEP abnormality was a 50% reduction in amplitude at occipital electrodes 20% lateral to the midline, O3 and O4, when using full field stimulation or when comparing right and left half field stimulation.

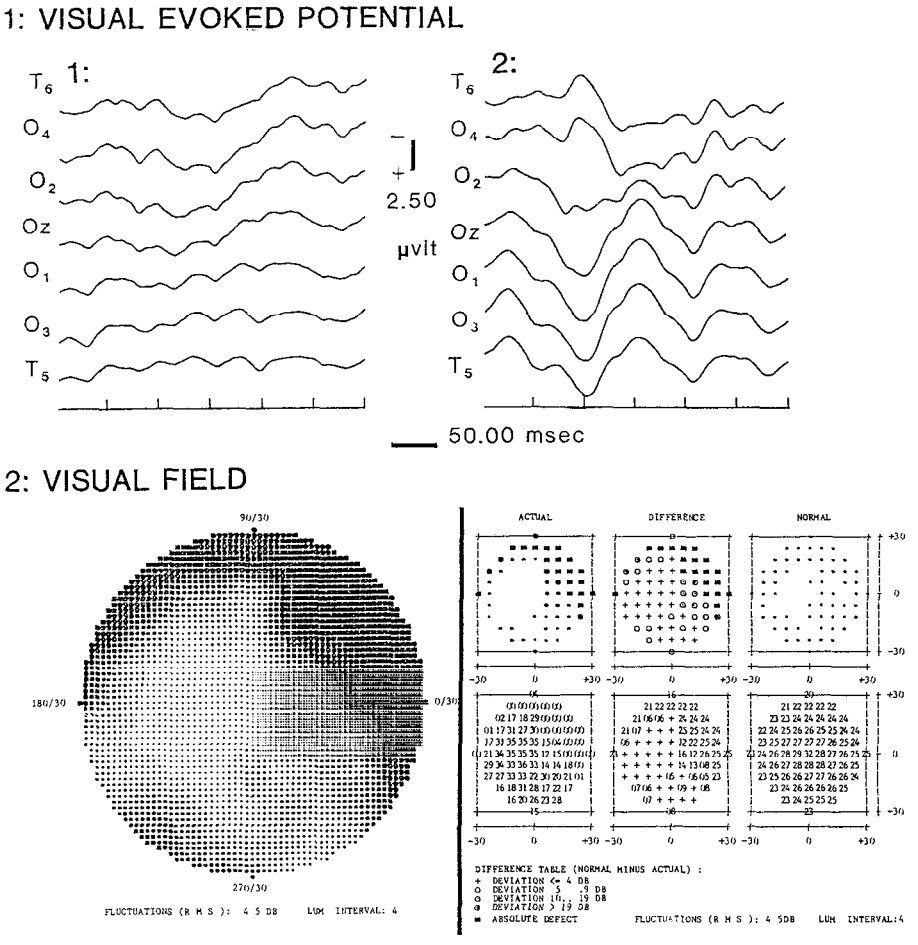

Fig 2 Typical half field results for a subject with pituitary adenoma (right eye of subject 4) 1. Right half field stimulation 2 Left half field stimulation

Results

Table 1 outlines the results in descending order of visual field Information Loss. Fig. 1 shows typical results for those subjects who were examined using the Octopus 201 perimeter and the Nicolet Pathfinder II. Fig. 2 illustrates typical half field results. Fig. 3 shows a typical result for a subject who was examined using the Bio-logic Brain Atlas III.

When the Information Loss was greater than 20% in the central 30° of the visual field, the largest field and check size stimulus elicited VEPs which were diagnostically conclusive following full field stimulation. The results were supported by half field stimulation.

When Information Loss was less than 15%, the largest field and check size, when presented as a full field stimulus, was generally not conclusive. Half field stimulation was more useful in five out of six subjects.

Five out of five eyes exhibiting no visual field abnormality, including peripheral isopters, demonstrated significant hemispherical asymmetry following half field stimulation.

Discussion

The results support those researchers who have found the VEP to be useful in detection of compressive chiasmal lesions[1-4]. They disagree with those of Amiroff and Maitland[5]. It is likely that the small 10° stimulus field size was responsible for their results, in spite of using a 50 min check size.

In summary, there was a clear correlation between the degree of Information

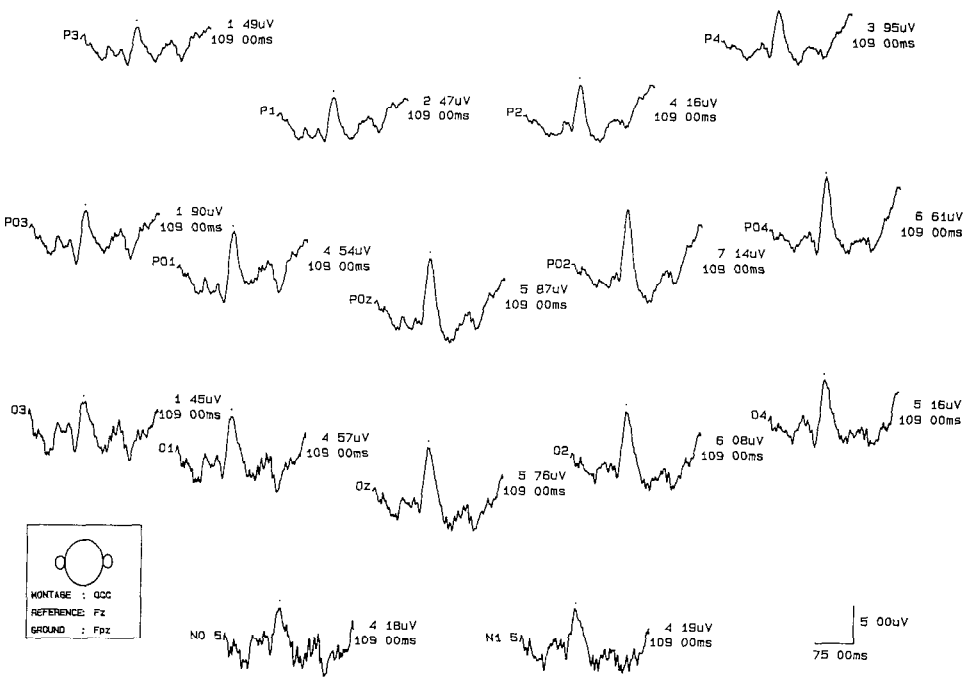

Fig 3 Typical result obtained from a subject with pituitary adenoma (subject 6, left eye) following 30° field stimulation, when recorded using a 16-channel, occipital montage, on the Bio-logic Brain Atlas III Note the gross lateral asymmetry when comparing electrodes O_3 and O_4

Loss, measured subjectively, and the diagnostic value of the VEP, a largely objective measurement. The VEP was, however, capable of detecting early compressive lesions of the chiasm before the visual field was noticeably affected, providing the correct stimulus and recording techniques were used. It is recommended that large field and check sizes, approximately 30° field and 60 min check, and half field stimulation are used. This should be accompanied by a montage which incorporates electrodes approximately 20% lateral to the midline in the occipital region. Smaller field and check sizes failed to add any useful clinical information.

Acknowledgements

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WATERSHED VISUAL FIELD LOSS

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Detailed automated static and manual kinetic perimetry were used to study the visual field loss in two young men, both of whom had suffered cardiopulmonary arrest with prolonged coma and resultant visual loss Both also had other objective neurologic loss and Magnetic Resonance imaging abnormalities

The basic visual field defect was a relative loss of sensitivity over the whole field of vision but one that varied considerably from locus to locus Most strikingly, however, the area of greatest loss was an irregular zone of 5-10 degrees on either side of the midline vertical line that stretched nearly from the top to the bottom of the field of vision Unexpectedly the visual field defect seemed to be denser when kinetic rather than static perimetry was used and with either a rapid kinetic rate or a short interval of static stimulation. Fatigue and concentration also appeared to affect results

It is postulated that this type of visual field loss is predictable in cardiopulmonary arrest since hypoxia is greatest in the border zone or watershed area where the middle cerebral and posterior cerebral artery terminations interdigitate and since this zone also approximates the edge of Brodmann area 17 and the vertical line through the field of vision

Introduction

Anatomic studies correlated with visual system analysis have consistently shown that there is a good correlation between the edge of the primary visual cortex, Brodmann area 17, and the vertical line of the field of vision. This line runs along the medial crest of the occipital cortex as it turns inward to form the coapted portion. There is a somewhat less precise relationship between this line and the area or zone of interdigitation between the terminal arteries of the posterior and middle cerebral arteries, the so-called watershed zone [1-4]. And yet, this terminal zone of circulation to the occipital lobe seems to approximate the central line of the field of vision well enough so that one might predict that occasionally a person with anoxic or ischemic damage in this area would exhibit a relative zone of depression on either side of the vertical line of the field of vision.

A review of the literature that deals with bilateral occipital disease of a vascular nature was done but reference to the type of visual field defect postulated here was found only occasionally and then more by default. Most of the reports, as might be expected, dealt with bilateral posterior cerebral artery occlusion from a variety of causes. The defects depicted in these studies are bilateral asymmetric but congruous sector defects that have a variable involvement of the macular portion of the field[5,6].

On the other hand, one patient with cardiac arrest had a variation of the bilateral visual field loss just mentioned but with the suggestion that each of the sector losses was most pronounced along the vertical line of the field of vision[1]. Another patient with cardiac arrest had bilateral, almost isolated macular defects and a third had the suggestion of a paravertical central defect in the field of vision[7,8]. This report details the findings in two young men who had border zone or watershed area infarction in the occipital cortex that was superimposed on diffuse cerebral damage and who exhibited a central zone of loss of the field of vision that straddled the vertical line.

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Case studies

Case 1 A 23-year-old man with Wolff-Parkinson-White syndrome had been drinking heavily at a party. He had also taken codeine for a headache and may have ingested some recreational drugs. A friend noticed his absence and upon looking for him found him on the floor in the bathroom unresponsive in a pool of vomitus. He was not able to arouse him and called for an ambulance. The paramedics arrived in ten minutes but could not find a pulse or any respiratory effort. After clearing the airway of debris they administered mouth to mouth resuscitation and closed chest compression. The patient was comatose for ten days.

He was examined two weeks after the cardio-pulmonary arrest and periodically for the next five years. During that period his neurologic function remained relatively stable except for visual acuity which improved from rough counting fingers to about 6/60 in each eye, general mental function which slowly improved in regard to memory, calculation etc. and the left hemiparesis and ataxia which converted into a left-sided dystonia even while becoming less dense.

The color vision was nearly normal with Hardy-Rand-Ritler (HRR) plates, but the visual field had a general but variable depression with an increased area of loss in an irregular zone covering about 5-10 degrees on either side of the vertical line of the visual field. This was essentially congruous and stretched from the top of the vertical line to the bottom, was wider at both the top and bottom and was demonstrated by kinetic and static perimetry (Figs. 1, 2). He also had a Balint's type syndrome with psychic gaze paresis, optic ataxia and simultanagnosia. In addition he had difficulty with space and time perception, constructional apraxia, memory and calculation, and personality change. The MR demonstrated the watershed infarcts and severe, diffuse cerebral atrophy that was most marked in the parietal and occipital lobes (Fig. 3).

Case 2 A 19-year-old man was taking Verapamil in an unregulated fashion and probably suffered a third degree AV block with cardiac arrest. This occurred in an emergency room and resuscitation was relatively prompt. The clinical picture was stable after three years but up to that point included a slowly improving visual acuity from about 6/60 bilaterally to 6/12 and 6/15, normal HRR color vision, and a visual field similar to the first case (Figs. 4, 5). Also present were simultanagnosia, problems with space and time perception and mild changes in memory, calculation and personality, speech and general balance and coordination of fine motor tasks. The MR was confirmatory for diffuse cerebral atrophy and subcortical infarcts (Fig. 6).

Discussion

Both of the cases presented here had typical neurologic sequelae for the severe anoxic-ischemic episodes they suffered. This is particularly true for the Balint's type syndrome each expressed with optic ataxia, psychic gaze paresis and simultanagnosia[9-14].

Both cases suffered cardiac arrest, the first perhaps secondary to aspiration of vomitus with associated airway obstruction and the second directly due to overdosage of a medication affecting cardiac conduction. Perhaps one could speculate on whether blood circulation after respiratory arrest is protective against watershed cerebral damage or enhances it for a period of time but neither the time sequence in our patients nor the literature on the subject seem to be sufficiently clear[15-17].

The clinical and imaging data clearly demonstrate that both of the patients in this study had cerebral damage that is characteristic for diffuse cerebral anoxia-ischemia as might be seen in cardiopulmonary arrest. While the damage is certainly

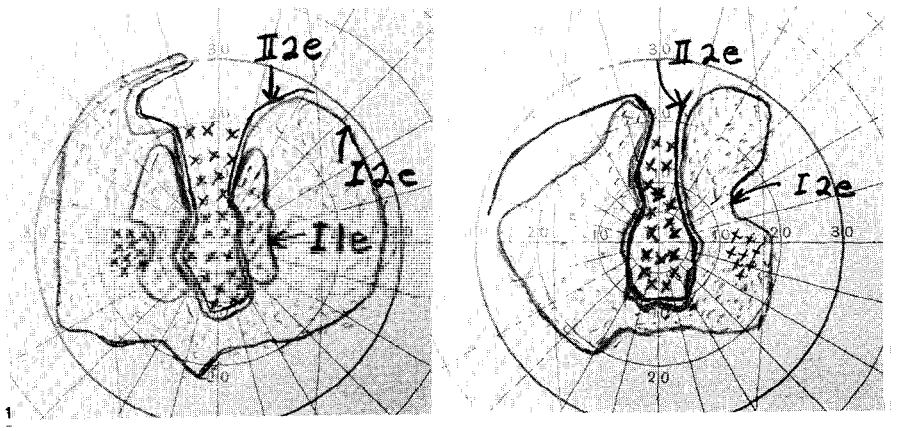

Fig 1 Goldmann kinetic field of vision for case 1 (right eye on right and left eye on left). The spots are static checks seen with I2e and x's are static checks with II2e not seen With the left eye, two additional small areas were seen with I1e.

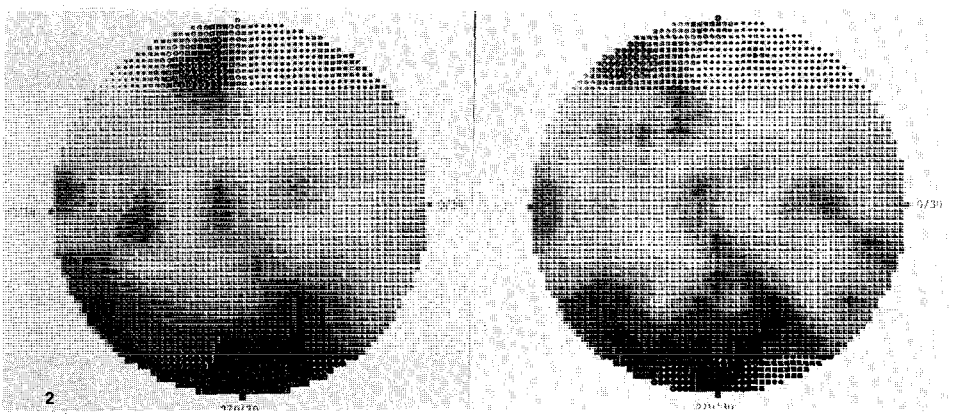

Fig 2 Octopus program 34 is shown for right and left eyes (case 1) OS left, OD right

not limited to watershed infarcts of the cortical and/or subcortical white matter in our patients, the greatest defects in the visual fields seem to occur in an area corresponding to the watershed zone. Knowing this, it seems logical that these patients might exhibit the type of visual field we describe. The relationship of the center line through the field of vision to the edge of Brodmann's area 17 is well known[1-4]. The relationship of these two to the border zone or watershed area between the posterior and middle cerebral arteries is probably not as close but the correlation is good enough to theorize that there might occasionally be a central bilateral field of vision defect as we describe. The relationships just mentioned are shown in Fig. 7. Here, attention is drawn to the zone of interdigitation between the

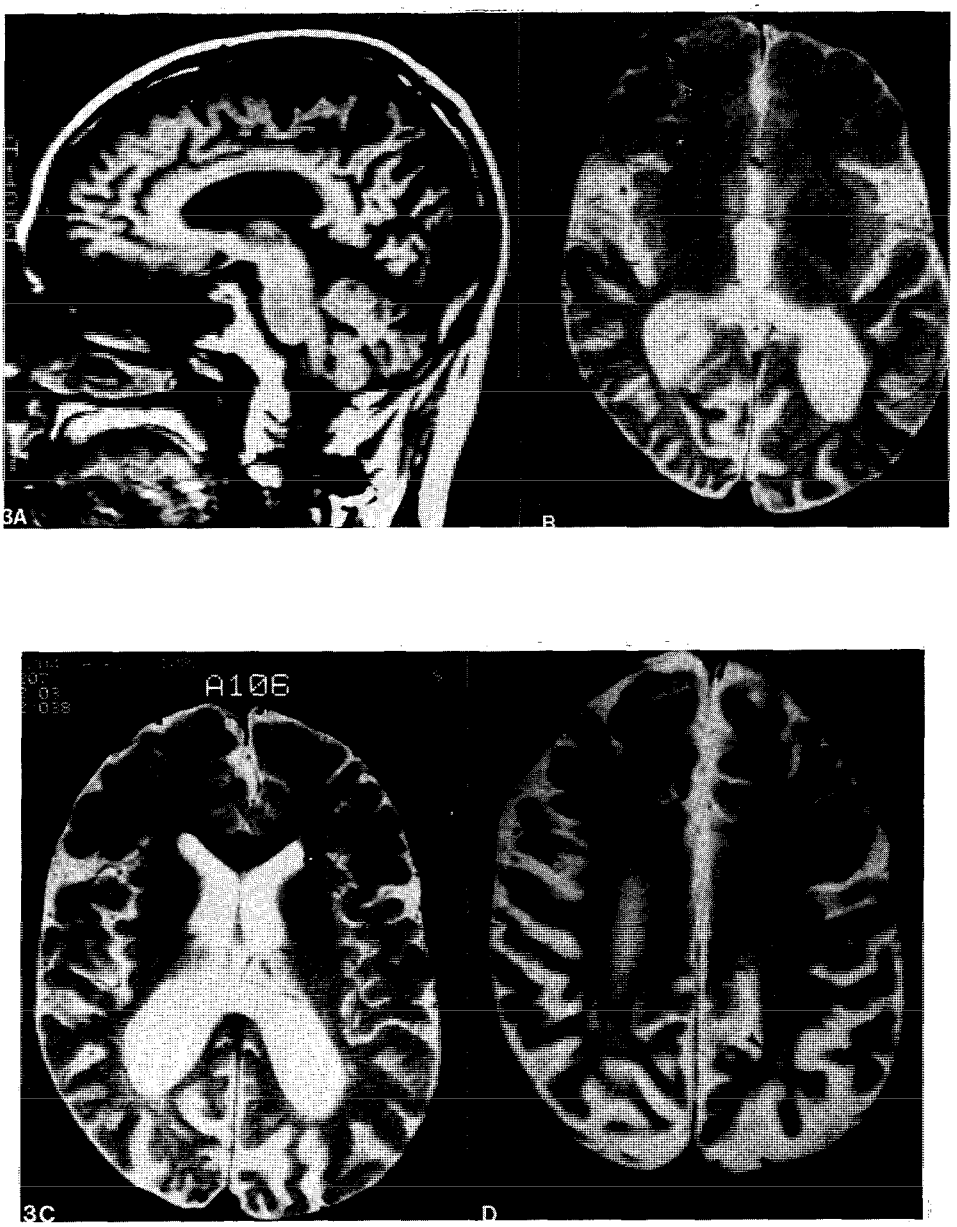

Fig 3 MR scan for case 1 Diffuse, severe atrophy (A-D) with large ventricles (B and C), and small watershed infarcts (D arrows) occur The atrophy is worst in the bilateral parieto-occipital areas but the basal ganglia are normal. A is a sagittal image (TR 600, TE 20) and B-D are transverse images (TR 2800, TE 90)

three major cerebral circulations which extends from the frontal lobe through the inferior temporal lobe (dotted stripe), the coapted but exposed left posterior brain (shaded area), the vertical line through the field of vision and the edge of area 17 (essentially as dotted stripe), and the horizontal line through the field of vision

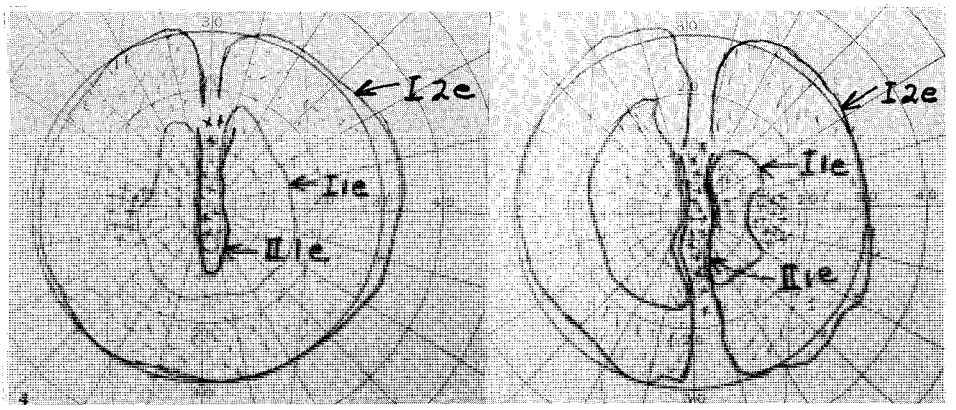

Fig 4 Goldmann kinetic visual fields for case 2 with static checks for both I2e and I13 (R and L). The x's are not seen with I2e and II1e is drawn for comparison

(following the calcarine artery and fissure).

The defects in the field of vision in these two patients were very similar. The basic defect was a reasonably congruous, bilateral general depression of the visual field that varied considerably from locus to locus. Superimposed on this was an area of increased loss that formed a somewhat irregular zone 5-10 degrees on either side of the vertical line of the field of vision and which broadened at the top and bottom extremes of the vertical line.

The paravertical zone of greatest loss is probably based on the fact that the area of greatest sensitivity of the brain to anoxia is the border zone or watershed area between the three major cerebral circulations. Along this zone the visual cortex, motor cortex, basal ganglia and cerebellum are probably more sensitive than others with layers 3 and 4 of the cerebral cortex being the most sensitive[18-27]. Even though our cases had small watershed infarcts, these were superimposed on diffuse cerebral atrophy without basal ganglia involvement, and probably represent one end of the spectrum seen with anoxia and ischemia. In fact, the pathogenesis of the brain damage in our cases is probably similar to that occurring in near drowning with

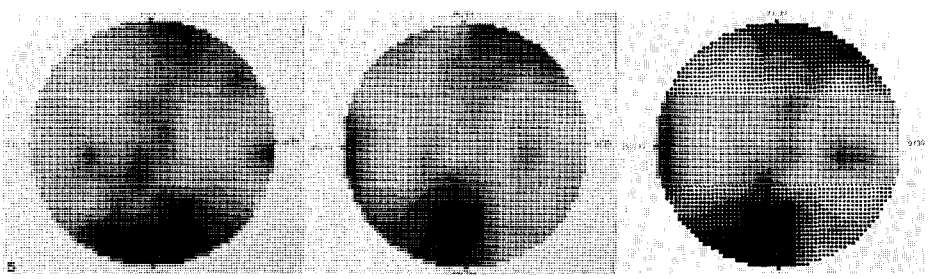

Fig 5 Octopus program 34 is shown for case 2 The far right field is of the R eye with short intervals, the middle with three second intervals and the left field of the L eye with short intervals

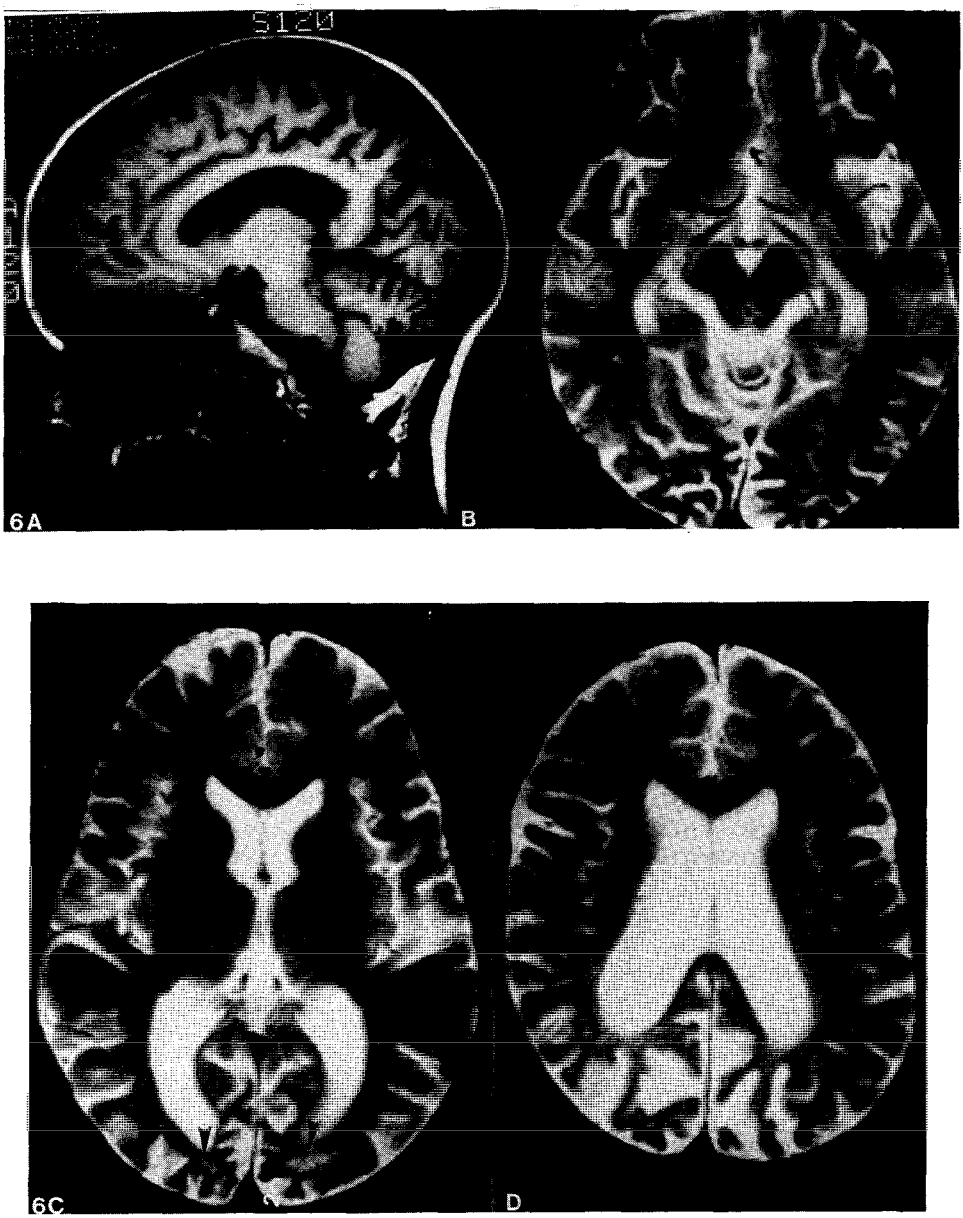

Fig 6 MR scans of case 2 with moderate diffuse atrophy, again with a similar parieto-occipital emphasis, and sub-cortical infarcts (C arrows). B-D are in the same order as Fig 3 but at slightly lower levels and the TR and TE data are the same as Fig 3

anaerobic glycolysis leading to an accumulation of toxic by-products, such as lactic acid, and finally cell death[23-27].

The general visual field loss would be expected because both patients suffered cardiopulmonary arrest that probably lasted 15 minutes or more and even though the watershed area might be most susceptible to anoxia, adjacent areas of the brain are very sensitive too. The broadening of the zone of visual field loss along the

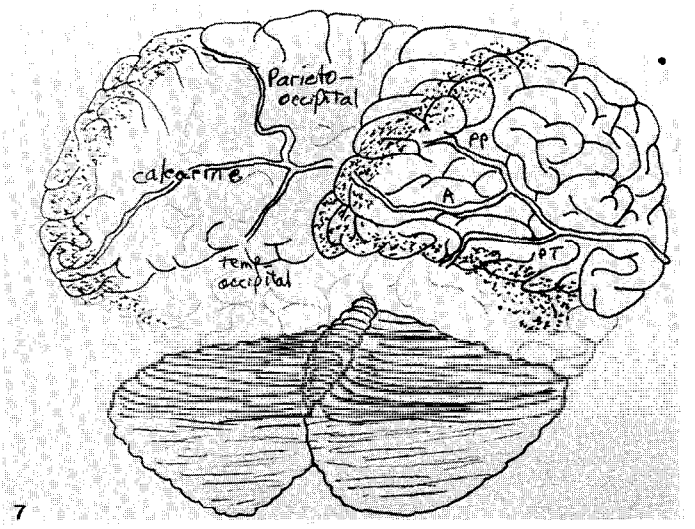

Fig 7 Posterior view of the brain with the left coapted portion opened to illustrate area of visual cortex PP is posterior parietal, A is angular and PT is posterior temporal (all from middle cerebral)

vertical line at the top and bottom of the line supports the fact that the area where the border zone and vertical line correlate least well is at these two extremes[1-3].

While it has been said that the Riddoch phenomenon is characteristic of occipital visual field defects, we found our patients seemed to demonstrate more clearly the central vertical zone of loss with kinetic stimuli, that is, a reverse stato-kinetic dissociation. It is possible that the damage to associated visual integration areas in addition to area 17 might make it more difficult for the brain to determine the direction of a stimulus than to merely ascertain its presence. It is possible that the task fatigue these patients demonstrate along with their attenuated mental function affect both the Riddoch phenomenon and the congruity we measured. It might also be that an abnormality exists in handling inputs from different retinal ganglion cells so that the message is either routed incorrectly or garbled[28].

A change from Goldmann I to II did little to affect the size of the defect of the field of vision but a change in brightness of one-half log unit produced quite noticeable changes. The kinetic strategy that produced the least visual field defect was a movement approximating 5 degrees per second, therefore exhibiting a rate of dependency. The static strategy that produced the least visual field defect was a duration of 2 seconds every 5 seconds with the Goldmann and 100 milliseconds every 3 seconds with the Octopus. Even with these slow strategies frequent rest periods seemed necessary to maintain fixation and reduce the false negative and positive trys. All of this is probably affected by the somewhat faulty and prolonged integration process in these patients. It is anticipated that, as more of these patients are studied, the exact parameters of the visual field defect we describe will be refined. It is also likely that the severity and chance distribution of the anoxic damage in these patients along with the timing of testing after injury will affect the findings [1,21,22].

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AMAUROSIS FUGAX AND VISUAL FIELD LOSS

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Abstract

Routine visual field examinations in 50 patients with amaurosis fugax have revealed a variety of field defects, the principal among these defects being arcuate depressions, isolated scotoma and nasal steps Hemianopic type changes have also been observed.

The relationship of the defect to ultrasonic Doppler flow signals coupled with Duplex scanning of the carotid bifurcation is analyzed Data on the incidence of Hollenhorst plaques and carotid bruits is also recorded. Reversal of the field defects after carotid endarterectomy has been highly significant in four out of ten patients and can be coupled with the improved parameters of carotid perfusion. Twenty percent (20%) of patients referred to the vascular studies unit for assessment had amaurosis fugax The results with endarterectomy over a five-year period are included and the value of carotid endarterectomies in patients presenting with amaurosis fugax are presented.

Introduction

A significant proportion of patients with transient ischemic attacks will present with amaurosis fugax[1]. The advent of new, non-invasive methods for investing their carotid bifurcation, the possibility of surgical endarterectomy and the reversibility of some cerebral damage accentuate the need for appraisal of patients with amaurosis fugax. Doppler ultrasound is an established method of investigation[2,3]. It has the advantage of accuracy, simplicity and reproducibility[4,5]. It presents both anatomical and physiological data. The time required for the examination along with the immediate information make it an ideal form of clinical measurement. It is now regarded as the primary investigation in most vascular units.

Positron emission tomography[6,7] and NMRI[8] have revealed the presence of unsuspected areas of brain ischemia amongst patients with transient ischemic attacks. These are either reversible or non-reversible. Diamox has been used to demonstrate reversibility and is used as a prelude to reconstructive surgery[9]. The presence of small infarcted areas in association with transient ischemic attacks raises the possibility of unsuspected field defects in patients with amaurosis fugax. Modern methods of perimetry with automation offer the possibility of identifying small, discrete lesions. The method developed by Henson[10] is based on normal population studies and offers a low rate of error and intertest variation. It will identify small, incomplete scotomata which can then be differentiated from dense focal lesions which are likely to be irreversible. This information is important to the vascular surgeon in decision making.

Materials and method

Patients attending at the routine Outpatient Department with transient blurring of vision had, in the majority, a true amaurosis fugax. A routine ophthalmological examination was undertaken and a visual field examination with standard

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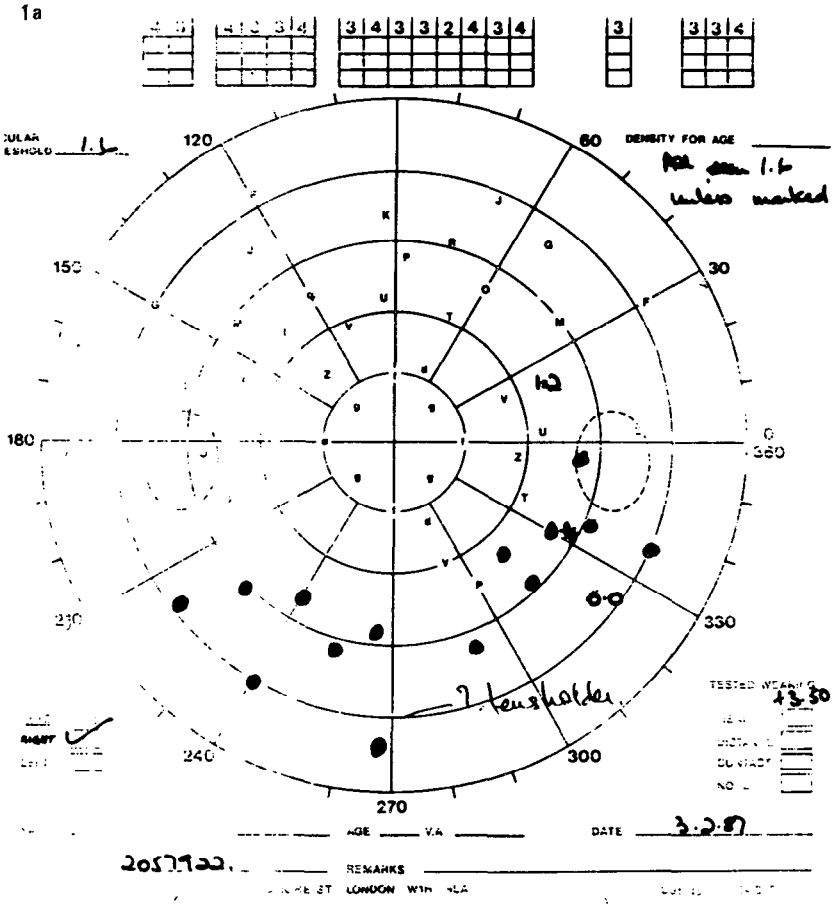
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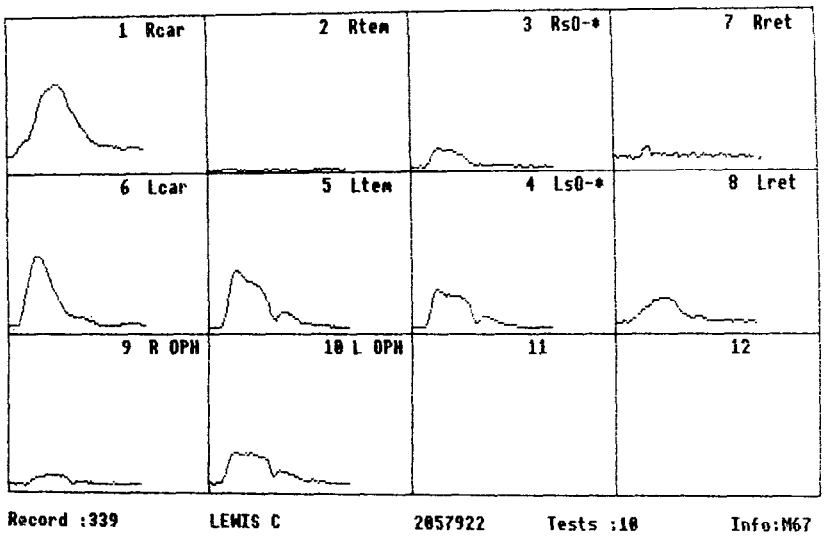

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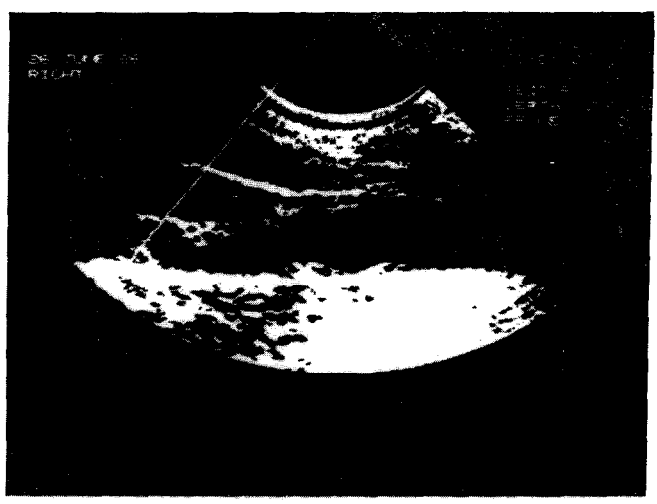
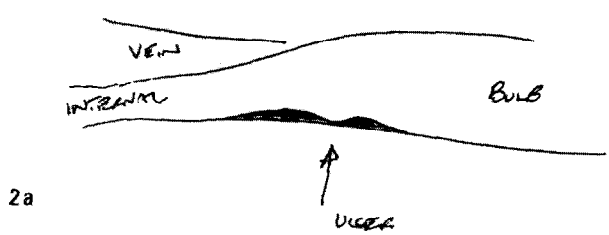
Fig 1 Optic disc photograph with ischemic changes in vessel (a), corresponding visual field (b) and continuous wave Doppler signals from ten sites with reverse flow in each supra orbital (c).





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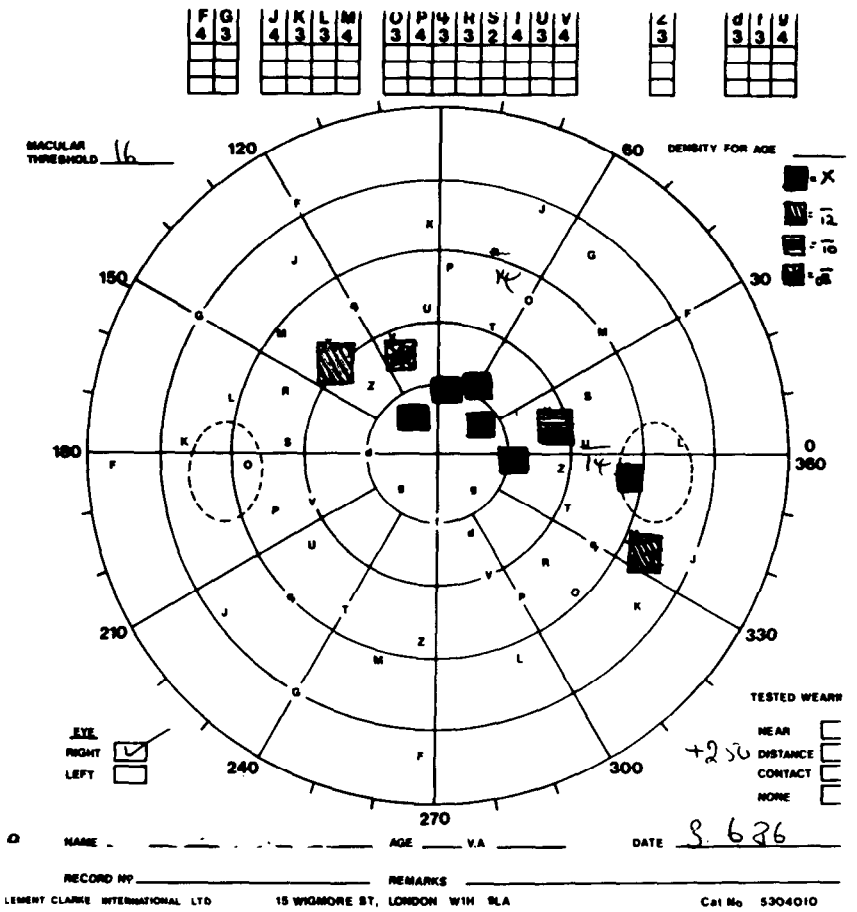

2b

Fig 2 Duplex scan right carotid bifurcation (a) and arcuate defect above fixation in right visual field (b).

perimetry, using Friedmann Field Analyser Mark II. The perimetrist was unaware of the diagnosis. The visual fields were classified into the type and extent of the defect. The examination of the carotid bifurcation was undertaken with a continuous wave Doppler as previously reported[11] with the purpose of establishing evidence of change in flow signals, especially reverse flow in the supraorbital (Fig. 1). The time delay sequence, that is the delay between the carotid and the supraorbital vessel was calculated by the computer using the R wave of ECG as standard reference point Pourcelot Index. Pourcelot indices were calculated by the computer using the formula as defined by Planiol and Pourcelot[12]. When significant disease was identified, patients were referred to the Vascular Studies Unit for appraisal of the carotid bifurcation by Duplex scanning (Fig. 2). Subsequently those who were within a defined age group and had had no significant general medical problems (severe cardiac disease, uncontrolled hypertension, smoking or uncontrolled diabetes), were referred to a vascular surgeon for an opinion about carotid endarterectomy. The criterion for a carotid endarterectomy was that there must be

more than a 50% occlusion of the lumen and the patient must have had several transient ischemic attacks.

Results

In the 50 patients examined, field loss was recorded with the Friedmann Visual Field Analyser on the side ipsilateral to the carotid stenosis in 34 out of the 50 cases. On the contralateral side, it was only recorded in ten out of the 50 cases. The type of field loss was as shown in Table 2, the principal type of defect being an arcuate loss. The type of field loss was examined in relation to the Pourcelot index and the time to half peak sequence. The Pourcelot index was higher on the affected side but not significantly so. There is a time difference between the affected side and the contralateral side which came close to significance at the 5% level. Duplex scan data was available for analysis in 27 of the 50 patients and the results of field loss in relation to the degree of stenosis presented in Table 3 does not suggest a clear-cut association with the degree of stenosis and field loss. Following carotid endarterectomy, the reversal of field loss was observed in four out of ten patients. In a further four there was no field loss prior to surgery and no field loss occurred after surgery. Ten untreated cases were reviewed and, in these, nine were unchanged and one had reverted to normal. Emboli of the Hollenhorst plaque type in the retinal circulation were observed in eight cases; field loss was present in seven; six arcuate defects and one hemianopia. No association was discovered between field loss and carotid bruits, neither was there any association between field loss and reverse flow through the supraorbital vessel. Table 4 shows the number of carotid endarterectomies performed per year and the mortality and morbidity over the period. There is a quarterly vascular audit to monitor the effectivity of procedures and the results are regarded as encouraging.

Discussion

Lees[4] has reviewed the natural history of transient ischemic attacks and draws attention to the duration over which these may recur before the onset of a cerebral

Table 1. Distribution of lesions in 50 patients presenting with amaurosis fugax

M/F ratio	24/26
Field loss incidence	34/50 ipsilateral
Field loss incidence	10/50 contralateral

Table 2 Amaurosis fugax. Type of field loss

34	Arcuate upper	12
	lower	7
	Nasal step	4
	Enlarged blind spot	3
	Hemianopia	3
	Discrete paracentral	4

Table 3 Duplex scanning of the carotid bifurcation ipsilateral to amaurosis fugax

27 Scans % stenosis	Field loss present	Field loss absent
75% plus	5	5
50 - 74%	5	0
25 - 49%	2	1
0 - 24%	5	7
	17	10

Table 4 Carotid endarterectomies 1980-1987

1980	1981	1982	1983	1984	1985	1986	1987
10	18	14	17	17	26	34	42

Total	178
Number of stroke deaths post-operatively over the period	5
Number of new deficits over period	6
A quarterly vascular audit is undertaken	

vascular accident. The longest period recorded in this series without a cerebral vascular accident was 12 years. At the other end of the scale, three patients proceeded very rapidly to a full CVA which was quickly fatal in one instance. Kuller[13] has suggested that bruits do not relate to strokes, yet Riles and co-workers[14] have indicated that there is inter-relationship of a linear type between bruits and degree of stenosis. This did not correlate with focal neurological symptoms. In this particular series there was no positive correlation between a bruit and the incidence of field loss. It has been claimed[15] that reverse flow through the supraorbital vessel is a good indication of a significant degree of stenosis. Approximately 80% of the anastomotic circulation will be through the superficial temporal into the supraorbital vessel and thence feeding into the circle of Willis. Were ischemia to be the basic patho-physiology of the visual field defects noted, then a high incidence of field loss would be expected where reverse flow was present; this was not found. Similarly there was no clear-cut association between the degree of stenosis recorded on Duplex scanning at the carotid bifurcation and the presence of field loss.

The technique of visual field examination is well established[10] and in the clinical setting has been proved to have low false positive levels and to be reproducible. Visual field testing being a simple, not too onerous task for a patient with a high degree of reproducibility, offers the possibility of a further parameter for investigation and long term management of patients with transient ischemic attacks. The evaluation prior to carotid endarterectomy can be enhanced and possibly the distinction between reversible and irreversible lesions made.

Significant lesions of the carotid bifurcation could be associated with silent areas of infarction. It is accepted that significant damage can take place after arrest of

circulation for between three and five minutes and many attacks of amaurosis fugax are of this duration. Modern perimetry provides a satisfactory way of clarifying the possibility of small, incomplete or complete areas of visual damage. This has been demonstrated in this study. Arteriosclerotic disease with plaque tends to be present bilaterally and therefore field loss on the contralateral side is to be expected to a degree as has been shown in these results. The absence of any significant correlation with reverse flow in the supraorbital vessel and the presence of a high incidence of field loss where emboli have been identified in the retinal microcirculation would suggest that the primary cause for the changes noted is probably microembolic rather than prolonged ischemia. Carotid lesions are, for a long period of time, asymptomatic[16]. Barnes and co-workers[17] have reported that a significant morbidity and mortality from CVAs occurs in patients undergoing cardiovascular surgery. Micro infarcted areas have also been reported on nuclear magnetic resonance imaging[8] and DeWitt and co-workers[18] have undertaken a neuropathological correlation and found that relaxation times on NMRI scanning were more extensive than expected in the areas of infarction noted pathologically. These were determined to be infarcts plus areas of adjacent Wallerian degeneration. Areas of damage that can be specifically identified are important as they can convert what has previously been a symptom into a positive sign thus aiding the overall evaluation of the patient.

Doppler ultrasound has become increasingly acceptable as an accurate and reproducible method for the investigation of carotid bifurcation[3,18]. It has been compared with spectral bruit analysis[19] and with digital subtraction angiography[5]. Duplex scanning of carotid bifurcation is now regarded as the baseline examination in a significant number of centers. It should provide evidence in at least 84% of plaques[5] from which emboli can arise. Apart from the micro-emboli, hemorrhage can occur from a plaque which, in turn, could be responsible for micro-infarction. The surgical success of endarterectomy in the long term would be partly dependent on the ability to prevent further hemorrhage or micro-emboli forming. Improved blood flow profiles have been observed in this series with Duplex scanning following endarterectomy. The restoration of normal flow in the supraorbital vessel improved Pourcelot indices and transit times have also been recorded. These changes are comparable with the alterations in fluorescein angiographic profiles as noted by Sarkeys and co-workers[20].

In this series, nine out of ten untreated patients had unchanged repeat fields. In three out of the ten patients with carotid endarterectomy there was complete resolution of the field defect and, in a further patient, the field defect gradually improved over a period of six months but did not resolve entirely. Visual field examinations could be a useful adjunct for the vascular surgeon appraising silent areas of damage and, where these are found, they could be used as another measure in the evaluation of modern forms of treatment of carotid artery disease.

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A NEURO-OPHTHALMOLOGICAL GLOBAL ANALYSIS PROGRAM (N1) DEVELOPED WITH THE OCTOPUS MEASUREMENT UNIT*

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Test location mainly allows assessment of horizontal and vertical meridian area, macula, temporal crescent, and blind spot area It also takes into account possible field rotation due to extraocular muscle imbalance, and avoids artefacts resulting from hemianopia or hemineglect The procedure involves three possible phases; each of these phases can be checked separately or successively.

Phase I is a screening test using a two-level strategy at the above locations, excluding blind spot area If necessary, evaluation can be interrupted at this stage, and the results printed out.

Phase II is a decision procedure It analyses with normal strategy the central 26 area only at locations where light spots were perceived during phase I. 'Visual field indices' are computed The printout combines data from phases I and II, in case phase II is performed following phase I.

Phase III examines blind spot area, using a single-level strategy at 15 dB.

Introduction

An automated perimetry global analysis program has been designed to define most of the visual field defects found in patients with neuro-ophthalmologic disorders. It also meets a number of requirements for assessment of various visual affections encountered in clinical practice.

This program has been developed with the 2000 R Octopus measurement unit, and an IBM PS/2 30 micro-computer. The program includes: (1) a test location adapted to specific neuro-ophthalmological requirements; and (2) an examination procedure, conceived to potentially shorten the evaluation time of the visual field.

Program description

1. Test location

With 73 tested points, the test pattern mainly allows assessment of horizontal and vertical meridians, macular area, and temporal crescent (Fig. 1); with one out of two additional optional grids, blind spot area can also be investigated (Fig. 2).

Test location also takes into account possible field rotation due to ocular torsion resulting from extraocular muscle imbalance, or abnormal head position. Thus, test points located near the horizontal and vertical meridians leave a 10^{o} test-free area on either side. In addition, blind spot search area can be circumferentially extended in case there is suspicion of field rotation (Fig. 3). Finally, in order to avoid artefacts resulting from hemineglect or hemianopia, test location allows a central fixation point. A large (5^{o} radius) ring fixation is used in case of severe central scotoma.

*Original concepts appearing in this program are the property of Geneva University, and cannot commercially be reproduced without its consent.

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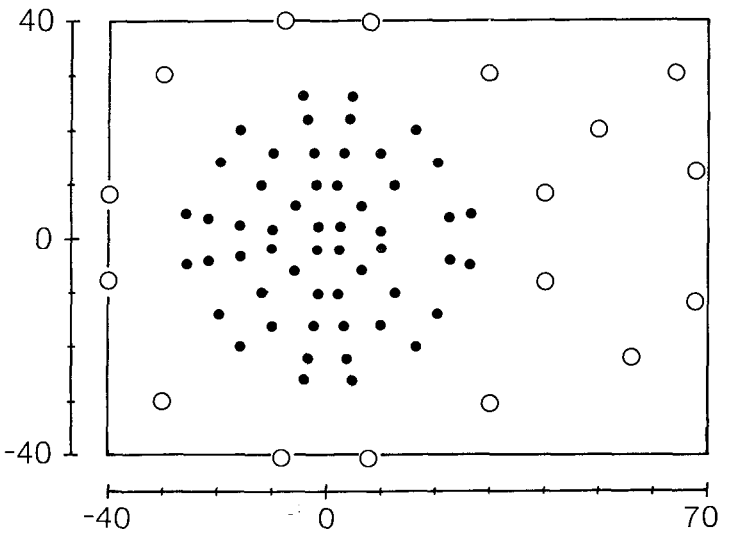

Fig 1 Text location pattern for phases I and II Locations for light spot projections are indicated with circles Full circles indicate locations of quantitative evaluation in phase II

2. Examination procedure

This involves three possible phases: *(2.1)* a screening phase, using a two-level strategy; *(2.2)* a central quantification phase (up to a 26° radius) with a normal strategy; and *(2.3)* blind spot plotting using a single-level strategy with 15 dB light spots.

Each of these phases can be checked separately or successively to allow adaptation to the individual patient's abilities and examination procedure time requirements.

2 1 Phase I. After performing phase I, results may be printed out and examination procedure stopped if the results appear to be normal or if the patient is too tired to sustain a prolonged examination. Otherwise, the procedure is allowed to continue to the - quantified - IInd phase.

2.2. Phase II. If phase II is performed after phase I, phase I is memorized for two purposes: (a) Test results of the peripheral visual field are added and combined to the printing of the quantified central area of phase II, and (b) if, at a number of locations, light is not perceived during the first screening, these locations are not tested again in phase II. This may substantially shorten phase II assessment.

However, if the screening phase I is not required, quantified phase II can be initiated directly. In this case, following assessment of central area (up to 26°) with a normal strategy, peripheral points are automatically checked using a two-level strategy, so that final printing of phase II always exhibits a full neuro-ophthalmological visual field.

In either procedure, assessment of phase II provides usual 'visual field indices', including separate evaluation of nasal and temporal halves of central test location; the presumed blind spot area and the corresponding points in the nasal area are excluded from index computation.

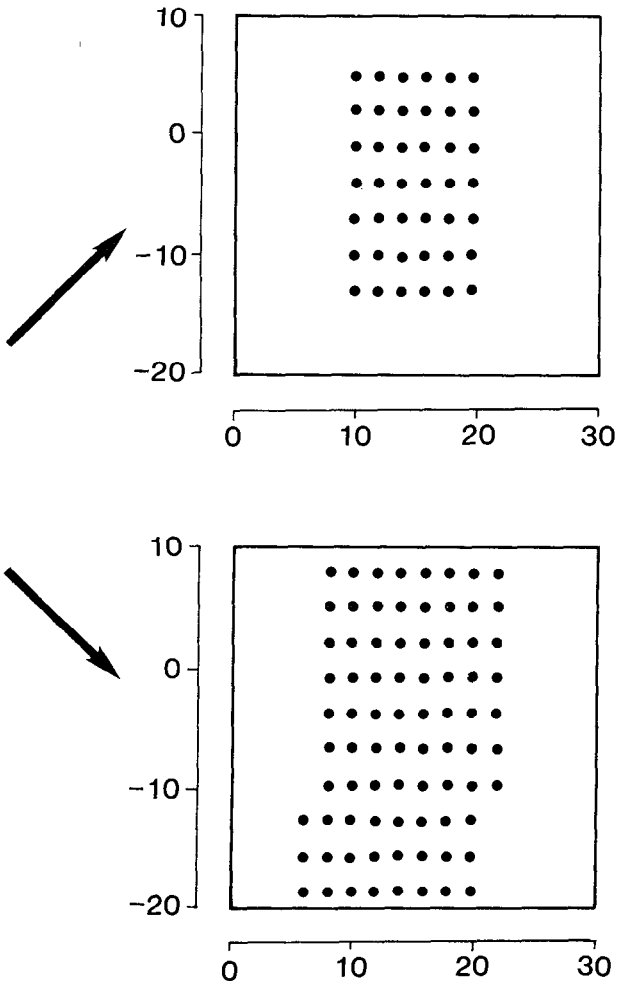

Fig 2 Blind spot search grid options: the regular (above) and enlarged one (below)

2.3. Blind spot area. For blind spot plotting, the examiner can choose between a 'regular' 42-point grid and a larger, 80-point one; in comparison with the former, the latter is mainly extended circumferentially (Fig. 2). After each five-spot projection in the blind spot area, one light spot is projected in the nasal field in order to prevent the subject shifting his gaze from the fixation point toward the blind spot area.

Discussion

Test location has been designed specifically to evaluate visual field defects found in patients presenting with neuro-ophthalmological diseases[1,2]. Most of the points tested are placed in the central (26^{o}) area, in which most visual field defects resulting from disorders in visual pathways can be detected[1], and are best quantified using a corrective lens. There are a few exceptions when peripheral visual field evaluation is helpful for the management of neurological patients, including

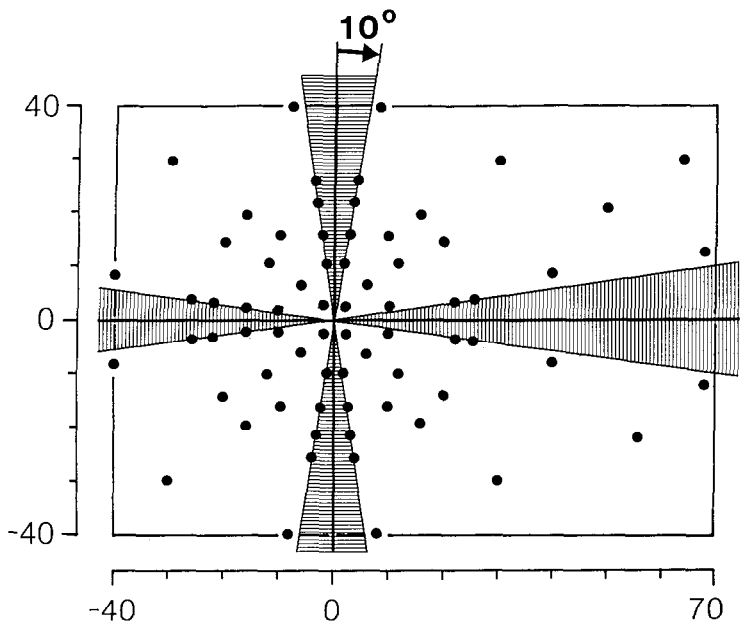

Fig 3 Location of 10° test-free areas near horizontal and vertical meridians Search grids for blind spot plottings are more precisely illustrated in Fig 2.

cerebral hemisphere lesions involving - or sparing - the temporal crescent of vision[1-3]; these conditions have been taken into account in the design of the pattern of peripherally-located test points (Fig. 1).

In order to avoid artefacts resulting from anatomical peculiarities of examined subjects, no test is located beyond 40° above the horizontal meridian or 40° radially towards the nasal side.

All peripheral locations are evaluated with a two-level strategy: in addition to speeding up the evaluation procedure, this avoids attempting to quantify light threshold sensitivity at locations outside the area which can be examined with a corrective lens. In addition, both inter- and intraindividual variability in threshold increase with visual field eccentricity[4]. Supragenículate defects are deeper in mid-periphery than in the central visual field[5], and since patients affected with such disorders usually demonstrate a limited ability to cooperate, semiquantitative evaluations generally deliver the clinically relevant information[6].

Since ocular torsion resulting from fourth nerve palsy is inferior to 10° [7], a 10° test-free area near the horizontal and vertical meridians, together with possible circumferential extension of blind spot search area, avoids artefacts due to abnormal ocular torsion (Fig. 3). Furthermore, the use of a single central fixation point during visual evaluation prevents the incorrect estimation of the center of a large fixation pattern (a four-dot lozenge or a circle) when dealing with a patient suffering from visual hemineglect[8], and obviates the need for continuous search of the center of the fixation pattern in cases of hemianopia[9]. It implies that no evaluation is made of central fixation area; however, this is of little concern, since it has been shown that paracentral points (*e.g.*, at least 5° from the center) are involved in inflammatory retrobulbar optic neuritis[10].

Obviously, there will always be patients suffering from neurological disorders which prevent them from undergoing automated perimetry. However, it should be

noted that the chosen test procedure, which includes a screening phase and memorization of phase I when performing phase II evaluation, helps shorten the examination in patients who may not be very cooperative. In addition, this program overcomes a number of limitations found with automated perimetry in neuro-ophthalmological patients.

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NORMAL AND ABNORMAL VARIABILITY

FLUCTUATION AND GENERAL HEALTH IN AUTOMATED PERIMETRY IN GLAUCOMA

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Abstract

Ten normal controls, ten ocular hypertensive patients, ten high tension, 12 normal tension and nine low tension glaucoma patients were studied prospectively by means of double threshold measurements of the 30 degree visual field during a time period from one to 36 months One of the aspects studied was the relation between general health based on the medical history on the one hand, and Short-term Fluctuation (SF), Long-term Fluctuation (LF) and Individual General Sensitivity (IGS) on the other

A relation was found between general health and short-term fluctuation and to a lesser degree long-term fluctuation, but there was no relation in our population between general health and general sensitivity of the visual field.

Introduction

In view of the considerable fluctuation encountered in automated perimetry[1], we studied factors possibly influencing fluctuation in 51 patients and normal subjects. The aim of this article is to describe the relation between general health parameters and short-term and long-term fluctuation as it was observed in our study population. In addition, we examined the relation between general health and the individual general sensitivity level of the visual field.

Material and methods

Subjects

We studied prospectively ten ocular hypertensive patients, 31 patients with primary open angle glaucoma, and ten age-matched controls. The glaucoma patients were subdivided into a high tension, a low tension, and an intermediate group. The definitions and inclusion criteria for the groups are listed below. The number of subjects in each group and the mean age are presented in Table 1.

NOR is the normal control group consisting of relatives or accompanying persons. They had no complaints about their eyes and no known eye disease. On clinical examination, they had a visual acuity of T≥0.6, clear media or incipient cataract, a normal optic disc, intraocular pressures ≤22 mm Hg, and a normal fundus.

OHT is the group of patients with ocular hypertension. The subjects had a visual acuity of ≥0.6, clear media or incipient cataract, either a normal or a suspect disc, a normal fundus otherwise, and an IOP of more than 22 mm Hg in a diurnal curve. They did not have any visual field defects as measured with our usual methods of investigation (the Peritest automated perimeter with manual checks). The length of

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Table 1 Composition of the 51 subjects measured repeatedly with the Scoperimeter

Group	Number of subjects	Male/female	Age (years)
NOR	10	6/4	67 8±10 1
OHT	10	7/3	55.7±13.8
MTG	12	8/4	65.6± 6.6
HTG	10	4/6	50.6±10.9
LTG	9	6/3	72.4± 8 8

time that these patients were known to have had ocular hypertension was 3.7±2.1 years.

MTG stands for "Medium Tension Glaucoma" as a distinction from the high and low tension groups defined below. MTG subjects had intraocular pressures without therapy of between 23 and 40 mm Hg in a diurnal curve. They had a visual acuity of ≥0.5 (average 0.8), clear media or incipient cataract, a suspect or overt glaucomatous optic disc excavation and no other ocular abnormalities. These patients had typical glaucomatous visual field defects[2] as measured with the Peritest and high resolution static perimetry along four meridians of the visual field.

HTG are patients with "High Tension Glaucoma". These patients had an IOP of more than 40 mm Hg without therapy in a diurnal curve, and typical field defects. They usually also had evidence of a late congenital aspect of the chamber angle at gonioscopy. This means that in the chamber angle extensions of the iris base could be seen, projecting onto or over the scleral spur or trabecular meshwork. The visual acuity was ≥0.6.

LTG are patients with "Low Tension Glaucoma", with intraocular pressures without therapy of less than 22 mm Hg in a diurnal curve, and typical glaucomatous field defects. The visual acuity in this group was ≥0.5. There were more patients with incipient cataract than in the other groups, but none had overt cataract. The LTG subjects usually had evidence of peripapillary atrophy, choroidal sclerosis and/or compromised retinal vasculature.

General health condition

For all subjects, a general health interview was performed and the results used for classification as 'healthy' or 'non-healthy'. None of the subjects was overtly diseased or disabled. We thus divided the subjects of the five research groups into three subpopulations:

1.'Healthy' subjects: those individuals who had no complaints about their health, were not under specialist care (except for their eyes), and were not taking medicine (except glaucoma medication).

2.Subjects with 'vascular diseases', such as arterial hypertension, myocardial infarction or other heart disease, generalized (manifest) atherosclerosis, hyperviscosity syndrome.

3.Subjects with 'non-vascular diseases', such as in this case: lung diseases, rheumatoid arthritis, diabetes mellitus, large abdominal surgery, urologic problems.

Method of testing

The subjects were tested at least four times over a period of four months to three years. All tests were done with threshold static perimetry by means of the Scoperimeter[3]. Within the 30 degree visual field, 60 locations were tested twice, providing double thresholds for all locations. Computer analysis of the double threshold measurements rendered estimates for the three parameters which will be used in this study:

1.The Individual General Sensitivity (IGS), based on a careful selection of 'healthy' locations[4], representing the non-defect level of the visual field.

2.The Short-term Fluctuation (SF) defined as the standard deviation of the double threshold measurements within one session. Because double thresholds were available for all locations, we could estimate the average SF for any subset of points, *e.g* , central *vs.* peripheral, or 'healthy' *vs.* pathological points. Here we will use the SFh, *i.e.*, the SF of the 'healthy' locations of the visual field under consideration.

3.The Long-term Fluctuation (LF) defined as the standard deviation of a variable between visual field sessions; in this study we will consider the LF of the Individual General Sensitivity.

For all variables, the mean values per individual were determined, and subsequently average values were computed per group.

Results

General health and Individual General Sensitivity

The mean IGS and mean age of the healthy and non-healthy groups are shown in Table 2. There was no significant difference in Individual General Sensitivity between the three groups.

General health and Short-term Fluctuation

During the study we got the impression, rather by accident, that non-healthy individuals seemed to have a higher SFh. We therefore grouped together all those subjects with what we considered a high SFh ($\geq$ 2.5 dB) and compared them with the remaining subjects (SFh <2.5 dB) with respect to general health condition. The result is shown in Table 3. It was confirmed that the proportion of non-healthy individuals was much larger in the high SFh group.

Table 2. Mean age and mean Individual General Sensitivity (IGS) in different general health conditions

	Healthy	Vascular	Non-vascular
Number of subjects	29	11	11
Age (years)	59.8±7.4	68.1±8 9	67 6±14.4
IGS (dB)	28.4±2.2	27.9±1.0	27 5± 3.4

General health and Long-term Fluctuation

We analyzed the relation between general health and the LF of the individual general sensitivity in the same manner as we did for the short-term fluctuation. We chose to look at the variable IGS because this is least likely to be influenced by glaucoma itself, thus permitting a less biased view on the influence of general health. An LF of >2.0 dB was defined as high (more than 1.5 sd from the mean LF for the whole population) and LF≤2.0 dB as low. The result is presented in Table 4. A larger proportion of non-healthy individuals was found in the high LF group. This group was relatively small. Otherwise there were no differences between the two groups.

Table 3 Difference in general health and glaucoma status between subjects with high versus low short-term fluctuation

	High SFh group 2 5 dB≤SFh	Low SFh group SFh< 2.5 dB
Number of subjects in the group	N = 17	N = 34
Age (years)	66.3±13.5	60.4±11.8
IGS (dB)	26.3± 2.2	29.2± 2.0
SFh (dB)	3 1± 0 5	2.0± 0.3
Number of healthy subjects	N = 6	N =24
Number of non-healthy subjects	N =11	N =10
Ratio non-healthy/healthy	1.8	0 4
Number of NOR and OHT subjects	N = 4	N =16
Number of POAG subjects	N =13	N =18
Ratio POAG/non-glaucoma	3.2	1 1

Discussion

Of the many factors influencing visual field behavior, 'general health' has not received much attention. The influence of alcohol on the outcome of automated perimetry was investigated[5] in 20 healthy volunteers from ten to 60 years of age, tested with the Octopus perimeter before and after moderate alcohol consumption. No influence was found on differential light threshold level. The short-term fluctuation increased somewhat, but this was not significant. In a different study[6], 30 healthy volunteers were tested with the Octopus JO program after 5 and 10 mg diazepam versus placebo. No difference was found between visual field parameters (among them differential light threshold and short-term fluctuation) with or without diazepam.

We did not try to influence the health status of healthy volunteers but subdivided our study population into three subgroups according to their actual health status based on the medical history. We found no difference between these groups with respect to the average 'true' general sensitivity of the visual field, represented by the IGS. With respect to Short-term Fluctuation, however, we did find a difference: in a group of subjects with a high SFh, the ratio of non-healthy to healthy persons was much larger than in the group with low SFh subjects. The mean age as shown in Table 3 was not different between the two groups. Attention should be paid to

Table 4 Difference in general health and glaucoma status between subjects with high versus low long-term fluctuation of the individual general sensitivity

	High LF group 2.0 dB<LF	*Low LF group* LF ≤2 0 dB
Number of subjects in the group	N = 10	N = 41
Age (years)	65.2±13.6	61 7±12.7
IGS (dB)	27 2± 2.7	28 5± 2 4
LF-IGS (dB)	2 5± 0 8	1 2± 0 4
Number of healthy subjects	N =4	N =25
Number of non-healthy subjects	N =6	N =16
Ratio non-healthy/healthy	1 5	0 6
Number of NOR and OHT subjects	N =4	N =16
Number of POAG subjects	N =6	N =25
Ratio POAG/non-glaucoma	1.5	1 6

the fact that the high SFh group contains proportionally more of the glaucoma cases and many authors have shown a higher SF in glaucoma patients than in normals[7]. It must be emphasized that in this study we only considered the SFh, *i.e.*, the SF in 'healthy' locations as determined by our algorithm. The SFh was not different between normal and glaucomatous visual fields in our prospective fluctuation study[8], but only the SFpa (of pathological points) was higher in the patients with visual field defects. Therefore, it does not seem likely that a higher proportion of glaucoma patients could be the explanation for the high SFh values. In Table 3, the IGS values seem to differ between these groups, but we have shown above that the IGS as such has no relation to general health.

What is the practical implication of a higher SFh value in the average subject with 'poor' general health? It has been suggested[6] that this indicates poorer cooperation of the patient and a less reliable visual field. This would seem to infer that follow-up of such fields would then also be unreliable. We did indeed find some relation between a long-term fluctuation parameter and general health condition. In our opinion, one should be a little bit more careful than usual in judging a visual field of a person with a general medical history, because the short-term and long-term fluctuation may be higher than expected.

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INTER-TEST VARIABILITY OF COMPUTER-MEASURED INDIVIDUAL DIFFERENTIAL LIGHT THRESHOLD VALUES IN GLAUCOMATOUS VISUAL FIELDS

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The large inter-test variability of computerized threshold fields renders the interpretation of consecutive fields difficult. Normal inter-test variability is high, and these changes are even larger in glaucomatous fields. Better knowledge of the variation of glaucomatous visual fields should facilitate follow-up of patients with this disease.

We studied inter-test variation in 51 glaucomatous eyes of 51 patients with threshold-measuring computerized perimetry. The 30-2 program of the Humphrey perimeter was used, and each eye was tested four times with one week inter-test intervals. Pointwise threshold variability was calculated as a function of defect depth.

The threshold variation was large, depending on and increasing with defect depth. Already at a defect depth of approximately 6 dB the 95% threshold prediction interval for individual points included all sensitivities from normal to a maximum luminosity defect. Variability also increased with eccentricity, just as in normal fields. There was a positive correlation between inter-test threshold changes at different points in the visual field, proving a homogeneous component of the long-term fluctuation. It should be noted, however, that this correlation had a clear geographical component. Thus the correlation was considerably higher between neighboring points than between points further away from each other.

The large threshold variation and its dependence on defect depth means that, even if the sensitivity is only moderately depressed, no conclusions can be drawn from the threshold changes between two tests at a single point, regardless of the magnitude of that change. In points with normal and near-normal differential light sensitivity, on the other hand, changes even in single points may reach statistical significance. Interpretation of pointwise inter-test threshold changes in glaucomatous fields could thus be considerably more effective if initial defect depth and point location were both taken into account. The importance of these two factors is even larger if averaged results from more than two tests are compared. The complex nature of the threshold variation makes it impossible to effectively interpret consecutive field charts using only a few simple rules of thumb. The increased knowledge of inter-test variability could be used clinically, if it was incorporated in new routines for computer-assisted visual field interpretation.

Despite the fact that all patients had previous experience of computerized perimetry, and that most patients were highly experienced, there was a significant but small effect of increasing perimetric learning. This effect was small compared to the other variation, but is nevertheless worth considering. It shows that perimetric studies, *e.g.*, regarding the effect of drug treatment, should be designed to eliminate the confounding effects of increased perimetric training.

The full article will be published elsewhere.

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VARIABILITY OF AUTOMATED VISUAL FIELDS IN CLINICALLY STABLE GLAUCOMA**

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The variability of the visual field was measured in 20 patients with open angle glaucoma who appeared to be clinically stable and well controlled on medical therapy. All patients had at least four visual fields performed on the Octopus 201 perimeter with at least 12 months follow-up since their first visual field. The four most recently performed visual fields were analyzed.

The visual field was divided into ten sectors reflecting the nerve fiber layer anatomy. Calculation of variability was based on the range over which the mean threshold of each sector varied Ninety-five percent of the sectors varied over a range of less than 7 dB

The authors discuss the possibility of using this type of data to develop criteria for detection of progressive visual field loss in glaucoma.

Introduction

It has been recognized since the inception of automated quantitative perimetry that the visual field of an individual appears to fluctuate on repeated testing. Techniques for measuring the fluctuation of the visual field over time have been developed by several workers[1-10]. It has now been established that larger amounts of variability are found in the visual fields of patients with glaucoma and glaucoma suspects than in normal subjects[7,9,11-19].

Various statistical techniques have been applied to the visual field in an effort to define progressive visual field loss by detecting statistically significant change[20-23]. None of these techniques has been clinically validated. It has recently been shown that experienced clinical observers and standard statistical tests do not agree well with each other in detecting progressive visual field loss in glaucoma patients[24].

The purpose of this study is to determine the total amount of visual field fluctuation which may be expected over a long period of time in a sample of clinically stable glaucoma patients. Using this information, we may be able to develop criteria for the amount of change in the visual field which must occur to be interpreted as significant when measured by automated perimetry.

Material and methods

The charts of all patients followed in the glaucoma service of the Scheie Eye Institute were reviewed. All subjects who met the following criteria were included in the study:

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1. Diagnosis of primary open angle glaucoma, pigmentary glaucoma or pseudoexfoliation with glaucoma;
2. At least four available automated visual field examinations with at least 12 months follow-up since the first visual field;
3. Presence of a definitive nerve fiber bundle visual field defect detected on manual (Goldmann) perimetry prior to the patient's first automated visual field examination;
4. Visual acuity of 20/40 or better with no change in visual acuity greater than one Snellen line during the follow-up period;
5. No intraocular pressure greater than 19 mm Hg at any time since the initiation of the patient's present medical therapy;
6. No clinically detectable change in the appearance of the optic nerve head during the follow-up period;
7. No change in medical therapy for glaucoma during the follow-up period;
8. No laser or surgical treatment for glaucoma during the follow-up period and the 12 preceding months.

All subjects were phakic and had no other known ocular, neurologic or systemic disease likely to affect the visual field or other visual functions. All visual fields were performed on the Octopus 201 perimeter using program 32.

Each visual field was divided into ten sectors roughly corresponding to the nerve fiber layer anatomy of the retina (Fig. 1). The number of threshold determinations in each sector varied between five and 13. A mean threshold was then calculated for each sector of each visual field for each individual subject. This value is called the sector threshold.

Using each sector threshold as a single data point, the range over which the mean threshold of each sector varied was calculated. The total variability of a sector threshold was defined as the range over which that sector threshold varied over the four visual fields.

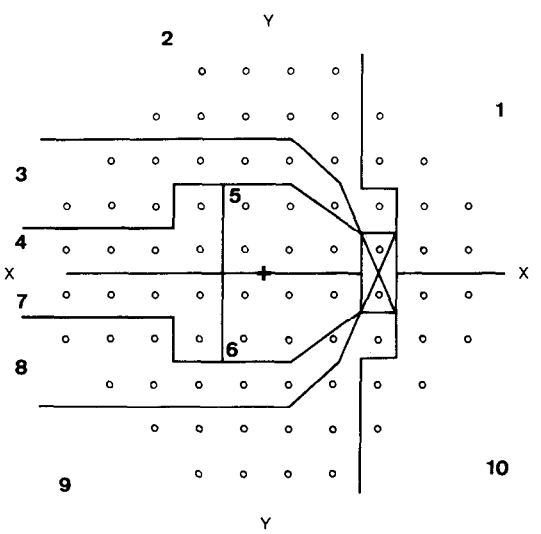

Fig 1 The pattern of test locations within the central 30 of the visual field on program 32 of the Octopus perimeter with the ten visual field sectors superimposed.

Table 1. Cumulative totals and percent of the total sample of 191 visual field sectors (20 subjects) relating total variability per sector to the number of sectors

Total variability per sector (dB)	Cumulative totals of visual field sectors and percent of total	
0	0	0.0%
1	19	9.9%
2	81	42.4%
3	123	64.4%
4	160	83 8%
5	171	89.5%
6	180	94 2%
7	184	96.3%
8	190	99 5%
9	191	100 0%

Results

Twenty subjects were found who satisfied the inclusion criteria. The average mean sensitivity of each subject's visual field for the entire sample was 15.8 dB (range 5.4 - 24.7 dB). The study, thus, included a sample of glaucoma patients ranging from minimal to severe damage. Of the 200 visual field sectors in the sample, there were nine sectors of four subjects whose sector threshold was always 0 dB. These sectors were also excluded from further calculations of variability.

Table 1 shows the cumulative frequency of the variabilities per visual field sector. Fig. 2 shows the frequency distribution of the sector threshold variability related to the number of visual field sectors in the sample.

As can be seen from Table 1, 95% of the sectors had a variability of less than 7 dB and 99% of the sectors had a variability of less than 8 dB.

Discussion

With one exception[4], previous studies of long-term fluctuation of glaucoma patients have evaluated multiple visual fields performed over a relatively short period of time[11,16,25]. Our study reproduces the usual clinical situation in which a patient is examined and perimetry is performed at intervals of several months over a period of one or more years.

In general, calculations of fluctuation in automated perimetry have been based upon the variance of repeated determinations of threshold. Some authors, however, have based variability calculations on the range[10,26]. In clinical practice, there are certain advances to using the range as the measure of variability. The range of a series of values is more readily obvious without calculation than the variance or standard deviation.

Based on our entire sample of 191 sector threshold determinations, one can now define the upper limit of change in visual thresholds which might be considered a result of random fluctuation. For example, a change of 7 dB or more in a single sector threshold will be observed due to random fluctuation only 5% of the time.

There are, however, ten sectors in each visual field. The probability that any number (r) of these 10 (n) sectors in a single patient's visual field will vary by at least 7 dB or any other specified amount due only to random fluctuation is given

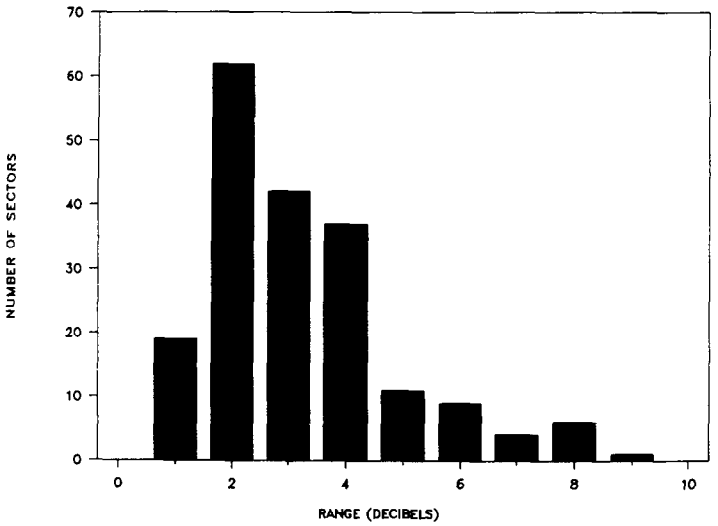

Fig 2 Frequency distribution showing the number of visual field sectors against the variability of the sector threshold calculated from the range of the sector thresholds over time.

by the following binomial formula[27]:

$$P = \frac{n!}{(n-r)!r!} \cdot p^r q^{n-r}$$

where

n = number of sectors in the visual field[10]
r = number of sectors in which the specified change occurs[1-9]
p =probability point will vary by the specified amount or more (0.05 or 0.01)
q =probability point will vary by less than the specified amount (0.95 or 0.99)

Thus, for one sector (r = 1), this probability is 0.264. In other words, even though the probability of a single sector varying over a range of 7 dB or more is less than 5%, the probability of observing any one of a patient's ten sectors varying by at least this amount due to random fluctuation alone is 26%. The probability, however, of any two sectors (r = 2) in the same visual field varying by at least 7 dB is only 0.046.

This analysis is not entirely valid because the binomial expansion formula cited above assumes that the factors being analyzed are independent variables. It has been shown that adjacent test locations do not vary independently. The same is probably true for adjacent sectors or other groups of test locations, although this has not yet been shown.

Our sample size was too small to allow analysis of the probabilities of finding various levels of fluctuation for each of the individual sectors. The confidence intervals would have been too large.

In any case, the methods and data outlined in this pilot study point the direction for development of rational criteria for progressive visual field loss in glaucoma based upon probabilities. Table 2 for instance shows the number of visual field sectors which would have to change by different specified amounts to be considered

Table 2 Number of visual field sectors whose sector threshold would have to change by various specified amounts to be considered outside the expected range of random variability at the 0.05 and 0.01 probability levels

Probability level	>0.05	>0.01
Number of sectors	Range of variability (dB)	
1	8	9
2	7	8
3	6	7
4	4	6

outside the range of random fluctuation at the 0.05 and 0.01 probability levels if we assume for the sake of demonstration that the sectors are varying independently. For example, if one sector varies by 8 dB, then this is expected to be due to physiologic fluctuation less than 5% of the time, or if three sectors vary by 7 dB, this is expected to be due to fluctuation less than 1% of the time, etc. When better data are available, these types of guidelines should prove useful both for clinicians who follow patients with automated perimetry as well as for researchers using the visual field to evaluate risk factors or therapy in glaucoma.

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RATE OF PROGRESSION OF DISCRETE AREAS OF THE VISUAL FIELD

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Recent studies have shown that analysis of discrete portions of the visual field, rather than the entire field, may be more useful in the management of glaucoma1,2 The theory investigated in the current study was that different areas of the visual field progress at different rates

Nineteen glaucoma patients were selected from a glaucoma referral practice in San Francisco. Each patient had at least five visual fields performed using the Humphrey Field Analyzer program 30-2 and met minimum requirements for visual acuity, pupil size, reliability indices, and fixation losses If both eyes of a given patient met these requirements, one eye was randomly selected for analysis

For each eye, 48 clusters of four points each were identified for analysis Regression analysis was used to analyze the progression of these 48 areas through the five fields The variability of the slopes of the resulting regression lines was examined using graphical means Preliminary findings indicate that different areas of the visual field progress at different rates

Introduction

In this study, the rates of sensitivity change of four-point cluster areas of the visual field for the eyes of glaucoma patients were measured. Our goal was to determine whether we could objectively recognize change in the visual field by analyzing smaller portions of the visual field. The results allow for evaluation of the statistical significance of changes in sensitivity of small areas of the visual field with time.

Methods

Glaucoma patients who had at least five visual fields performed with the Humphrey Field Analyzer program 30-2 were selected from a glaucoma referral practice in San Francisco. Only those eyes that met minimum reliability requirements for all five sequential examinations were used in the analysis. If both eyes of a given patient were eligible for the study, the eye to be analyzed was randomly selected using a random numbers table.

Criteria for inclusion were: a visual acuity of 20/40 or better on each examination, a pupil size of at least three millimeters at each field, and less than 20% false negative and/or false positive responses on any of the five visual fields. No more than 20% fixation losses were allowed at any field. In addition, eyes were excluded from the study if they had laser treatment or surgery during the study period. Nineteen eyes met all eligibility criteria for all five examinations and were included in this study.

For each eye, 48 clusters of four Humphrey visual field points were identified for analysis. These clusters were formed by grouping every possible square of four contiguous points. Overlapping squares were possible, but no area crossed the horizontal midline. The mean sensitivity (S) at each visual field was computed by averaging the sensitivities of the four points included in each cluster.

Regression analysis was used to analyze the progression of these 48 areas through the five fields. These mean sensitivities were used as the dependent variable, with time between fields as the independent variable, according to the following regression equation:

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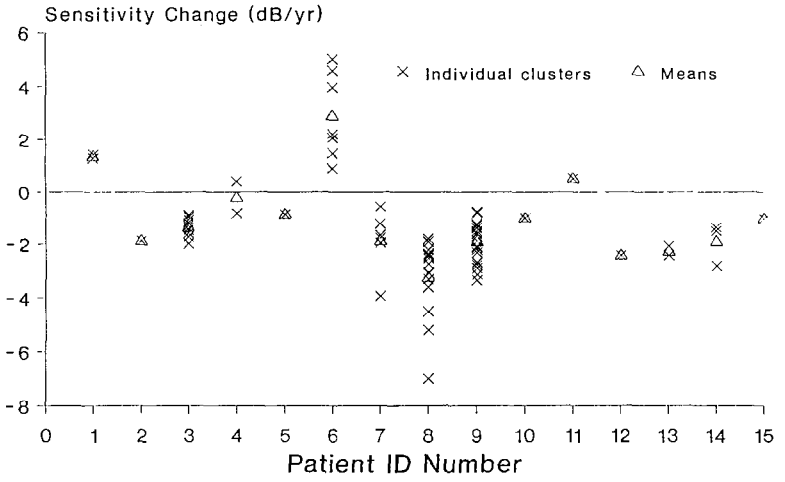

Fig 1 Rates of sensitivity change of four-point clusters for 15 patients. The values of the rates of sensitivity change (slope) (y-axis) are given for each patient (x-axis). Both individual slopes (crosses) and mean slopes (open triangles) are shown

$$S = a + b(T)$$

where S = mean sensitivity of each cluster, a = mean sensitivity intercept, b = slope of the regression line, and T = time from the first field to subsequent fields.

This analysis was repeated for each of the 48 clusters of the field identified above for each eye. Clusters that had a significantly positive ($p<0.05$) regression slope were classified as getting better. Clusters with a significantly negative slope ($p<0.05$) were classified as getting worse, and clusters with a regression slope that did not differ significantly from zero were said to be unchanged.

Results

Of the 912 four-point clusters followed over five fields in 19 eyes of different patients, 85 four-point clusters in 15 eyes showed statistically significant rates of change in sensitivity or slopes. The large fluctuations in measurements obtained from individual clusters limit the number of slopes that can be determined to be significantly different from zero. This limitation is more pronounced among the areas in which sensitivity is initially more severely depressed. Nevertheless, sufficient numbers of areas have been followed over successive fields to indicate correlations and trends. This study produced several findings.

1. Within a given eye, the rate of change of the various four-point clusters is highly variable (Fig. 1.).
2. The location of a specific four-point cluster was not a factor that contributed to its having a significant rate of change.
3. Four-point cluster analysis indicates that higher mean initial sensitivity correlates with higher mean rate of loss of sensitivity among the population of eyes

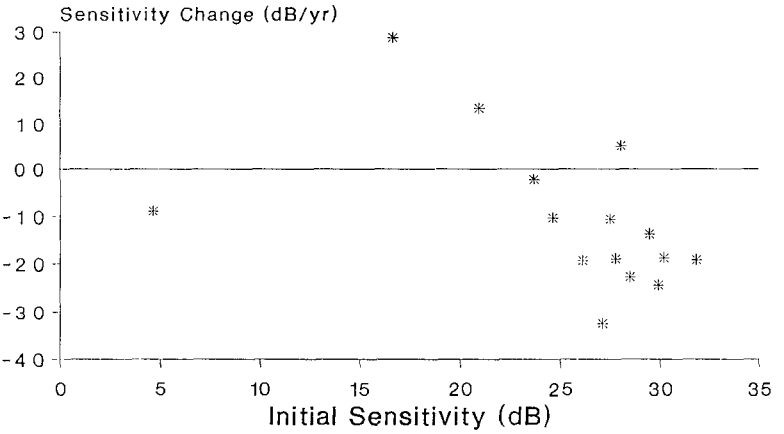

Fig 2 Scattergram of mean rate of change of sensitivity (slope) vs mean initial sensitivity Each point represents the values of mean slope (y-axis) and mean initial sensitivity (x-axis) The averages were taken over measurements of sensitivity in all four-point clusters showing significant change in a given patient. The correlation coefficient between mean slope and mean sensitivity is $r = 0\ 6$ ($p = 0\ 03$)

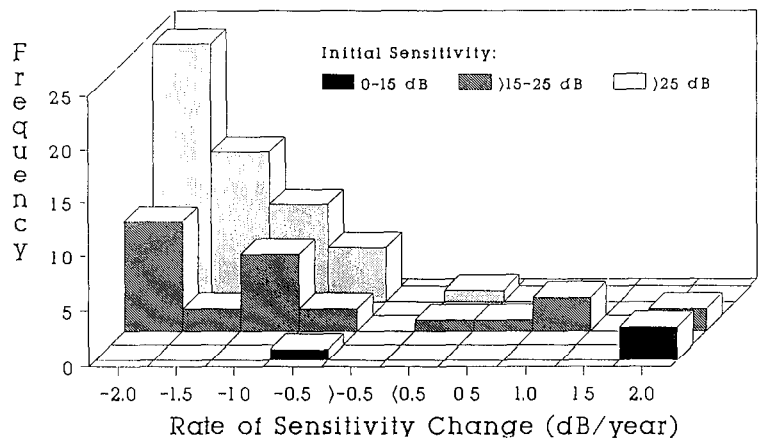

Fig 3 Frequency of significant slopes by initial sensitivity range Four-point clusters were divided into three groups according to their initial sensitivities: 0-15 dB (black bars), 15-25 dB (gray bars) and 25 dB (shaded bars). The number of clusters of each of these groups (vertical axis) having different positive and negative slopes (horizontal axis) is shown

that were examined ($r = -0.6$, $p = 0.3$), although there is a large variation of initial sensitivities and slopes for different areas within individual clusters and among different eyes (Fig. 2).

4. The number of four-point clusters with slopes that are significantly different from zero is proportionally greater among clusters whose initial sensitivity is greater than 25 dB than among clusters whose initial sensitivity is less than 25 dB, with few significant changes in four-point clusters with initial sensitivities that are less than 15 dB (Fig. 3).
5. The number of four-point clusters with significant rates of change of sensitivity that are respectively positive or negative is proportionally greater among clusters with initial sensitivities that are respectively less or greater than 25 dB (Fig. 3).

Discussion

The small number of significant changes in sensitivity observed among four-point clusters in the group with the lowest values of initial sensitivity may be a result of several factors: (1) A previous study has shown that fluctuation in sensitivity increases with decreasing sensitivity[3]. (2) Clusters with low initial sensitivity cannot decrease greatly and therefore may not diminish sufficiently to establish statistical significance. (3) The lower limit of the perimeter (absolute scotoma, dB = 0) limits the measurement of negative progression of defects.

These and previous findings suggest that analysis of four-point clusters, rather than analysis of larger areas of the field, allow earlier recognition of statistically significant change. Change in visual sensitivity can be recognized in individual four-point clusters although similar sequential measurements taken over the entire field may not show significant change.

In addition, there is the question of whether increasing the stimulus would broaden the range of measurement and allow earlier detection of change in clusters with higher initial sensitivities and more reliable detection of change in clusters with lower initial sensitivities.

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INTER-POINT CORRELATIONS OF DEVIATIONS OF THRESHOLD VALUES IN NORMAL AND GLAUCOMATOUS VISUAL FIELDS

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Abstract

The authors studied the dependence of measured threshold values within individual visual fields in 84 fields of 84 normal subjects and 90 fields of 90 patients with glaucoma of varying severity Central 30° full threshold fields obtained with the 30-2 program of the Humphrey Field Analyzer were used In each visual field, they computed the correlations between the pointwise deviations of the measured threshold values from the age-corrected normal threshold values as obtained with the Statpac program These deviations were more closely correlated for neighboring points than for points situated further away from one another. The correlations were larger in pathological than in normal fields.

The visual field was also divided into 15 sectors according to the projection of the retinal nerve fiber layer. In the glaucoma fields, mean correlation coefficients were approximately 0 1 units higher for points within the same sector, than for points located at the same distance but in another sector. This difference was largest in moderately disturbed fields (MD between -6 and -15 dB), but was also present in almost normal fields from glaucomatous eyes In the normal group of subjects, on the other hand, there was no statistically significant difference between correlations for pairs of points situated in the same sector and pairs not located in the same sector

The results show that in both normal and abnormal fields, points with particularly low or high sensitivities tend to cluster This is of importance for the interpretation of visual field data. It also emphasizes the importance not to regard individual threshold measurements in one field chart as independent measurements. It should be possible to use inter-point correlations for the classification of visual fields, particularly if correlation coefficients are separately calculated within and between sectors.

Introduction

With the introduction of computerized perimetry, it has become increasingly apparent that recognizing pathological field loss is a question of discriminating between normal and pathological field variation. In pathological visual fields, points with reduced sensitivity are of course usually not randomly distributed across the field but rather grouped together in areas of more or less recognizable shapes, *e.g.*, the typical arcuate defects in glaucoma. However, it seemed to us that, in normal fields as well, points with low sensitivity often occurred in the vicinity of each other. Knowledge of such covariation of deviations of threshold values from age-corrected normal values should be useful when algorithms for visual field interpretation are to be developed.

The aim of this study was to investigate such covariation of deviations in normal and glaucomatous eyes and especially to investigate whether points located within a given sector defined by the courses of nerve fibers across the retina would show covariations different from those of points in different sectors.

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Material and methods

Subjects

We studied 84 eyes from 84 normal subjects and 90 eyes from 90 patients with glaucoma of varying severity. The normal subjects were randomly chosen from a normal population with ages ranging from 20 to 80 years (mean 52). From these subjects, abnormal subjects had been excluded according to predetermined criteria[1]. The glaucoma patients were followed at the glaucoma clinic of the Eye Department at Malmö General Hospital. Their ages ranged from 33 to 82 years (mean 66). Most eyes had previously documented field loss, but some eyes were included despite the fact that previous field tests were seemingly normal. In these eyes, the diagnosis of glaucoma was founded on combinations of findings of documented glaucoma with field loss in the fellow eye in conjunction with abnormal disc topography and elevated intraocular pressure in the eye studied. All patients and normal subjects had previous experience of computerized perimetry.

All participants were tested with the 30-2 program of the Humphrey perimeter. This program measures the differential light threshold at 76 points in the central 30° field using a repetitive up-and-down staircase technique with steps of 4 and 2 dB[2,3].

Correlations

In each field we calculated the deviations of the measured threshold values at each point from the age-corrected normal mean threshold values. The latter are included in the Statpac statistical analysis program of the instrument[4,5]. The correlation between the pointwise deviations of the measured threshold values from the age-corrected normal threshold value was then computed as a function of the distance between the points.

The distance between two neighboring points in the 30-2 test fields is 6°. Then the possible distances between two points in the visual field are 6°, $\sqrt{2}\cdot 6^{\circ}$, $2\cdot 6^{\circ}$, $\sqrt{5}\cdot 6^{\circ}$,..., $\sqrt{90}\cdot 6^{\circ}$. These distances were divided into eight intervals to achieve greater accuracy in the estimation of the correlations. This results in a larger number of pairs of points at each distance. Interval indices for the distance between points number i and j were defined as a_{ij} where

$$a_{ij} = 1,2,...,8 \quad \text{if} \quad i \neq j \quad \text{and} \quad a_{ii} = 0, \quad i,j = 1,2,...,n,$$

where n (=74) is the number of points in the field charts (excluding two points in the blind spot). With x_i as the measured threshold value and N_i as the age-corrected normal value, the deviation from the normal value at point number i is $y_i - x_i - N_i$, i=1,...,n.

For each field test the covariance c(a) between the deviation from the normal value in points at distances with index a was calculated as

$$c(a) = \frac{1}{m_a - 1} \sum_{i=1}^{n} \sum_{j;a_{ij}=a} (y_i - \bar{y}) \cdot (y_j - \bar{y}), \quad a = 0,\ldots,8,$$

where m_a is the number of terms in the sum, *i e* , the number of point-pairs with inter-point distance index a, and

$$\bar{y} = \Sigma_{i=1}^{n} y_i / n$$

is the mean of the deviations over the field. Thus, c(a) represents the covariation

of the deviations of the sensitivity from the age-corrected field, adjusted to the individual mean sensitivity level. Not subtracting the mean deviation $\bar{y}$, would just mean that the spatial covariation in the individual pattern would be masked by a dominating individual shift of the general sensitivity level. Subtraction of the mean deviation will automatically cause some correlations to be negative, with the most positive values being associated with point pairings which are most closely correlated.

The variance of the deviations in the field is the same as c(0). Thus the correlation $\rho(a)$ for each distance is

$$\rho(a) = c(a)/c(0), \quad a=1,...,8.$$

Sectorization

The visual field was then divided into 15 sectors according to the anatomy of the nerve fiber layer (Fig. 1). We used the pattern devised by Wirtschafter *et al.*[6]. Covariances were then calculated separately for pairs where points were located within the same sector, $c_s(a)$, with possible distances a=1,2,...6, and for pairs of points in different sectors, $c_d(a)$, a=1,2,...,8. This gave us the corresponding correlations

$$\rho_s(a) = c_s(a)/c(0), \quad a=1,...,6,$$

and

$$\rho_d(a) = c_d(a)/c(0), \quad a=1,...,8.$$

Mean correlations were calculated separately for normal and glaucomatous eyes. Glaucoma fields were divided into groups with increasingly severe field loss:

	MD > −6 dB	mild or no field loss
−6 dB≥	MD > −15 dB	moderate field loss
−15 dB≥	MD > −24 dB	severe field loss
−24 dB≥	MD	very severe field loss

The Mean Deviations (MD) for each test were calculated as

$$MD = \frac{\sum_{i=1}^{n} y_i/\delta_i^2}{\sum_{i=1}^{n} 1/\delta_i^2},$$

where δ_i^2 is the normal inter-patient variance at point i[4]. In the normal group, all tests had MD values above -6 dB.

Results

The mean correlations in the two groups are illustrated in Fig. 2. As seen in Fig. 2a, the mean correlation between the deviations was larger for neighboring points than for points further away from one another. This was true in normal eyes as well as in the eyes with glaucoma. Correlations were generally larger in glaucoma ($p<0.001$ for a=1,2,3; *t*-test).

In the glaucoma group, the correlation at neighboring points (a=1,2) also increased with the severity of the field loss ($p<0.001$; *t*-test) (Fig. 2b).

In the fields from the glaucomatous eyes, correlations were higher for points within the same nerve fiber sector than for points in different sectors (Fig. 3). The

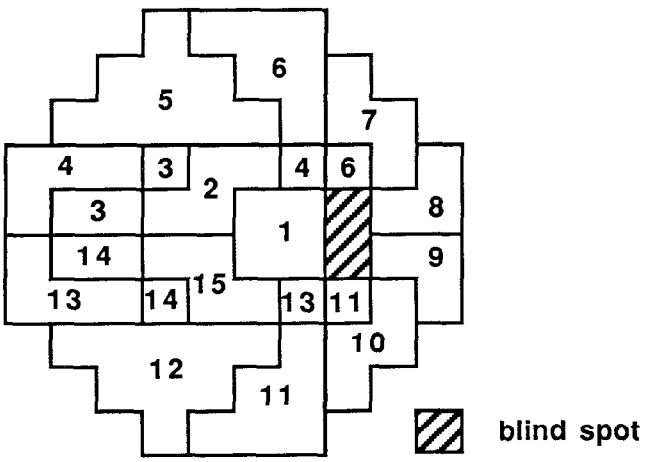

Fig 1 The 76 points in the visual field chart divided into 15 sectors according to the nerve fiber anatomy.

difference was largest in moderately disturbed fields (MD between -6 and -15) but was also still present in almost normal fields (Figs. 3a-d).

In fields of normal subjects on the other hand, the correlations were generally smaller. Here differences in correlations between points located in the same sector and points not located in the same sector were small (and not statistically significant) (Fig. 4).

Discussion

It has long been understood that there is a strong correlation among threshold sensitivities at the various points in the visual field; this is the essence of the concept of the normal hill of vision. Our analysis does not deal with correlations between such sensitivities, but with deviations of measured threshold values from the age-corrected normal threshold values of the normal hill of vision.

Our results suggest that when normal subjects produce visual field results that differ significantly from expected values, these deviations tend to cluster together more than would be predicted by chance. This confirms other recent findings[7] and indicates that a test result should not be classified as abnormal just because the measured threshold happens to be slightly lower in a few neighboring points than in the rest of the field. It seems as if normal hills of vision may vary slightly in shape among individuals, instead of showing only random variation around the age corrected normal reference field.

Second, our findings quantify the expected pathophysiologically-based spatial correlations found among abnormal points in glaucoma. Currently available visual field indices such as MD, LV, and PSD[4,8] do not make use of these correlations, and it is thus not surprising that they often fail to detect obviously abnormal visual fields. Thus, to date, these indices have been useful mostly in longitudinal follow-up and not in diagnosis of individual fields.

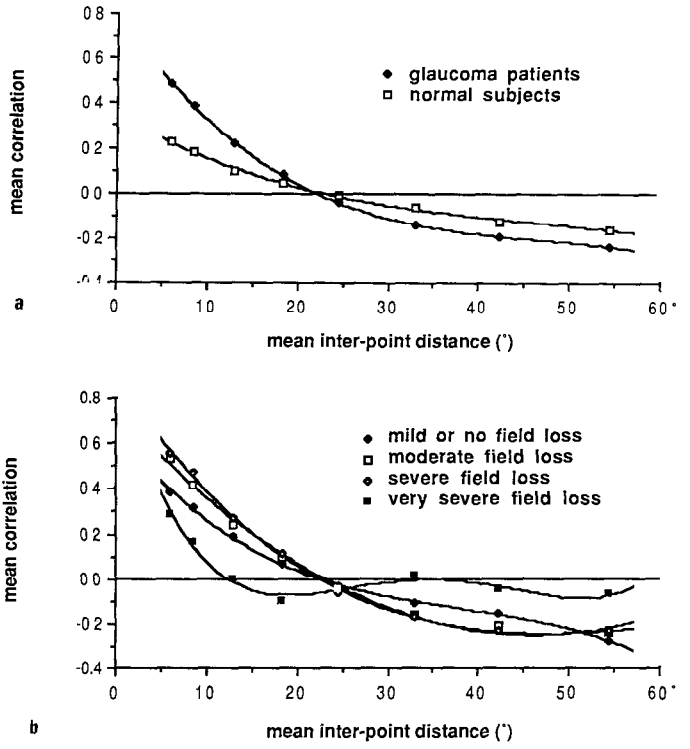

Fig 2 Mean correlation as a function of distance. a Mean correlations for 84 normal and 90 glaucomatous eyes b Mean correlations for 90 glaucomatous eyes grouped according to the severity of their field loss

The results of this study indicate that it should be possible to improve separation between normal and abnormal results if correlation between neighboring points is used. The recognition of glaucomatous field loss should be facilitated if correlation is divided into correlations within and between nerve fiber layer sectors.

Part of the observed covariation of measured threshold values is probably due to test artifacts. Disturbances induced, *e.g.*, by ptosis or rims of correcting lenses, may lead to covariation of results in neighboring points. Such disturbances should be limited to the peripheral part of the tested field, however. Therefore, they cannot be the only explanation for the observed covariation, since dependence between results at neighboring points was also found paracentrally.

The thresholding algorithm tests points in a growing pattern starting from four primary points[2,3], and therefore introduces some dependence. The transfer of measured threshold values as starting values for the thresholding staircases in neighboring points and the temporal sequencing of points combined with fatigue[9] could both contribute to this. These effects would not, however, explain the higher within vs across sector correlations found in glaucoma.

The sectorization pattern used in this study[6] was not optimal. We know that the true pattern of the retinal nerve fiber layer is asymmetric around the horizontal meridian. It is therefore possible that correlation differences between points within and across sectors may increase if the sectorization is brought into closer agreement with normal anatomy. This work is currently under way.

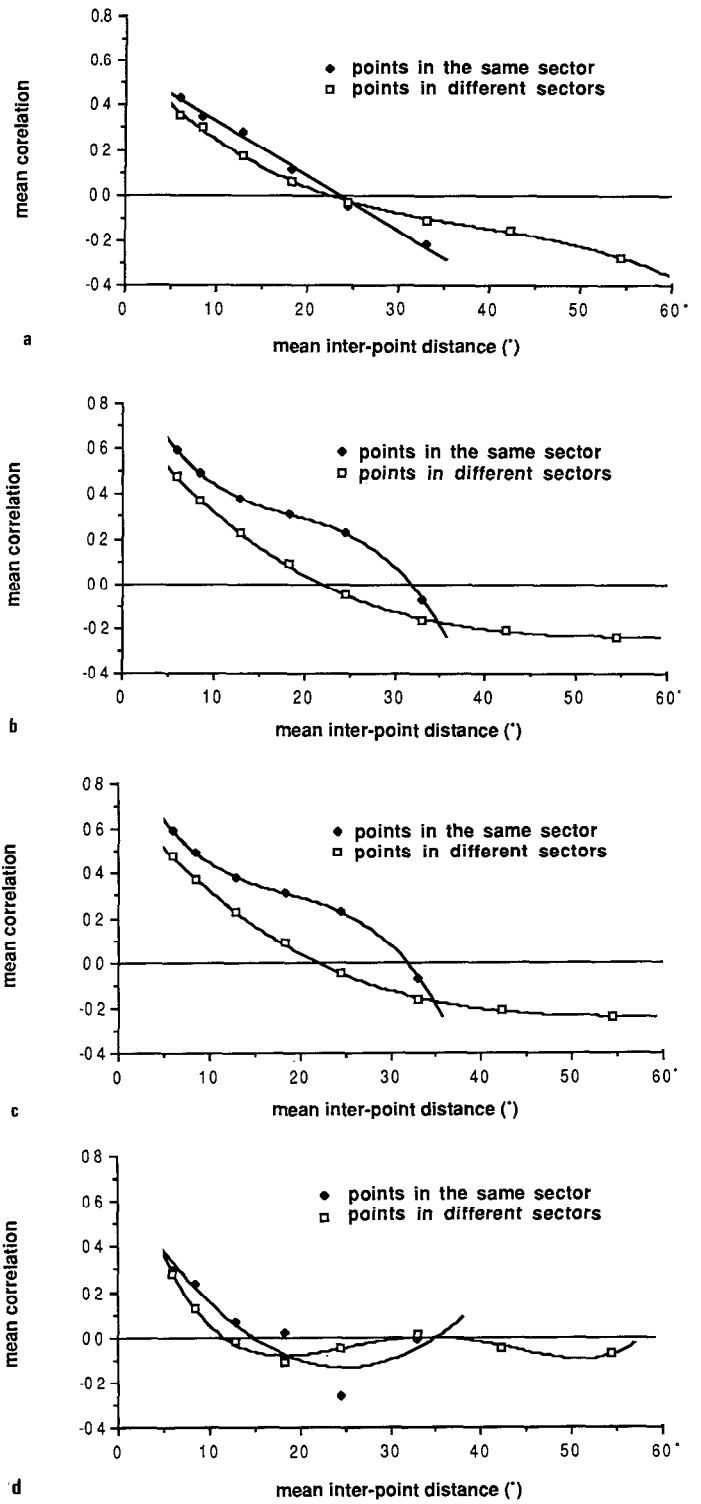

Fig 3 Mean correlations with respect to sector affiliation in 90 glaucomatous eyes a 25 eyes with mild or no field loss (MD > –6 dB) b. 41 eyes with moderate field loss (–15 dB < MD < –6 dB) c. 19 eyes with severe field loss (–24 dB < MD <–15 dB) d. five eyes with very severe field loss (MD < –24 dB)

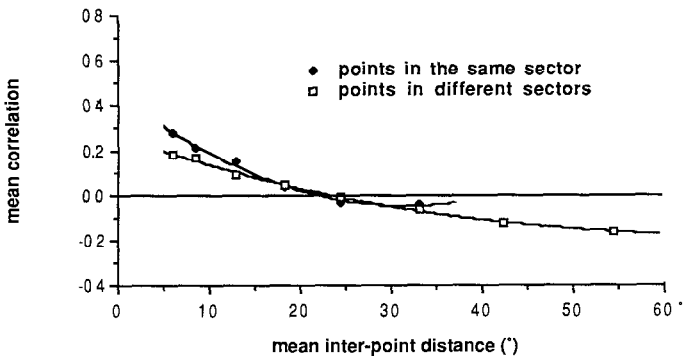

Fig 4 Mean correlations with respect to sector affiliation in 84 normal eyes

In summary, it is clear that in the interpretation of visual fields, one should remember that even in field charts from normal subjects, points with particularly high or low threshold values are not randomly distributed, but are often grouped. In glaucomatous fields this covariation is larger within nerve fiber sectors than between sectors. The diagnostic value of an arcuate defect is therefore larger than that of a defect which does not respect the normal nerve fiber pattern.

It should be possible to enhance existing statistical programs for visual field interpretation, if these physiological and abnormal correlations are taken into account.

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CLUSTERING OF DEPRESSED POINTS IN THE NORMAL VISUAL FIELD

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We studied the tendency of depressed points in normal fields to occur in groups. One hundred and thirty-four eyes of 134 normal subjects were subjected to static threshold perimetry using the 30-2 program of the Humphrey perimeter Points were defined as abnormal if significantly depressed ($p<0$ 05 or $p<0.01$, respectively) in the probability maps of the Statpac program In each field, we counted the number of abnormal points at these two levels, and the percentage of such points which appeared in clusters. These percentages were plotted versus total number of abnormal points, and the results were compared to the outcome of computer simulations where abnormal points were randomly distributed.

The depressed points of actually measured fields were clustered to a much greater extent than those of the simulated fields The differences were most pronounced in fields with moderate numbers of depressed points, or when using the stricter of the two criteria for abnormality Our results indicate that in fields from normals, depressed points have a tendency to occur in clusters In interpretation of visual fields, individual threshold values should not be regarded as independent observations Small clusters of depressed points are no proof of pathology, even if each point reaches statistical significance

Introduction

Computerized threshold perimetry is now generally accepted as a more sensitive method for the detection of early field loss than standard manual perimetry[1-4]. However, computerized fields include significant amounts of physiological variation and thus the interpretation of fields in the zone between unquestionable normality and obvious pathology is often difficult. The interpretation of fields with only a few subnormal threshold values is especially difficult. A relative defect including only one test location is usually not immediately regarded as pathological since such a result often occurs by chance alone. Anderson[5] has suggested that even tests with several such depressed points should not be considered definitely pathological if the points are scattered randomly. Abnormal points located adjacent to each other have, however, often been assumed to be indicative of pathology[5-7]. Recent studies of normal subjects have shown that threshold deviations, from the age-corrected normal values, are positively correlated in neighboring points[8]. This suggests that, in a normal visual field, depressed points, if present, would have a tendency to occur in groups. The evaluation of this tendency was the purpose of the present study.

Material and methods

Selection of material

We studied 134 eyes of 134 normal subjects. Their mean age was 59 years (range 22-89). Two groups were included. One hundred and twenty-five were healthy volunteers invited for eye examination and visual field testing, and nine were patients treated for minor external eye disorders not influencing the visual field.

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All eyes were normal on slit lamp examination and ophthalmoscopy and had an IOP< 22 mm Hg and a corrected visual acuity in the tested eye of 0.5 or better. A majority (119 subjects) had some previous experience of automated perimetry. Each subject underwent static threshold field testing using the 30-2 threshold program of the Humphrey perimeter (Full Threshold mode). This program measures differential light sensitivity at 76 points in the central 30° field using a repetitive staircase technique with steps of 4 and 2 dB[9,10]. Test points are equally distributed with an interpoint distance of 6°.

Analysis

Points were defined as abnormally depressed if reaching significance in Statpac pattern deviation probability maps.

The Statpac program produces these probability maps by calculating the decibel deviation from age-corrected normal threshold at each point in the field[11]. Two points in the blind spot area are excluded (x = 15, y =± 3). In the pattern deviation maps, all deviations are then uniformly adjusted in order to correct for any overall deviation from normal of the height of the measured hill of vision. The purpose of this procedure is to eliminate the disturbing influence of, *e.g.*, media opacities[11,12]. The statistical significance of each of these height-adjusted deviations is then determined by comparison with the normal reference values of the program[11].

We analyzed our results in the following way: First the number of abnormal points in each field was counted, as well as the number of clustered points. A clustered point was defined as having at least one neighboring significantly depressed point. Neighboring points were located at a distance of 6° (therefore each test location was surrounded by four neighboring points, except in the most peripheral ring and in the vicinity of the blind spot). The percentage of clustered abnormal points was then calculated for each field. Calculations were repeated defining an abnormal point in two different ways. The first criterion used all points reaching at least the $p<0.05$ level; the second and stricter criterion counted as abnormal only points at the $p<0.01$ level or higher.

Computer simulations

A computer was programmed to create visual fields where abnormal points were randomly distributed. One thousand simulated visual fields were created for each possible number of abnormal points between 2 and 74. We analyzed the resulting 73000 simulated fields in the same way as the actual fields from our normals. The percentage of clustered points was calculated in each field chart. The median of these percentages was calculated in each group of 1000 fields, where all fields in one group had the same number of significant points (from 2 to 74). The percentages from the simulated fields were compared to the data from the measured fields.

Results

The frequencies of clustering for both normal and simulated data are shown in Fig. 1. The measured fields showed significantly more clustering than was predicted from the simulated fields. This difference was most marked in the range of three to six abnormal points and when the $p<0.01$ criterion for abnormality was used.

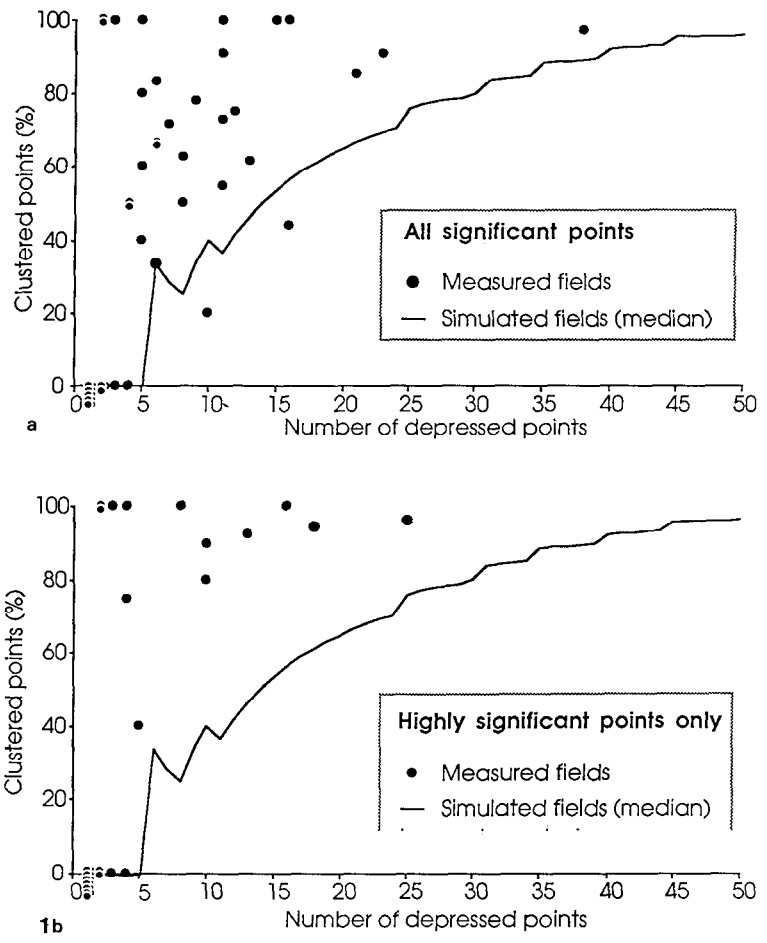

Fig 1 Scatterplot showing the total number of abnormal points (x-axis) using the $p<0.05$ criterion (a) and the $p<0.01$ criterion (b) in each field and the percentage of these points that had at least one neighboring depressed point (y-axis). Measured fields are represented by solid squares and the median values of the simulated fields are represented by a line In normals, significant points appeared in clusters to a significantly greater extent than that predicted from random situations.

Discussion

Our results call into doubt a commonly applied rule of thumb for evaluating perimetric results. Contrary to this rule of thumb, we found that depressed points in normal fields are not randomly distributed. Instead, depressed points occurred in clusters much more often than expected based on chance alone.

In some instances this was due to trial lens artifacts or ptosis (Fig. 2a). However, areas with clusters of depressed points were often located more centrally, where these disturbing factors should not interfere (Fig. 2b). The reason for the clustering might be that tested fields really contained regions with diminished differential light sensitivity. Such depressions would be expected to be reasonably reproducible on repeated testing. In fact, some indications of such reproducibility have been found[13].

Another contributing factor may be that irrelevant pathology had gone undetected

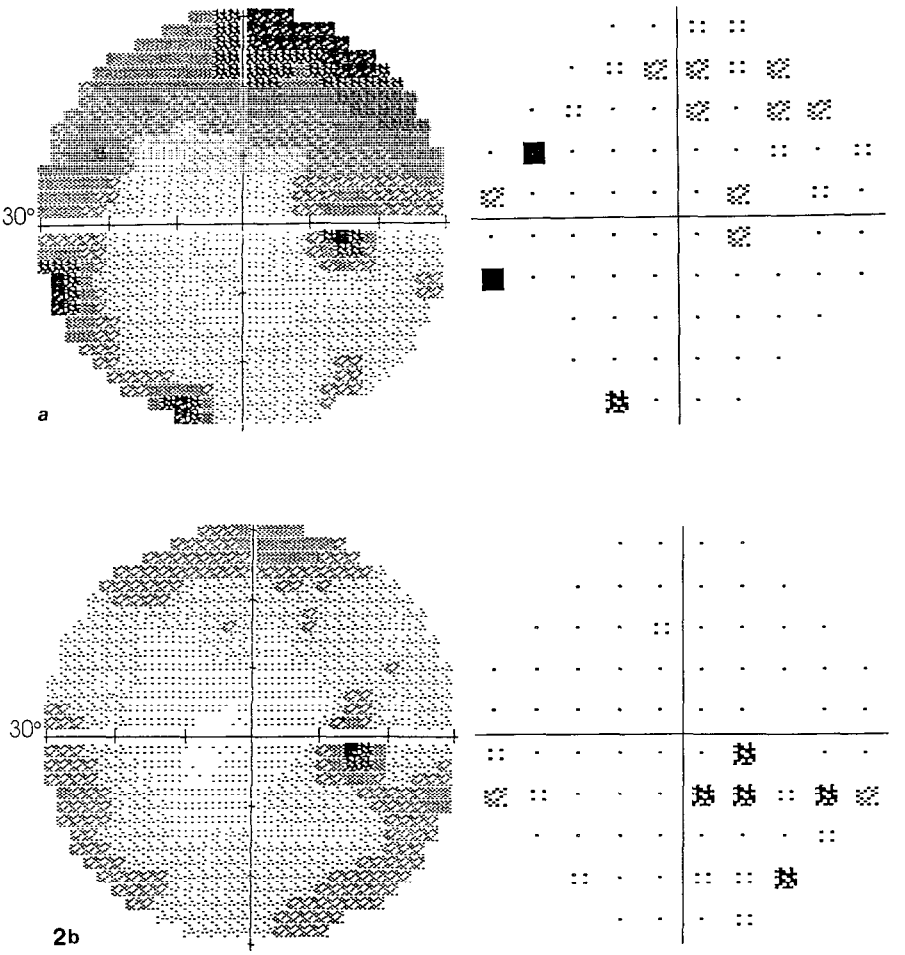

Fig 2 a Clusters of depressed points in the upper midperiphery are frequently due to ptosis. b. In normals, areas of diminished sensitivity also occur in the paracentral part of the field, where ptosis and trial lens artifacts should not play a role

in some subjects. Visual field defects are not uncommon in randomly chosen subjects, and the reason for such defects may easily escape detection[14]. Also the thresholding algorithm may play a role, since the starting levels of the bracketing procedure are determined from measured thresholds at neighboring points.

Nevertheless, the present results have clear clinical implications. The results indicate that, in the absence of obvious ocular disease, great caution should be used before classifying field charts containing small areas with depressed sensitivity as definitely abnormal. In view of the present results, it now seems desirable to find the normal limits for these clusters of points with low differential light sensitivity. These limits will probably vary in different areas of the visual field. It is also important to find out whether these depressions in the hill of vision of normal subjects are commonly reproducible.

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THRESHOLDS USING SINGLE AND MULTIPLE STIMULUS PRESENTATIONS

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The objective of this research was to see if new threshold strategies could reduce the variance of results found with the widely practiced single stimulus techniques Three different strategies were used to measure the differential light threshold, (1) multiple stimulus, (2) single stimulus, and (3) a two alternative forced choice strategy Thresholds measured with the multiple stimulus technique were found to be lower (difference 0.95 dB) and to have a smaller standard deviation (1.36 versus 1 64 dB) than those measured with the single stimulus technique. The improved performance of the multiple stimulus technique is believed to be due to psychological factors related to the examination strategies The dialogue between the patient and the perimetrist, which is inherent in the semi-automated multiple stimulus technique, helps to maintain patient attention throughout the period of the examination

1. Introduction

There are many different strategies that can be utilized to statically test the visual field[1]. For threshold measures, the most widely practiced technique is the repetitive up/down strategy[2,3] while for screening it is a suprathreshold technique usually combined with gradient adaptation and patient threshold compensation. A modification to the suprathreshold technique, which was initially introduced by Harrington and Flocks[4], is that of presenting several stimuli at the same time, the multiple stimulus technique[5]. This technique has several advantages over the single stimulus technique, it speeds up the examination, it reduces the likelihood of the patient guessing and by being semi-automated[6] it promotes a dialogue between the patient and the perimetrist which has certain psychological advantages[7].

Greve[8] reported that when the stimuli in a multiple stimulus pattern are separated by more than 2 degrees, they had no interactive effect upon each other and that the results could therefore be treated in the same way as if each stimulus had been presented singly. The procedure adopted by Greve collected data from multiple and single stimulus procedures within the same experimental trial. Any psychological effects upon the threshold[7] would have been masked by this procedure.

In the present study, we are going to measure thresholds with both multiple and single stimulus strategies, only this time we will be using techniques which closely mirror those used in routine clinical perimetry. Our objective is to see if alternative strategies can reduce the variance of results found with single stimulus techniques and thereby point the way to new improved strategies for threshold perimetry.

We are also going to report upon the results from a two alternative forced choice technique which, by its nature, is free from the effects of subjects' criteria[9]. The results from this experiment will give an indication as to whether any differences between the single and multiple stimulus techniques are the effect of shifts in subject criteria.

2. Method

The data were collected with a Henson CFS2000 visual field screener[10,11] for which three special threshold programs had been written, a multiple stimulus

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program, a single stimulus program and a two alternative forced choice program. All three programs used the same 25 stimulus locations whose eccentricity fell between 10 and 15 degrees and whose radial position avoided the blind spot regions. Prior to running the programs, an estimate of the patient's threshold was made with the CFS2000 operating in its normal mode. All three test programs presented stimuli at intensities which ranged from 0.3 log units below to 0.3 log units above the estimated threshold in 0.1 log unit steps. At least 20 stimulus presentations were made at each of the seven intensity levels. The intensity of each presentation was randomly selected from one of the seven levels with the condition that an even number of presentations at each intensity level would be obtained after the first, second, third and fourth quarters of each session. This condition allowed us to check the results for any systematic changes in threshold throughout a single recording session. The subjects were informed as to the nature of each program and informed that, on occasions, they may not see the stimulus/stimuli. Each presentation was preceded by an audible tone and the results were stored on magnetic disc for later analysis. The order in which the programs were presented varied in such a way that each occupied approximately equal numbers of first, second and third positions. Only one eye from each subject was used. The time taken to run each program was automatically recorded by the computer, this did not include the time taken in the initial estimate of the threshold or instructing and aligning the subject.

2.1. Subjects

Eighteen subjects were tested with each of the three programs. They were selected from the students and staff of the University. Their ages ranged from 20 to 63 and they wore any habitually worn near correction throughout the tests.

2 2. The multiple stimulus program

Each pattern consisted of either two, three or four stimuli, the subject's task was to verbally report the number seen, which was subsequently entered into the computer by the operator who then selected and presented the next stimulus pattern. The dialogue between the subject and the operator was essentially one-way. The operator did not comment on the responses made by the subject. The results from the first four presentations were discarded.

2.3. Single stimulus program

The subjects were instructed to press a stimulus response key every time they saw the stimulus. If the subject failed to press it within two seconds, the computer recorded a miss and proceeded with the next presentation. The results from the first ten stimulus presentations were discarded.

2.4 Two alternative forced choice procedure

The subjects were given two response keys and were instructed to press the upper one if they saw the stimulus in the upper field and the lower one if they saw the stimulus in the lower field. After each presentation they had to respond and when they could not see a stimulus they had to guess. The computer would not proceed with the next presentation until one of the two keys had been pressed. The results from the first ten stimulus presentations were discarded.

2.5 Analysis

The data were analyzed with the summation method[9,12] to give estimates of the threshold and its standard deviation. The results from each program were not only analyzed as a whole but also in four stages corresponding to the data collected in the first, second, third and fourth quartiles.

3. Results

3.1. Multiple stimulus versus single stimulus thresholds

Sixteen out of the 18 subjects had a lower threshold with the multiple stimulus program as compared to the single stimulus one. The mean difference was 0.95 log units which was highly significant ($p<0.001$) (Table 1). The mean standard deviation of the threshold estimates was also found to differ between the two techniques. For the multiple stimulus program it was 1.36, while for the single stimulus program it was 1.64; again this difference was highly significant ($p<0.001$)

3.2. Two alternative forced choice versus multiple and single stimulus techniques

The two alternative forced choice program gave, on average, results that fell between those of the single stimulus and multiple stimulus programs, being slightly closer to that of the single stimulus program (Table 1).

3.3. Quartile responses

The thresholds for the first quartile are found to be lower than those from the subsequent quartiles (Fig. 1). This effect is seen to be much greater with the single

Table 1 Mean thresholds and mean threshold standard deviations from the sample of 18 subjects Numbers in brackets represent the standard deviation of the subject's thresholds Intensity levels given in dB LED luminance 0.16 cd/m when at 30 dB, 0 10 cd/m when off.

Program	Overall means		Quartile means				Last half means	
	Threshold	SD	1st	2nd	3rd	4th	Threshold	SD
Multiple stimulus	32.53(1.05)	1 36	32 89	32 55	32 14	32 34	32 25(1.03)	1 20
Single stimulus	31.58(1.32)	1 64	32 37	31 65	31 30	31.34	31 28(1 33)	1 53
Two alternative forced choice	31.97(1.48)	1 76	32 69	31 80	32 16	31.58	31 89(1 59)	1 93

stimulus program than with the multiple stimulus one. When the data from the last half of each program are analyzed separately, the mean threshold is seen to increase (0.28 dB for the multiple stimulus technique and 0.3 dB for the single stimulus technique), while the overall variability of responses decreased (standard deviation figures of Table 1).

3.4. Duration of different techniques

The mean duration of the multiple stimulus program was 3.6 min versus 7.7. min for the single stimulus program and 6.9 min for the two alternative forced choice program.

4. Discussion

The clinical value of any particular threshold strategy can be assessed by looking at the derived frequency of seeing curve and seeing if the overall variability, which is represented by the standard deviation of the distribution, can be reduced. The lower this value can be made the greater confidence we can apply to the results.

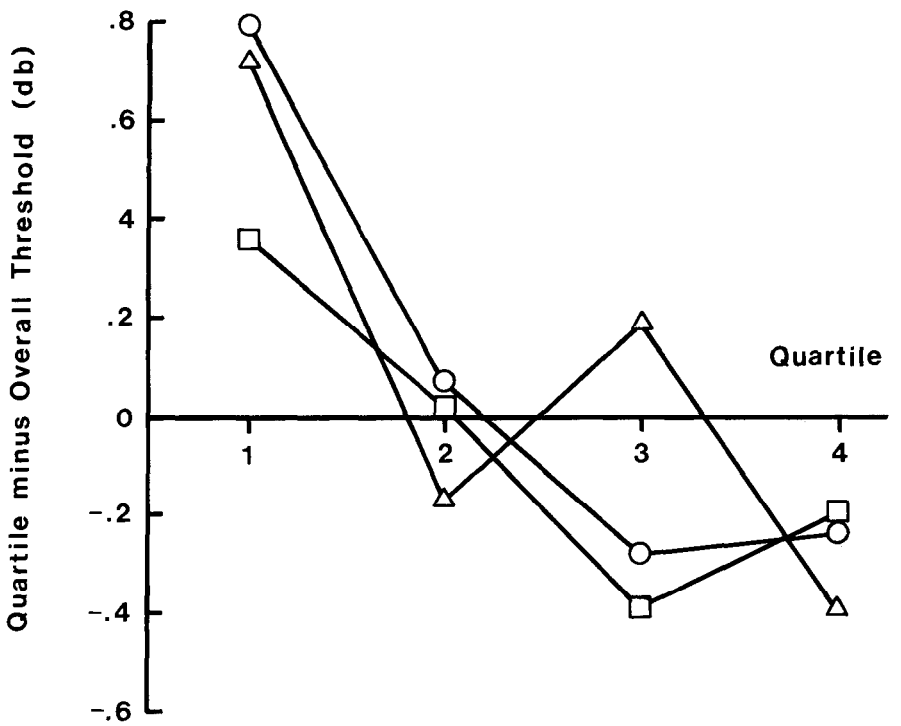

Fig 1 The mean difference in threshold, for each strategy, between the overall estimate and the estimate during each quarter
Multiple stimulus program
Single stimulus program
Two alternative forced choice programs

This in turn should lead to higher sensitivities and specificities.

The results reported here show that the standard deviation of threshold measures is lower with a multiple stimulus strategy, in which the subject verbally reports the number of stimuli seen to the operator, than in a single stimulus strategy in which the patient is given a response key to press whenever they see a stimulus. This reduction in the standard deviation is approximately 0.3 dB over the whole period of each session and 0.33 dB in the last half of each session. The reduction is not therefore solely due to the initial loss of sensitivity shown to exist at the beginning of each session (as shown in Fig. 1).

The results also indicate that the threshold is lower with a multiple stimulus strategy than with the single stimulus one (0.95 dB). This difference may in part be explained by the subjects adopting different criteria for the two tests. The two alternative forced choice strategy which is designed to remove the effects of subjects' criteria gave a mean threshold value below that of the single stimulus strategy, although again it was significantly higher than that of the multiple stimulus strategy.

The threshold differences between the multiple and single stimulus strategies are much less in the first quartile of each experiment (0.53 dB) than from the experiment as a whole (0.95 dB). It is as if the subjects fatigued more with the single stimulus strategies than with the multiple stimulus one.

In post-experiment discussions with the subjects, they all reported that the single stimulus technique was more demanding than the multiple stimulus one and that they had a great deal of trouble maintaining their attention throughout the period of this test. Obviously any shift in the subjects' level of attention will result in a drop in sensitivity and an overall increase in the standard deviation of the threshold measures, a factor which could explain the differences between the two strategies.

The effect of different interrogation methods and different types of stimulus presentations upon the level of attentiveness and subsequent threshold measures is a topic of research that has received relatively little attention. The computer evaluations of Bebié et al.[2] which have formed the basis of the now widely practiced repetitive bracketing strategy specifically excluded 'different levels of attention due to different interrogation methods'. Yet, clearly, the nature of the examination can have a significant effect upon the estimated thresholds. If a patient is rushed through an examination then he is likely to become flustered and make an increasing number of errors. If a patient is verbally encouraged throughout the examination and given feedback as to the quality of his responses, then this often reduces the overall variability and improves the quality of the data[6,7].

While computers are very good at controlling the physical parameters of a visual field examination and ensuring that they remain the same from one session to another, they, at present, do not give any encouragement/feedback to the patient even though the importance of this has been well documented[9]. Whether computers can ever give the same amount of encouragement/comfort as a sympathetic perimetrist is open to debate. The results reported here indicate that fully automated procedures, in which the subject enters his responses into the computer with a stimulus response key, are not as reliable as semi-automated procedures in which the subject verbally reports what he sees to the operator who then keys in the response and proceeds with the next presentation, a finding that is in complete agreement with those of De Jong et al.[6].

The threshold increase, both in single and multiple stimulus strategies, during the first few minutes of the recording implies that there is a settling down phase during which the sensitivity decreases. While this phase occurred in all three strategies evaluated in this paper, its magnitude was least for the multiple stimulus program (0.55 dB versus 0.94 dB for the single stimulus program and 0.84 dB for the two alternative forced choice program; these values have been obtained by taking the

mean of the last three quartiles and subtracting it from that of the first quartile).

Heijl[13] also reported a slight but consistent increase in threshold in six normal subjects when tested with a repetitive up/down strategy over an average period of 28 min. This increase was less than that reported here even though the recording sessions were much longer. When analyzing his data, Heijl ignored the results from the first few minutes (approximately 2.3 min) of each session. In this experiment we removed the first ten responses, which corresponds to approximately 0.5 min of data. If we had removed a further 1.8 min of data, this would have removed/reduced the large initial drop in sensitivity shown in Fig. 1.

This early change in the threshold has several clinical implications. With the fast threshold strategies[1] and the threshold related suprathreshold strategies that are incorporated in many of the current generations of visual field equipment, an estimate of the threshold is obtained at the beginning of the test before the intensity is incremented by a given amount (usually 0.4-0.6 log units) and the rest of the field tested. If the initial estimate of the threshold is an underestimate of the final threshold, as the data in this report indicates, then the suprathreshold section of these strategies will be testing at a value closer to the threshold than was originally intended. It would be of value to see if this effect could be reduced even further by the adoption of new threshold techniques.

The objective of this research was to see if alternative threshold strategies could reduce the variance of results found with the widely practiced single stimulus techniques. The results indicate that the variance can be reduced with a semi-automatic technique which involves a limited dialogue between the subject and perimetrist. More research is now needed to ascertain how these improvements can be incorporated into new threshold strategies for routine clinical use.

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VARIABILITY OF THE FRISÉN RING PERIMETER

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The Frisén ring perimeter is a resolution or acuity perimeter whose variability of results has not been established. Using normals, ocular hypertensives, and glaucomas, all of whom were tested five times, a total intergroup variation of 0 370 dB to 1 043 dB was found The reliability factor was 0.928 The results indicate low variation on a machine which is easy to use, fast, and may test different visual channels compared to standard perimetry.

Introduction

The Frisén ring perimeter[1] is a new device which uses high pass frequency stimuli[2] to test the central visual field. These are resolution or acuity targets rather than differential light sensitivity stimuli. The former represent a novel psychophysical mode of testing the visual field. This method requires validation with respect to its variation. To determine the intrapatient and interpatient variation, a group of normal, ocularly hypertensive, and glaucomatous subjects had repeated examinations and the 50 points in each of the visual fields were analyzed.

Methods

Thirty-seven subjects (15 normals, 10 glaucoma suspects, and 12 glaucomas) each had one eye examined sequentially five times. They all had Snellen acuities of 6/12 or better, refractions of no more than +4.00 D, and their ages were between 29 and 78 years. There was no preselection based upon age or past perimetric experience. Perimetric testing was usually accomplished within one day.

Method of statistical analysis

The total scores, individual quadrantic scores, and central, mid-field, and peripheral groupings of the five replicated sets of points were examined by analysis of variance (components of variation) estimating diagnostic group effects and patient effects. From these analyses, the coefficients of reliability were calculated.

Results

The components of variation within individuals, between individuals but within groups, and between groups are contained in Table 1. For the total score, they ranged from 0.370 dB (MSE) to 1.043 dB for intergroup variation. The reliability factor, which is the proportion of total variation in data which accounts for variation among the three groups versus variation among individuals, is a 'signal to noise' ratio and equalled 0.928. Variation among zones was not statistically different. The same could be said for the quadrants where the reliability factors ranged from 0.838 to 0.916.

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Table 1 Analysis of variation

Variation components	Intraindividual (MSE)	Interindividual intragroup (Sp)	Intergroup (Sg)	Reliability (R)
Total score	0.370 dB	0.828 dB	1 043 dB	0 928
Zones				
central	0.481 dB			0 894
middle	0 460 dB			0 909
peripheral	0.378 dB			0 922
			Quadrants	
			superonasal	0 909
			inferonasal	0.838
			superotemporal	0 911
			inferotemporal	0 916

Discussion

In the ring perimeter, 50 points are examined in the central visual field using high pass frequency stimuli. The test is rapidly done and offers frequent feedback to the patient. This device utilizes resolution targets which vary in size rather than in contrast against a uniform background as in differential light sensitivity perimetry. One decibel (dB) change equals 0.1 log 10 *diameter*. As a result of this fundamental difference, comparison with standard perimetry must be done cautiously. Any attempt to do so quantitatively would be even more adventurous. Test reliability (total score) was 92.8%. Within quadrants, the interpatient variation was found to be least inferonasally and greatest inferotemporally. Patient variation in the middle zone was higher than in either the central or peripheral zones; however, these differences were not statistically significant. The significance of these findings is unknown as yet and may represent local variability due to the small sample size. As indicated, neither the zonal nor the quadrantic division of the field tested provided additional information.

Analysis of the effects of age on values demonstrated an increase of variation of 0.035 dB per year over the entire field. This is a reflection of the lack of age-corrected values for this instrument. Our data indicates that over the age range of our sample there was an increase in variation over the total field of this amount.

Conclusions

The Frisén ring perimeter provides threshold information from the central visual field quickly and reliably. Very acceptable levels of variation were established for three diagnostic groups following repeated testing. Like all other forms of perimetry, greater variation was found in the glaucomas than in the normals and glaucoma suspects.

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THE LEARNING EFFECT OF THE FRISÉN HIGH PASS RESOLUTION PERIMETER*

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The authors studied the visual field on the high spatial frequency ring perimeter five times in one eye of 37 subjects who included normals, glaucoma suspects and glaucoma patients. The results for the total field and its quadrants were regressed over time A significant improvement in sensitivity was found between the second and first examinations and amounted to a mean change of 0.297 dB ($p< 0\ 005$)

Introduction

Introduction of computerized perimeters has removed the variability introduced into the examination by the perimetrist. The objective nature of the examination remains and accounts for variations in the visual field which includes both a short term and a longer term fluctuation. These cause difficulties both in the interpretation of suspicious areas within an examination, and in the evaluation of changes in the visual field over time. The effects of prior perimetric experience was studied by Wood *et al.*[1] who found in a homogeneous sample of young subjects that there were three types of individuals, namely those in whom the greatest learning effects occurred between the first and second examination, those who continued to improve over five examinations, and those who showed no discernible learning effect at all. These authors also found that the learning effect was greater in the upper part of the visual field, and was more marked in the periphery than in the center. They also showed for the first time that the increase in sensitivity, as a result of the learning effect persisted at follow-up examinations on days 15, 16 and 44. The learning effect has previously been studied with manual perimetry by Aulhorn and Harms[2] who reported an increase of approximately one long unit of sensitivity in all of their subjects, after 20 consecutive manual perimetric threshold determinations in one day. They found the greatest sensitivity increases to take place early in the examination.

The introduction of the visual field screener using a high spatial frequency resolution target with multiple feedback devices has introduced a new modality of threshold determination[3]. It is important to verify whether the resolution threshold has the same fluctuation and learning effects as the differential light threshold.

Method

Thirty-seven subjects, 15 normals, 10 glaucoma suspects and 12 patients with glaucoma, were studied. Each patient had one eye examined sequentially five times on the Frisén high spatial frequency ring perimeter. All of the patients had Snellen acuities of 6/12 or better, and refractive errors of less than +4D. Their ages ranged

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between 29 and 78 years. No pre-selection was based upon age, refraction, or past perimetric experience. The five examinations were usually done within 24 hours.

Statistical methods

The score of each individual on each occasion was regressed on the order of the corresponding observation. Regression slopes were derived using analysis of co-variance methods. Total scores and quadrant scores were analyzed in each group, and in the combined group. In addition, successive scores were regressed on their immediate antecedent scores over each time interval. Mean differences in scores over consecutive determinations were adjusted for initial scores, and then tested for significance by analysis of co-variance techniques.

Results

Means and standard deviations of scores from the entire central field for each group of patients and for the total group are shown in Table 1. No significant time trends were found when the five consecutive observations were regressed on the order of the observations. The regression analysis of successive total scores on their immediate antecedent scores showed a significant (p 0.01) flattening of the line predicting the second score from the corresponding first score in the normal group. The regression equation was given by X_2 the second score in the normal group. The equation indicated that in the normal the lower second score (improvement of resolution) would be expected at any level of the initial score, but that the relative lowering was significantly larger as the initial score was higher.

In the glaucoma group, the regression line was $X_2 = 1.1\ X_2 - 0.73$, indicating that in this group the second scores were systematically significantly lower than the initial scores, but that the lowering effect was roughly constant at all levels. A

Table 1 Mean scores in dB from the entire central field and their standard deviations

	Examination 1	2	3	4	5
Normals	3 80 dB ± 1 08	3 27 dB ±0 85	3 53 dB ±0 90	3 55 dB ±1 20	3 57 dB ±1 07
Glaucoma suspects	3 92 dB ±0 41	3.80 dB ±0 43	3 81 dB ±0 37	3 86 dB ±0 42	3 85 dB ±0 49
Glaucoma patients	5 32 dB ±1 38	5 16 dB ±1 64	5 21 dB ±1 54	5 09 dB ±1 47	5 03 dB ±1 48
All eyes	4 32 dB ±1.25	4 03 dB ±1 35	4.15 dB ±1 28	4 14 dB ±1.31	5.12 dB ±1.27

similar result was obtained for the combined group, with the regression equation of $X_2 = 0.98\ X_2 - 0.23$.

Analogous results were obtained for the quadrant scores, and no systematic improvements would be demonstrated in any of the later pairs of successive readings. Analysis of co-variance was carried out to test the significance of the change in the total score between the second and first examinations, after adjustment for initial score. The mean difference in total score for the combined group was -0.297 dB which was statistically highly significant (p 0.05). Quadrant scores again showed similar differences. Mean differences in the subsequent scores adjusted for the initial score showed no further score improvement.

Discussion

Statistical comparisons of five consecutive scores obtained on the Frisén perimeter showed a significant learning effect as reflected by the decrease in the score which occurred between the first and the second determinations. The learning effect was identified by regressing the second score on the corresponding initial score, and supported by the significance of the mean difference in the two scores, after adjustment for the initial score level. The learning effect could be observed in normal individuals and in patients with glaucoma. It was similar in all quadrants. Further improvements which might have suggested further learning beyond the second determination could not be detected. It should, however, be pointed out that our studies confirm the variability of the learning effect between individuals, and that there are some individuals in whom the learning effect may continue longer than suggested by the statistical treatment of the group as a whole, while in some others the learning effect may be negligible. In the majority, however, most of the significant learning effects take place between the first and second examination.

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COMPUTER-ASSISTED ANALYSIS

COMPUTERIZED VISUAL FIELD ANALYSIS

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Abstract

A decision algorithm as an aid for localization of visual field defects is presented The guidelines of the presented algorithm had been chosen to represent the underlying anatomical structures, represented in the visual field as the vertical and horizontal borders, the blind spot and the temporal crescent This will be the basis of a computerized analysis of visual field results gained by static or kinetic perimetry The aim is a program leading the user to the clinical localization of the underlying lesion by simple 'yes/no' questions Finally, the visual field data obtained by means of a computerized static perimeter will be directly transferred to this program, permitting the localization of the lesion within the visual pathways

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REGRESSION TECHNIQUES IN THE ANALYSIS OF VISUAL FIELD LOSS

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Inter- and intra-subject variability between and within perimetric examinations limits the accuracy with which both early field loss and small changes in loss can be evaluated, particularly when the interpretation utilizes normative age-matched values of sensitivity for comparative purposes Using clinical data obtained from central field examinations with the Octopus 201 and Humphrey 630 perimeters and data from computer simulations, the study investigated the suitability of two novel and distinctly different approaches to visual field analysis.

Firstly, the pointwise distribution of sensitivity was modelled by a polynomial function $Z = a_0 + a1_x + b1_y + a2x^2 + b2y^2 + c11xy + \ldots\ldots\ b_ny^n$ where Z is sensitivity and x and y are the individual stimulus locations. The normal field could be modelled to a precision (adjusted R^2) of $\geq 85\%$. For a sample of 34 consecutive patients attending a glaucoma clinic, the precision was $\leq 79\%$ (4th order polynomial) The constant correlated highly with mean defect (deviation), corrected loss variance (corrected pattern standard deviation) and well with short-term fluctuation Secondly, the pointwise regression of sensitivity between any two examinations of a given patient was used with suitable estimates of the short term fluctuation in sensitivity at each location to provide an indication of abnormality.

Introduction

The psychophysical determination of any threshold response exhibits a variation in the measured result from one threshold evaluation to another. This variability is apparent in the detection of the spot stimuli used in clinical perimetry where the intra-examination variation in threshold at a given stimulus location has been designated the short-term fluctuation and the inter-examination variation in the threshold the long-term fluctuation[1].

The presence of short-term and long-term fluctuations confounds the interpretation of abnormality, particularly in cases of early loss and in small changes in sensitivity. In addition, the interpretation of abnormality is traditionally undertaken by comparison with data from surrounding points or more commonly with data representative of the normal age-matched population. The efficiency of these approaches is limited in cases of early loss and in small changes in sensitivity by the presence of intra-subject variations[2] and by considerable inter-subject variation, both in sensitivity and in fluctuation of sensitivity within the normal population[3-5]. Indeed, it is recognized that, in addition to age[4,6,7], the intra- and inter-subject format of the sensitivity gradient can be modified by such factors as the pupil size[8], the learning effect[4,9] and the degree of intraocular light scatter[10,11].

A system of visual field evaluation and analysis based upon the response from the individual subject alone and yet capable of describing the intra-subject variations in the field, would thus seem to offer some advantages in both single field and serial field analysis.

The mathematical technique of least squares and its use in fitting dependent variables in terms of one or more controlled, or independent, variables is well documented in many areas of science. Indeed, regression techniques and other closely related procedures have previously been applied to visual field indices and used in serial visual field analysis[5,12,13].

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Materials and methods

Clinical data was obtained in the normal manner using stimulus size III with Program G1 of the Octopus Automated Perimeter 201 and Program 30-2 of the Humphrey Field Analyser 630. The study was undertaken with specific reference to cases of early glaucoma.

Polynomial regression fit of the sensitivity function - Snap shot analysis

The stimulus locations corresponding to each of the various programs were each described in terms of their respective x and y coordinates (x_i, y_i), (i = 1,2, ... n) and the corresponding sensitivity values as zi (i = 1,2 ..... n). Analysis was then carried out using an IBM personal computer and associated software package (Statgraphics) to explore the possibility of fitting the sensitivity function in terms of its location coordinates. The most appropriate function from preliminary investigations was considered to be of the polynomial type. A particular sensitivity value, z, is compared with a fitted or modelled theoretical value, Z, where

$$Z = a_0 + a_1x+b_1y+a_2x^2+b_2y^2+c_{11}xy+ .....b_ny^n$$

The actual values of the coefficients a_0, a_1, b_1, b_n..... etc. were derived by minimizing $\Sigma(z_i - Z_i)^2$. The accuracy of the fit of individual points could be gauged by inspecting the separate residuals ($z_i - Z_i$) at each stimulus location while the overall fit could be assessed by reference to the coefficient of determination (R^2) which provides a measure of the variation in z explained by the polynomial function. The cross terms were omitted from the model since preliminary work suggested that these terms did not produce a significant increase in the precision of the model.

The model for the Octopus G1 field was developed using right eye data from a sample of 20 consecutive subjects drawn from a glaucoma clinic and comprised nine primary open angle glaucomas, five low tension glaucomas, one narrow angle glaucoma and five ocular hypertensives. The group mean for the mean defect index was 2.33 (one standard error of the mean 1.46) and that for the CLV 31.06 (one standard error of the mean 7.62). The model for the Humphrey 30-2 field was developed using right eye data from 20 consecutive cases. Of these, 18 were drawn from a glaucoma clinic and comprised eight primary open angle glaucomas, one low tension glaucoma, one narrow angle glaucoma and six ocular hypertensives and two glaucoma suspects. The group mean for the mean deviation was -3.34 (one standard error of the mean 1.32) and that for the corrected pattern standard deviation 4.513 (one standard error of the mean 0.88). Six subjects, five of whom were ocular hypertensives, were common to each sample.

Time series regression of the sensitivity function - longitudinal analysis

Derivatives of simple linear regression were used to illustrate the pointwise distribution of sensitivity between any two fields obtained from serial investigation. In this mode of analysis, sensitivity values $Z_i(t)$, where $Z_i(t)$ is the sensitivity recorded at location (x_i, y_i) at time t (t = 1,2,.....k), are compared serially with previous values $Z_i(t-T)$, i = 1,2,...n (where T = 1,2,.....t-1). The linear regression is of the type

$$Z_i(t) = b+aZ_i(t-T).$$

With this type of approach, autoregression becomes a problem, but a complete analysis is generally not possible because of the short nature of the time series data applicable in the clinical situation.

Two techniques in particular were considered to warrant further investigation; both resembled procedures used in quality control analysis. In the first, the pointwise distribution of sensitivity for a given field was plotted against that for a subsequent field. The data was evaluated in two parts, within 12 eccentricity and beyond 12 in order to account for the heterogeneous nature of the short-term fluctuation[1,4,14]. In the second, the difference between the mean sensitivity and the sensitivity at each location for a given field was plotted graphically against the corresponding differences for a subsequent field referenced to the subsequent mean sensitivity. The data was similarly analyzed in terms of eccentricity. An Ormstead-Tukey test could then be applied to test for an association between the data from the two sets of fields.

Results and discussion

Polynomial regression of the normal field

The results of central field examination in normal individuals can be modelled by a second order polynomial.

The Octopus G1 (stimulus size III) normal field can be modelled to a precision (adjusted R^2) of 85% with a second order polynomial and can be improved to 87% by the use of a fourth order polynomial (Table 1). The precision of the model is valid for all ages of the designated normative data since, for the Octopus system, sensitivity in the normal eye is assumed to decrease uniformly by 1 dB per decade at each location. The asymmetric nature of the field[2] precludes a better fit to the data. For the second order polynomial, all functions in the regression equation are significant. The constant, y, x^2, and y^2 are significant for the third order equation whilst the y^4 term additionally becomes significant for the fourth order equation. The significance of the y term may be due to an artificial origin compounded by less symmetry between the upper and lower field than the nasal and temporal which is present in both normal and abnormal data.

Similarly, the normal Humphrey 30-2 (stimulus size III) field, excluding the sensitivity values corresponding to the blind spot at 15° eccentricity 3° above and below the horizontal, can be described to an accuracy of up to 94% with a second order polynomial and can be improved to 96% by the use of a fourth order

Table 1 Adjusted R-squared values (%) against the order of polynomial for the normative data of Octopus G1 and Humphrey 30-2 programs

	Order of polynomial		
	2nd	3rd	4th
Octopus G1	85 5	85 0	87.2
Humphrey 30-2			
20 years	88 4	90 6	90.5
40 years	92 5	95 4	95 5
60 years	94 4	95 7	95 9
70 years	92 7	93 9	93.9

polynomial (Table 1). The degree of precision varies with age group, being lowest for the 20-year-old category and highest for the 60-year-old category. All functions up to the third order are significant with the exception of the x term in the third and fourth order polynomials for the 20- and 70-year-old groups. Inclusion of the sensitivity values corresponding to the blind spot would result in a lower coefficient of determination since the model is influenced by sudden localized discontinuity in sensitivity. The extraordinarily good fit of the Humphrey central field normal data undoubtedly stems from the use of polynomial modelling of data obtained from normal subjects to generate a representative normative data base for subsequent comparative purposes[5].

Polynomial regression of the abnormal field

The field for 11 of the sample of 20 consecutive glaucomatous subjects examined with Octopus Program G1 could be modelled by a fourth order polynomial with a precision (adjusted R^2) of 60% or more (Fig. 1). The constant term for each of the four orders of polynomial correlated highly with the Octopus indices mean sensitivity and mean defect and well with the corrected loss variance (Table 2). The highest correlations were obtained for the second and third order polynomials. The magnitude of the correlations demonstrate that the constant is mainly influenced by the overall reduction in sensitivity but is also relatively sensitive to localized loss. The statistical significance of the x and y coefficients varies dependent upon the nature of the field loss and is a function of the predominant characteristic of the loss (Fig. 2). A correlation was also present between the constant and the global short-term fluctuation (Table 2). Indeed, this is not surprising since the short-term fluctuation increases as sensitivity decreases[1] and is higher in glaucoma patients than normals[14]. The coefficient of determination R^2 correlates weakly with mean sensitivity, mean defect and corrected loss variance being highest for the third order polynomial (Table 3).

The field for 12 of the sample of 20 consecutive mainly glaucomatous subjects examined with Program 30-2, could be modelled by a fourth order polynomial with a precision of 60% or more (Fig. 1). The model provides similar results to that of the Octopus: the constant term for each of the four orders of polynomial correlated highly with the Humphrey indices mean deviation and corrected pattern standard deviation (Table 2). Similarly, the x and y coefficients alter in the level of statistical significance depending upon the type and level of loss. The constant also correlates well with the short-term fluctuation. As with the Octopus G1 model, the coefficient of determination R^2 correlates weakly with mean sensitivity, mean defect and corrected loss variance being highest for the third order polynomial (Table 3).

The constant in both perimetric models relates to the value of perimetric sensitivity derived by the Monte Carlo Integral[9,15]. This arises because the integration of the polynomial equation over the relevant domain is dominated by the large value of the constant. The Monte Carlo Integral is approximated by the mean sensitivity[9].

It would seem that conditions involving a general depression in sensitivity or exhibiting uniform changes in sensitivity in both the x and y directions can be modelled well. The model breaks down as the degree of non-uniform loss in sensitivity increases and particularly as the number of discrete or focal areas of loss increases. The model can be further refined by incorporating an allowance for the presence of the short-term fluctuation.

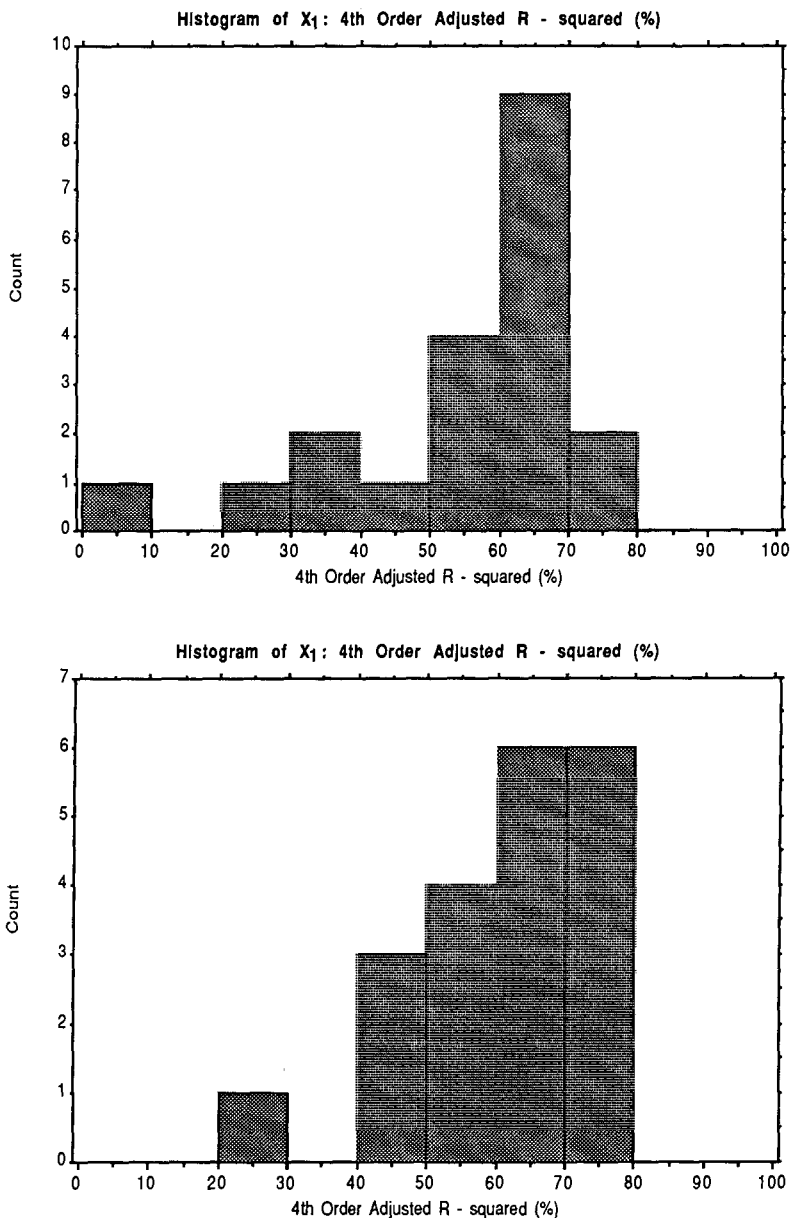
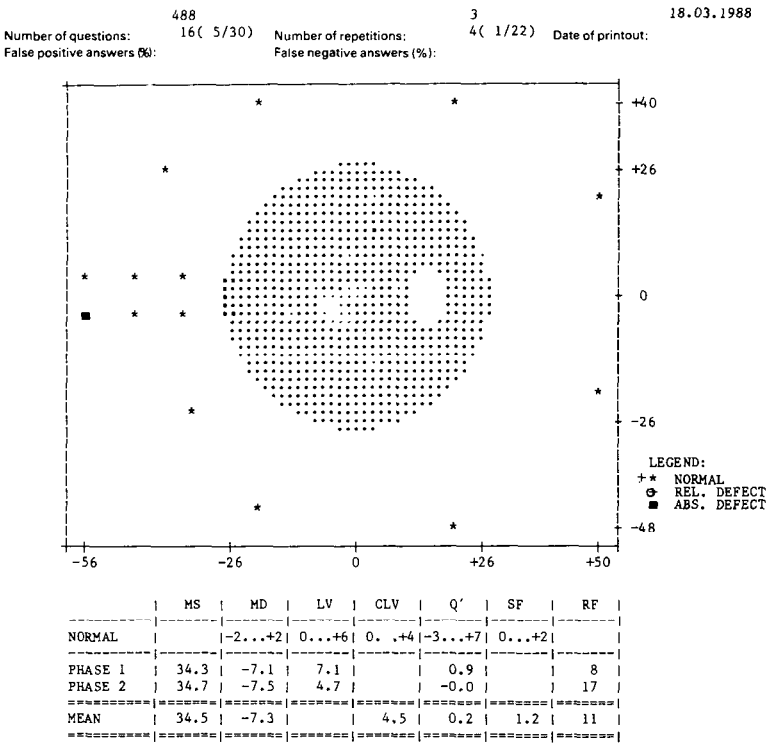
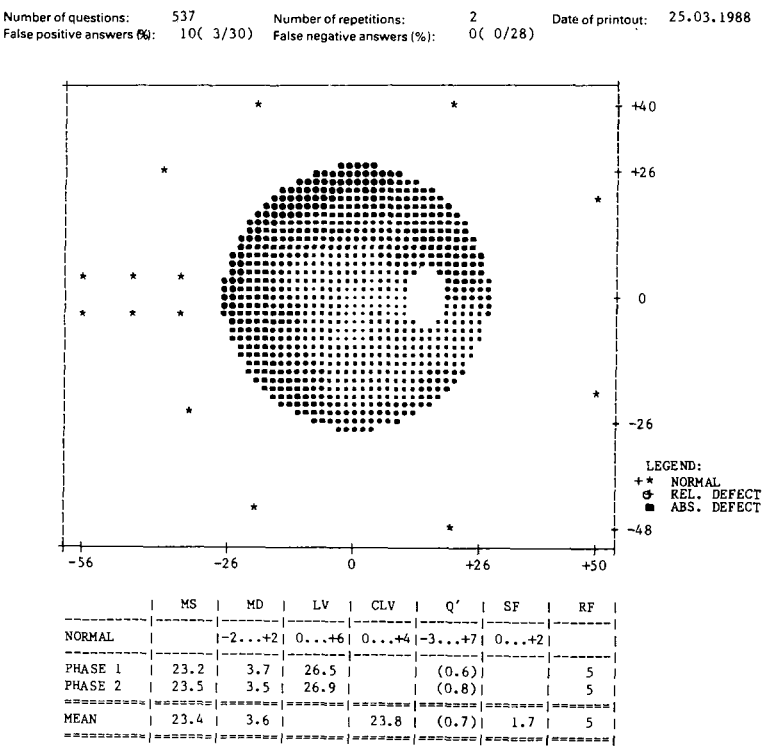


Fig 1 Frequency distribution of the adjusted coefficient of determination R2 for the fourth order polynomial fit of the Octopus Program G1 (top) and of the Humphrey Program 30-2 (bottom) field for glaucomatous eyes.

A change in the magnitude of the constant, when interpreted in conjunction with the standard error, can be used to indicate loss either in comparison to normative age-matched values or in comparison to a previous examination, whilst inspection of the significance level associated with the x and y coefficients may be equally useful. In addition, the value of the coefficient of determination R^2 provides a



	MS	MD	LV	CLV	Q'	SF	RF
NORMAL		-2...+2	0...+6	0. .+4	-3...+7	0...+2	
PHASE 1	34.3	-7.1	7.1		0.9		8
PHASE 2	34.7	-7.5	4.7		-0.0		17
MEAN	34.5	-7.3		4.5	0.2	1.2	11



	MS	MD	LV	CLV	Q'	SF	RF
NORMAL		-2...+2	0...+6	0...+4	-3...+7	0...+2	
PHASE 1	23.2	3.7	26.5		(0.6)		5
PHASE 2	23.5	3.5	26.9		(0.8)		5
MEAN	23.4	3.6		23.8	(0.7)	1.7	5

Fig 2 (Top) Octopus Program G1 field of a 57-year-old patient with primary open angle glaucoma. The field models with a precision of 35% to the fourth order polynomial equation: $Z = 34\,95 - 0.07x - 0.05y - 8.92\,E^{-6}.x^4 + 2\,0\,E^{-4}\,x^3$ (Bottom) Octopus Program G1 field of a 61-year-old patient with primary open angle glaucoma The field models with a precision of 79% to the fourth order polynomial equation: $Z = 30.92 - 0.31y - 0.02x^2 - 0\,03y^2 + 3.21E^{-4}.y^3$

Table 2 Product moment correlation between the visual field indices for glaucomatous eyes derived by the Octopus Program G1 (top) and the Humphrey Program 30–2 (bottom) and the constant for the second, third and fourth order polynomials

Visual field index	Order of polynomial		
	2nd	3rd	4th
Octopus program G1			
Mean sensitivity	0.945	0 945	0 914
Mean defect	0.939	0 938	0 908
Short-term fluctuation	-0 488	-0 488	-0.453
Corrected loss variance	-0 756	-0 754	-0.751
Humphrey program 30-2			
Mean deviation	0 898	0.897	0 905
Short-term fluctuation	-0 586	-0.584	-0 581
Corrected pattern standard deviation	-0 782	-0.781	-0 852

Table 3 Product moment correlation between the visual field indices for glaucomatous eyes derived by the Octopus Program G1 (top) and the Humphrey Program 30–2 (bottom) and the adjusted coefficient of determination R^2 for the second, third and fourth order polynomials

Visual field index	Order of polynomial		
	2nd	3rd	4th
Octopus program G1			
Mean sensitivity	0 075	0 128	0 077
Mean defect	-0.073	-0.121 -	0 070
Short-term fluctuation	-0 011	-0 023	-0 023
Corrected loss variance	0.077	0 133	0.131
Humphrey program 30-2			
Mean deviation	0 337	0 218	0 186
Short-term fluctuation	-0 329	-0.340	-0 262
Corrected pattern standard deviation	-0.388	-0.302	-0 215

further commentary on the state of the field.

The pointwise distribution of residuals, i.e., the deviation of the observed value from the value predicted by the model may also offer a further guide to clinical diagnosis and management. The pattern of residuals exhibits a strikingly linear trait in the normal eye (Fig. 3). Given this very distinct pattern of residuals, the standard techniques of analysis would not seem to be appropriate. It is theoretically possible to graph two dimensional residuals, however, and this is presently being investigated.

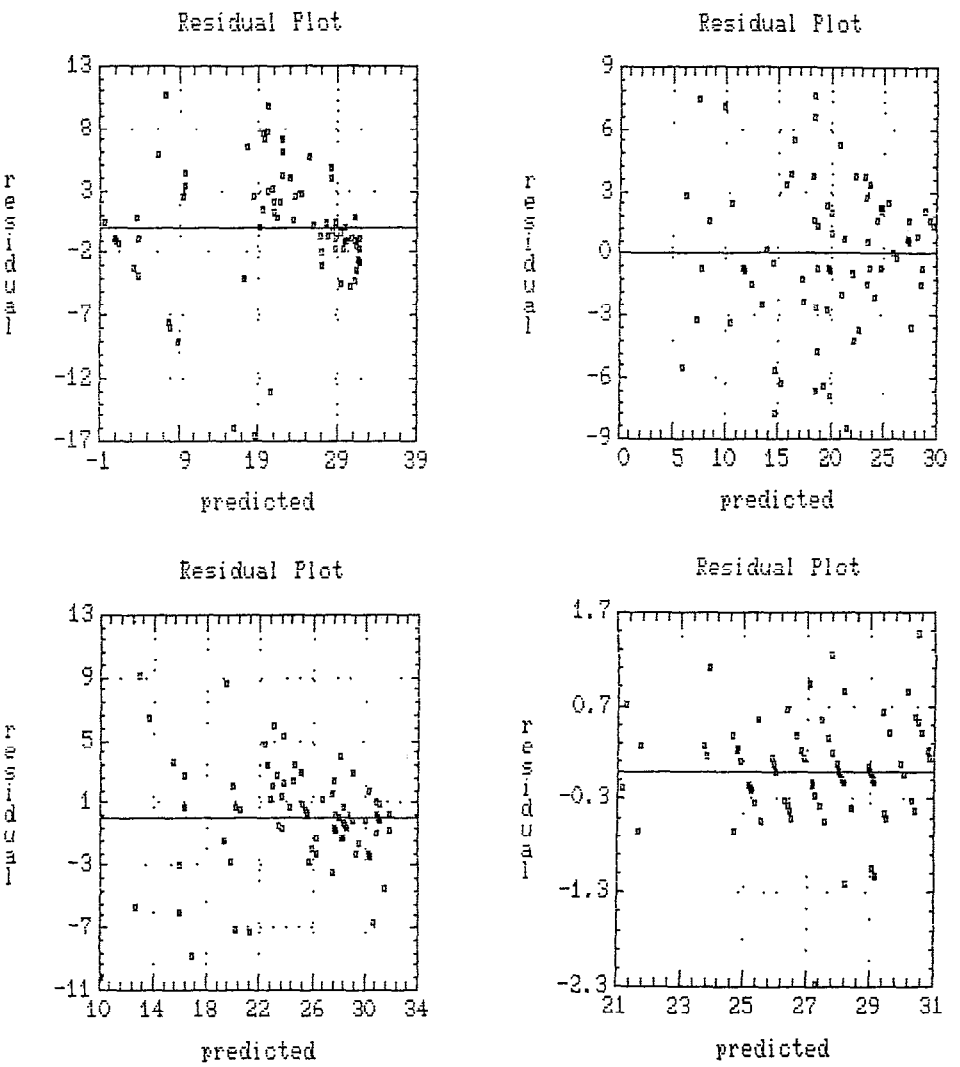


Fig 3 Residual plots showing pointwise differences between the actual sensitivity value (z) recorded with the Humphrey program 30-2 and that predicted by the fourth order polynomial model (Z) for three glaucomatous 70-year-old patients The age-matched normative plot is shown at the bottom right.

Time series regression of the sensitivity function - longitudinal analysis

Using pointwise regression of sensitivity, an immediate visual comparison of any two fields of a given individual is possible (Figs. 4 and 5). The stimulus locations can be coded to indicate the specific region of the field and confidence limits of twice the particular short-term fluctuation can be included at any given eccentricity to aid diagnosis of abnormality. The initial field is necessarily compared with the normal values of sensitivity and short-term fluctuation, whilst subsequent fields are compared with the corresponding values of the most previous field. The methods must be considered in relation to the long-term fluctuation and with respect to the normal age-related depression of the field.

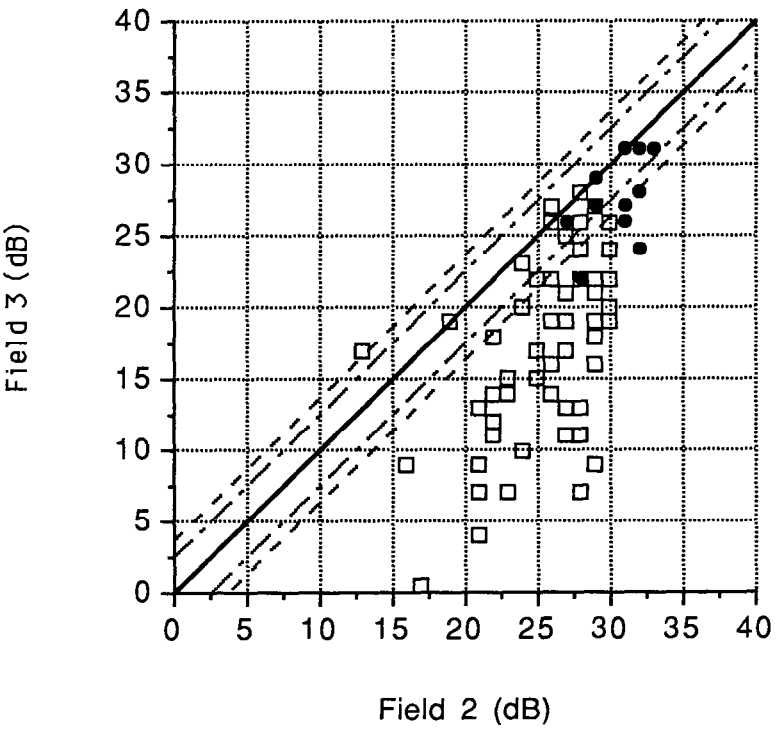


Fig 4. Scattergram illustrating the graphical analysis of the computer simulated pointwise distribution of sensitivity in a Humphrey 30–2 serial field examination of a glaucomatous patient (filled circles represent points within 12° eccentricity: open squares points beyond 12 °eccentricity; inner broken lines indicate twice the short-term fluctuation for the central region, and the outer lines that for the peripheral region

Acknowledgements

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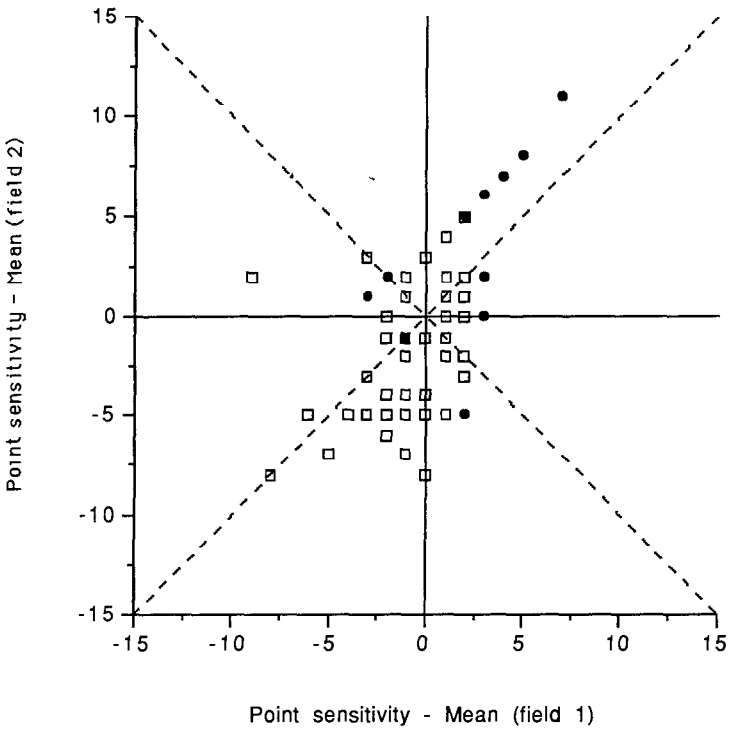

Fig 5. Scattergram showing differences between pointwise sensitivity values (dB) and the mean sensitivity for each of two serial fields of a glaucomatous eye. (Filled circles represent stimulus locations within 12° eccentricity: open square locations beyond 12° eccentricity). Points exhibiting no change in sensitivity should fall within the upper right and lower left quadrants

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CLUSTER ANALYSIS IN SUPRATHRESHOLD PERIMETRY

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Abstract

Although several quantification indices are available for the analysis and interpretation of visual field loss, they do not utilize the spatial relationship between locations with depressed sensitivities. The purpose of this investigation was to examine this relationship and develop a technique, or a cluster analysis, for the evaluation of visual field data.

The central visual fields of 1105 normal and 87 glaucoma patients were measured using a threshold related suprathreshold strategy Approximately 13% of normals have clusters; the great majority of these individuals have one cluster of two defects Most clusters in normals are formed artifactually due to angioscotoma and/or physiological variations in the blind spot position Analysis of the foci or centroids of the clusters show that they are found with equal frequency in the superior and inferior fields in normal patients but with greater frequency in the superior fields of glaucoma patients

Using the results from this large normal sample and looking at other visual field properties, such as depth and location of defects, it is possible to devise an accurate scoring system The incorporation of cluster analysis in visual field quantification is both sensitive and specific in the detection of glaucomatous visual field defects

Introduction

Cluster analysis is a technique for investigating the spatial relationship between two or more, usually geographical, observations. In static perimetry, a cluster is defined as a group of two or more locations with reduced sensitivities and with a given spatial relationship. Cluster analysis is a method by which clusters are formed and analyzed.

In suprathreshold perimetry, normal patients often 'miss' stimuli due to inattention or fatigue[1,2]. Assuming that there are no local factors, such as the upper lid, to affect the sensitivity, then these defects in normals (ignoring the blind spot) can be assumed to be distributed approximately randomly in the visual field. It is not unusual to find an individual with three shallow isolated defects with an instrument that tests 100 locations; however, the theoretical probability of a normal patient producing three clustered defects is very small. On the other hand, a small localized scotoma deeper than the suprathreshold testing level could easily produce a cluster of three defects. This indicates that studying the spatial relationship between defects may provide valuable information, especially in screening for glaucoma.

The purpose of this investigation was to study clusters in both normal and glaucoma patients and to note the differences between the clusters in the two groups with regard to their number, size and location.

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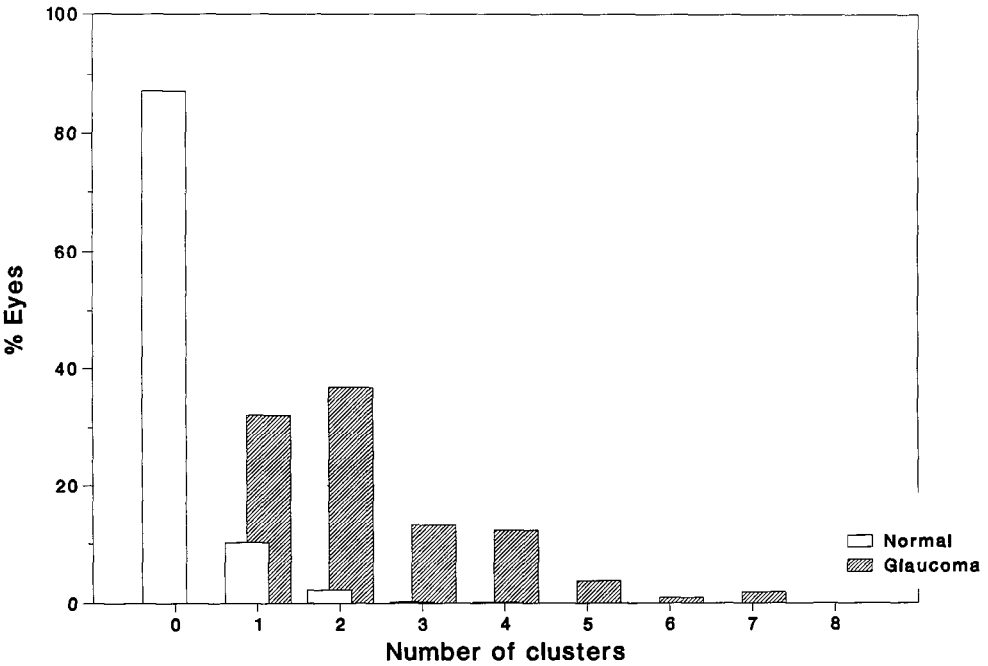

Fig 1 The distributions of the number of clusters in the two groups Approximately 13% of the normal and all of the glaucoma patients have a cluster of two or more defects

Material and methods

The material consisted of 2165 eyes of 1105 normal patients and 106 eyes of 87 glaucoma patients with early visual field disturbances (defined as a total defect area of less than one quadrant of the central 25 degrees). The material and the inclusion criteria are described in detail elsewhere[3].

The visual fields were measured using a threshold related suprathreshold strategy with the Friedmann Visual Field Analyser mk 2 (FVFA). The thresholds at some preselected locations were first determined to the nearest 0.1 log unit (lu). The 98 stimuli were then presented at a suprathreshold increment of 0.4 lu. Any missed stimuli were re-presented later in the examination and if missed a second time were quantified and termed defects.

The data were digitized and entered into a minicomputer with the four stimuli falling within the charted blind spot removed from the analysis. For each eye, the computer was instructed to select each defect entry and search for any defects within a radius of 5.5 degrees. After clusters in the whole visual field were formed in this manner, the number of clusters per field and the size and centroid (mean x- and mean y-coordinate) of each cluster were calculated.

Results

The frequency distributions of the number of clusters of two or more defects in normal and glaucomatous visual fields are quite different (Fig. 1). Approximately 87% of the normal eyes had no clusters, 10% had one cluster and 2% had two clusters. By contrast, all glaucomatous eyes had clusters, with 31% having more than two clusters. Since the glaucoma patients in this study had early localized

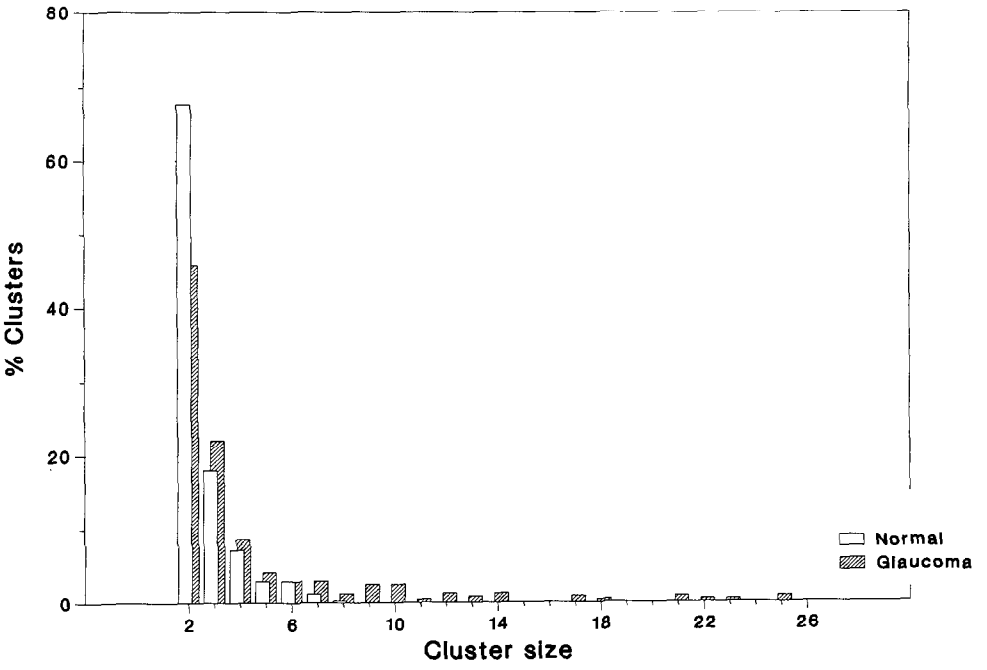

Fig 2 The distributions of the size of normal and glaucomatous clusters Both distributions have similar shapes.

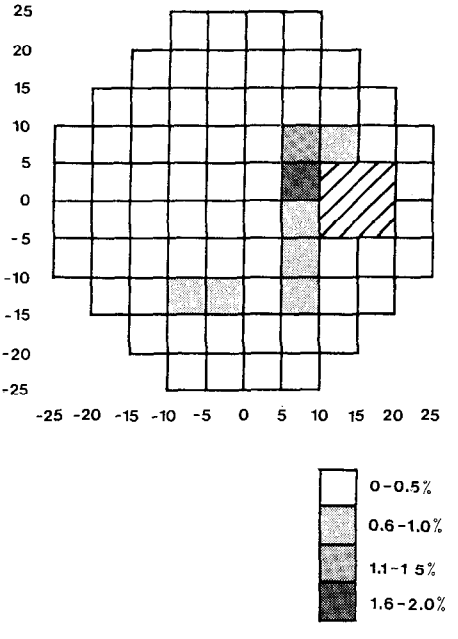

Fig 3. The topographic frequency distribution of cluster centroids in normal eyes Clusters occur with an equal frequency in the superior and inferior fields with most clusters situated adjacent to the blind spot. (From Chauhan et al : Cluster analysis in visual field quantification Doc Ophthalmol 69:25, 1988 Reproduced with the perimission of Kluwer Academic Publishers)

defects not exceeding a total defect area of one quadrant, the eyes with a larger number of clusters were likely to have had small and isolated scotomas.

The frequency distribution of the cluster sizes, that is the number of defects in a cluster for both normal and glaucomatous clusters is shown in Fig. 2. The group distributions have a similar shape and although around 16% of the glaucomatous clusters were larger than six defects, the majority of all clusters (86% of normal and 68% of glaucoma clusters) were of either two or three defects.

The topographic frequency distribution of the cluster centroids in normal eyes (Fig. 3) shows that most clusters occurred adjacent to the blind spot area (hatched square), the highest frequency area being nasal and superior to the hatched square (1.7% of normal eyes). It is likely that these clusters occur due to physiological variations in the blind spot and/or angioscotomas of the large vessel trunks. Clusters were also found in the inferior arcuate area unconnected to the blind spot. A similar pattern around the blind spot was evident in glaucomatous eyes (Fig.4), however there were high frequency areas in the superior and inferior arcuate areas, though generally the latter were further from the horizontal midline. In normal eyes, clusters were found with approximately equal frequency in the superior field (51%) and inferior field (49%); however in glaucomatous eyes, they occurred with a higher frequency in the superior field (60%) compared to the inferior field (40%).

Discussion

The low incidence of clusters in normal visual fields and the correspondingly high incidence in glaucomatous fields indicates that cluster analysis provides useful information in visual field screening for glaucoma.

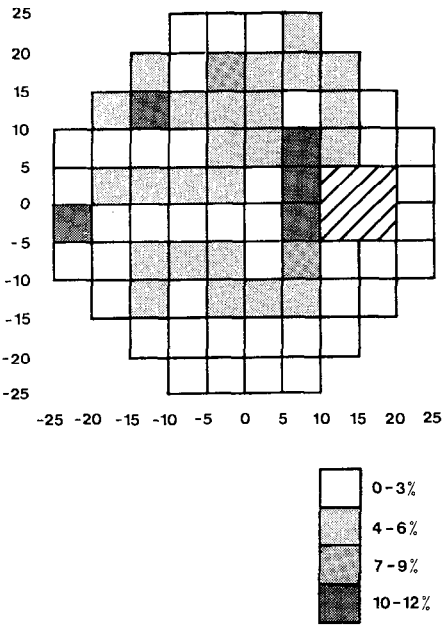

Fig 4 The topographic frequency distribution of cluster centroids in glaucomatous eyes Superior field clusters are found closer to the horizontal midline than inferior field clusters and are 1 5 times more likely to occur than their inferior field counterparts (From Chauhan et al.: Cluster analysis in visual field quantification Doc. Ophthalmol. 69:25, 1988 Reproduced with the permission of Kluwer Academic Publishers)

The data reduction techniques described for threshold perimetry[4,5] have aided in the interpretation of visual field data. However, the quantification indices used currently to indicate localized loss are not sensitive to the spatial relationship between locations with reduced sensitivities and, therefore, a distinction is not made between scattered localized loss and clustered localized loss. We will report elsewhere a similar cluster analysis developed for use with results from threshold perimetry obtained with the Octopus 201 perimeter.

A limitation of the cluster analysis on the FVFA lies in the fact that the stimuli are not distributed on an even matrix. Consequently, the cluster 'catchment' cannot be in terms of nearest neighboring stimuli. The problem is to some extent overcome by specifying a cluster radius, but this form of analysis is easier when the locations tested are approximately equally spaced.

Visual field screening for glaucoma requires efficient strategies. A sound knowledge of the properties of the glaucomatous and especially the normal visual field aids not only in the design of these strategies but also increases the amount of information gained from a given visual field. The results of this analysis have been included in the development of a weighted scoring system[3]. The consideration of not only the depth and location of defects, but also their spatial relationship allows high specificity and sensitivity in visual field screening.

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KINETIC VISUAL FIELD INDICES

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Abstract

One of the advantages of computerized perimetry is the possibility of processing data recorded during one or more visual field examinations in order to obtain statistical informations. The visual field indices suggested by Flammer for the Octopus perimeter and modified by Heijl for the Humphrey perimeter represent a valuable aid for the correct evaluation of a single visual field or for the comparison of successive perimetric results during follow-up

We have tried to transfer these concepts to kinetic perimetry, elaborating indices obtainable with the computerized Goldmann kinetic perimeter 'Perikon' The results of this study, based on normal visual fields recorded over five years, allow us to identify the following parameters: (1) Kinetic Short-term Fluctuation (KSF); (2) Kinetic Mean Defect (KMD); (3) Kinetic Loss Variance (KLV); (4) Kinetic Corrected Loss Variance (KCLV).

The results of the utilization of these indices on a sample of normal subjects are reported

Introduction

The automation of perimetry enables us to draw a large amount of data from a single test. This surely is an important advancement, but it also creates difficulties in the interpretation of perimetric results. Problems arise especially in distinguishing slight defects from physiological fluctuations of the responses linked to retinal sensitivity unsteadiness, patient cooperation loss or examination strategy characteristics.

Thanks to the speed and precision of computers, which also drive the perimeter, it is possible to facilitate analysis of the results by means of the so-called 'perimetric indices'. These parameters synthetically represent, by means of numerical values, the global features of a single visual field and also make it easier to compare different perimetric results[1]. The visual field indices studied by Flammer *et al* [2] for the Octopus perimeter and modified by Heijl *et al.*[3] for the Humphrey perimeter have been exhaustively illustrated[4].

In Goldmann kinetic traditional perimetry, evaluation of the normality of results has always been entrusted to empirical criteria and to the perimetrist's experience[5,6].

Automation of the Goldmann perimeter (Perikon)[7] has permitted good standardization of the examination strategies and the removal of many factors influencing the results, such as variables due to the examiner. In the present study, we have tried to transfer to kinetic perimetry the concepts of 'visual field indices'.

The difficulty we encounter when defining standards with regard to the shape and surface of an isopter is a common experience. Many parameters have to be taken into account, such as the physiological sensitivity decay with aging and the normal scattering of the psychosensorial responses due to threshold fluctuation. In our opinion, the 'kinetic visual field indices' are an indispensable aid to the perimetrist

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in evaluating the normality of a visual field and the true importance of the modifications detected in successive examinations.

Material and methods

1. *Assessment of normal values*

Calculation of a perimetric index requires knowledge of the normal threshold eccentricities of the various targets for all tested meridians, according to the patient's age[1,3,4]

We analyzed 220 visual fields, recorded examining both eyes of 110 normal subjects equally distributed into five age groups (five decades from 20 to 70 years). All subjects had ametropias of below 2 diopters and showed good cooperation during preliminary perimetric tests performed with random kinetic target presentations.

We utilized the program 'Standard Kinetic Perimetry'[8], carried out by the automatic Goldmann perimeter Perikon and characterized by four isopters drawn along 16 meridional trajectories for every target (I/4, I/3, I/2 and I/1).

Ten double presentations were randomly made in order to assess the kinetic short-term threshold fluctuation. The blind spot was tested, but not considered in this study. Proper correction was utilized inside the central 30 degrees.

The mathematical routine elaborated for the visual field indices calculation was carried out by means of an XT IBM PC connected to the perimeter. Only data obtained with target I/1 along the meridians 5 and 355 (RE) or 175 and 185 (LE) were not included in the calculation, in order to avoid the disturbing influence due to the baring of the blind spot.

Our results were in agreement with those of other authors[5,9-12].

2. *Calculation of kinetic visual field indices*

a. Kinetic mean defect (KMD) this index indicates the arithmetic mean of the differences between the recorded values of threshold eccentricity and the age-corrected normal values for every test location[1].

KMD is expressed in degrees and informs us of the contraction of a single isopter or of all the isopters obtained by means of the selected stimuli. High values of KMD mean that a global sensitivity loss is present.

This index is sensitive to isopter contraction and is independent of the shape and uniformity of the results.

$$KMD = \frac{1}{m} \sum_{i=1}^{m} (z_i - x_i)$$

were m is the number of test locations (m = 62); z is the age-corrected normal value at test location i; x is the value obtained at test location i.

b. Kinetic short-term fluctuation (KSF). KSF represents the scatter found in ten double threshold determinations performed with the same stimulus during a single examination. It is expressed as RMS (Root Mean Square)[8,11,13]

This index is increased in disturbed visual field areas and is influenced by cooperation.

$$KSF = \sqrt{\frac{1}{n}\sum_{i=1}^{n}(x_{1i} - x_{2i})^2}$$

where x1 and x2 are the values obtained in the double presentations in the same location i and n is the number of test locations (n = 10)

c. Kinetic loss variance (KLV): as in static perimetry for the Loss Variance[1], KLV represents the variance of the differences detected between the results obtained and the age-corrected threshold eccentricities in normals.

High values of KLV are a sign of irregular isopteric shape, even if KMD values are normal[14].

$$KLV = \frac{1}{(m-1)}\sum_{i=1}^{m}(z_i - KMD - x_i)^2$$

where m = 62

where m = 62.

d. Kinetic corrected loss variance (KCLV): this index indicates the variance of the differences between the results obtained and the age-corrected normal values, taking into account the influence of KSF.

As in static perimetry, this index, compared to KLV, permits a more reliable evaluation of the uniformity of sensitivity[1,2]

$$KCLV = KLV - \frac{1}{n}(KSF)^2$$

Table 1 Kinetic Visual Field Indices Mean ± SD of visual field indices in normal subjects

Kinetic indices	Mean ± SD (degrees)	Normal range (degrees)
KMD	0 9 ± 4 32	0 4 4
KSF	2.31 ± 1.77	0 4 0
KLV	18 37± 8.16	0 26 5
KCLV	17 70± 8 21	0. 25 8

Results

In Table 1 the mean values and the SD of the kinetic visual field indices are illustrated.

KMD is scattered around zero in normals and is independent of age. KLV is increased in the presence of non-uniformity of the isopters and is not related to age. Eccentricity does not influence this parameter.

Conclusions

Evaluation of the normality of manual kinetic perimetric results has always been performed by means of empirical criteria, mainly based on the perimetrist's experience.

Automatic Goldmann perimetry allows examiner-related variables to be avoided, but also causes elimination of continuous correction, retest and interpretation of the patient's responses performed by the perimetrist during the examination. Therefore, interpretation and evaluation of normality are now more difficult because of

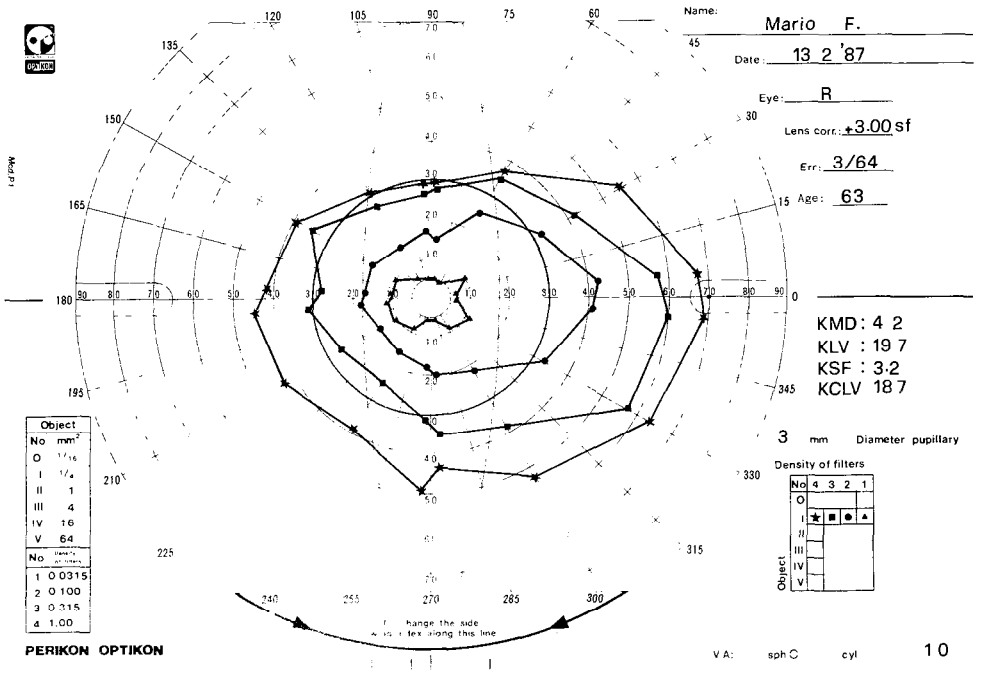

Fig 1 The visual field illustrated in this figure seems to be irregular and contracted On the contrary, the visual field indices indicate that both isopteric width and shape are inside normal range.

the irregularity of the isopter's shape. There is need for a precise and objective method for comparison of results during follow-up of perimetric defects.

In this field, perimetric indices represent a valuable aid to the ophthalmologist. For instance, the visual field represented in Fig. 1 reveals at first glance a general contraction with an irregular isopteric shape.

The visual field indices, on the contrary, indicate that the isopteric width is normal for the patient's age (KMD = 4.2) and the isopteric irregularities are within normal limits (KLV = 19.7; KCLV = 18.7; KSF = 3.2). This confirms the need for

a reliable and rigorous evaluation of a kinetic visual field abnormality.

In conclusion, in our opinion, the 'kinetic visual field indices' represent a noticeable advancement in perimetry, but they cannot completely replace the experience of a good perimetrist.

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THE Q-STATISTIC IN GLAUCOMA AND OCULAR HYPERTENSION

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Brecher and Whalen have suggested that the Q-statistic, a calculation based on third moment calculations, may be useful in the early detection of glaucoma defects. From our early experience in the use of this statistic and based on theoretical considerations, we questioned its value in the interpretation of automated visual field data We therefore analyzed the visual fields of 30 glaucoma suspects and 15 patients with established chronic open angle glaucoma (OAG).

All visual fields were performed on the Octopus 2000R perimeter using Program 32 and target size III Visual fields were downloaded to an IBM compatible microcomputer and the visual field indices mean defect (MD), corrected loss variance (CLV) and Q were calculated using the formula of Flammer, Brechner and Whalen

Our analysis showed: (1) No correlation between Q and MD (r=-0.23, p=0.12, n=45) or CLV (r=0 17, p=0.23, n=45). (2) In our glaucoma patients population, all of whose visual fields were abnormal, only one of 30 visual fields was judged as abnormal based on the Q criteria of Brechner and Whalen. (3) In the glaucoma suspect population, the incidence of abnormal Q values increased as the field was judged more normal by MD and CLV criteria. Upon repeat testing, positive Q values were not found to be predictive for increasing abnormality on MD or CLV criteria, and could not predict subsequent Q abnormality.

We conclude that the Q statistic is of little or no use in the analysis of visual fields

Introduction

Because perimetric testing strategies are statistical samplings of the true visual field, there is a growing realization that statistical analysis is necessary for the interpretation of visual field data. Point by point analysis is possible but is attended by severe statistical constraints[1]. More promising are the whole field indices popularized by Flammer *et al.* [2]. Brechner and Whalen have suggested the use of the Q statistic as an aid in the early detection of abnormal visual fields[3]. The Q statistic is designed to detect a small subset of abnormal values. It is based on third moment calculations and is represented mathematically by Equation 1:

$$Q = \frac{\dfrac{\sum_{i=1}^{I} (z_{ijk} - \bar{Z}_{\cdot jk})^3}{I}}{\left[\dfrac{\sum_{i=1}^{I} (Z_{ijk} - \bar{Z}_{\cdot jk})^2}{I}\right]^{3/2}}$$

where Z_{ijk} is the threshold corrected by the normal value at location i, session j, for patient k; $Z_{\cdot jk}$ is the mean of all Z_{ijk} in the examination (the mean defect) and I is the number of thresholds used in the calculation.

This formula differs from that published by Brechner and Whalen in that the Q statistic computed by this formula will have a reversal of sign[1].

By raising the difference of the observed threshold and normal value to the third

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power, a small subset of depressed values will have a large impact on the final global Q statistic. The Q statistic becomes less sensitive as the field becomes more abnormal; likewise the Q statistic would not be affected if the entire visual field were evenly depressed. Brechner and Whalen therefore proposed that this statistic may be useful in the detection of early glaucomatous field loss if there is a small subset of depressed values.

The measurement of retinal sensitivity by the automated perimeter is accompanied by both measurement error and fluctuation[1]. Short term fluctuation of several decibels has been demonstrated by Wilensky *et al.* in normal eyes[4]. Moreover, short term fluctuation may be increased in early glaucoma [5-7]. For theoretical reasons, we questioned whether the variability inherent in the testing process might decrease the usefulness of the Q statistic as a reliable indicator of visual field abnormality. We therefore computed the Q statistic in glaucoma suspects and glaucoma patients and compared them to the critical values suggested by Brechner and Whalen. We also compared the Q statistic to the standard field indices, mean defect (MD) and corrected loss variance (CLV).

Patients and methods

Patient population

1. *Glaucoma patients:* All patients suffering from chronic open angle glaucoma in the Glaucoma Service at the University of Kentucky were reviewed. In order to have been selected for inclusion in this study, the patients must have had bilateral chronic open angle glaucoma with no other cause for visual field defects. Specifically, the inclusion criteria were documented intraocular pressure (IOP) greater than 21 mm Hg in both eyes, disc changes, and visual field defects characteristic of chronic open angle glaucoma in at least one eye. Specifically excluded were any patients with corneal disease, cataract or media opacities decreasing visual acuity to less than 20/40 in either eye and other retinal, macular, or neurologic causes of field defect. Using these criteria, 15 patients were identified whose visual fields represented, as far as we could tell, pure glaucomatous loss.

2. *Glaucoma suspects:* These visual fields were collected from patients from the Massachusetts Eye and Ear Infirmary Glaucoma Service who had been recruited into a study of Timolol versus no treatment in glaucoma suspects. Inclusion criteria included visual acuity of greater than 20/30, IOP greater than 22 mm Hg in both eyes, and no evidence of characteristic disc changes due to glaucoma or visual field defects on Goldmann testing. One hundred and twenty-five fields of 30 subjects were obtained.

Visual field testing

All visual fields were performed on the Octopus 2000R automated perimeter using program 32. Parameters of testing are listed in Table 1.

Statistical analysis

All visual field data indices were calculated using Lotus 123. All graphs were created directly from the Pgraph function of this program. The Mean Defect (MD) was computed according to the formula of Flammer[2]. The Q statistic was computed

Table 1. Parameters of testing Octopus 2000R Program 32

True threshold algorithm (double-crossing technique)
Infrared television fixation monitor
76 points tested (60 grid)
Spot size Goldmann III
Stimulus duration, 0.1 second
Background 4 Asb (apostilbs)
Maximum target luminance, 1000 Asb

according to the formula of Whalen and Spaeth as modified by Hirsch1,3. The Q statistic of each visual field was plotted against the MD. For statistical analysis, in order to avoid covariance effects for patients and eyes, only the right eye of the last visual field of each subject was selected and an analysis of variance (ANOVA) procedure applied to the data.

The critical Q statistic values were obtained from Brechner and Whalen[3] and are:

Q 10% = 0.7952
Q 5% = 1.0645
Q 1% = 1.8000

Test parameters were identical to those used by Brechner and Whalen to determine these critical values. The reversal of sign from the published values is necessary to conform to the different equation format.

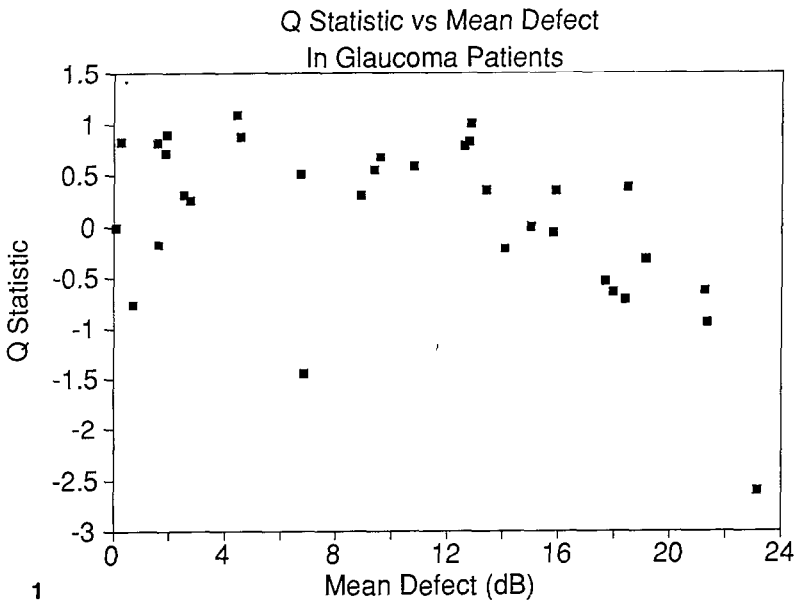
Results

The plots of the Q statistic versus MD for glaucoma patients and glaucoma suspects are shown in Figs. 1 and 2. There is no relationship between the Q statistic and the MD except that there are no significant Q values with a large MD. Only one of 33 eyes tested in the glaucoma patients had a Q value significant above the 5% confidence level. Approximately 30% of the visual fields in the glaucoma suspects had Q values significant above the 5% confidence level. However, each patient who had one or more test results in the 'abnormal' range also had one or more 'normal' results. Furthermore, there was no pattern in the occurrence of the 'abnormalities'.

Discussion

There are several theoretical reasons why we question the usefulness of the Q statistic. Undoubtedly the nature of the calculation allows for determining whether small numbers of values in a large set of homogeneous data differ from the normal. In practical application, this makes the Q statistic useful for such things as quality control. In that instance, where nearly all of the values are normal, the rare value that deviates will be easily detected using the Q statistic.

Visual field measurements have inherent variability both over the short and long term[7,8]. Wilensky *et al.*[4] have shown that in normal eyes it is common to have at least one point differ from normal by greater than 4 dB over the short term. Bebié *et al.*[8] suggest that if retinal sensitivity measurements are repeated at 12 points, on a statistical basis alone, three of these points will show an apparent deterioration of 2 dB and one will differ by 4 dB or more. Unquestionably, the threshold determinations in normal eyes do not fall on the expected but rather vary around the normal. This poses some theoretical problems when applying the Q statistic to



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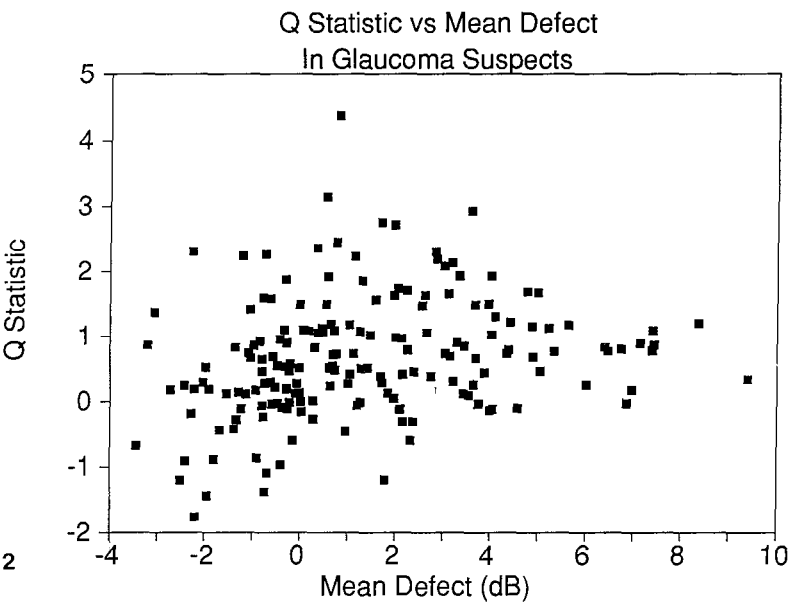

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visual field data. If all of the values vary equally around the normal, the differences will cancel and the Q value will be zero, a statistically normal field. If, however, a single point is asymmetrically depressed, even by only 4 dB, the field will be judged statistically abnormal at greater than the 1% confidence level. Thus, there will inevitably be false positives in clearly normal fields[4].

It has been proposed that the earliest field abnormality in glaucoma may be increased scatter or increased short term fluctuation[5,7]. As the variability around the normal increases, by definition the sensitivity of the Q statistic decreases. In a sufficiently variable field, the Q statistic will miss a defect independent of its size. Thus the very nature of the disease mitigates against its detection using the Q statistic.

In our group of glaucoma patients, there was only one visual field with a Q value significant at the 5% confidence level. This patient had a mean defect of approximately 4.5 dB. As the mean defect increases, the sensitivity of the Q value decreases and thus it is not surprising that in none of the glaucoma patients with a large mean defect was the Q significantly abnormal. In our series, however, even in those patients with relatively small mean defects, the Q was not significant at the 5% level. The fact that this occurred emphasizes that the earliest lesion in glaucoma is not a localized defect at a single point but is more likely an increase in the short term fluctuation, a group of depressed points, or a generalized depression. None of these defects would produce a significant Q value.

Similarly, in the glaucoma suspect group the Q statistic was unhelpful. In this group, each subject performed multiple tests at intervals of three months to one year. Although approximately 30% of the Q results were significant at the 5% confidence level, the 'abnormal' results occurred sporadically interspersed with 'normal' examinations in individual patients.

The Q statistic is useful as a measure of sample skewness. It is formulated to detect isolated aberrations in populations with low variance. Because of intrinsic fluctuations in visual potential and inherent limitations in the sampling strategies used in perimetry, the results of visual field examinations do not resemble such populations. Furthermore, in dealing with glaucoma, the nature of the disease process decreases the likelihood that the Q statistic will be helpful. Analysis of visual field data in glaucoma suspects and patients with definite chronic open angle glaucoma confirms the theoretical suspicion that the Q statistic is of little or no value in the management of this disease.

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CLINICAL EXPERIENCE WITH THE BEBIÉ-CURVE

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A visual field can have diffuse and local changes. In the absence of local defects, diffuse damage can easily be recognized with the help of the visual field indices In the presence of scotomas, diffuse damage in the remaining better or 'normal' part of the retina is more difficult to recognize and quantify Bebié et al published a new method to present the outcome of a visual field in relation to the normal values. They represented the results with the help of a cumulative defect curve, a method which we called the 'Bebié-curve' This method allows easy recognition of diffuse as well as local damage. This study evaluates the clinical application of the Bebié-curve in different diseases and for the follow-up of the visual fields.

Introduction

The results of visual field measurements can be represented by different methods, numerically or graphically. A visual field measured by static perimetry can be shown numerically by a numerical list, a numerical grid or the so-called visual field

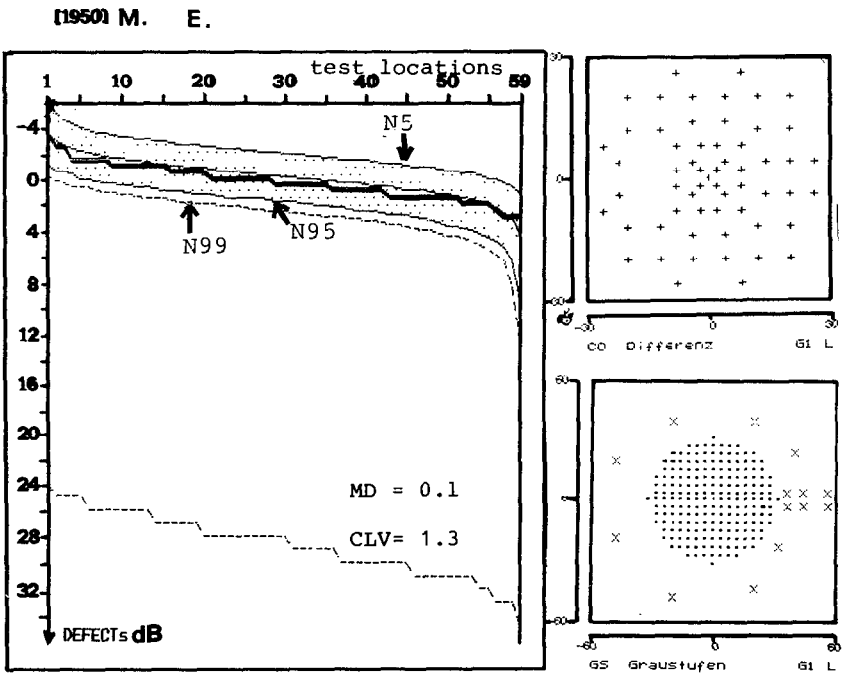

Fig 1 Example of a normal visual field On the left hand side of this combined printout is the Bebié-curve (together with the visual field indices) and on the right hand side a CO-printout and a GS-printout of the 59 test locations of the central 26-field. The normal range of a Bebié-curve is displayed by the shaded zone The thick black line represents the Bebié-curve of the individual case. The N5, N95 and N99 curves indicate the defect value which is not exceeded by 5%, 95% or 99% of normals

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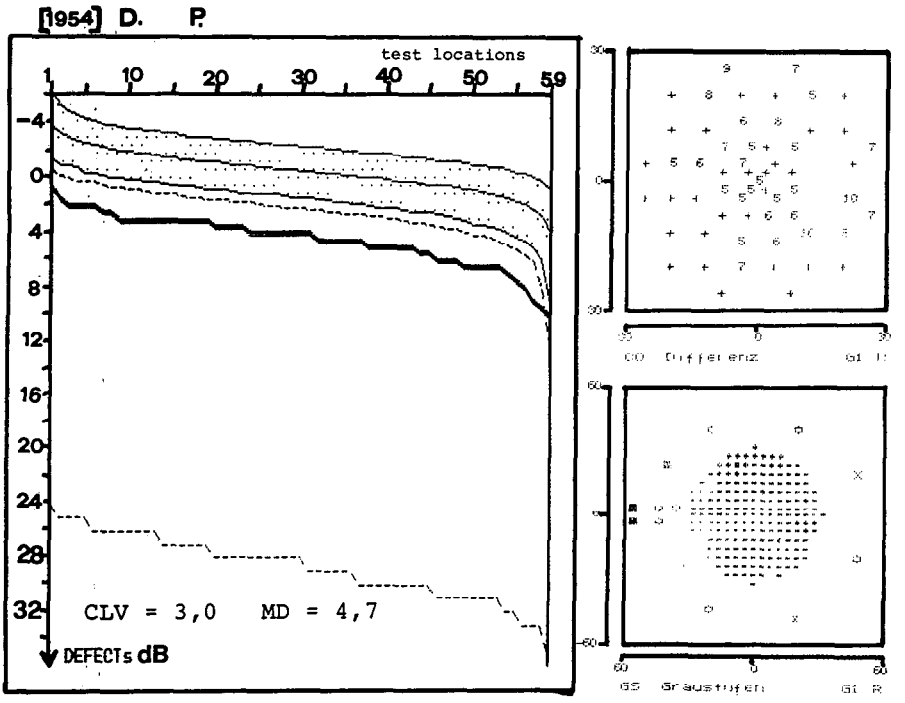

Fig 2 Example of a Bebié-curve, CO-printout, GS-printout and visual field indices of a glaucoma patient with diffuse damage The Bebié-curve is shifted down, more or less parallel to the normal range

indices, as well as graphically by a CO-printout (Comparison table), a GS-printout (Grey Scales), a 3-D-printout (3-dimensional) or, finally, a Profile-printout. Although all these modes are available, we normally use the CO-printout combined with a list of the visual field indices for the Octopus Program G1. Whereas the visual field indices provide global and quantitative information about the entire visual field, the topography of damage can be seen on the CO-display. Local damages (scotomas) can easily be displayed with each method, especially if they are deep. It is, however, more difficult to recognize diffuse damage. It is easy to recognize diffuse damage with the help of the visual field indices in the absence of scotomas (increased Mean Defect, MD, and normal Corrected Loss Variance, CLV). In the presence of scotomas (increased MD *and* increased CLV), however, it is difficult to quantify the amount of potential additional diffuse damage.

To solve this problem, Bebié *et al.*[1] described a method to represent the perimetric results with the help of a cumulative defect curve. We will refer to this method as the 'Bebié-curve'. The aim of the present study was to test the usefulness of this method for clinical purposes.

Methods

The principle of the Bebié-curve is the arrangement of the depth of the defects of all test locations in a cumulative curve. With this curve, it is easier to quantify

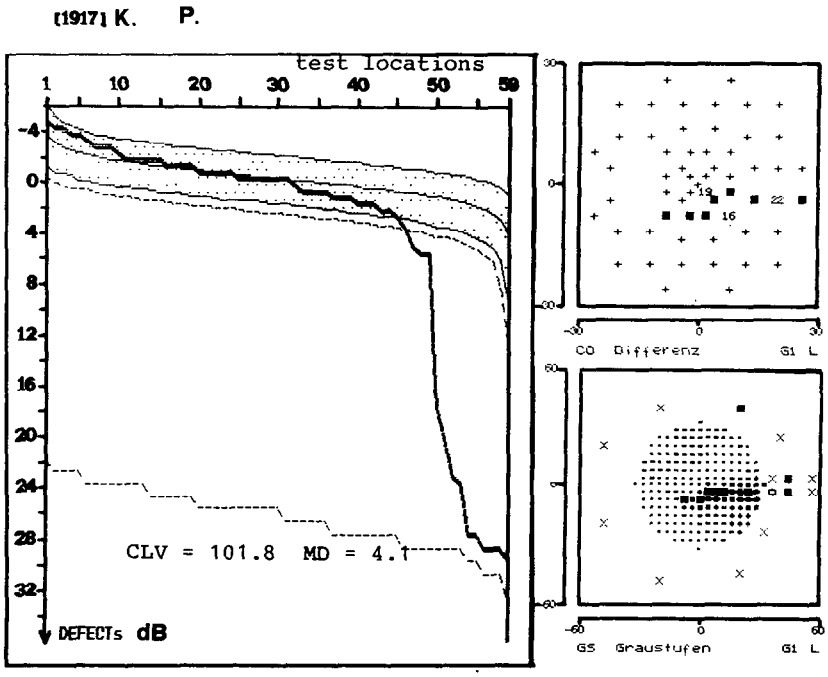

Fig 3 Further example of a visual field of a glaucomatous eye. This patient has a typical scotoma without any additional diffuse damage. The Bebié-curve has a steep fall showing local damage

the damage in the scotoma as well as in the remaining 'normal' area. The visual field damages, measured in the 59 central test locations of the program G1, are displayed in a cumulative mode, this means in an ascending line. On the *x*-axis, the single test locations are lined, on the *y*-axis there are defects in dB. The test locations with the lowest dB loss, compared with normal values, are shown on the left hand side, the test locations with the highest dB loss on the right hand side of the curve. With the help of a pool of normal values, Bebié *et al.* defined the normal range of these cumulative curves (Fig. 1). This enables the program to represent the Bebié-curve in relation to the normal population. This method is presently available for the Octopus program G1. It can, however, in principle be applied to any type of quantitative program, if normal values are available. In our study, we applied this program to a large number of patients, especially glaucoma patients, and tested the usefulness for the recognition of local, diffuse and combined damage for the follow-up of visual fields.

Results and discussion

After having explained the method to clinicians working in our department, they adopted the method very quickly and uniformly experienced an improvement in the interpretation of the visual fields. The following examples show some typical clinical situations. Pure diffuse damage is shown by a curve displayed below but parallel to the normal range (Fig. 2). Local defects show up as a steep fall in the Bebié-curve (Fig. 3), and a combination of diffuse and local damage can be seen

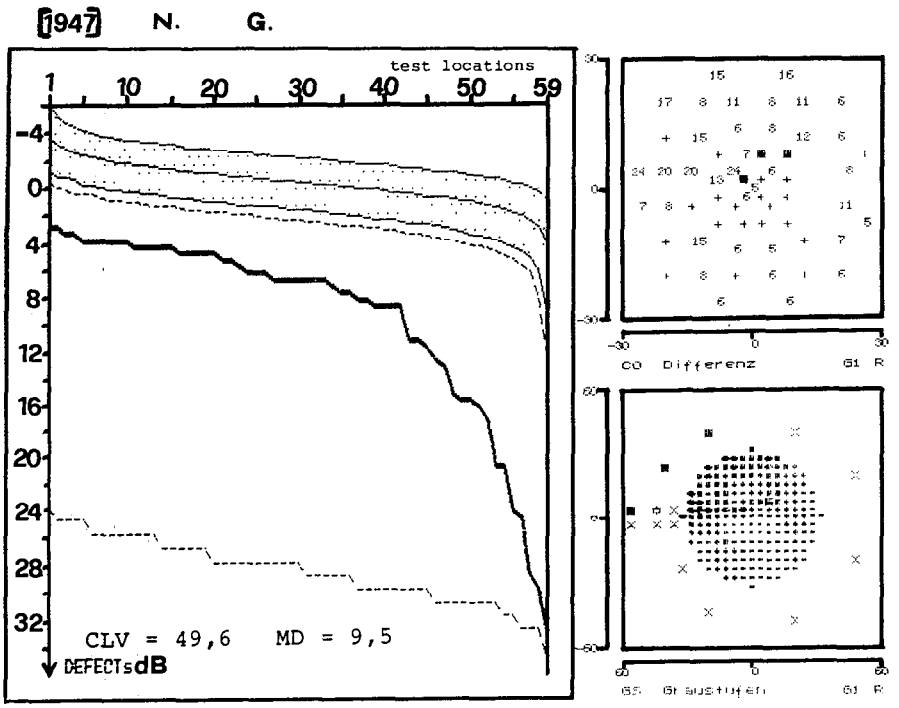

Fig 4 This example has combined diffuse and local damage. Both visual field indices, MD and CLV, are increased. The CO-printout and the GS-printout represent the topography of the individual relative and absolute scotomas. The Bebié-curve indicates clearly the combination of diffuse and local damage.

in Fig. 4. With the help of the Bebié-curve, the diffuse and local damage are clearly visible on the graph. It is however not possible to see the topography of the defects. It should therefore only be used in combination with another type of display, such as the CO- or GS-display. Based on experience with the Bebié-curve, we learned that the diffuse damage in glaucoma patients is often greater than one would expect by using the Comparison-table-display or Grey Scales. It is further possible to see differences between high and low tension glaucoma, a topic which will be dealt with in a further study. We would like to indicate at that stage that the Bebié-curve is of great help, not only in clinical work but especially in evaluating clinical studies.

Acknowledgement

We are grateful to Dr Suzette Franklin for her help

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THE ANALYSIS OF NORMAL FIELDS WITH THE HUMPHREY STATPAC

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Abstract

We evaluated the effect of changing the definition of normality in the statistical package of the Humphrey perimeter (STATPAC) One hundred-thirty eyes of 100 normal consecutive subjects were subjected to static threshold perimetry using the 30-2 program of the Humphrey perimeter The criteria for entry and reliability were purposely made stricter than those used in STATPAC The statistical package found that 3.0% of all tested point locations deviated from expected age-corrected normal values at the p<5% level (Total Deviation Plot), while 2.7% deviated at this level of significance after correction for the overall height of the hill of vision of each subject (Pattern Deviation Plot) Similarly, 0.02% of all tested points on the Total Deviation Plot and 0 06% on the Pattern Deviation Plot were significant at the p<0.5% level

The incidence of eyes with global indices significant at p<5% was 2 3% for Mean Deviation, and 1 5% for Short-term Fluctuation, Pattern Standard Deviation, and Corrected Pattern Standard Deviation None of the eyes had global indices significant at p<0 5%

We believe that the most likely reason for our consistently lower than expected incidence of statistically significant findings was the application of stricter entry and reliability criteria to our study population than those applied to the normals in STATPAC

Our results emphasize the importance of agreement and consistency in the definition of normality in statistical diagnosis packages

Introduction

It is not always easy to interpret with certainty whether a field measured by means of an automated perimeter is normal or not. The Humphrey STATPAC is a statistical package devised for the statistical analysis of computerized visual fields[1]. Implicit in the design of this package are definitions and assumptions of what is to be called normal and what is not[2]. We wished to demonstrate the effect of a change in those definitions.

Subjects, material and methods

Among the analyses offered by STATPAC is one called the single field analysis. This analysis is specifically designed to help one interpret whether any given field is normal or not, and presents data in a number of ways. Decibel deviations from age-corrected normal values are plotted at each test point location along with an indication of the frequency with which each point's observed deviation was seen in the STATPAC normal data base; these are called the Total Deviation Plots (TD), The Pattern Deviation Plots (PD) are similar to Total Deviation except that the data have been corrected for any overall depression or elevation of the hill of vision,

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e g. due to miosis or media opacities. Also presented on the single field analysis are four global indices, intended for use in longitudinal follow-up. These indices indicate the deviation of height (Mean Deviation or MD), intra-test reliability (Short-term Fluctuation or SF), and shape consistency (Pattern Standard Deviation or PSD, and Corrected Pattern Standard Deviation or CPSD)[1].

We defined subjects as normal who met all of the following criteria: (1) best corrected visual acuity equal to or better than 20/20, (2) no ocular disorders except for refractive errors equal to or less than 3 diopters, (3) ophthalmoscopically normal optic discs, and (4) absence of family history of glaucoma. One hundred-sixty subjects (190 eyes) who fulfilled the criteria were tested with the Humphrey Field Analyzer Model 620 or 630. The central 30-2 threshold test was used. Stimulus size III was used and each stimulus was presented for the standard 0.2 seconds at the standard test speed.

Table 1. Age distribution

Age (years)	10-19	20-29	30-39	40-49	50-59	60-	Total
No of patients	. 14	15	16	19	17	19	100
No of eyes	17	23	20	27	21	22	130

Table 2 Incidence of p<5% and p<0.5% points in all the tested points

Age (yrs)	No of eyes	Total points examined (76 x No. of eyes)	No. of p<5% points		No of p<0 5% points	
			TD	PD	TD	PD
10-19	17	1292	57(4 4)	26(2.4)	0	1(0.08)
20-29	23	1748	67(3 8)	42(2.4)	0	0
30-39	20	1520	25(1.6)	37(2 4)	0	0
40-49	27	2052	24(1.2)	25(1.2)	0	0
50-59	21	1596	73(4 6)	72(4 5)	2 (0.1)	4(0.25)
60-	22	1672	50(3.0)	66(3 9)	0	1(0.06)
Total	130	9880(100)	296(3 0)	268(2 7)	2(0.02)	6(0.06)

( ): %

Results

1. *Reliability and age distribution of subjects*

Among 190 eyes tested, 60 eyes were excluded, as they failed to meet minimum reliability criteria (<20% fixation loss, *and* <10% false positive responses, *and* <10% false negative responses). The fields of the remaining 130 eyes of 100 subjects were subjected to analysis. The age distribution of the adopted subjects is shown in Table 1.

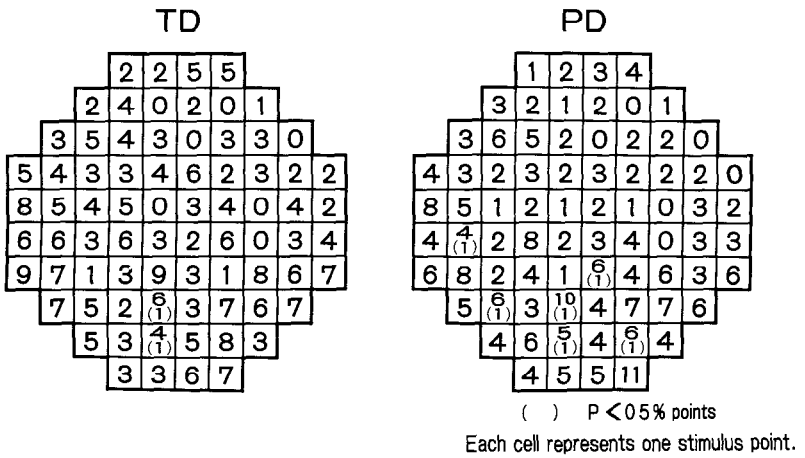

Fig 1 Number of $p<5\%$ and $p<0.5\%$ points in all the examined points ($n = 130$ in each cell)

Table 3 Incidence of eyes with global indices of p<5% and p<0.5%

Age (yrs)	No of eyes	MD		SF		PSD		CPSD	
		p<5%	p<0.5%	p<5%	p<0.5%	p<5%	p<0.5%	p<5%	p<0.5%
10–19	17	2	0	0	0	0	0	0	0
20–29	23	1	0	0	0	0	0	0	0
30–39	20	0	0	0	0	0	0	0	0
40–49	27	0	0	0	0	0	0	0	0
50–59	21	0	0	1	0	0	0	0	0
60–	22	0	0	1	0	2	0	2	0
Total	130	3	0	2	0	2	0	2	0
	(100)	(2 3)	(0)	(1.5)	(0)	(1 5)	(0)	(1.5)	(0)

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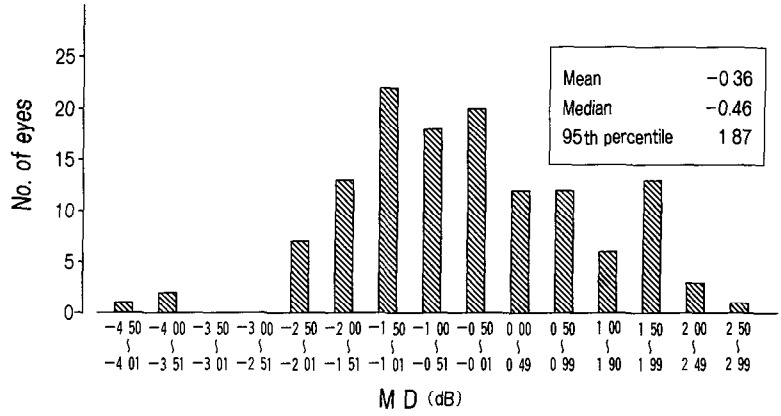

Fig 2 Frequency distribution of Mean Deviation.

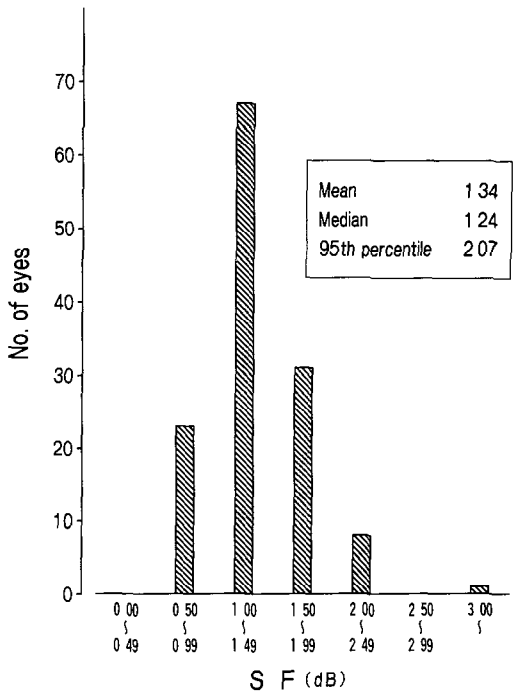

Fig. 3 Frequency distribution of Short-term Fluctuation

2. *Total and pattern deviation*

The incidence of p<5% and p<0.5% points is illustrated as the number of eyes at each test point for TD and PD (Fig. 1). The incidence of p<5% and p<0.5% points is listed for each decade of age (Table 2). The overall incidence of the test points of p<5% was 3.0% for TD, and 2.7% for PD in all the tested points (76 points per eye x 130 eyes). The incidence of test points of p<0.5% was 0.02% for TD and 0.06% for PD.

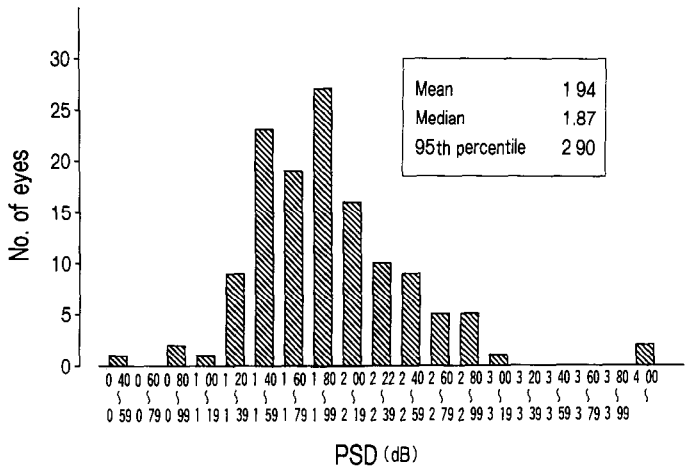

Fig 4. Frequency distribution of Pattern Standard Deviation

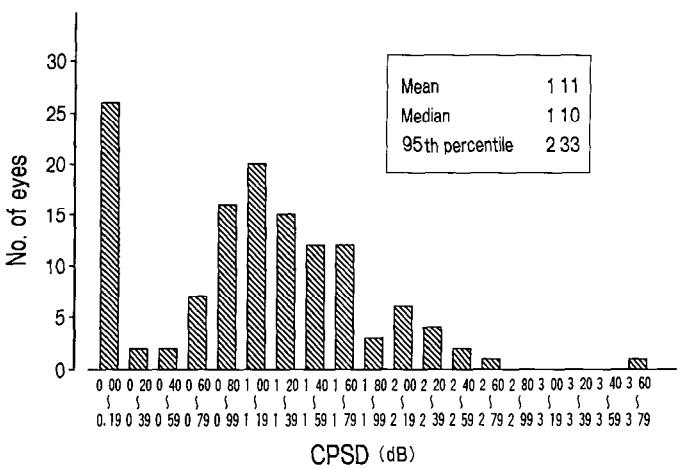

Fig 5 Frequency distribution of Corrected Pattern Standard Deviation

3. *Global indices*

The incidence of eyes with global indices of p<5% was 2.3% for MD, and 1.5% for SF, PSD, and CPSD (Table 3). The frequency distribution of global indices is illustrated with the mean, median, and 95th percentile in Figs. 2-5.

Comments

The choice of criteria defining normality is always a difficult one. If highly restrictive criteria are applied, then only results from supranormal subjects will be

used and, presumably, a high number of false positive results will be generated in the clinical population. Likewise, if the chosen criteria are lax, it would be expected that many pathological cases will be missed in the clinic.

Our results demonstrate that specification of strict criteria does in fact lead to more exacting standards for normality. We found fewer statistically significant values in the results of our normal subjects than might be expected based on the STATPAC analysis. We suggest that the most likely reason for this was the application of stricter entry and reliability criteria to our study population than those applied to the normals originally used in STATPAC.

Intuitively, one would expect subjects meeting stricter criteria to produce field results showing higher pointwise sensitivities, and more internal consistency. Our results suggest that to be the case, and emphasize the importance of agreement and consistency in the choice of definitions of normality.

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MAXIMUM LIKELIHOOD ESTIMATION OF THE FREQUENCY OF FALSE POSITIVE AND FALSE NEGATIVE ANSWERS FROM THE UP-AND-DOWN STAIRCASES OF COMPUTERIZED THRESHOLD PERIMETRY

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Knowledge of the frequency of false positive and false negative answers facilitates the interpretation of computerized visual fields. These parameters are usually estimated by catch trials.

The authors have devised and investigated a new method in which maximum likelihood techniques are used to estimate the frequency of false answers It utilizes all data in the up-and-down staircases of the threshold determination sequences as well as results from catch trials The results achieved with this new method were compared with those of the conventional method, theoretically and in simulations

For healthy and reliable observers, the new method gave sufficiently good results without any catch trials at all, while the number of catch trials may be reduced by about 50% for observers with visual field loss

Introduction

Knowledge of the frequency of false positive and false negative answers facilitates the interpretation of computerized visual fields. These ratios are usually estimated by catch trials[1,2]. In false negative (FN) catch trials, a strong supraliminal stimulus is exposed at a location where the threshold has already been measured. In false positive (FP) catch trials, no stimulus is shown while the perimeter produces the same sound as when displaying a stimulus.

In computerized perimetry the differential light threshold is usually estimated by an up-and-down staircase procedure. In each measured point a sequence of stimulus intensities and responses is produced, resulting in a staircase of exposed stimulus intensities. The field test consists of an aggregate of staircases.

The aim of the present study was to find out if the actual staircases of the thresholding algorithm could be used to estimate efficiently the frequency of false positive and false negative answers. A new method of analysis was devised. The theoretical possibilities of this method were investigated, and results obtained with it compared with those of traditional catch trials.

Method

We used a modified maximum likelihood method to estimate the ratio of false positive and false negative answers. In maximum likelihood estimation[3] the parameters of a model are estimated by adjusting them to maximize the likelihood of the observed data. Knowing the numerical values of the parameters in a mathematical model, one may calculate the probability (or likelihood) of the various observations. In computerized threshold perimetry, if we know the threshold value, the slope of the frequency-of-seeing curve and the frequencies of false positive and

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false negative responses, we may compute the probabilities of all observed test stimulus and response sequences. The maximum likelihood estimates are those values of the parameters (*e.g.*, frequencies of false positive and false negative responses) which make the numerical value of the probability of the aggregate of staircases actually observed as large as possible.

Model

The following perimetric model was used:

A. The frequency-of-seeing curve, $P(z|\mu)$, was defined as the probability of a positive response to a stimulus of intensity z, and is given by

$$P(z \mid \mu) = FP + (1 - FN - FP) * \Phi\left(\frac{z-\mu}{\sigma}\right), \qquad (1)$$

where the true threshold level (probability of perceiving the stimulus = 50%) is μ, and FP and FN are the ratios of false positive and false negative answers, respectively. The standard Gaussian distribution function is denoted by Φ. The slope of the frequency-of-seeing curve is determined by the parameter σ.

B. The threshold-measuring staircase algorithm used steps of 4 dB until the first reversal of the test process. Testing then continued in 2 dB steps, stopping at the second reversal.

C. The differences between initial stimulus levels of the thresholding algorithm and the true threshold levels at each location were assumed to be independent and normally distributed, with expectation and standard deviation denoted by m_p and σ_p, respectively. This assumption is reasonable since the initial level at a point was assumed to be derived from measured thresholds at adjoining points, starting at an intensity m_p above the expected threshold value.

Thus the model had a total of five parameters (FP, FN, Φ, m_p,σd_p).

Calculation of probabilities of staircases

The conditional probability $L(i|\mu)$ of obtaining a staircase of a specific category (here denoted by i) when the threshold level is μ, can be calculated as the product (denoted by π in (2) below) of response probabilities for each stimulus intensity level z_j in the staircase,

$$L(i \mid \mu) = \prod_{j \in \text{stimuli with responses}} P(Z_j \mid \mu) * \prod_{j \in \text{stimuli without responses}} (1 - P(z_j \mid \mu)), \qquad (2)$$

with $P(z|\mu)$ given by (1). Thus the probability L(i) of obtaining a staircase of category i is,

$$L(i) = \int_{-\infty} L(i \mid z_1 - x)\, f(x)dx,$$

where z_1 is the initial stimulus level and f is the probability density function of the normal distribution with expectation m_p and standard deviation σd_p.

In most threshold field tests the differential light threshold is measured at a reasonably large number of test locations (50-100). The likelihood function L is the probability of the entire set of measurements observed in the visual field and therefore the product of the probabilities of the observed staircases,

$$L = \prod_{i=1}^{* \text{ staircase categories}} (L(i))^{n_i}, \qquad (3)$$

where n_i is the number of staircases of category i.

The results from traditional catch trials were incorporated in the model by multiplying equation (3) with the likelihood of the catch trial results.

Estimation of FP and FN

The values of σd, m_p and σd_p were kept constant during the iterations of FP and FN which were performed to find those values of FP and FN which gave the maximum of the probability of the observed aggregate of staircases and catch trials. The maximum likelihood values were calculated using the E04JAF program of the NAG library[4]. The parameters m_p and σp were estimated by the mean and the standard deviation of the difference between the initial stimulus level of each staircase and each threshold level as determined in the standard way (mean of the last two stimulus intensities). Five different values of σ were inserted into the likelihood function (1, 3, 5, 8, 12 dB). These were considered to cover a large enough range for most clinical situations. Each choice of σ gave a different estimate of FP and FN, and of the likelihood. The values of FP, FN and σ giving the maximum likelihood were chosen as estimates.

Consequently, although we have been primarily interested in the FP and FN ratio parameters, the method also yields an estimate of σ.

Testing the method

The results of the new method were compared with those obtained from traditional catch trials. We used data from 74 staircases (74 because this is the number of points outside the blind spot in the commonly used test programs 30-2 and 32 of the Humphrey and Octopus perimeters, respectively). Catch trials data consisted of answers from ten FP and ten FN trials.

Four artificial 'subjects' were introduced to facilitate the comparison. Two of the artificial 'subjects' had normal visual fields and two were abnormal. One normal

Table 1. Characteristics of the artificial subjects

Subject	Description	m_p(dB)	σ_p(dB)	σ(dB)	FN(%)	FP(%)
1	Normal field, reliable observer	3	3	1	5	5
2	Normal field, non-reliable observer	3	3	1	25	25
3	Abnormal field, reliable observer	3	7	5	5	5
4	Abnormal field, non-reliable observer	3	7	5	25	25

Table 2. Means and rms errors of FN and FP estimates. (All measures in %)

		Subject 1 *Normal, reliable*				*Subject 2* *Normal, non-reliable*				*Subject 3* *Abnormal, reliable*				*Subject 4* *Abnormal, non-reliable*			
		FN		*FP*		*FN*		*FP*		*FN*		*FP*		*FN*		*FP*	
		mean	*rms*	*mean*	*rms*	*mean*	*rms*	*mean*	*rms*	*mean*	*rms*	*mean*	*rms*	*mean*	*rms*	*mean*	*rms*
New method with catch trials	Theoretical	5	3.6	5	4.6	25	6.9	25	8.4	5	6.2	5	6.7	25	12.8	25	13.4
	Simulated	3.5	2.6	4.9	3.6	16.1	10.4	21.0	8.1	3.2	4.2	5.6	5.5	20.1	9.9	25.6	9.2
New method without catch trials	Theoretical	5	4.2	5	6.3	25	8.0	25	10.7	5	15.5	5	29 4	25	44.3	25.	72.0
	Simulated	3.5	2.9	5.6	4.1	11.4	15.7	16.5	11.9	6.6	9.1	12.0	13.7	12.9	16.8	18.0	14.8
Old method		5	6.9	5	6.9	25	13.7	25	13.7	5	6.9	5	6.9	25	13.7	25	13.7

and one abnormal 'subject' were reliable observers, one of each was unreliable (Table 1). For each of the 'subjects' we compared the results of the new method with those of traditional catch trials. The new method was evaluated both with and without the use of catch trials.

The new and the traditional methods were compared using means and rms errors of the FP and FN estimates. The rms error includes systematic error and standard deviation of the estimate. Means and rms errors were obtained both through theoretical calculations and computer simulations.

It is known[3] that with a very large number of observations (*e.g.*, staircases) the maximum likelihood estimator is optimal, *i.e.*, it has no systematic error and its rms error achieves the lowest possible value. We calculated the theoretically lowest possible rms error for the given perimetric model of 74 staircases. The Fisher information matrix[3], for estimation of all five parameters, was calculated in order to find these theoretical lower bounds of an unbiased estimator.

We generated 100 simulated visual fields for each of the four artificial 'subjects', using the perimetric model described. Our estimation method was subsequently applied to each of these fields, with and without catch trials data.

Means and rms errors of the catch trial method are easily calculated. The traditional estimates are unbiased and the rms errors equal the standard deviations.

The results of the simulations were also expressed by computing the number of extra catch trials which would have been required in order to give the same precision (rms error) as the new method.

Results

The results from the new and the traditional method for each of the four simulated 'subjects' are shown in Table 2. The mean of the estimates for FP and FN, and the rms error of the differences between the estimates and the correct parameter values are shown. In the normal and reliable 'subject' (#1) the new method, with no catch trials at all, gave better estimates than the traditional method. The new method (without catch trials) was at least as good as the traditional one, even in the unreliable observer with a normal field (#2). In abnormal fields the new method made it possible to reduce the number of catch trials, while maintaining the precision of the traditional estimates. The precision of the FN estimate was better than that of FP. Theoretical and simulated results agreed quite well except when the new method was used without any catch trials in abnormal fields.

In Table 3 the results are expressed in a different way. The table shows the number of catch trials, using the old method, needed to achieve the rms error of the new method. In most cases, the new method added information which otherwise would have required a large number of catch trials.

Discussion

We have devised and tested a new statistical approach to estimate false answers during perimetric test sessions. It utilizes all data in the up-and-down staircases of the thresholding algorithm and catch trials data if available. The method, based on maximum likelihood estimation, was tested by theoretical calculations and in computer simulations and its results were compared to those of conventional catch trials.

Our findings indicate that in healthy and reliable observers, the new method may replace traditional catch trials and at the same time give significantly better estimates of the false positive and false negative ratios than those obtained by

currently used techniques. In observers with visual field loss, the method allows the number of catch trials to be reduced by about 50% relative to the conventional method. Because of the construction of the tested threshold algorithm (first stimulus is likely to be seen), the improvement of rms error is greater for FN than FP, although substantial for FP as well.

A drawback of the new method is that for some subjects the estimates have a systematic error. However, this bias is included in the rms error (which is the square root of the sum of square bias and variance), and has therefore been taken into account in the comparisons.

Some of the simulations resulted in rms errors which were smaller than those expected from the theoretical calculations. The reason for this might be that theoretical results assumed no prior knowledge of the parameters, while in the simulations only a limited number of values for σ were allowed. This indicates that prior knowledge about the value of σ could improve the precision of the estimates considerably. Future analyses of σ in empirical perimetric data may therefore offer the possibility of further improving the present method.

In principle, all five parameters of the visual field could have been estimated by simultaneous iterations. However, in doing so we encountered considerable numerical difficulties in finding the maxima of the likelihood function. This was the reason for estimating m_p and σ_p directly from the data and for inserting only a limited number of values for σ.

It is logical and attractive to use simulated fields, in which the frequencies of false answers are known, for the evaluation of the new method. An alternative would have been to collect empirical data, perhaps using custom-made test programs with very large numbers of catch trials. The validity of our theoretical and simulated results requires that the perimetric model is sufficiently close to reality. We believe our model to be realistic. However, moderate deviations from the assumptions of the model are only expected to lead to a minor deterioration of the properties of the new method. The frequency-of-seeing curve is usually assumed to be Gaussian. An analysis of actual field data indicated that our assumption of a Gaussian distribution of the differences between initial stimulus levels and threshold values is warranted. The initial stimulus levels at different locations are certainly interdependent, as are the threshold values. However, the interdependence across the field between successive differences of initial levels and threshold values are probably small. The assumption of a constant slope, σ, across the visual field is certainly a simplification and here the model would probably benefit from a refinement. Some available studies indicate that σ may vary with test point location[5] and be higher in defective parts of the visual field[6]. This simplification was necessary because the empirical knowledge of σ is insufficient. In the abnormal fields only a small amount of information about the slope is available in the staircases. Values of FP and FN are realistic and based on results from previous studies[1,2]. The parameter m_p was set to the value 3 dB, a value which is commonly used in clinical perimetry. The values of σ and σp were determined after analyzing actual tests from normal and abnormal subjects.

We conclude that a major improvement in the FP and FN estimates can be achieved if our new method is applied to actual fields. This can be achieved without any increase in test time. The only cost is the computation time. The method requires extensive computations, however, and cannot be successfully implemented with the simple microprocessors used in today's computerized perimeters. The present fast development of computer technology makes it realistic to implement the method in the next generation of automated perimeters.

The error of the estimates for the new method depends on the subject and the visual field. There is a trade-off between saved test time and increased precision. We envision a procedure where the parameters are estimated during the test and

catch trials are used only to the extent needed to guarantee sufficient precision of the estimates.

The method should of course be carefully evaluated clinically before it is implemented in standard clinical perimetry. This is necessary to ensure the validity of the assumptions of the perimetric model. We have performed some initial practical trials which have been reasonably successful.

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GLAUCOMA

THE EFFECT OF LONG-TERM INTRAOCULAR PRESSURE REDUCTION ON THE DIFFERENTIAL LIGHT SENSITIVITY IN GLAUCOMA SUSPECTS

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Abstract

This study was undertaken to observe the effect on the differential light sensitivity in glaucoma suspects produced by a long-term reduction in intraocular pressure (IOP) with timolol maleate. The results are taken from an ongoing six-year follow-up study of glaucoma suspects randomly selected for treatment and non-treatment. We present fine-grid meridional data, recorded every four months by automated perimetry, of all 46 patients (24 treated and 22 untreated) who completed the six-year follow-up without developing localized visual field defects, acquired optic disc changes, and whose IOP was not judged clinically dangerous during the follow-up Methods of analyzing the profile sensitivity, the profile slope and the sensitivity of specific locations over the follow-up are described The results show that the long-term fluctuation in differential light sensitivity of the two groups was not significantly different ($p = 0.395$) and that the sensitivity at most of the locations remained stable The number of stable locations was not significantly different in the two groups ($p = 0.412$) and there was also no difference in the number of locations where the sensitivity appeared to decrease ($p = 0.193$) or increase ($p = 0\ 540$) Analysis of covariance showed no group difference in the profile sensitivity or the profile slope and that these variables remained stable in both groups over the six-year period Although the treated group maintained a consistently lower IOP than the untreated controls, the results showed that long-term pressure reduction with timolol in glaucoma suspects appeared not to influence the differential light sensitivity in the tested meridian

Acknowledgements

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(From Chauhan *et al* : The effect of long-term intraocular pressure reduction on the differential light sensitivity in glaucoma suspects. Invest Ophthalmol. Vis. Sci. 29:1478, 1988. Reproduced with permission)

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EFFECTS OF ORAL ACETAZOLAMIDE ON GLAUCOMATOUS VISUAL FIELD CHANGES

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Abstract

A total of 750 mg of acetazolamide was orally administered to 11 patients (15 eyes) with primary open angle glaucoma showing an intraocular pressure of 22 mm Hg or more and with glaucomatous visual field changes, to examine the effect on glaucomatous visual field changes using program 31 of the Octopus perimeter

Reduction in intraocular pressure with administration of acetazolamide was significant

The mean threshold changes per one test point with respect to the whole field, in addition to pathological and normal areas of the field before and after oral administration of acetazolamide showed no significant improvement compared with those in the control group The effect of oral acetazolamide was evaluated according to the degree of retinal sensitivity, although tendencies towards improved thresholds were observed at retinal sensitivity levels of 0 dB to -11 dB below the age-corrected normal value; a similar trend was also observed in the control group When mean threshold changes were compared with the control group, according to the retinal sensitivity graded at 5 dB intervals, a significant improvement was observed from 0 dB to -4 dB However, improvement of mean threshold changes remained between 0.06 dB and 2 03 dB.

The present results thus differ from previous reports which indicated that administration of acetazolamide improved glaucomatous visual field changes, orally or intravenously.

Introduction

It has been reported that oral or intravenous administration of acetazolamide improves glaucomatous visual field changes[1,2]. We examined not only whether oral administration of acetazolamide improves glaucomatous retinal function but also whether the effect is limited to pathological areas of the field or covers the whole field, and also whether it differs according to the disturbance of visual field sensitivity.

Material and methods

We examined 15 eyes of 11 patients diagnosed with primary open angle glaucoma (POAG) whose intraocular pressure (IOP) was above 22 mm Hg and with glaucomatous visual field changes detected by Goldmann perimeter. The age of the patients ranged from 41 to 69, average 60.9 years.

The visual field was measured twice with program 31 of the Octopus perimeter. First visual field examination was performed on the day that an IOP of 22 mm Hg or more was noted.

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Three 250 mg doses of acetazolamide were administered orally on the occasion of the second examination one week later (one dose the night before, one dose on the morning of the day of examination, and one dose at noon two hours before the examination).

IOP was measured again after visual field examination. Controls consisted of 23 eyes of 13 patients with POAG whose IOP was controlled below 21 mm Hg with glaucomatous visual field changes and otherwise on the same medication, apart from acetazolamide.

The average age of the control group was 52.3 years, ranging from 48 to 70. In these control patients, visual field examination was performed twice at one-week intervals without administration of acetazolamide.

The analysis of the effect of acetazolamide was made with 69 test points, excluding four test points at the blind spot. Any test points showing 0 dB on both examinations were excluded.

The difference in threshold between the initial result and the age-corrected normal value, and the threshold change between the initial and the second threshold, were obtained for each test point.

Among the thresholds of the initial examination, test points showing a decreased sensitivity of 5 dB or more compared to the age-corrected normal value were designated pathological areas of the field and those of 4 dB or less were considered to be normal areas of the field.

Mean threshold changes per one test point with respect to the whole field, as well as pathological and normal areas of the field, were calculated for each visual field and were compared with those in the control group.

Mean threshold changes corresponding to the retinal sensitivity based on the difference from the age-corrected normal value of all test points in the acetazolamide administration group were statistically compared with those of the control group.

Table 1. Mean threshold changes per one test point with respect to the whole field, pathological areas of the field and normal areas of the field in both groups

	Acetazolamide administration group	Control group	t test
Number of eyes	15	23	
Age (years)	60 9 ±10.2	56.4 ±10.2	t=2.080 NS
Reduction of IOP (mm Hg)	8 1 ± 4.2	−0.74 ± 1 7	t=2,416 p<0,001
Whole field (dB)	0.23 ± 2.26	−0.48 ± 1.37	t=1,094 NS
Pathological areas of the field	2 63 ± 4 38	0.55 ± 3.27	t=1,605 NS
Normal areas of the field	−0.14 ± 1.37	−0.62 ± 1 09	t=1.188

NS: Not Significant

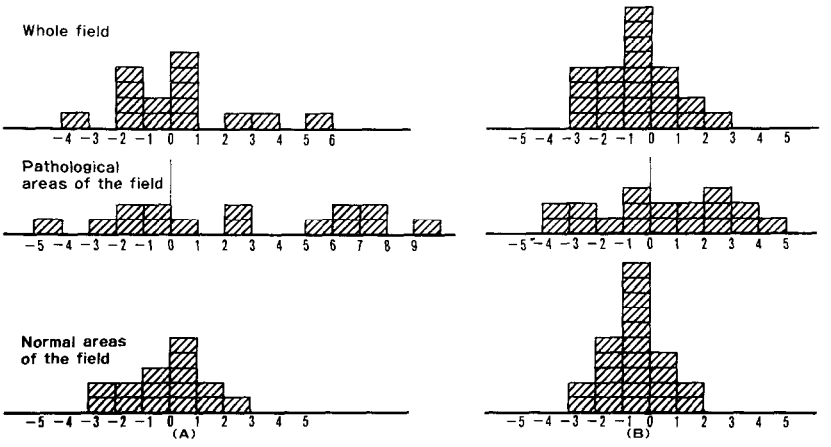

Fig 1 Frequency distribution of mean threshold changes per one test point with respect to the whole field, pathological areas of the field and normal areas of the field in the administration of acetazolamide (group A) and the control group (group B).

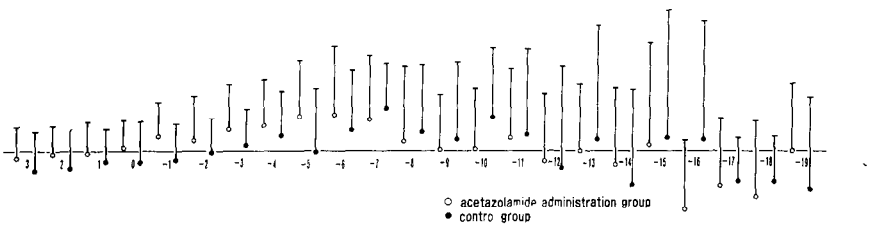

Fig 2 Mean threshold changes and SD of all test points corresponding to the difference between the initial program 31 results and the age-corrected normal value. Ordinate: mean threshold change in dB; abscissa: retinal sensitivity according to age-corrected normal value

Results

The decrease of IOP ranged between 2 and 18 mm Hg, average 8.1 ± 4.2 mm Hg, with administration of acetazolamide. The IOP changes in the control group ranged from 0 to 4 mm Hg, average -0.74 ± 1.7 mm Hg. This indicates a significant difference between the two groups ($p<0.001$).

Table 1 shows the mean threshold changes per one test point in both groups with respect to the whole field, pathological and normal areas of the field. Fig. 1 shows the frequency distributions.

Mean threshold changes with regard to the whole field, pathological and normal areas of the field in both groups, show similar distribution and no significant difference between those of the two groups was observed, as shown in Table 1.

In order to estimate the effect of acetazolamide on the degree of retinal sensitivity, mean threshold changes of all test points were calculated according to the difference between the initial result and the age-corrected normal value as shown in Fig. 2.

Table 2 Mean threshold changes of all test points compared with the control group according to the retinal sensitivity which was divided into 6 grades at 5 dB intervals

	Acetazolamide administration group	Control group	t test
	Mean threshold changes ± SD	Mean threshold changes ± SD	
+5 ~ +1 dB	−0 36 ± 1.87 dB (241)	−1.15 ± 2 28 (551)	4.764**
0 ~ −4	0 73 ± 2.34 (420)	−0.21 ± 2 34 (678)	6 469**
-5 ~ −9	1 47 ± 3.80 (142)	0 93 ± 3 88 (200)	1.265
-10 ~−14	−0 1 ± 4.57 (50)	1.75 ± 4 75 (32)	1.762
-15 ~−19	−1 70 ± 5.53 (33)	0.10 ± 5 9 (31)	1.252
-20 ~−24	−1.81 ± 1 83 (26)	−0 53 ± 3.56 (15)	1.517

**$p<0.01$ ( ) number of test points

Although improved mean thresholds were observed at retinal sensitivity levels from 0 dB to -11 dB in the acetazolamide administration group, a similar trend was also observed in the control group.

When mean threshold changes were compared with the control group according to the retinal sensitivity graded at 5 dB intervals, a significant improvement was observed from 0 dB to -4 dB ($p<0.001$, Table 2). Mean threshold changes in this grade ranged between 0.06 and 2.03 dB.

No significant correlation was observed with regression analysis between reduction of the IOP and mean threshold changes with respect to the whole field, pathological and normal areas of the field.

Discussion

In spite of the recent development of new types of anti-glaucoma agents, only a few studies have been performed on the effect of anti-glaucoma agents on retinal sensitivity[3].

It is not easy to evaluate true therapeutic efficacy, because the influence of aging or fluctuation accompanies the determination of differential light thresholds.

Some investigators have reported that increased retinal sensitivity or improved glaucomatous visual field defects were noted after administration of acetazolamide or hyperosmotic agents[1,2,4]

Although various mechanisms have been postulated for nerve fiber damage at the optic disc in POAG and low tension glaucoma, IOP plays a major role. Glaucomatous visual field changes have generally been considered to be irreversible.

From this point of view, the findings mentioned above deserve re-examination. Therefore, the authors planned this study to re-evaluate the effects of administration of acetazolamide on retinal sensitivity.

In 15 eyes of POAG with an IOP of 22 mm Hg or more and with glaucomatous

visual field changes, the effect of orally administered acetazolamide was examined with reference to the mean threshold changes per one test point for the whole field, as well as normal and pathological areas of the field.

The distribution of mean threshold changes was similar to that of the control group and no significant improvement was observed.

The effect of acetazolamide was evaluated with reference to the retinal sensitivity of all test points. As a result, a trend towards improvement was observed at retinal sensitivity levels from 0 dB to -11 dB lower than the age-corrected normal value; however, a similar tendency was also shown in the control group.

When the retinal sensitivity was graded at 5dB intervals, a significant improvement was demonstrated at 0 dB to -4 dB of retinal sensitivity compared to the age-corrected normal value.

Mean threshold changes in this range were from 0.06 to 2.03 dB. If the long-term fluctuation in stable glaucoma is estimated as 2 ± 1.64 dB, these mean threshold changes may fall within this fluctuation range[5].

In conclusion, the results of this study differ from previous reports that administration of acetazolamide improved the retinal sensitivity of glaucoma patients and that the improvement trend was noted especially in lower retinal sensitivities. However, a significant reduction in IOP was noted.

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THE EFFECT OF ACUTE INTRAOCULAR PRESSURE REDUCTION ON PSYCHOPHYSICAL AND ANATOMICAL OPTIC DISC PARAMETERS IN OCULAR HYPERTENSIVES**

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Abstract

We studied the effect of acute medical reduction of intraocular pressure in ocular hypertensives using oral glycerol Fifteen eyes of 15 patients underwent automated perimetry, Farnsworth Munsell 100 Hue color testing, spatial contrast sensitivity measurement with a laser interferometer, and automated optic disc analysis The relationship of intraocular pressure reduction to the change of the psychophysical and structural parameters was studied There was no significant relationship between absolute or relative change in intraocular pressure and corresponding change in any of the visual field indices or optic disc parameters measures. There was a statistically significant relationship ($p = 0\ 02976$) between the absolute change in intraocular pressure and the change in performance on the Farnsworth Munsell 100 Hue test, indicating an increase in color score with decrease in intraocular pressure There was a statistically significant relationship between absolute change in intraocular pressure and change in the logarithm of contrast sensitivity at the 3 and 7 5 cycles per degree grating ($p = 0\ 00748$ and $0\ 05073$, respectively), indicating that for decreasing intraocular pressure there was a reduction in contrast sensitivity function.

Introduction

The effects of acute reduction of intraocular pressure on the visual field in glaucomatous patients have been described previously[1-9] Paterson reported an improvement in both absolute and relative scotomas 30 minutes after the intravenous injection of acetazolamide[1]. Flammer et al., utilizing 750 mg of acetazolamide during a 12-hour period, showed a significant partial reversibility of glaucoma defects without changes in the visual fields of ocular hypertensives[6]. Younger patients showed a greater reversibility and strongly disturbed parts of the visual field showed a relatively greater improvement than did less disturbed areas. There was no correlation between the change in the visual field and the intraocular pressure reduction. Virno et al. studied the effect of glycerol reduction of intraocular pressure in 49 ocular hypertensive eyes and 21 glaucomatous eyes. Seventy-nine percent of these eyes revealed improvement in the central visual field 30-45 minutes after testing[9].

We studied the effect of acute medical reduction of intraocular pressure in ocular hypertensive patients using oral glycerol.

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Methods

Fifteen patients with intraocular pressure elevation of 20 mm Hg or more in either one or both eyes, normal optic discs, and normal visual fields as tested with manual perimetry, were studied. There were ten females and five males, the ages ranged from 28-72 years, with a mean of 60.8 years. Octopus program G1 was used on the Octopus 201 automated perimeter. The Farnsworth Munsell 100 Hue test was used to measure color vision, and spatial contrast sensitivity was measured with the laser interferometer. The neuroretinal rim area, optic disc cupping and optic disc pallor were recorded on the Rodenstock Disc Analyzer. Only one eye of each patient was studied. In individuals with elevated intraocular pressure in only one eye, that eye was chosen. If both eyes had ocular hypertension, the eye with the higher pressure was chosen for the study.

On the preliminary visit, regarded as a learning visit, each patient had an Octopus G1 field recorded, a Farnsworth Munsell 100 Hue test, laser interferometry, applanation tonometry and, after pupillary dilatation, optic disc analysis with the Rodenstock Disc Analyzer followed by a subsequent applanation tonometry. The optic disc analyzer measurements performed on this day were considered the baseline measurements.

On the treatment day the patient again had Octopus G1 perimetry, Farnsworth Munsell 100 Hue test, laser interferometry and applanation tonometry. Glycerol 50% solution in a dosage of 2 ml/kg body weight was then given orally. Sixty minutes after the glycerol, Octopus G1, color vision, laser interferometry and tonometry were repeated. The patient's pupils were then dilated with one drop of Mydriacyl 1% and Neosynephrine 2.5% and the optic disc measurements were repeated followed by tonometry.

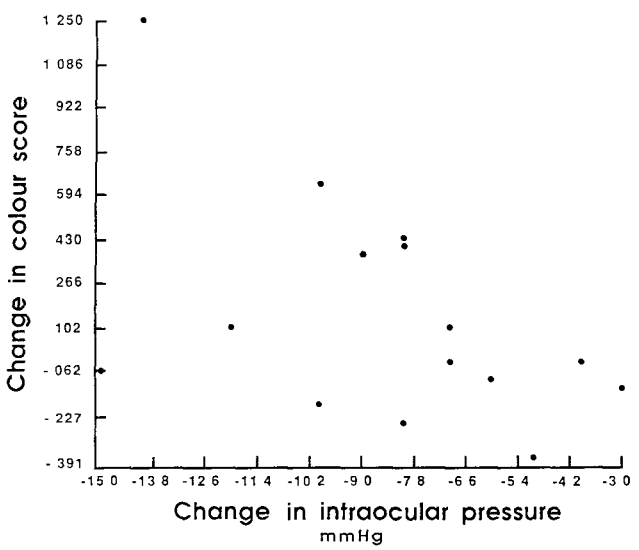

Fig 1 Scattergram illustrating the relationship between change in intraocular pressure and change in the color score

Results

The relationship of intraocular pressure reduction to the change of the psychophysical and structural parameters was studied. The mean intraocular pressure reduction was 8.4 mm Hg. Regression analysis was carried out, relating both the absolute change and the relative change in the intraocular pressure from baseline to the corresponding absolute and relative changes in each of the covariants studied. There was no significant relationship between absolute or relative changes in intraocular pressure and corresponding changes in any of the visual field indices, *i.e.*, mean sensitivity, mean defect, corrected loss variance and short-term fluctuation, nor with any of the optic disc parameters measured including neuroretinal rim area, disc cup volume and optic disc pallor. There was a statistically significant relationship ($p = 0.02976$) between the absolute change in intraocular pressure and in the performance on the Farnsworth Munsell 100 Hue test. As intraocular pressure decreased, the color score increased, indicating a slight deterioration in performance with reduction of intraocular pressure (Fig. 1). There was a statistically significant relationship between absolute change in intraocular pressure and in the logarithm of contrast sensitivity at the 3 and 7.5 cycle per degree grating ($p = 0.00748$ and 0.05073, respectively) (Figs. 2 and 3). The relationship again was such that for decreasing intraocular pressure, there was a reduction in contrast sensitivity function. There was no significant relationship to higher and lower contrast sensitivity gratings

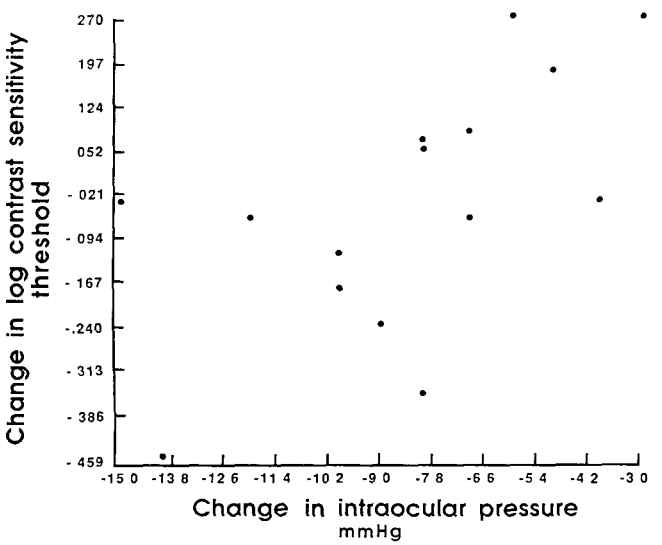

Fig 2 Scattergram illustrating the relationship between change in intraocular pressure and change in the logarithm of contrast sensitivity at 3 cycles/degree grating size

Discussion

In this study the effect of acute intraocular pressure reduction in patients with ocular hypertension was studied. We evaluated the effects both on psychophysical

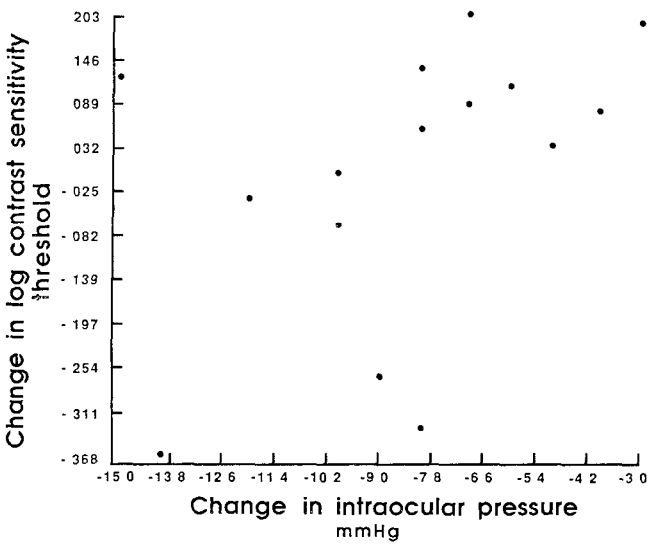

Fig 3 Scattergram illustrating the relationship between change in intraocular pressure and change in the logarithm of contrast sensitivity at 7.5 cycles/degree grating size

as well as anatomical parameters. None of the parameters measured showed any significant improvement with acute intraocular pressure reduction. Only color vision and mid-range contract sensitivity showed any significant relationship. In both cases, the relationship was a deterioration of function with decrease in intraocular pressure.

All patients studied had ocular hypertension. They therefore had normal appearing optic discs and fields. It is possible that the lack of improvement in the psychophysical or anatomical parameters was due to the normal state of these parameters prior to testing. If this were the case, then pressure lowering medication would not cause an improvement in the supposedly normal values.

The use of glycerol as a pressure lowering medication may have significantly altered the results. Flammer *et al.* have previously shown a deleterious effect of timolol on the differential light threshold and improvement in differential light threshold with acetazolamide [10]. Perhaps any pressure lowering effect of glycerol was offset by a potential unknown neurotoxic or retinal mechanism. Glycerol does have transient systemic toxicity with headache and nausea and this did appear to have a deleterious effect on patient concentration and performance. This may explain the slight worsening in Farnsworth Munsell 100 Hue testing as well as in contrast sensitivity testing.

There were no significant changes in the neuroretinal rim area, optic disc cupping or pallor. The optic disc analysis with the Rodenstock Analyzer was the only anatomical measurement performed in this study and as it is purely objective, patient interaction is not necessary [11-18]. The lack of change in these parameters with acute pressure reduction may also be due to the fact that the discs were all normal and, therefore, improvement could not be expected.

Although our study did not show any significant improvement in psychophysical or anatomical parameters in patients with elevated intraocular pressure following acute pressure reduction, we feel that such changes may occur with chronic lowering of the intraocular pressure

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UNEQUAL INTRAOCULAR PRESSURE AND ITS RELATION TO ASYMMETRIC VISUAL FIELD DEFECTS IN LOW TENSION GLAUCOMA*

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Key words: low tension glaucoma; visual field asymmetry, intraocular pressure asymmetry

Abstract

Fifty-nine low tension glaucoma patients were reviewed with respect to asymmetry of intraocular pressure and visual field defects. In the presence of unequal intraocular pressure, the visual field damage is almost always greater on the side with higher mean intraocular pressure. However, only 13 of 47 patients with asymmetric visual field defects had a mean intraocular pressure difference between the two eyes of greater than or equal to 1 mm Hg. Although in the case of intraocular pressure asymmetry visual field damage is greater in the eye with higher mean intraocular pressure, other factors must also play an important role in the development of visual field defects in low tension glaucoma

Introduction

The goal of glaucoma therapy should be primarily directed at the prevention of further visual field loss which is presently attempted by lowering intraocular pressure. Long-term studies have suggested but not conclusively proved that intraocular pressure reduction is effective in decreasing visual field progression in primary open angle glaucoma[1]. Some reports have even shown that despite good postoperative intraocular pressure control, progression of visual field loss can still occur[2,3]. Whether intraocular pressure reduction is of much benefit in the management of low tension glaucoma is even less clear. Reduction of intraocular pressure to a level less than 10 mm Hg is claimed to arrest progression of visual field loss in some low tension glaucoma patients[4]. It has recently been reported that even in low tension glaucoma intraocular pressure may be an important factor associated with visual field loss[5].

If intraocular pressure is a risk factor for patients with low tension glaucoma then the eye with higher pressure would be expected to have the greater visual field damage. One study reported that 50% of primary open angle glaucoma patients with monocular visual field loss had no detectable reason for their asymmetry[6]. Other studies found no congruence between intraocular pressure and visual field loss in low tension glaucoma[7,8]. In this study we have attempted to confirm whether asymmetric intraocular pressure in low tension glaucoma is associated with greater visual field loss in the eye with higher intraocular pressure.

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Methods

Fifty-nine low tension glaucoma patients whose pressures were never greater than 24 mm Hg were selected from the records of our practice, in whom at least five intraocular pressure readings had been recorded personally by two of us (SMD, GRD) or the referring ophthalmologist. All patients had a mean intraocular pressure of less than 21 mm Hg. Patients were either on no medication or symmetric medication. A few patients were included in the study who were on asymmetric medications, but only if more medication was used in the eye that still had the higher intraocular pressure. Snellen visual acuity was within two lines between the two eyes unless the difference was due to glaucomatous damage. Patients with a history of other ocular pathology such as old retinal detachment, macular degeneration or vascular occlusion were excluded. Extensive bilateral visual field loss led to exclusion from the study because of the difficulty in assessing visual field asymmetry. The visual field data and the intraocular pressure recordings were evaluated separately. All data following laser or surgical intervention were disregarded.

Patients had between five and 27 pressure readings. The degree of difference in pressure between eyes was categorized using all the paired pressure readings. To use the same number of intraocular pressure readings, we also classified the pressure asymmetry by using only the first five pressure readings or the last five pressure readings which were available for all patients. The patients were divided into symmetric or asymmetric pressure groups according to the amount of difference between the mean pressures of the two eyes. The classification of asymmetry excluded any patients in whom the intraocular pressure in any of the pairs of pressure readings was higher by more than 1 mm Hg in the eye with the lower mean intraocular pressure. The visual fields were plotted on Goldmann or Oculus perimeters manually or by perimetry on the Octopus or Humphrey computerized visual field analyzers. Visual fields were judged to be clearly asymmetric if the more affected eye had more glaucomatous scotomata than the other (*e.g.*, both hemifields involved in one eye and only one in the other). In the absence of such obvious asymmetry, the defects were quantitated. This was done by using the visual field indices from automated perimetry. When only Goldmann perimetry was available, planimetric assessment of the isopter with the smallest stimulus which delineated the visual field defects and was available from both eyes was done. Fields were judged to be asymmetric when the more affected eye had a scotoma three times greater than the fellow eye upon evaluation of mean defect on automatic perimetry or the planimetrized area derived from manual visual fields. Symmetry was said to be present if the difference between the defects was less than one-third on evaluation of the same parameters. Patients with visual fields falling between these definitions were called borderline and were classified as asymmetric by forced choice. There were 36 patients with obviously asymmetric visual fields, 12 with asymmetric visual fields, and 11 with borderline visual fields as defined.

The association between the pressure and the field classifications was examined statistically. For each table, the chi-square statistic was calculated. In addition, the Goodman-Kruskal measures of association (lambda)[9] and Cohen's coefficient of agreement (kappa)[10] were computed in each case.

Results

A mean intraocular pressure difference between the pairs of eyes greater than or equal to 2 mm Hg was found in only five of our patients and all five showed a corresponding asymmetry of their visual field defects. A mean intraocular pressure

Table 1: 3 x 3 contingency table dividing low tension glaucoma patients by mean intraocular pressure asymmetry and visual field asymmetry

	Field defect asymmetry		
Mean intraocular pressure asymmetry ≥1 mm Hg	R>L	R = L	L>R
R>L	4	3	0
R = L	14	8	20
L>R	0	1	9

$X^2 = 13.95$ p 0 0

difference of 0.5 mm Hg or greater occurred in 32 patients, 22 of whom showed a corresponding visual field defect asymmetry. Forty-seven patients on the other hand had an asymmetry of their visual field defects and only 13 of these had a mean corresponding pressure asymmetry greater than or equal to 1 mm Hg.

The patients were cross-classified into a 3x3 contingency table (Table 1) in which the rows classified mean intraocular pressure difference 1 mm Hg, (RL, R=L, R) and the columns classified the visual field defect differences (right field defect greater than left, right equal to left, right less than left). For mean intraocular pressure difference of 1.0 mm Hg, the X was 13.95 (p 0.01) suggesting therefore an association between these classifications. Calculating the Goodman and Kruskal index of agreement reveals that knowing the classification of the intraocular pressure asymmetry reduces the mis-classification error of the category of visual field asymmetry by 13% ($\lambda = 0.13$). Knowing the classification of the field defect asymmetry does not reduce the mis-classification of the category of intraocular pressure asymmetry ($\lambda = 0$). The overall coefficient of agreement k was 14%, which is statistically significant but low.

Using a mean intraocular pressure difference of 0.5 mm Hg and 1.5 mm Hg to classify the pressure asymmetry produces similar and statistically significant results. Mean pressure differences of 2 mm Hg or more show identical trends but the numbers are so small as to lose statistical significance.

Discussion

Our study shows that when intraocular pressure is asymmetric in low tension glaucoma the visual field defect appears to be greater on the side with the higher mean intraocular pressure, confirming recently reported findings[5]. The greater the intraocular pressure asymmetry, the greater the prevalence of correspondingly asymmetric visual fields. There are however many patients with asymmetric visual field defects who do not have appropriately unequal intraocular pressure. This finding explains the lack of congruence previously reported between intraocular pressure and visual field defects in low tension glaucoma patients[6,7] Although intraocular pressure inequality was not necessarily present in the patients with asymmetric field defects, when intraocular pressure inequality was present the

visual field was usually more damaged on the side with higher intraocular pressure. Although factors other than intraocular pressures would seem to play a part in the development of visual field defects in low tension glaucoma, intraocular pressure appears to be involved in field damage even in patients with low tension glaucoma. Further studies are needed to identify those patients in whom pressure is an important damaging factor and to identify the other factors which influence the disease. We also need to know whether pressure reduction modifies the course of the disease. Such studies are currently being undertaken.

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THE EFFECT OF A Ca^{2+}-ANTAGONIST ON THE VISUAL FIELD IN LOW-TENSION GLAUCOMA

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Introduction

The mechanism of damage to the optic nerve in low-tension glaucoma and primary open-angle glaucoma remains unknown. There is now much evidence that ischemia of the optic nerve head might be responsible for the damage. However, whether ischemia is mechanically induced by intraocular pressure (IOP) or due to primarily vascular pathology is not clear.

In 1985 Phelps and Corbett reported on the high incidence of migraine in low-tension glaucoma patients and suggested for the first time that vasospastic events might play a role in the optic nerve changes in low-tension glaucoma[1]. In 1986 Gasser and associates described an ocular vasospastic syndrome in which patients with glaucomatous field defects, but without elevated IOP, had abnormal capillaroscopic responses to cold in the nail fold of the finger[2]. They noted that visual field defects became aggravated by the immersion of a hand in cold water and that the scotomas often improved after a calcium channel blocker. Recently, Drance and associates measured blood flow in the finger of normal subjects and low-tension glaucoma patients using a Doppler flow meter[3]. They found that the mean baseline flow and the flow after exposure to cold was significantly lower in patients with low-tension glaucoma than in normal subjects.

We conducted a prospective study in an attempt to evaluate the effect of a Ca^{2+}-antagonist on the visual field in low-tension glaucoma.

Patients and methods

Twenty-five patients with low-tension glaucoma (50 eyes) were randomly selected for the study. Their demographic data and clinical background are set out in Table 1. Low-tension glaucoma was defined as a characteristic optic disc change with classical visual field defects of the nerve fiber bundle type. IOP including diurnal measurements was no greater than 21 mm Hg.

The patients received nifedipine hydrochloride 30 mg/day per os for six months. Prior to, during, and after the oral administration of nifedipine, the following clinical factors were determined: IOP, visual field, resting systemic blood pressure and pulse rate, and the reactivity of peripheral vessels. IOP was measured with a Goldmann applanation tonometer. Visual field was tested with the Octopus 201 (program G1) at least three times prior to the administration of nifedipine, and the last perimetric data were used as the baseline. The reactivity of peripheral vessels was estimated as follows: a probe of Thermister (Shibaura Electrics, Inc., Model MG II) was attached to the skin of the middle finger[4]. A baseline skin temperature was recorded until a steady baseline reading was achieved. The hand was then immersed

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Table 1. Demographic and clinical background of patients' data

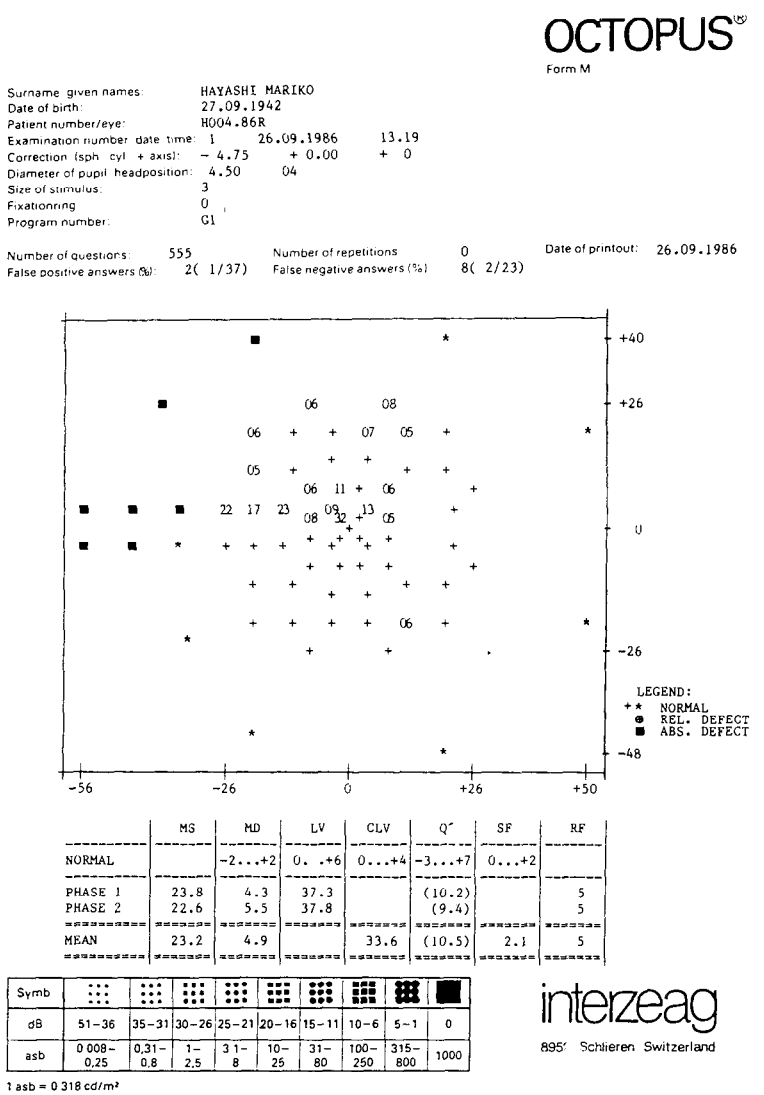
Number of patients	25
Number of eyes	50
Sex (male/female)	13/12
Age (years)	53 7 ±11.5
IOP (mm Hg)	12 5 ± 3 1
Visual field changes (Aulhorn's classification)	
I - II	27
III - IV	23
Disc hemorrhage (eyes)	8
Migraine headache (case)	0
Cold hands (case)	1

in ice cold water (4°C) for ten seconds, and the temperature was monitored every minute for the next ten minutes. The change in skin temperature after the immersion in cold water was expressed as the percentage recovery from the lowest to the baseline temperature at each measurement. None of the patients had typical migraine headache. One patient admitted she had cold hands even in spring and summertime. In no case were any antiglaucoma drugs used for at least three months prior to and during the period of nifedipine administration. Univariate analyses of variance and covariance, and discriminant analyses, were performed. The latter were performed to separate the patients who showed improvement of the visual field with systemic administration of nifedipine from those who failed to improve.

Table 2 Demographic and clinical data in the improved and unimproved groups

	Improved	Unimproved
Number of patients	6	19
Number of eyes	12	38
Sex (male/female)	3/3	10/9
IOP (mm Hg) before nifedipine administration	12.7 ±3.8	12.5 ±2.9
Visual field changes (Aulhorn's classification)		
I - II	8	19
III - IV	4	19
Disc hemorrhage (eyes)*	2	6
Cold recovery rate at 4 minutes (%)		
Before nifedipine administration	80 5 ±6.4	75 1 ±8 4
		p<0.05
During nifedipine administration	87.2 ±6 9	79.3 ±6 9
		p<0.01

*including all hemorrhagic episodes in the past and during the present study

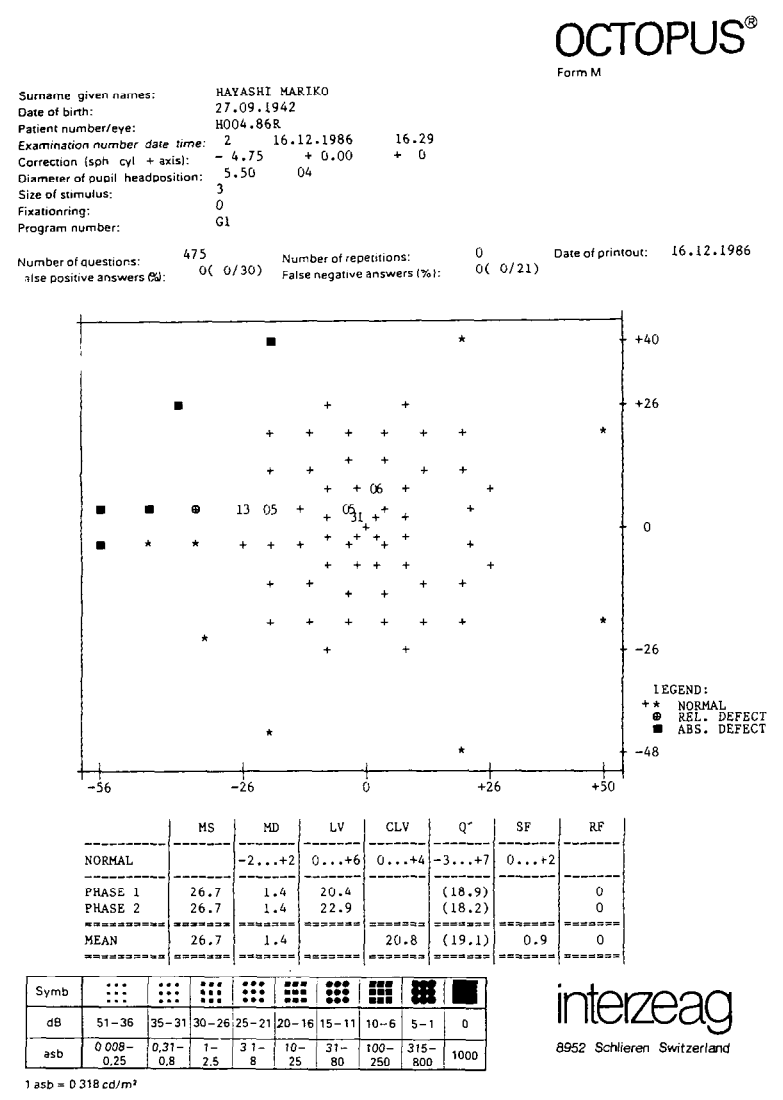


1a

Fig 1 Example of three visual fields of a patient: a before nifedipine treatment; b at four weeks of nifedipine treatment, and c at eight weeks of nifedipine treatment b: page 290, c: page 291

Results

Twelve eyes (six patients) showed an increase in mean sensitivity (MS) at each perimetric examination throughout the six-month follow-up and were judged to be improved[5,6]. An example of three visual fields of a patient is illustrated in Fig. 1. In the remaining 38 eyes (19 patients) MS failed to show a constant improvement compared with the baseline value and the cases were classified as unimproved; in no case had MS a constant decrease during the follow-up period. The demographic and clinical data of the improved and unimproved groups are listed in Table 2. Apart from the mean age, factors were not significantly different between the improved and unimproved groups. The mean age of the improved patients was 45.8 ±8.3

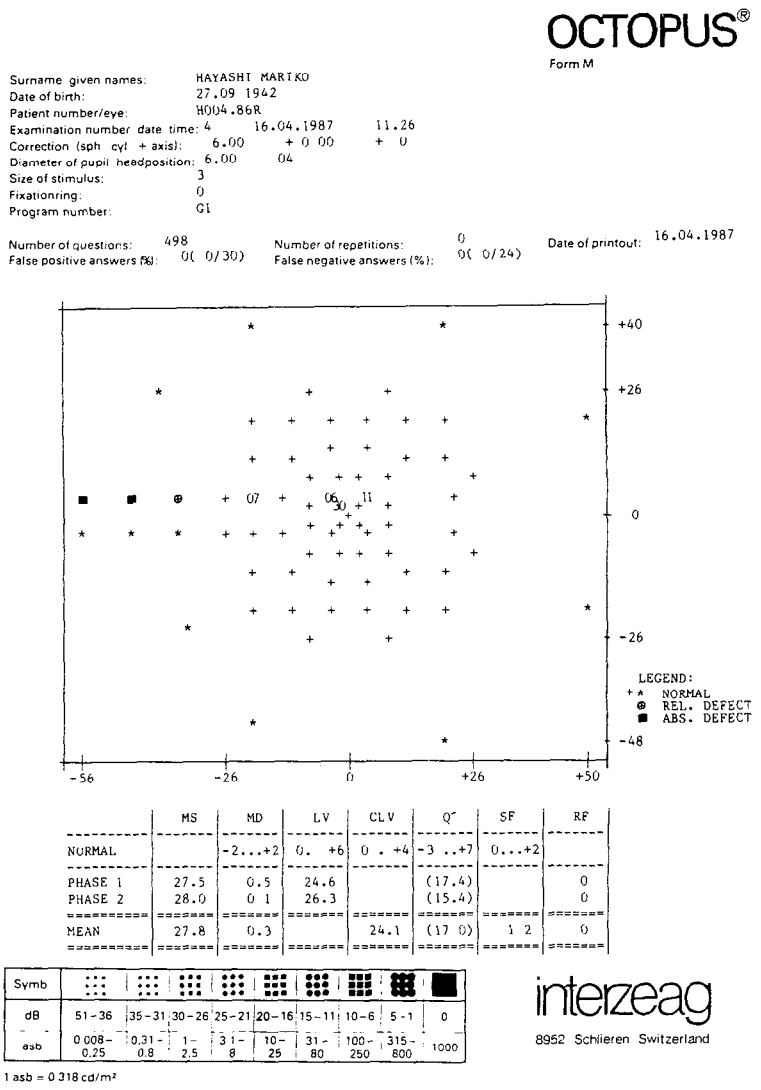


1b

years, whereas the unimproved patients had a mean age of 56.3 ±11.3 years. This difference was statistically significant ($p < 0.05$).

Visual field

The global indices before, during, and after nifedipine administration are summarized in Table 3. As expected from the criteria for the improved visual field, MS and mean defect (MD) significantly differed before and after treatment with nifedipine ($p < 0.05$, Wilcoxon rank-sum test). At four weeks after the withdrawal of nifedipine, MS and MD numerically deteriorated but the difference was not of statistical significance ($p > 0.10$). Among the global indices, only corrected loss variance (CLV) was significantly smaller in the improved group than in the unimproved group throughout the study ($p < 0.01$).



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Systemic blood pressure and pulse rate

There was no significant difference in blood pressure and pulse rate between the improved and unimproved groups throughout the period of observation. Within the unimproved group, systolic, diastolic and mean blood pressures were decreased during nifedipine administration, compared with the pretreatment value ($p< 0.05$, $p< 0.01$ and $p< 0.01$, respectively) (Table 4).

Table 3 Global indices (dB) during the study

Group of patients	Nifedipine	MS	MD	CLV	SF
Improved	Before	20 9± 6 1	7 6± 8 4	47.7± 14 0	1 8± 0 3
	During	22.9± 6 5	5 4± 8 8	42.1± 14 3	1 9± 0 4
	After	21 8± 7 8	6.5± 8 1	45 3± 13 9	1 8± 0 3
Unimproved	Before	18 0± 8.0	9 5± 7 5	85 4± 11 6	2 3± 1 3
	During	17.7± 7 6	9 7± 8 1	82.1± 11 9	2 4± 1 4
	After	17.4± 7 4	9 9± 8 3	82.6± 11 7	2 1± 1 3

* $p<0$ 05; ** $p<0$ 01

Table 4 Systemic blood pressure (mm Hg) during the study

Group of patients	Nifedipine	Systolic	Diastolic	Mean
Improved	Before	116.4± 12.6	77 6± 5 9	89.8± 8.8
	During	116 0± 15 4	74.4± 8 3	88 3± 11 9
	After	117.5± 14 2	70 0± 11 6	85.8± 12.5
Unimproved	Before	125 4± 19 5	80 0± 10 4	95 2± 12 1
	During	115 3± 15 6	71 1± 12 5	85 7± 14 0
	After	118.5± 21.9	77 3± 12 0	91.1± 14.5

* $p<0$ 05; ** $p<0$ 01

The diastolic blood pressure was significantly lower, not only during nifedipine administration but also after the cessation of the administration, than in the pretreatment period ($p<0.01$ and $p<0.05$, respectively). In the improved group, no significant change in blood pressures was noted throughout the study period. The resting pulse rate failed to show any significant change in either group or between the two groups throughout the observation period.

Cold recovery rate

Prior to nifedipine administration, the cold recovery rate was not significantly different between the improved and unimproved groups. With the administration

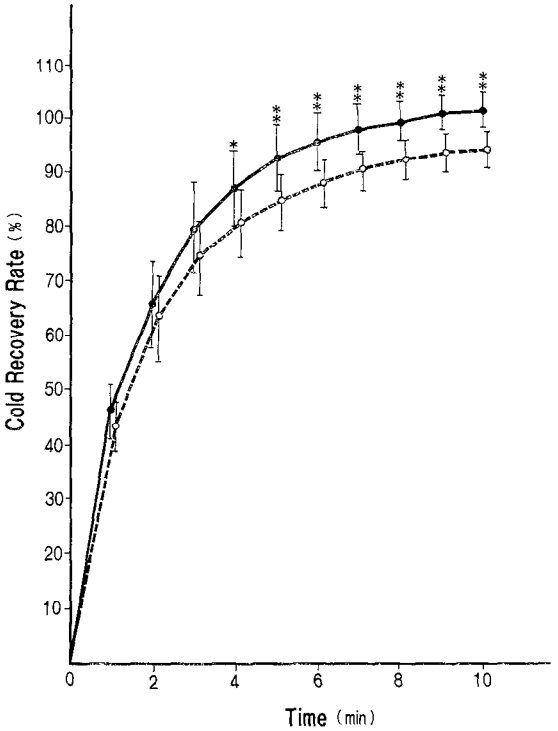

Fig 2 The cold recovery rate in the improved patients; the dashed line indicates the cold recovery rate prior to oral nifedipine and the solid line denotes the rate during oral nifedipine treatment Each vertical bar indicates SEM (n = 6) Note that the difference is of statistical significance between the with- and without-treatment values at each measurement from four to ten minutes after the immersion of a hand in cold water

of nifedipine, the improved group showed a significantly better cold recovery rate compared with the pretreatment value at 4, 5, 6, 7, 8, 9 and 10 minutes ($p<0.05$ at four minutes, $p<0.01$ from five to ten minutes, respectively) (Fig. 2), while, in the unimproved group, the cold recovery rate failed to improve with the administration of nifedipine (Fig. 3). During the period of nifedipine administration, the cold recovery rate was significantly better in the improved group than in the unimproved group at 3, 4, 5 and 6 minutes ($p<0.05$, $p<0.01$, $p<0.01$ and $p<0.05$, respectively).

Other factors

IOP was not significantly different throughout the observation period within each group or between the two groups. One among 12 improved eyes (8.3%) had disc hemorrhages, while three eyes developed disc hemorrhages among 38 eyes (7.9%). This difference was not of statistical significance.

Correlation between the change in visual fields during nifedipine administration and clinical factors

The relationship between the visual field changes, as represented by MS, during the administration of nifedipine and the clinical factors was tested with non-

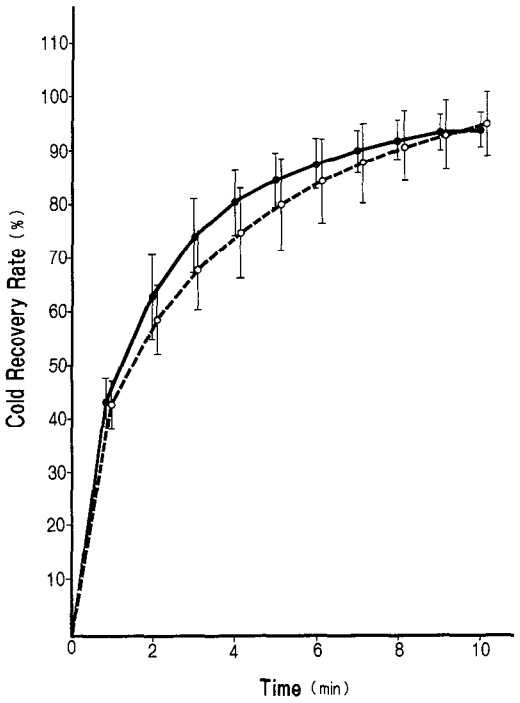

Fig 3 The cold recovery rate in unimproved patients; the dashed line indicates the rate prior to oral nifedipine and the solid line indicates the rate during oral nifedipine therapy Each vertical bar indicates SEM Note that there is no significant difference in the cold recovery rate between the with– and without–treatment values

parametric measures of correlation (Spearman rank correlation). During administration of nifedipine, MS was significantly related to age ($p = 0.0037$), cold recovery rate at four minutes prior to and during the administration of nifedipine ($p = 0.0258$ and $p = 0.0026$, respectively), diastolic blood pressure during nifedipine administration ($p = 0.0480$), and MS prior to nifedipine therapy ($p = 0.0491$) (Table 5).

Canonical discriminant analysis revealed that the discriminant function containing five variables (age, cold recovery rate prior to nifedipine administration, the maximum diurnal IOP, the mean diastolic blood pressure during nifedipine therapy, and the degree of visual field defects) gives the best separation between the improved and the unimproved groups (sensitivity: 93.8 %; specificity: 82.4%; and discriminant efficacy: 86.0%) (Table 6).

Discussion

Our observations indicate that the visual field can improve with oral administration of nifedipine, a Ca^{2+}-antagonist, in some cases of low-tension glaucoma. The cases who responded favorably to the Ca^{2+}-antagonist were found to share certain clinical features. They were younger than those who failed to respond with improvement of MS. It is of particular interest to note that patients whose visual field improved with nifedipine had significantly lower CLV prior to nifedipine therapy, although MS was not significantly different between those who improved with nifedipine and those who did not.

Table 5 Correlation between the change of mean sensitivity (MS) during nifedipine administration and clinical factors

Factor	Spearman rank correlation coefficient	*p*–value
Age	–0.40302	0 0037
Cold recovery rate		
Prior to nifedipine	0.32856	0.0258
During nifedipine	0 47547	0 0026
Mean diastolic blood pressure during nifedipine	0 30829	0 0480
Mean sensitivity prior to nifedipine	0.29280	0.0491

Table 6 Standardized canonical discriminant function coefficients

Variable	Coefficient
Age	–0.67244
Cold recovery rate prior to nifedipine	0 65524
Maximal diurnal IOP	–0 32440
Mean diastolic blood pressure during nifedipine	0 34162
Severity of visual field defects	–0.01145

This finding seems to indicate the possibility that cases with localized, marked depression reflecting a selective loss of nerve fiber bundles, are less likely to respond to oral administration of a Ca^{2+}-antagonist with improvement of visual field changes. Another clinical feature that seems to deserve attention is that the responsive cases had a significant improvement of the cold provocative test when they were kept on nifedipine, while the non-responsive cases failed to show a significant change in the cold recovery rate with the administration of nifedipine. Since the cold recovery rate is the measure of the rate of recovery from the vasospasm induced by exposure to cold, those who showed improvement of the visual field may still retain reactivity of the peripheral vessels to a Ca^{2+}-antagonist with vasodilatation resulting in increased blood supply to the optic nerve. The analytical result that the cold recovery rate, before nifedipine administration, is a reliable indicator of its effect lends further support to this possibility, but neither proves nor disproves the notion that the vasospastic events are not responsible for field defects in patients who fail to show improvement with nifedipine.

Our results appear to support what has been reported by Flammer and associates[2,7,8]; in some cases of low-tension glaucoma, vasospasm plays a significant role in the development of visual field defects and a Ca^{2+}-antagonist may be effective in improving the visual field by reversing the vasospastic events.

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DETECTION OF DEVELOPING GLAUCOMA WITH COMPUTERIZED THRESHOLD PERIMETRY AND FLICKER COMPARISMS OF DISC PHOTOGRAPHS

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We followed prospectively 131 eyes with high risk ocular hypertension for nine to 72 (mean 40 months). Computerized threshold-measuring perimetry (Competer standard central 20 degrees test) and monocular disc photography was performed every three months. Visual fields were classified according to predetermined criteria. Questionable fields were repeated immediately, and the standard visual field protocol often supplemented with computerized profile perimetry or manual perimetry. Disc photographs were compared with baseline photographs using a specially designed instrument based on flicker chronoscopy. With this technique, projections of two serial photographs from the same eye are optically aligned and superimposed; analysis is achieved by viewing a flickered image where the two slides are shown in rapid succession. Changed areas appear moving in the flickered image. Analyzed pairs of disc photographs were classified into one of four groups: no change (–), slight (+??) and high (+?) suspicion of change, and definite change (+).

Using this sensitive method of disc analysis, correspondence between the development of glaucomatous visual field defects and disc changes was surprisingly high (Table 1). Changes of disc anatomy did not precede disturbances in the visual field more often than vice versa.

Alterations in disc anatomy were usually very discrete, and were often not detected by a panel comparing masked pairs of photographs in the standard way, without using the flicker method.

The results indicate that, when patients with ocular hypertension are followed, computerized threshold perimetry can detect developing glaucoma as early as very careful and sensitive comparisons of serially obtained disc photographs. Furthermore, repeated computerized threshold perimetry is more sensitive than standard comparisons of monocular disc photographs.

The parallelism between the detection of optic disc changes and the development of field loss is also interesting from another point of view. It may indicate that

Table 1 Correspondence between change of optic disc configuration and development of glaucomatous visual field defects (GLVFD)

Change in disc anatomy	–	+??	+?	+
No of eyes with GLVFD	1	1	2	8
No of eyes without GLVFD	108	7	2	2

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flicker comparisons of disc photographs could sometimes replace perimetry in the detection of glaucoma. This would be particularly valuable in the very aged or in other patients who have difficulty in performing adequately at computerized perimetry.

Flicker chronoscopy is now time consuming. If the alignment of images could be facilitated by computerized image analysis techniques, this method could become a clinically practicable method. It could then offer a considerable improvement over current standard methods of analyzing serial photographs, and be a very useful complement to routine computerized perimetry.

THE CORRELATION BETWEEN NEURORETINAL RIM AND VISUAL FIELD INDICES*

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Abstract

The authors studied 110 eyes of 110 patients who had open angle glaucoma, low tension glaucoma, were glaucoma suspects or normal. The neuroretinal rim area, corrected for magnification, was calculated and the width of the neuroretinal rim was measured in a number of sites on the disc The visual field index MD determined by program G1 on the Octopus perimeter was available for all the eyes A stepwise regression between MD and various measurements of variability of the temporal rim and the neuroretinal rim measurements was carried out. The coefficient of determination (R^2) of MD on rim area was 23% but could be improved to 27% by using some of the temporal width measurements which reflect localized rim loss. When the loss of the neuroretinal rim area was regressed against MD, the R^2 could be improved from 26% to 32% by the addition of the measurements of variability of the neuroretinal rim width

Introduction

Chronic open angle glaucoma leads to a chronic optic neuropathy which causes localized nerve fiber bundle scotomas as well as diffuse changes in the visual field. Characteristic changes occur at the optic nerve head which usually precede the classical localized visual field defects. Glaucoma suspects can lose diffusely 40% of their nerve fiber layer[1] without clear-cut localized visual field defects. It is not yet clear which psychophysical disturbances best reflect this diffuse axonal loss. The aging process also leads to diffuse axonal loss at the rate of approximately 5000 per year[2]. The aging process is also accompanied by some losses in almost all psychophysical functions. The neuroretinal rim area which contains the entire complement of axons of the ganglion cells, the supporting glial tissue and blood vessels diminishes in size with the severity of glaucomatous damage[3], but there is a significant overlap between the neuroretinal rim measurements of glaucomatous and normal subjects. This is probably due to the large inter-patient variation of the size of the optic nerve head, to which the cup area and the neuroretinal rim area are related[4]. On a cross-sectional basis therefore the area of the neuroretinal rim alone can still be within normal statistical levels but might already have undergone considerable change from what was previously normal for that individual. We showed that the neuroretinal rim area was correlated with a number of psychophysical functions[5], including the visual field indices obtained on automatic perimetry. The significant linear correlation between the neuroretinal rim area and the 'mean defect' had a coefficient of determination (R^2) of 32%, while the quadratic function increased this to 40.6%[6]. This means that while 40% of the variation of the neuroretinal rim can be accounted for by the measurement of the 'mean defect' the remaining 60% variation was however not accounted for by this measurement. This may be due to the fact that the 'mean defect' reflects both diffuse as well as

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localized loss of the visual field while small localized losses of the rim may be too small to be detected in the overall neuroretinal rim area measurement. The present study was conducted to see whether estimates of localized change of the neuroretinal rim would improve the correlation between the 'mean defect' and the structural components of the optic disc.

Method

One hundred and ten eyes of 110 patients were included in this study, 43 suffered from open angle glaucoma, 16 had low tension glaucoma, 32 had elevated intraocular pressures only and 19 were judged to be normal. All of them had a visual acuity of 6/9 or better and had a manual neuroretinal rim measurement as well as a G_1 field on the Octopus perimeter carried out. The 'mean defect' was therefore available. The neuroretinal rim area was corrected using Littman's magnification Q value[7] obtained from the axial length and refraction of the eye. The width of the neuroretinal rim was measured linearly at 30 degree intervals clockwise from the 11 o'clock to the 7 o'clock position (right eye) and six measurements on the temporal side from 7 o'clock clockwise to 11 o'clock (Fig. 1). The linear measurements were transformed into millimeters using the Q values. Only the rim width of the temporal ten points including the 6 o'clock and 12 o'clock positions were used because the visual field indices of the central field which corresponds to the temporal part of the optic nerve. A quadratic regression was carried out between MD and the difference between the expected neuroretinal rim area calculated from the size of the optic nerve head and the actually measured neuroretinal rim[4]. A stepwise regression was then carried out between MD and the square of the neuroretinal rim area and various measurements of the variability of the temporal rim which included the logarithm of the variance of the rim width, the ratio minimum over maximum of the temporal rim widths, the number of temporal widths equal to or less than the mean of the temporal width measurements and the range of the widths divided by the mean width.

Results

In the 110 randomly selected eyes of the 110 patients the quadratic regression of MD on rim area was statistically very significant ($p = 0.000$). The coefficient of determination (R^2) was 23%. The quadratic regression of MD on the difference between the expected rim area and the measured rim area was also very significant ($p = 0.000$), with a coefficient of determination (R^2) of 26%. On stepwise quadratic regression the coefficient of determination of MD on rim area was maximally improved by the number of temporal width measurements less than or equal to the mean of the observed rim width of the temporal neuroretinal rim which improved the R^2 from 23% to 27%. The next best measurement was the ratio of minimum over maximum rim width which improved it from 23% to 26%. In stepwise quadratic regression of MD on the loss of neuroretinal rim area determined from the expected and the measured, the addition of the minimum over maximum ratio raised the R^2 from 26% to 29% while the number of temporal widths equal to or narrower than the mean width of the neuroretinal rim raised it from 26% to 32%.

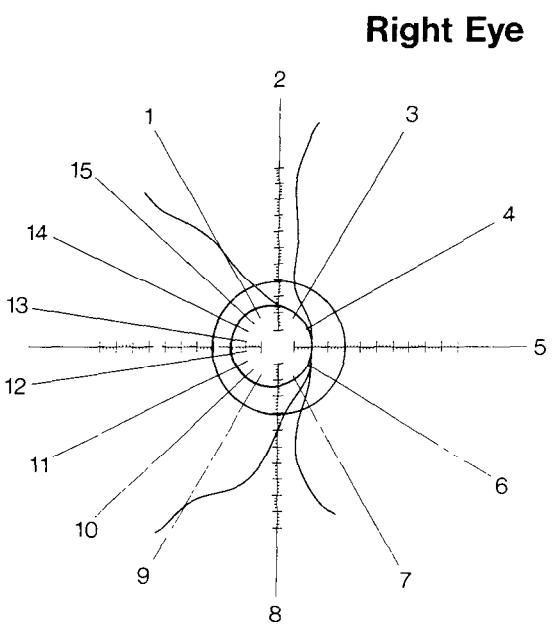

Fig 1 A schematic representation of a right optic disc showing the sites where the widths of the neuroretinal rim were measured.

Discussion

The present study confirmed that there is a statistically significant quadratic relationship between the MD and the neuroretinal rim area and an even better relationship between the MD and the difference between the rim area as calculated from the measured size of the disc and the measured rim area. The relationship between MD and the structural parameters of the disc are improved by adding some measurements of the localized disc disturbance, the best of which appear to be the ratio minimum/maximal temporal rim width and the number of rim width measurements of the temporal part of the disc less than or equal to the mean width of the temporal rim. In view of the fact that MD is composed of both local and generalized visual field loss, it is not surprising that the addition of measurements of localized disc change should add to the relationship between MD and disc appearance and therefore account for more of the variability of the MD.

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CLINICOPATHOLOGICAL STUDIES OF THE RETINAL NERVE FIBER LAYER IN EARLY GLAUCOMATOUS VISUAL FIELD DAMAGE

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Abstract

We examined the retina of a human glaucomatous eye by light and electron microscopy and correlated its histopathological features with visual field damage

A 51-year-old female had a small scotoma in the upper Bjerrum area and wedge-shaped retinal nerve fiber layer defect (NFLD) in the lower arcuate area of her right eye, while no visual field damage was observed in her left eye Marked thinning of retinal nerve fiber layer was observed, corresponding to the area of clinically detected NFLD Many axons had dropped out and remaining axons were also affected In the area without visual field damage, cystic spaces were also seen by electron microscopy Furthermore, the quantitative study showed 25-40% loss of the axons compared with the fellow eye

In conclusion, our findings suggest that nerve fiber damage occurs in the whole retina even in the early stages of glaucoma

Introduction

Retinal nerve fiber layer defects (NFLD) are frequently observed in patients with lesions of the optic nerve[1]. In glaucoma, it has been suggested that NFLD occurs prior to detectable visual field defects[2,3]. NFLD is one of the most important ophthalmoscopical factors in the diagnosis of early glaucoma.

Reports exist concerning the histopathological features of NFLD induced by retinal photocoagulation or by optic nerve trauma in experimental animals[4,5]. However, the pathogenesis of NFLD in glaucoma is different from that in these artificial NFLD. In addition, the correlation between the histopathological features of NFLD and those of visual function have not been evaluated.

In this study, we examined the retina of a human glaucomatous eye by light and electron microscopy and correlated its histopathological features with visual field damage.

Material and methods

A 51-year-old female had been treated medically for open angle glaucoma. In 1984, she died due to metastatic lung cancer and we obtained her eyes with consent from her family.

At the last examination six months prior to death, visual acuity was 1.0 in each eye and intraocular pressure was controlled under 16 mm Hg by timolol.

In the right eye, there was a small scotoma in the upper Bjerrum area, while no visual field damage was observed in the left eye (Fig. 1). The optic disc in the right eye had a vertical cup/disc ratio of 0.7 and notching of the lower optic rim. A wedge

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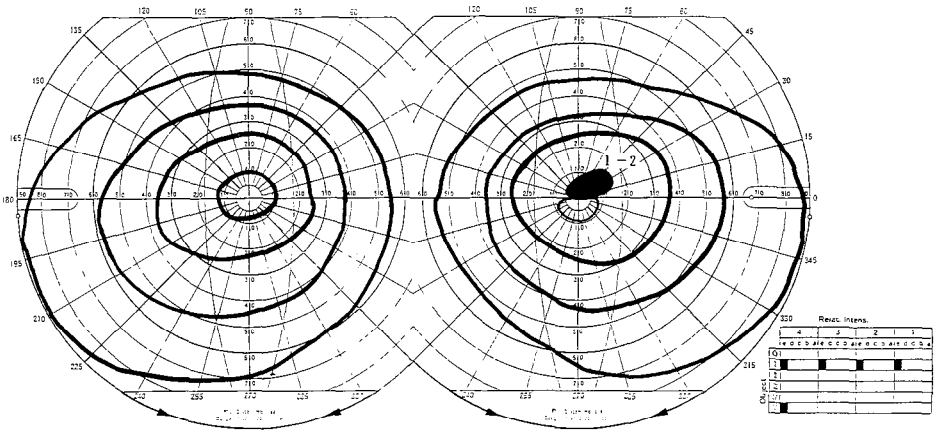

Fig 1 Right visual field showing a scotoma in the upper Bjerrum area

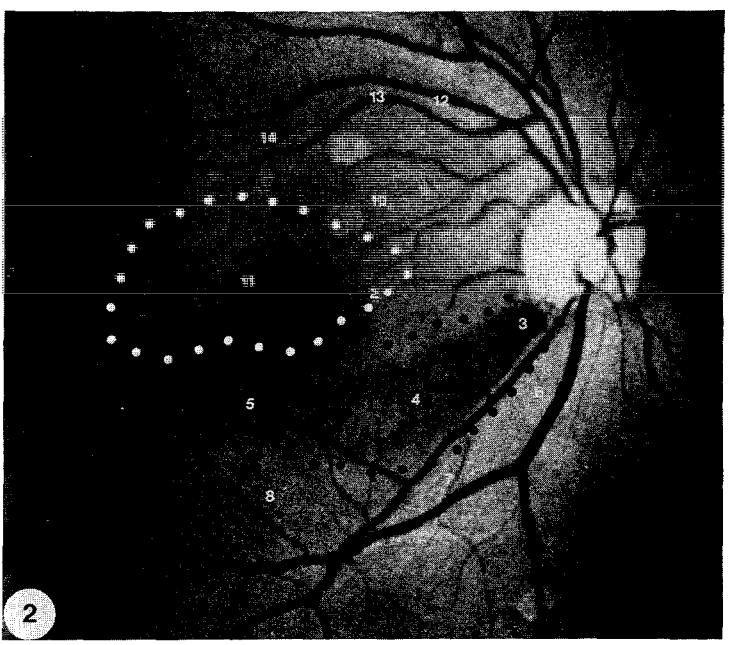

Fig 2 Red-free fundus photograph with superimposed Goldmann visual field Black dots indicate a scotoma to I/2, white dots indicate the border to I/1 Numbers are the location of measurement of the nerve fiber thickness, the number of ganglion cells and the number of axons

shaped NFLD was observed in the lower arcuate area (Fig. 2)

Immediately after enucleation, the eyes were fixed in 2.5% phosphate buffered glutaraldehyde. Retinal specimens were excised to obtain the perpendicular plane of section to the course of retinal nerve fiber bundles. The specimens were post-fixed in osmium tetroxide and embedded in epoxy resin. Thick sections were stained with paraphenylenediamine and examined by light microscopy. Thin sec-

tions were counter-stained with uranyl acetate and lead citrate and examined by electron microscopy (JEM-T8).

The posterior pole retina was divided into 14 areas according to the course of the retinal nerve fiber bundles (Fig. 2). The areas No. 1 and 2 corresponded to the papillomacular fiber bundles, Nos. 3, 4 and 5 to NFLD, and Nos. 6, 7 and 8 to the arcuate fiber bundles adjacent to NFLD. Clinically unaffected upper arcuate fiber bundles were also numbered 9, 10, 11 and 12, 13, 14, corresponding to the dividing of lower arcuate fiber bundles (3, 4, 5 and 6, 7, 8). The thickness of the nerve fiber layer, the number of retinal ganglion cells (/360 x 240) and the number of axons (/14 x 11) were measured in each area. The results in the eye with glaucomatous visual field damage were compared with the results in the same areas from the fellow eye with normal visual field.

Results

Fig. 3 shows a red-free fundus photograph with superimposed Goldmann visual field. The area surrounded by black dots is a scotoma to the I/2 test object and the white dots are the border to the I/1 test object. The white lines A, B, C and D correspond to the retinal specimens (Fig. 4).

In specimen A, taken from the retina close to the disc, thinning of the retinal nerve fiber layer (NFL) was observed which corresponded to the area of clinically detected NFLD. In this area, axon drop-out and glial column collapse were seen.

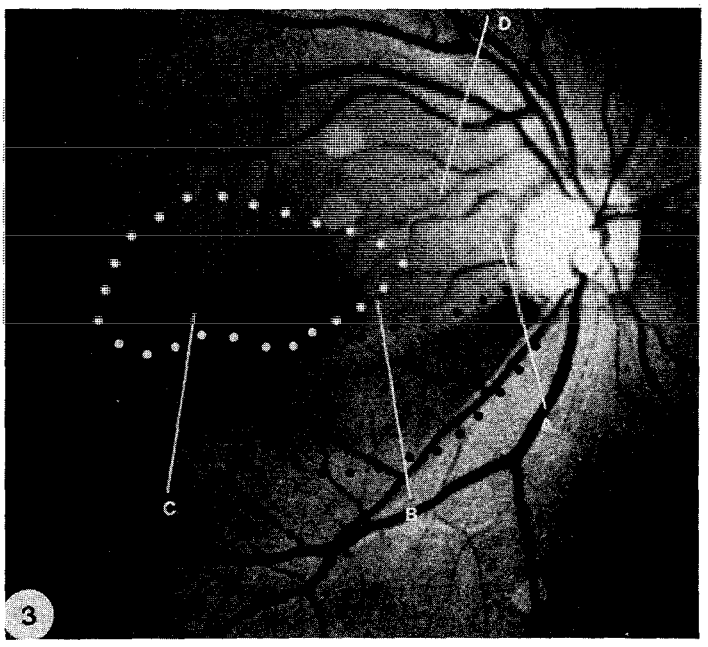

Fig 3 Red-free fundus photograph with superimposed Goldmann visual field Black dots indicate a scotoma to I/2, white dots indicate the border to I/1 White lines A-D correspond to the retinal specimens (Fig. 4).

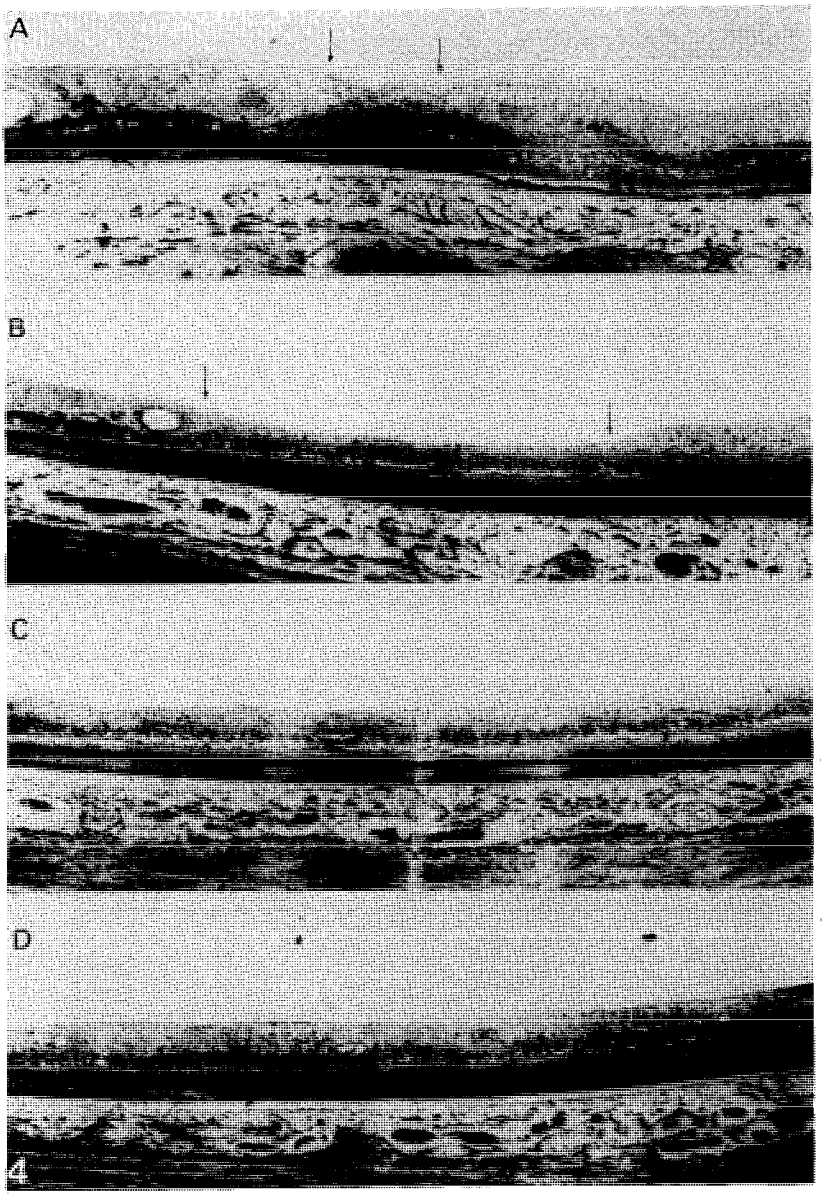

Fig 4 Retinal specimens taken from an eye with glaucomatous visual field defect (x 25). Right side is macular side Arrows indicate the clinically detected NFLD

Furthermore, the NFL adjacent to such a region showed numerous cystic spaces enclosed with Müller's cell processes especially in the superficial layer (Fig. 5). In the deep layers many axons remained, but disruption of microtubules was seen in these axons.

In specimen B, thinning of NFL was more remarkable and extended in width. Glial columns had collapsed completely and ganglion cells were recognized just under the internal limiting membrane. Only a few axons remained and were affected. Accumulation of mitochondria in the ganglion cells was also seen.

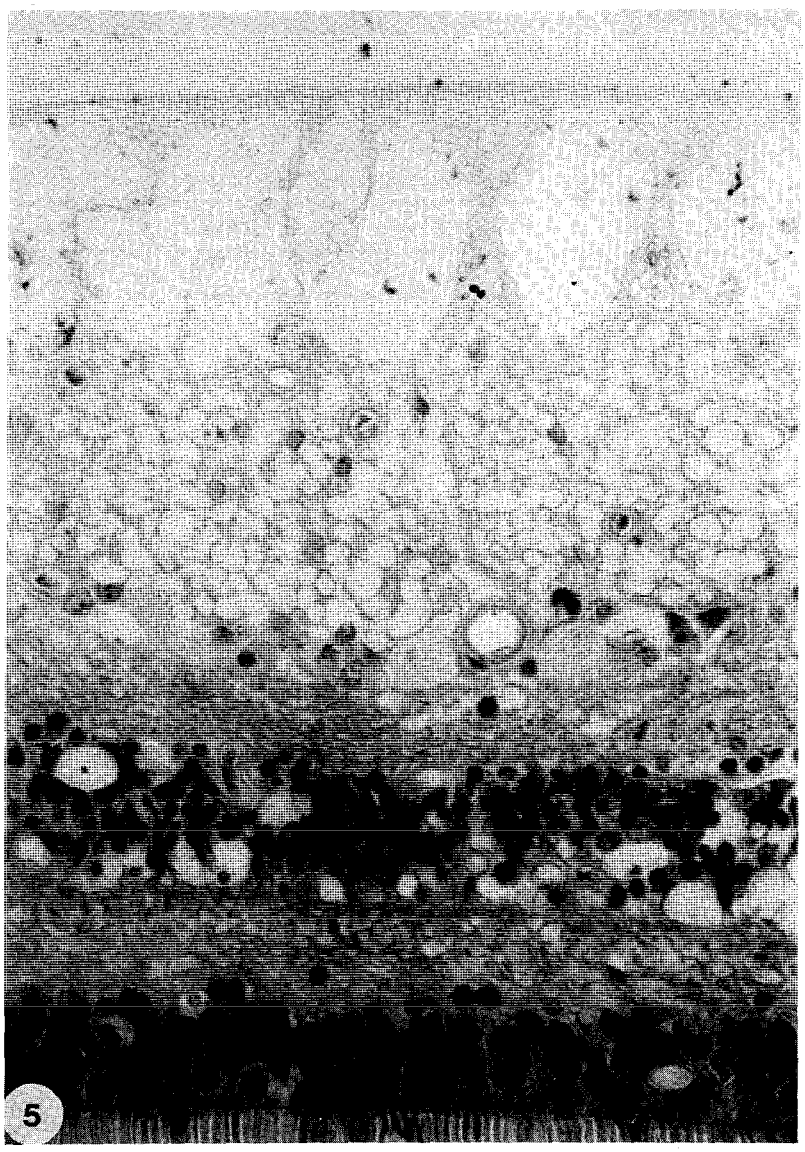

Fig 5 High magnification view of specimen A shows numerous cystic spaces enclosed with Muller's cell processes in the superficial layer (x 100) (reduced 10%)

In specimen D, with clinically normal appearance of NFL, the thickness of NFL was almost normal. By electron microscopy, however, numerous cystic spaces in NFL were detected.

Table 1 shows measurements of the thickness of NFL, the number of ganglion cells and the number of axons in the eye with visual field damage and the eye with normal visual field.

Table 1. The thickness of the retinal nerve fiber layer, the number of the ganglion cells and the number of the axons.

Retinal area		NFL thickness			Ganglion cell number			Axonal number		
		GL	NOR	GL/NOR	GL	NOR	GL/NOR	GL	NOR	GL/NOR
PM bundle	1	130.0±11.9	191.7±16.1	68.1	20.5± 1.1	21.8± 1.5	94.0	80.1± 6.6	106.6±12.4	75.5
	2	38.6± 6.9	41.3± 4.5	93.5	64.2±14.2	70.2±12.8	91.5			
NFLD	3	36.6	216.7	16.9	12.0	18.0	66.7			
	4	6.8± 1.1	72.0±10.3	9.4	24.0± 4.3	23.3± 5.9	103.0	11.2± 1.6	68.2± 5.9	16.4
	5	10.6± 3.6	28.0± 3.4	37.9	24.0± 4.4	20.2± 4.9	118.8			
Lower temporal	6	117.3±20.2	119.3±41.3	98.3	17.2± 2.9	19.4± 3.6	88.7			
	7	56.7±13.6	62.5±10.4	90.7	12.0± 3.3	18.5± 3.9	64.9			
	8	24.0± 7.7	30.0± 6.7	80.0	15.2± 4.5	10.2± 2.2	149.0			
Upper temporal	9	54.0± 5.3	68.6± 8.1	78.7	45.4± 5.9	40.0± 9.9	113.5			
	10	57.1±10.6	57.0± 9.1	100.2	39.3± 7.8	36.4± 8.6	108.0	40.2± 8.6	65.8± 6.4	61.1
	11	40.7±12.0	39.3± 6.9	103.6	28.6± 9.5	39.2±11.9	73.0			
Upper temporal	12	61.1±14.0	60.3± 8.7	101.3	18.7± 2.1	19.4± 4.3	96.4			
	13	57.8± 7.7	54.3±10.3	106.4	18.6± 5.2	17.5± 4.9	106.3			
	14	38.0± 6.9	37.2± 4.9	102.2	19.6± 3.6	18.3± 2.5	107.1			

GL: glaucomatous visual field eye, NOR: normal visual field eye, GL/NOR: %

NFL thickness: μm, Ganglion cell number: /360μ×240μ, Axonal number: 14μ×11μ

In the visual field damaged eye, areas 3, 4 and 5, which corresponded to NLD, showed a remarkable decrease in NFL thickness and these thicknesses were 9.4-37.9% compared to those of normal visual field eyes. The adjacent areas 1, 7 and 8 showed a 10-30% decrease. Upper arcuate areas 10, 11 and 12, 13, 14 without visual damage had, however, normally thick NFL.

The number of the ganglion cells of the visual field damaged eye was 64.9-149% in each area. No characteristic corresponding to visual field damage and fundus appearance was observed.

In the area of NFLD, the number of axons was only 16.4% and axon drop-out was remarkable. In the upper arcuate area without visual field damage, a 40% decrease in the number of axons was seen. In addition, in the area of the papillomacular fiber bundles, 25% of axons was lost.

Discussion

NFLD is one of the most important factors in the diagnosis of early glaucoma. The correlation between histopathological features of NFLD and visual field damage has been evaluated in this study.

Thinning of NFL was observed in the area of clinically detected NFLD. By electron microscopy, degeneration of axons and collapse of glial columns were obvious. Radius and Anderson studied experimental NFLD induced by retinal photocoagulation[4] and their findings were similar to our results. It is clear that ophthalmoscopical NFLD is histopathologically the thinning of NFL caused by axon drop-out and that a scotoma detected by Goldmann perimetry corresponds to the area of thin NFL.

In the area adjacent to NFLD, NFL was also affected though NFL thickness was normal and there was no visual field damage. Especially in the superficial layer, numerous cystic spaces were seen. In the deeper layer, many axons remained but some of them showed mild change. Quigley *et al.* reported that clinical detection of NFL atrophy was possible after loss of 50% of nerve tissue[5]. It seems that these NFL abnormalities are the early changes of NFL which could not be detected by ophthalmoscopy and by Goldmann perimetry.

Pederson and Anderson reported that the mode of early progression was usually a generalized expansion of the cup and it seemed to be possible that a generalized expansion of the cup was due to diffuse axon loss [6] Airaksinen *et al* reported generalized reduction of nerve fibers in glaucoma patients[7]. In our quantitative study, the number of axons in the area of NFLD was only 16% compared to that of the fellow eye. In the upper arcuate area with normal visual field, a 40% loss of fibers had already occurred. In POAG, it was believed that foveal function was preserved until very late in the course of the disease. However, in our study the area of the papillomacular fiber bundles showed 25% loss of nerve fibers. In conclusion, our findings suggest that nerve fiber damage occurs in the whole retina including the papillomacular fiber bundles, even in the early stages of glaucoma.

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CONTRAST SENSITIVITY, VISUAL FIELD DEFECT AND RETINAL NERVE FIBER LAYER DEFECT IN GLAUCOMA

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Abstract

The authors examined the relationship between macular nerve fiber layer defects and contrast sensitivity function (CSF) in 130 eyes with chronic open angle glaucoma The correlation between the abnormality of CSF and perimetric total loss scores was low, but the correlation between CSF and the macular nerve fiber layer defects was high Early loss of visual function in glaucoma is more easily detected by CSF than by quantitative perimetry or visual acuity

Introduction

Diffuse involvement of the visual field in the form of generalized depression can at times be recognized as an early glaucomatous defect. Foveal involvement in glaucoma is not limited to patients with severe glaucomatous optic nerve damage[1]. However, the mode of the damage and the correlation between peripheral and macular dysfunction are not yet clear. In this study, we examined the relationship between macular nerve fiber layer defects and the contrast sensitivity function in chronic open angle glaucoma cases.

Material and methods

We examined 130 eyes of 69 patients (age 24-69 years, average 47.1±4.12) with early to middle stage chronic open angle glaucoma. The eyes studied had visual acuities over 1.0. Visual field damage within 30 degrees was classified by the total loss score in the Octopus automatic perimeter, program 31.

According to these scores, the subjects were divided into four stages: 0-99 dB, 100-199, 200-799, and over 800.

Contrast sensitivity (CSF) was measured by a modified TV-display system[2]. This system is composed of a television CRT (PM-121T, Ikegami Tsushinki Co. Ltd., Tokyo, Japan), a pattern generator, a stimulus field splitting circuit and a personal computer system. Sensitivity was determined by adjusting the modulation amplitude of a sinusoidal grating pattern on the CRT screen to the point at which the pattern was first perceived. The CRT screen was presented to the subjects through a square aperture (a cover over the face of the picture tube). The aperture was 5.7 horizontally and 4 vertically when the CRT was viewed from a distance of 2 m; the surround was darkened.

The space-average luminance of the CRT screen was 16 cd/m. The measurements

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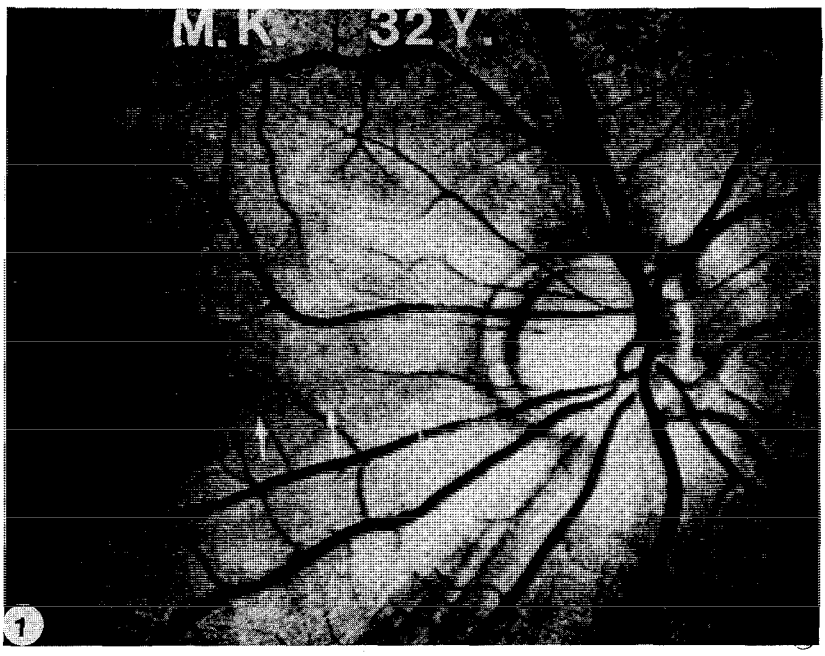

Fig 1 Bundle-like macular nerve fiber layer defect (arrows)

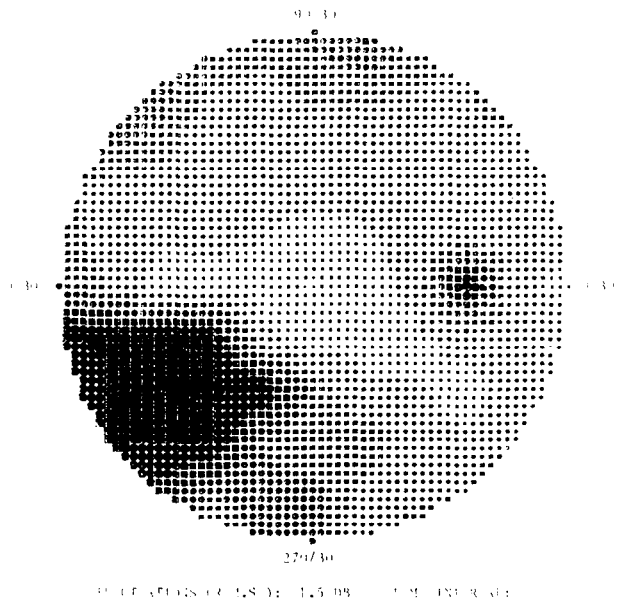

Fig 2 Visual field in case of Fig 1 Total loss, 487 dB; CSF, 0.7-57, 1 4-108, 2 5-130, 3.5-134, 0-130, 15 0-45

were automatically repeated six times at each spatial frequency. CSF was measured at the spatial frequencies of 0.7, 1.4, 2.5, 3.5, 7.0 and 15.0 cpd.

Red-free fundus photographs of 114 eyes were used to assess macular nerve fiber layer defect (M-NFLD). The eyes were classified into four groups: no nerve fiber layer defect (NFLD), slit-like NFLD, bundle-like NFLD (Fig. 1), and diffuse NFLD (Fig. 3).

Results

The average total loss score was 452 dB range (5-1674 dB). Fifty-five eyes scored in the 5-99 dB total loss range; 15 in the 100-199 range; 39 in the 200-799 range; and 23 in the 800-1674 dB range. Fig. 5 shows the correlation between the total loss score and CSF. Significant CSF differences between eyes in various stages of glaucoma were seen only at the lowest and highest spatial frequencies (0.7 cpd - p; 15.0 - p, Student's t-test).

No M-NFLD was observed in 36 eyes (32%). M-NFLD was slit-like in 28 (25%), bundle-like in 38 (33%), and diffuse in 12 (11%) eyes (Table 1). Macular nerve fiber layer defects were frequently seen, even in eyes of the lowest total loss group (22/45 eyes). Fig. 6 shows the correlation between CSF deficiency and the grade of M-NFLD.

There were significant CSF differences between eyes in the grade of M-NFLD at every spatial frequency used (0.7 cpd - p, 1.4 cpd - p, 2.5 cpd , 3.5 cpd , 7.0 cpd , 14.0 cpd , Student's t-test).

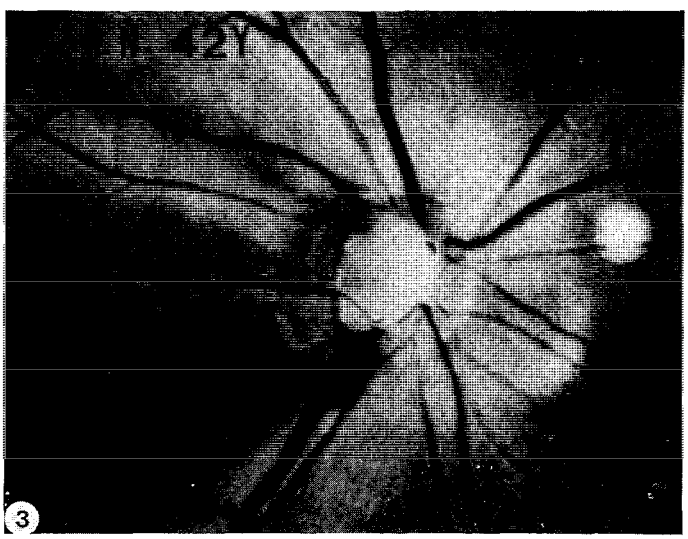

Fig 3 Diffuse macular nerve fiber layer defect

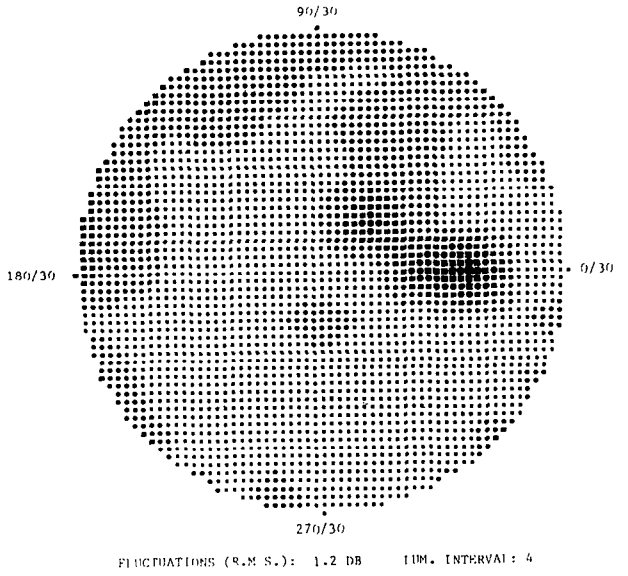

Fig 4 Visual field in case of Fig. 3 Total loss, 130 dB; CSF, 0.7-21, 1.4-40, 2 5-54, 3 5-63, 7.0-44, 15 0-8

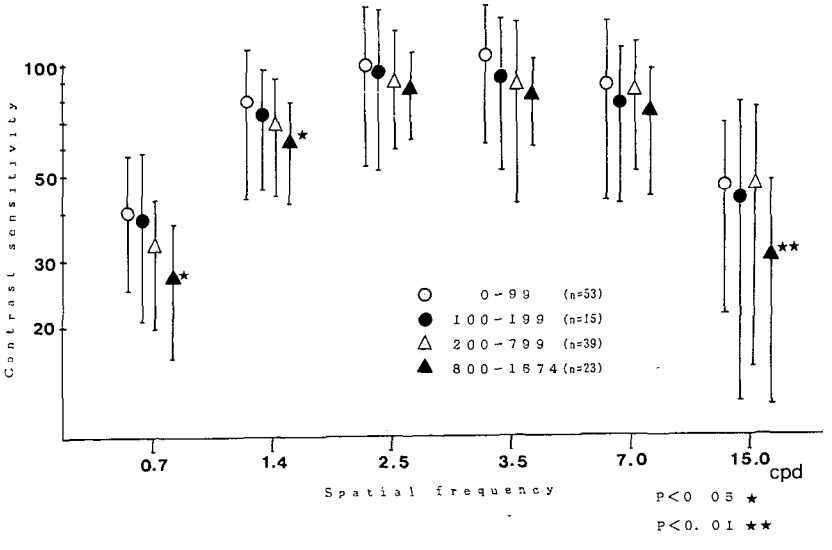

Fig 5 Total loss and CSF.

Table 1 Appearance of M-NFLD and visual field damage

Total loss M–NFLD	None	Slit	Bundle	Diffuse
5— 99	23	14	8	0
100— 199	2	2	6	2
200— 799	10	8	16	3
800—1674	1	1	8	7
	36	28	38	12

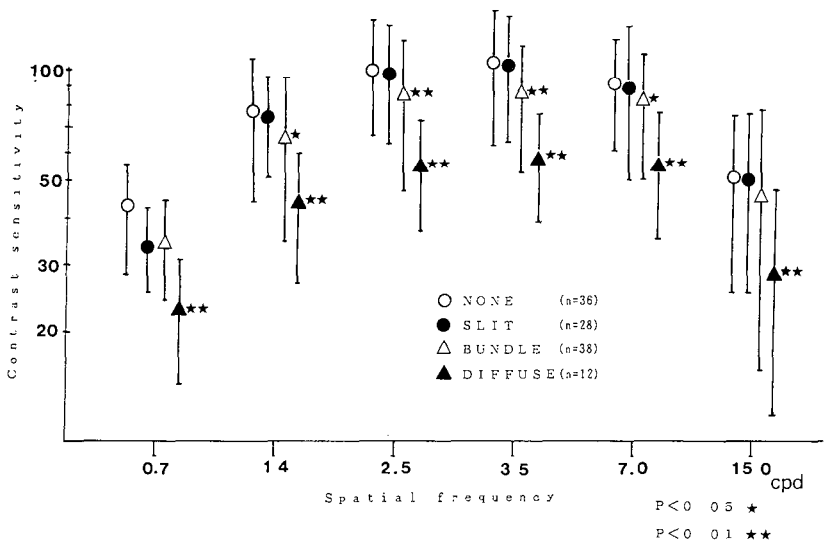

Fig 6 M-NFLD and CSF.

Discussion

Previously, contrast sensitivity function (CSF) was reported to be lost in glaucomatous eyes[3]. CSF damage does not, however, develop parallel to visual field damage in glaucoma[4].

In this study, the value of CSF deficiency was not closely correlated to the degree of visual field damage, but CSF was correlated to the appearance of the macular nerve fiber layer. Macular nerve fiber layer defects were frequently observed even in cases with only mild visual field damage.

According to a recent study[5], contrast sensitivity mediating ganglion cells are different to those the loss of which results in the first glaucomatous field defect.

Therefore, in some patients with early stage glaucoma, M-NFLD may be present and CSF may be reduced, while the visual field and the visual acuity are still normal.

Thus we found the measurement of CSF more useful in the detection of early central glaucomatous functional damage than quantitative perimetry or visual acuity testing.

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VISUAL FIELD INDICES AND THEIR CORRELATION WITH STATIC CONTRAST SENSITIVITY IN GLAUCOMA

Preliminary results

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Abstract

The aim of the study was to investigate a potential correlation between visual field indices and contrast sensitivity in glaucoma patients. If the correlations would be high, perhaps one test could to some extent replace the other in clinical practice However, the study was not designed to investigate the sensitivity or the specificity of the two tests.

Sixty eyes of 60 patients (20 glaucoma suspects with normal visual field indices, 20 eyes with moderately disturbed visual fields, and 20 eyes with severely damaged visual fields) were included in the study The visual field was tested with program G1 of the automated perimeter Octopus 201 The visual field indices, calculated by this program, were correlated with the contrast sensitivity measured with a modified Lotmar visometer (Haag-Streit). Contrast sensitivity was measured three times for the following spatial frequencies: 1 5, 3, 6, 12, 24 cycles/degree.

The correlations of the visual field indices with contrast sensitivity were similar for all spatial frequencies measured Therefore, the overall mean contrast sensitivity of all three measurements of all spatial frequencies was calculated for each eye The overall mean contrast sensitivity correlated best with the mean differential light sensitivity of the central five test locations of the visual field ($r = 0.74$, Pearson's test: $p<0.001$). The correlation with the visual field index MS, *i e* , the mean differential light sensitivity of the entire visual field, was lower ($r = 0\ 6$, $p<0\ 001$). Weak correlations were found with the square root of the index CLV, *i e* , the corrected loss variation ($r = 0\ 38$, $p<0.003$), and the index SF, *i e* , the short-term fluctuation ($r = -0\ 36$, $p<0\ 005$)

It is concluded that the correlation between the visual field indices, especially the central visual field areas, correlate statistically significantly with the static contrast sensitivity measured in the central area of the visual field Nevertheless, in a given patient the outcome of the two tests may differ considerably

A detailed presentation of this study will be published elsewhere

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THE NASAL STEP IN THE NORMAL AND GLAUCOMATOUS VISUAL FIELD

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The average difference of four pairs of test locations within the 26° visual field situated above and below the horizontal nasal meridian called the local index NDIFF was used to measure asymmetry in the differential light sensitivity characterizing the nasal step 755 examinations (of 446 normal eyes) and 539 examinations (of 194 glaucoma suspect eyes) were measured The distribution of NDIFF of the glaucoma suspect population had a much larger spread than normals (s d. of 6 7 dB as compared with 0 9 dB), suggesting a disturbance of the spatial correlations The global G1 visual field index CLV and the local index describing asymmetrical behavior around the nasal horizontal meridian (NDIFF) are strongly correlated (r = 0 67). An index derived from four pairs of test locations (TDIFF) arbitrarily distributed over the visual field having about the same separation and eccentricity as the NDIFF test location pairs does not differ significantly from NDIFF This suggests that the phenomenon of the nasal step has no or no great local specificity as compared to the CLV index and represents an expression of the disturbance of the spatial correlations found in glaucoma

Introduction

The phenomenon of the nasal step has not decreased in attraction since it was first described by Rönne in 1909[1] and continues to be an important sign possessing significant diagnostic and prognostic value in glaucoma[2-11]. A more profound knowledge of this disturbance may be obtained by studying its occurrence in a large population of normals[12] and glaucoma suspect eyes on the one hand, while on the other hand an estimate of its importance may be obtained by comparing it with a number of indices characterizing various aspects of the normal and pathological visual field[13,14].

Material and methods

539 examinations (194 patient eyes) were measured using both phases of the Octopus G1 program. All eyes had been referred because of suspected glaucoma. The criterion for 'suspect' were several IOP measurements above 23, a disc and/or anomalies of the visual field considered suspicious for glaucoma. The decision for inclusion or exclusion of the glaucoma suspect group was done by one of us (FF).

G1 was performed on another population of 755 examinations (446 normal eyes) in the context of a study oriented towards establishing normal values[12].

Global field indices MD (mean defect), SF (short term fluctuation) and CLV (corrected loss variance) were calculated for every examination. Four pairs of test locations (eight test locations in all) situated above and below the nasal horizontal meridian were selected to characterize asymmetry of the DLS in the nasal region (Fig. 1).

The difference (NDIFF) of the average differential light sensitivity (DLS) of the test locations above (U) and below (L) the nasal horizontal meridian was computed according to equation 1:

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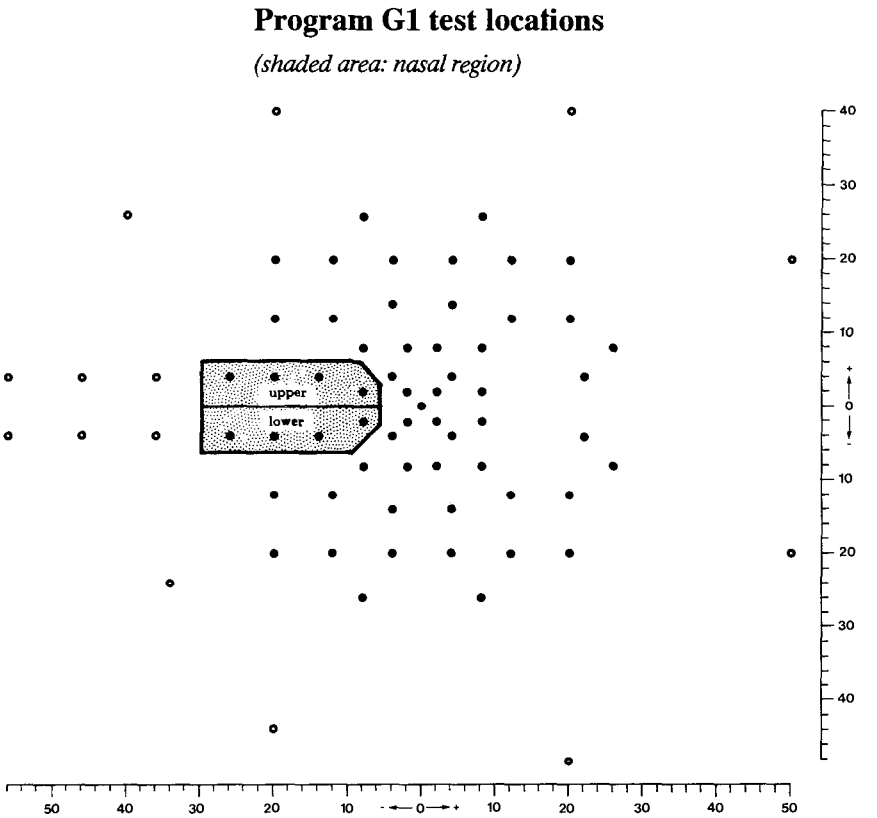


Fig 1 Coordinates of the test locations selected for the measurement of asymmetry of the differential light sensitivity around the nasal horizontal meridian.

$$NDIFF = [(U1 - L1) + (U2 - L2) + (U3 - L3) + (U4 - L4)]/4 \qquad (1)$$

Here, a positive value of NDIFF indicates a lower DLS in the lower nasal quadrant relative to the upper quadrant, while a negative value indicates the reverse situation.

In an arbitrary selection, four test location pairs were determined which had a comparable eccentricity and spatial separation to the nasal locations but which were non-specific with respect to their position in the visual field. Also, the four test location pairs were equally distributed across the four quadrants of the field (Fig. 2).

Each test location pair used for the computation of NDIFF thus had a corresponding pair of test locations in a new TDIFF variable with the same eccentricity and about the same separation. TDIFF was computed according to equation 2 (below). The direction in which the differences between the test location pairs (A,B,C,D) were included was random.

$$TDIFF = [\pm(A1 - A2)\pm(B1 - B2)\pm(C1 - C2)\pm(D1 - D2)]/4 \qquad (2)$$

Out of the population of glaucoma suspects, all NDIFF values exceeding the 95th

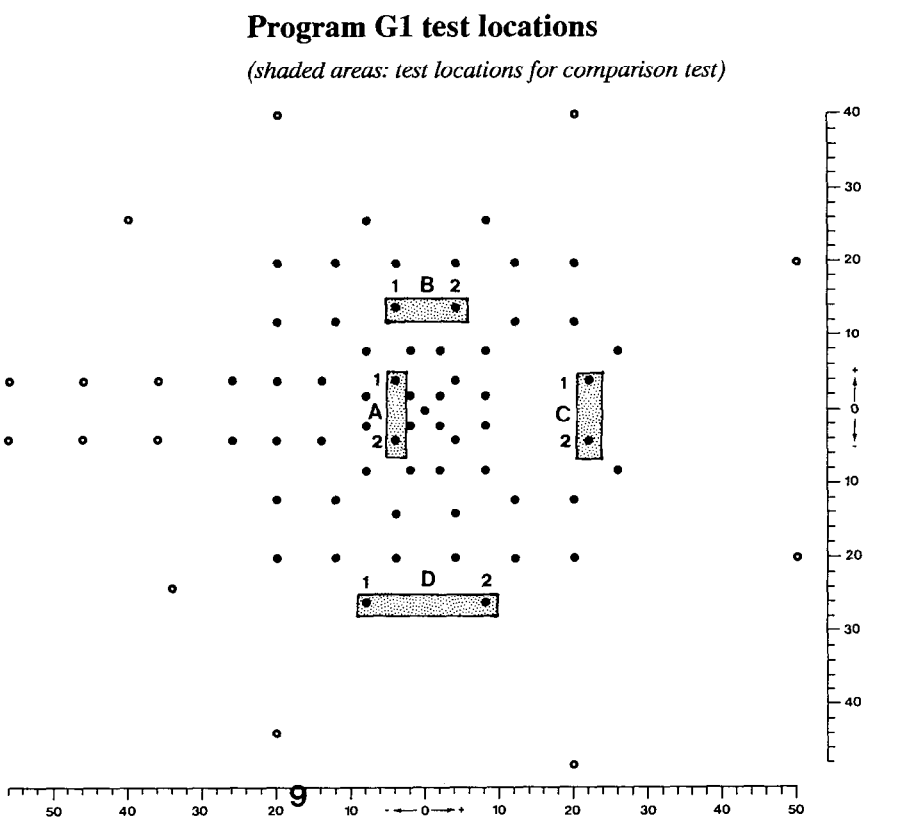


Fig 2 Coordinates of four test location pairs comparable to four pairs of test locations used to measure asymmetry around the horizontal nasal meridian.

percentile of the NDIFF distribution of normals but having normal MD, SF and CLV values (total 119 examinations) were identified and plotted in Fig. 5.

The results were subjected to a number of statistical manipulations.

Results

The distribution of NDIFF values in the control group is shown in Fig. 3 as shaded columns. A slight asymmetry in the upper nasal quadrant towards lower DLS values is apparent (skewness = 0.024). The mean value and the standard deviation amount to -0.0213 dB (mean) and 0.895 dB (SD), respectively. Due to the slight asymmetry in the distribution of the measured values, the lower percentage limit (5%, NDIFF = -1.625 dB) is somewhat closer to the mean value (-0.213 dB) than the upper percentage limit (95% NDIFF= 1.375 dB).

The distribution of the NDIFF values in the population of glaucoma suspects is shown in Fig. 3 as dark columns. Here, a much broader spread as compared to the normals is obvious amounting to a standard deviation equal to 6.7 dB. The mean value of the two populations is about the same (mean = -0.16 dB). An analysis of variance ($F = 56.24$) indicates a highly significant difference ($p < 0.001$) between suspects and normals.

A correlation computation was performed between the absolute value of NDIFF

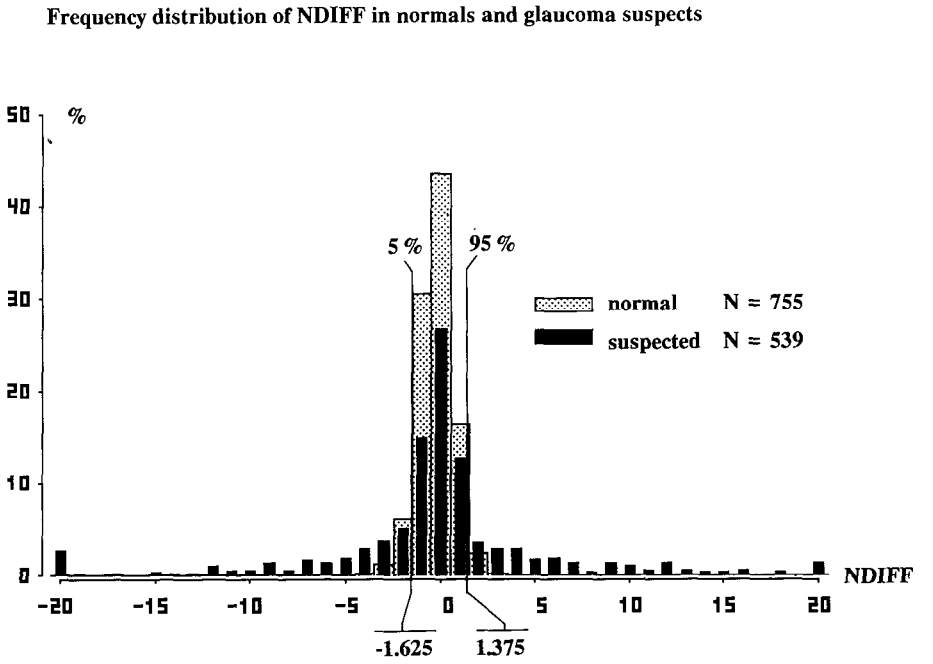


Fig 3 Distribution of NDIFF Shaded columns for normals with 5th and 95th percentile limits, dark columns for glaucoma suspects.

of the glaucoma suspects and the MD, SF and CLV indices. A good relationship between |NDIFF| and CLV (r = 0.674) was found, while the correlation both between |NDIFF| and MD (r = 0.21) and |NDIFF| and SF (r = 0.14) was poor. A scattergram of |NDIFF| versus CLV is shown in Fig. 4.

In Fig. 5 the covariance of |NDIFF| with CLV is shown for a subset of glaucoma suspects having values for SF, MD and CLV within their normal ranges (119 examinations G1, 46 eyes). The shaded area indicates the normal range of |NDIFF| (90%). No nasal step is present in the majority of cases. The six exceptions lying outside the normal range of |NDIFF| can be explained as artifacts.

The distribution of TDIFF as compared to NDIFF in Fig. 6 (a) for normals and (b) for the glaucoma suspects is shown. As the figures show, the two distributions are very similar. Nevertheless, a systematic difference is present which consists of the differing width and asymmetry of the two distributions of glaucoma suspects (Wilcoxon-White test, $p < 0.05$).

Discussion

Because the analysis of the nasal horizontal asymmetry is restricted to the central 26° visual field, the statements made below cannot be extrapolated to field areas beyond an eccentricity of 26°. There is however increasing evidence that the peripheral nasal field should not be neglected because it is likely to yield additional important information[2,16].

The distribution of asymmetries of the DLS around the nasal horizontal meridian in normals is narrow (SD = 0.895 dB), with a slight shift of the mean value from the zero point (-0.213 dB) indicating a lower DLS in the upper quadrant, and a

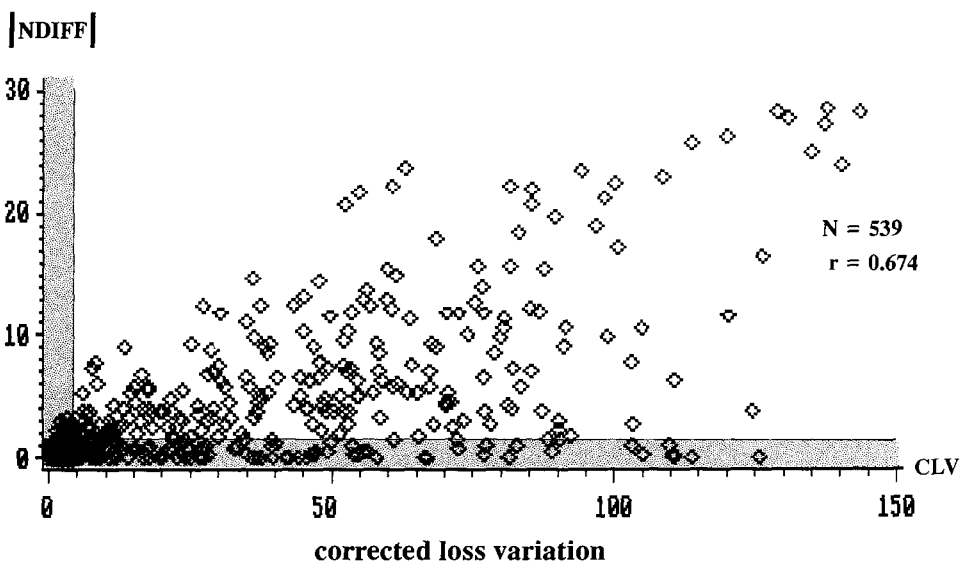


Fig 4 Correlation of |NDIFF| with visual field index CLV Shaded areas indicate the normal range for CLV and the 90% limit for |NDIFF|

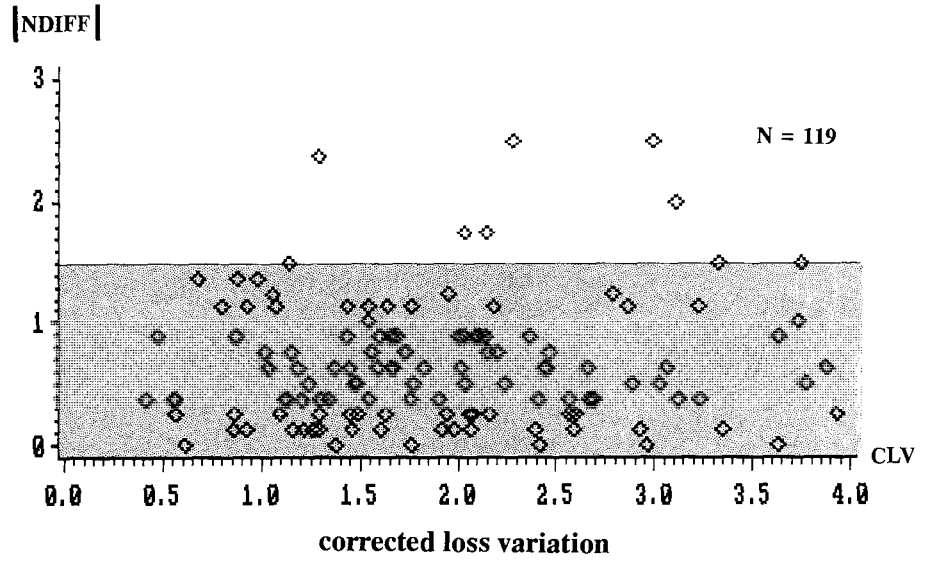
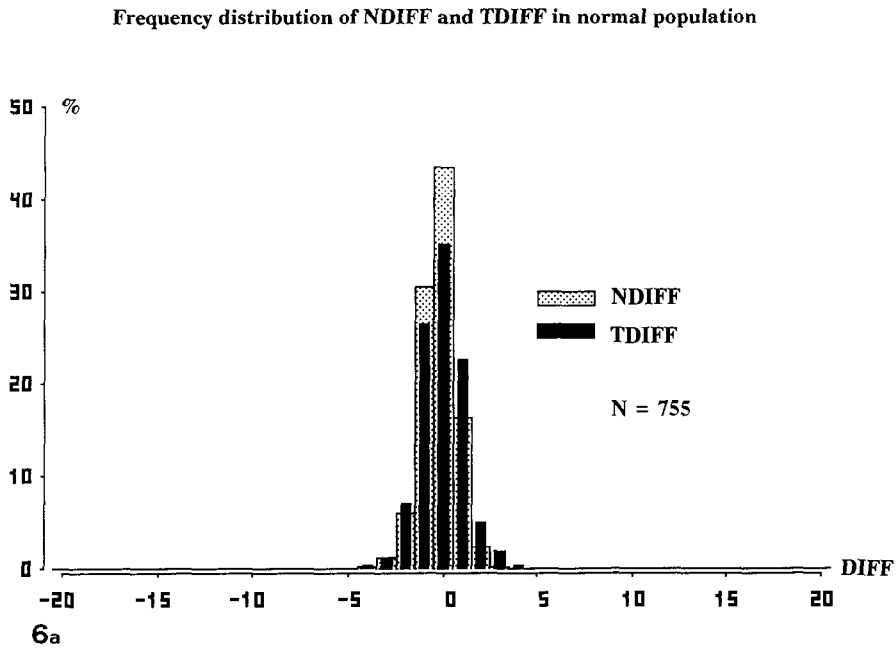


Fig 5 Subset of glaucoma suspect examinations having normal values for LV, MD and CLV indices, where |NDIFF| exceeds the 90% limit. (Normal ranges: SF 0 2 dB; MD -2... +2 dB; CLV 0 4 dB)

slight skewness (0.024) (Fig. 3, shaded columns).

The greater spread of the NDIFF distribution in the suspect eyes may be explained by contamination of this group with true glaucomas displaying positive and negative nasal steps, caused by glaucoma (Fig. 3, dark columns).

The pronounced correlation of |NDIFF| with CLV suggests that a test of the asymmetry in the DLS around the nasal horizontal meridian may be used to estimate the CLV index measurement in the G1 program. Here, it must be kept in mind that the noise attenuation when calculating NDIFF is based on a few test locations and



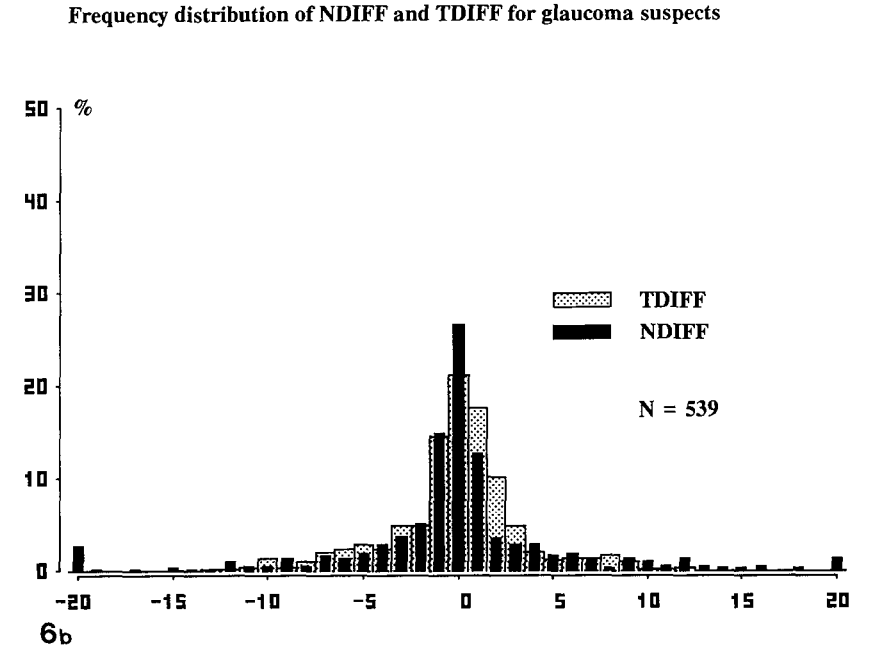


Fig 6 Distribution of NDIFF in comparison with TDIFF a: for normals; b: for glaucoma suspect population.

is thus less than that for the other indices which are determined using all 59 test locations of program G1. Since, as expected, there is neither a correlation between |NDIFF| with MD nor with SF, one would forego the information contained in MD and SF if one would rely only on the NDIFF determination. The efforts as described here, *i.e.*, to use a sample of limited size as a predictor of disturbances which have a more global distribution parallel rather closely those of other authors[16].

The finding that in a number of cases (six out of 119 glaucoma suspect examinations) only NDIFF exceeded its normal limits (5% resp. 95%) while CLV, MD, and SF were normal, can be explained as an artifact due to random scatter of the measured values and does not signify additional information obtained with NDIFF, which would not otherwise be available (Fig. 5).

Most important: Differences of the DLS (TDIFF) between a number of test locations being separated by about the same distance as the test locations used to determine nasal asymmetry is another expression of the disturbance of the spatial correlations within the Bjerrum region as already indicated by the disturbed CLV index.

In order to restrict the number of test stimuli in a future screening program ('a reduced G1 program'), we have embarked on a study[15] to find out whether and where there are regions in the visual field, including the nasal region, which yield optimum reliability in predicting global visual field indices such as MD, SF and CLV.

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CLINICAL IMPORTANCE OF SPATIAL SUMMATION IN GLAUCOMA

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Using static automated perimetry in eyes with advanced glaucoma, the authors have observed repeatedly an improvement in perimetric threshold which far exceeded the predicted 6 to 10 dB when test object size III was changed to size V Therefore, they studied the mean thresholds and mean differences between thresholds using these different large test sizes at two different backgrounds (3.15/31 5 asb) in 15 normal and 19 glaucomatous eyes. The mean differences in thresholds were evaluated further as a function of eccentricity and retinal sensitivity. In the hope of understanding the mechanisms of spatial summation in glaucoma, 38 spot locations were tested further by adding 18 size III spots that covered the same area as was occupied by the size V test object (bomb cluster analysis)

In glaucoma patients, a 1 2 log unit increase in test object size was more effective in improving reported retinal sensitivity than a 1.0 log unit decrease in background luminance. The opposite was found in normals, where increasing the contrast was more helpful in improving threshold reports than enlarging test object size

The worst seeing areas of the visual field caused the greatest change in thresholds from size III to size V test objects The bomb cluster analysis was applied to the two spot locations in each field which exhibited the greatest difference in thresholds. This difference could be accounted for 73% of the time by (1) recruitment of nearby areas of nearly normal sensitivity, and (2) classic spatial summation These intensely studied small areas of the visual field (19 spots in 1 72 degrees) revealed widespread hidden microscotomas As a clinical corollary, this may explain glaucomatous optic nerve damage without apparent visual field loss.

The remaining 27% exhibited a marked improvement in threshold far beyond normal physiologic expectations. We believe the unmasking of large, less sensitive receptive fields may facilitate summation over a much broader region This may explain why increasing test object size was effective in uncovering previously blind areas of the visual field in patients with advanced glaucoma

Introduction

The goal of perimetry is to find and follow visual field defects. Small test objects are needed to probe a relatively healthy field, but may fail to find remaining useful vision in badly damaged eyes. An equivalent Goldmann test target size III is most commonly utilized during static automated perimetry. With this test object, large areas of the visual field may appear blind in patients with advanced glaucomatous disease. When a larger test object is used to explore the visual field, remaining useful vision may be uncovered and followed[1].

The relationship between test object area and threshold luminance has been clinically evaluated by several investigators[2-6]. This interchangeable relationship between brightness and size of a test object can be expressed mathematically as log L + klog A = C, or $LA^k = C$. L is the light difference threshold, A is the area of the test object, C is a constant and k is the summation coefficient. The summation coefficient measures the additive effect of stimuli from contiguous areas of the retina[4].

Spatial summation is the ability to recognize a change in threshold when the test object area is increased or decreased while all other test variables are kept constant. When there is no change in threshold with change in area, k equals zero, and spatial summation is nil. When a given increase in target area stimulus causes the same amount of decrease in threshold luminance, spatial summation is complete and k is equal to unity or one.

Using kinetic techniques, Goldmann investigated area-intensity relationships and

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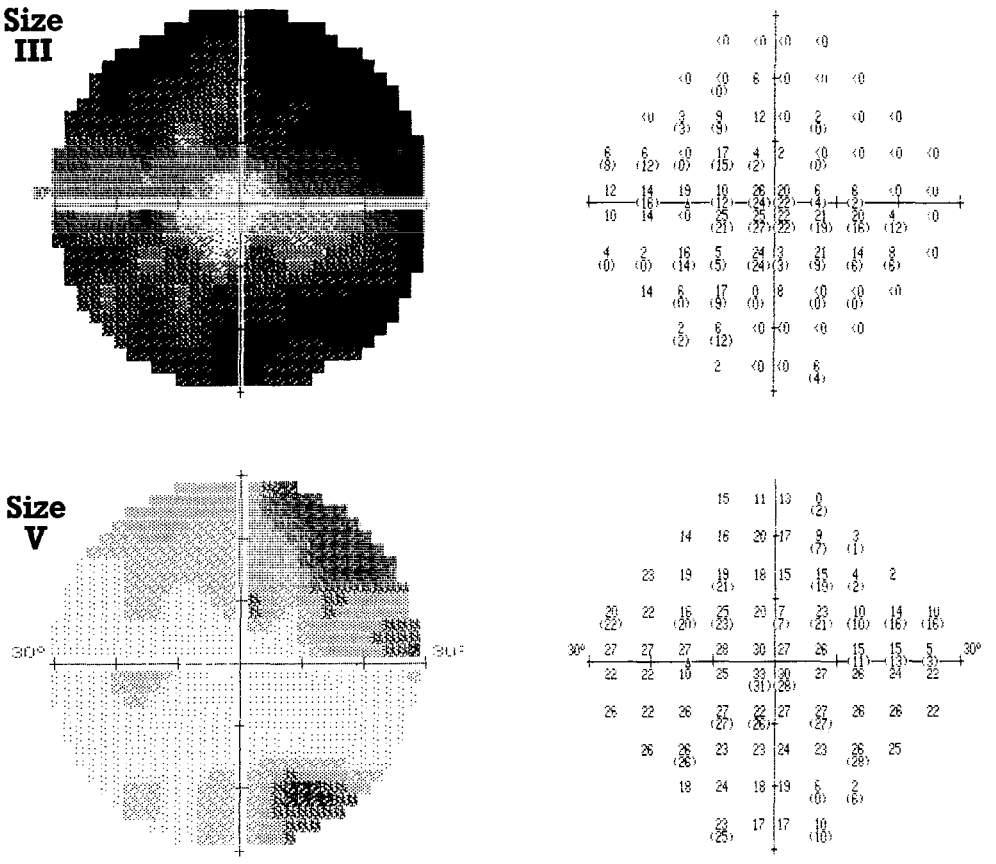

Fig 1 Marked improvement in perimetric threshold obtained clinically by enlarging the test object size This 30-2 Humphrey visual field was essentially blind over most of its area when it was studied using the Goldmann test size III Typically, a 5 to 10 dB increase in sensitivity occurs in normals by changing from a size III to a size V In this patient with advanced glaucoma, many areas that appeared devoid of retinal sensitivity showed a dramatic improvement in reported threshold when the stimulus size was changed to a V. Several repetitions of this experience were the impetus for the present study.

demonstrated that a four-fold change in test object area is approximately equivalent to a 3.16 change in intensity, yielding a summation coefficient of 0.83 (log 3.16/log 4.0). Further work by Fankhauser and Schmidt revealed that summation increases gradually from center to periphery of the field[6]. Louise Sloan thoroughly studied area-intensity relations with static techniques and found that spatial summation increased with decrease in the size of the test object and with increasing distance from the fovea. For example, in normal eyes, the summation coefficient ranges from 0.55 at the fovea to 0.9 at 45° nasal to fixation[4].

Changing from a Goldmann test object size III to a V is equivalent to a 1.2 log unit or 16-fold change in area (4 mm^2 to 64 mm^2). If the summation coefficient were equal to 1, this would correspond to a 1.2 log unit change in luminance or a 12-decibel (dB) increase in retinal sensitivity. In the normal eye, this only occurs when small test objects are used in the retinal periphery at 50° nasally and 60° temporally. Larger spot sizes tested in central retinal locations provide less spatial

summation, and a 1.2 log unit change in area commonly produces a minor change in the normal threshold.

Using static automated perimetry in eyes with advanced glaucoma, the authors repeatedly observed an improvement in perimetric threshold which far exceeded the predicted 6 to 10 dB when test object size III was changed to size V (Fig. 1). This prompted us to study spatial summation in our glaucoma patients.

Material and methods

Eighteen glaucoma patients (19 eyes) with an average age of 65 years and ten normals (15 eyes), average age 53 years, were evaluated. All patients were tested on the programmable Squid 300 automated perimeter with a maximal test target intensity of 3160 apostilbs (asb) (minus 5 dB). Threshold was obtained without region growing, using a 4-2-2 algorithm[7]. Goldmann test sizes III and V, subtending visual angles of 0.43° and 1.72° diameter, respectively, were used as the test objects.

Each patient had a total of four visual fields equally divided between two test sessions. The test order at each session was alternated for successive patients.

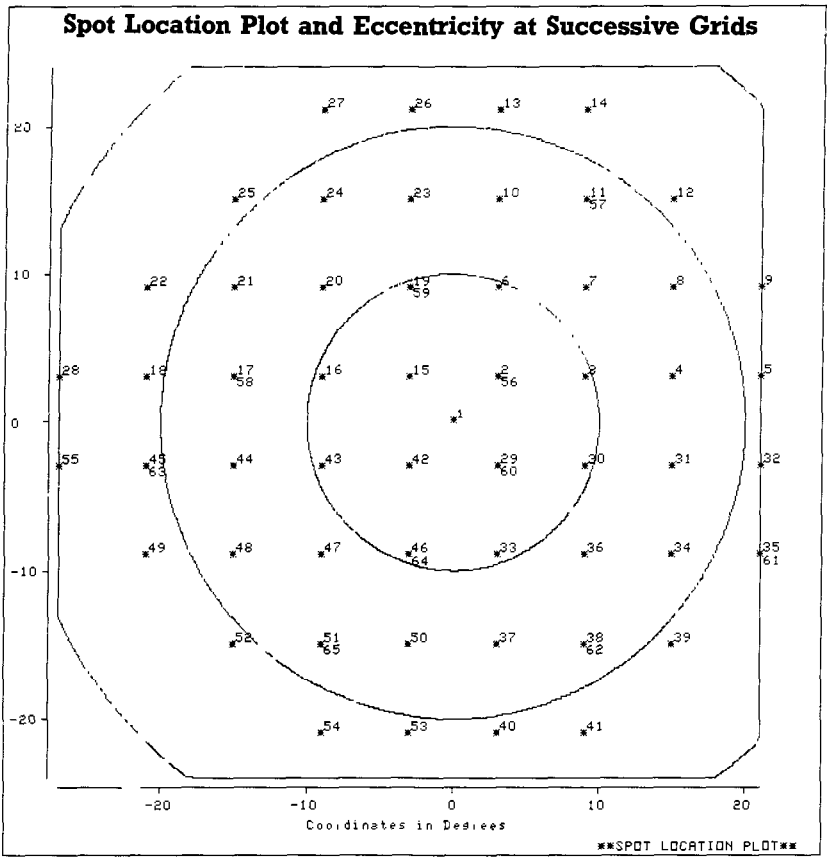

Fig 2 Spot location plot A six degree grid consisting of 55 loci covered the central 21° of the visual field, except for nasally where two extra points were programmed at 27° eccentricity. When threshold was calculated as a function of eccentricity, an average threshold for each successive square grid that crossed the meridia at 3°, 9°, 15°, and 21° was determined For 27°, the two available thresholds were averaged.

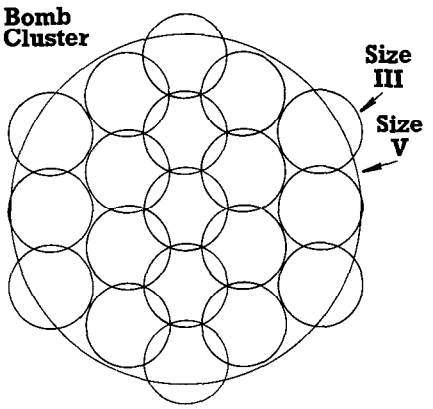

Fig 3 Bomb cluster analysis Coverage of a single spot size V area with multiple size III test objects The area of a Goldmann test size V (visual angle 1 72°) is 16 times greater than a size III (visual angle 0 43°) Eighteen additional size III test objects were chosen to cover the same area occupied by a size V test target. Analysis of line function shows that the edge of the size V test image on the retina follows the same spread as the edge of the size III retinal image.

Subjects were dark adapted for ten minutes before visual field testing and were allowed a 30-minute rest interval between tests. The duration of the test object stimulus was always 0.2 seconds. A six-degree grid covered the visual field with general limits at 21°, except for nasally where two extra points were programmed at 27° eccentricity. This grid consisted of 55 locations selected to avoid midline and horizontal meridia except at the fovea (Fig. 2). Ten more points were rethresholded in order to calculate root mean square, a measure of variance.

In the first session, patients were tested with a background of 31.5 asb. In test 1, the stimulus size was III, and in test 2 the stimulus size was V. Within a four-week period, subjects returned for the second session. Test 3 consisted of a size III stimulus and the same 55 point 6° grid, but the background was reduced to 3.15 asb. Test 4 was carried out with a background of 31.5 asb and stimulus size III. In this test, the familiar 55 point 6 grid was augmented by the addition of 18 spots near each of two locations that exhibited a large difference in thresholds during session one. Both spot locations were surrounded in two rings by 18 size III spots, corresponding to the area occupied by a size V test target. We refer to this test as a bomb cluster analysis (Fig. 3). The 36 additional size III test spots were randomly tested throughout the visual field to keep attention global. Therefore, a total of 91 points (55 + 18 + 18) were thresholded during test 4. Each patient had a total of four visual fields, three for statistical analysis (tests 1, 2 and 3) and test 4, the bomb cluster analysis, to ascertain mechanisms of summation. In the normal and glaucoma groups, an average threshold at every spot location was determined for each of the three tests. At each spot location, the differences in average threshold for tests 1 and 2, 1 and 3, and 2 and 3 were recorded for each group. The means and standard deviations at each point in the normal patients served as physiological standards for differences between thresholds in both groups. To create these standards, the mean differences between thresholds using different test size and backgrounds in the normals were subtracted from the corresponding point differences in each glaucoma patient's field and divided by the normal group's standard deviation at each spot location. This number represented how many standard deviations of difference from the normals existed at each spot location. This

Table 1 The mean thresholds and mean differences between thresholds for tests 1, 2, and 3

	Mean threshold ± standard deviation (dB)			Mean threshold difference (dB) between		
	Test 1	Test 2	Test 3	Test 2-1	Test 3-2	Test 3-1
	(III-31 5 asb)	(V-31 5 asb)	(III-3.15 asb)			
Normal	20 8 ± 3.4	25 7 ± 2 6	27.4 ± 3.0	4 9	1 7	6.6
Glaucoma	8 8 ± 9 3	15 4 ± 9 7	14.0 ± 16 3	6 6	-1.4	5 2

information was obtained for each patient and for each group.

The mean differences in threshold were also determined as a function of eccentricity for each group. Mean threshold was calculated at the fovea and each successive grid that crossed the meridia at 3°, 9°, 15°, 21° and 27°.

The bomb clusters were analyzed by calculating the mean and standard deviation for the 19 test size III locations that covered the spot size V area. These clusters were then grouped according to the difference between the thresholds to the size V test and the best seen stimulus size III.

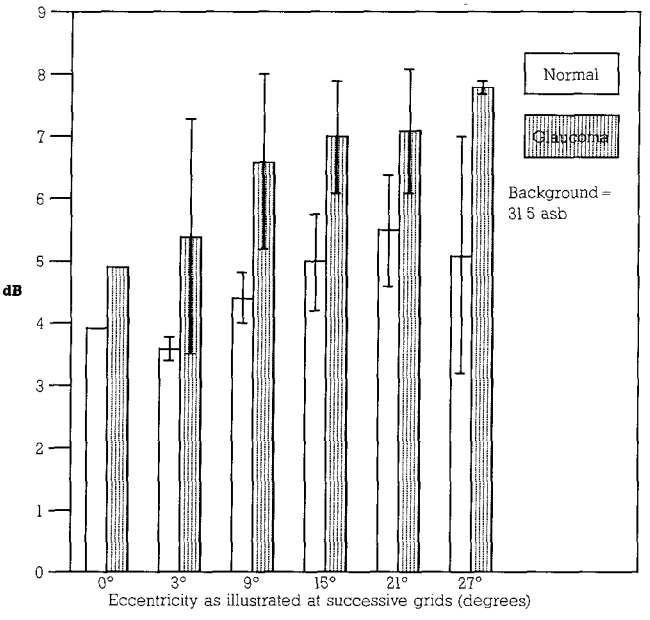

Fig 4 Mean threshold differences from size III and V test objects as a function of eccentricity.

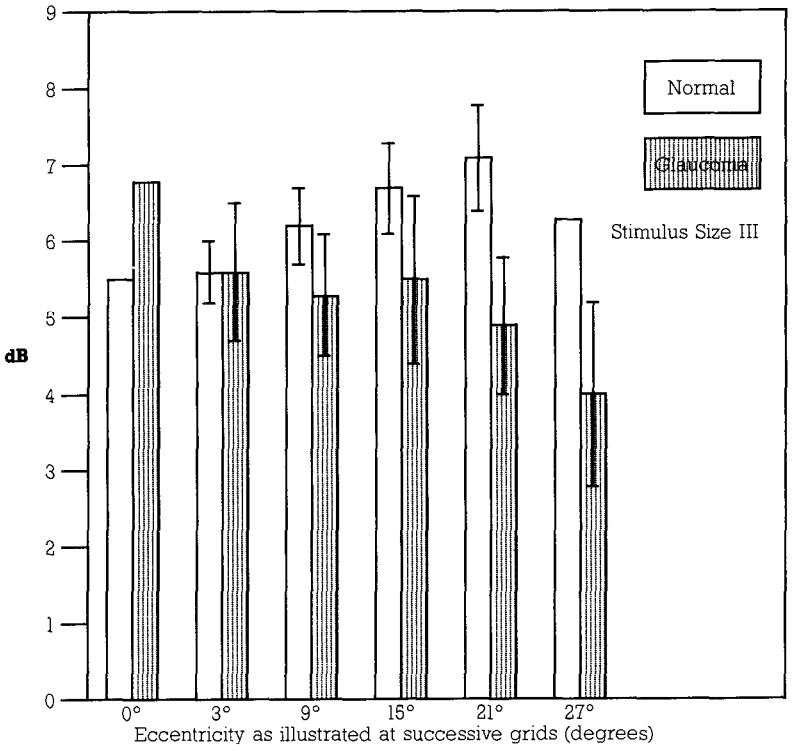

Fig 5 Mean threshold differences from 3.15 asb and 31 5 asb background luminances, both using test size III, as a function of eccentricity

Results

The mean thresholds and mean differences between thresholds using different test sizes and backgrounds in normals and glaucoma patients are illustrated in Table 1. The improvement in mean visual field threshold upon increasing test object size by 1.2 log units (test 2 minus test 1) was 4.9 dB for the normal and 6.6 dB for the glaucoma group. The increase in mean visual field sensitivity upon lowering background by 1.0 log unit (test 3-1) was 6.6 dB and 5.2 dB for the normal and glaucoma groups, respectively. The change in mean visual field threshold obtained by varying both background and spot size (test 3-2) was 1.7 dB for the normals, and -1.4 for the glaucoma group.

The mean differences in the visual field were dependent on eccentricity. Figs. 4, 5 and 6 illustrate the mean difference between thresholds as a function of eccentricity using different test sizes and backgrounds. Spatial summation increased with increasing distance from the fovea and was larger at each successive grid for the glaucoma group (Fig. 4). Dimming the background luminance by 1 log unit improved threshold in both groups. This improvement in retinal sensitivity was greater for the normal group, and simultaneously amplified by increasing eccentricity. In the glaucoma group, this improvement in sensitivity declined with increasing eccentricity (Fig. 5). In the normal group, a 1 log unit decrease in background was more effective in improving sensitivity than a 1.2 log unit increase in test object size. The opposite was found for the glaucoma group (Fig. 6). The

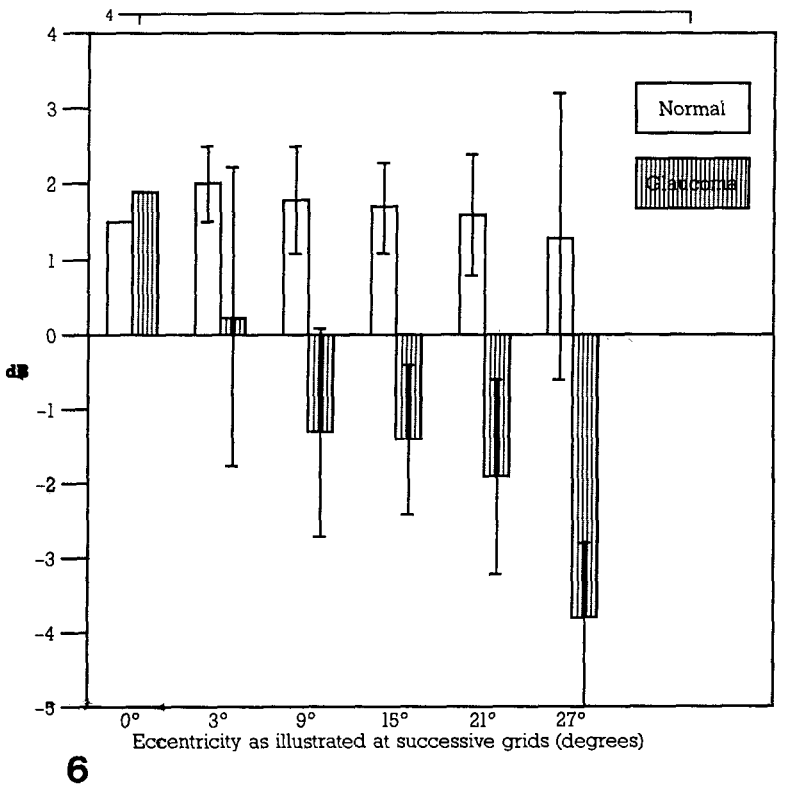

Fig 6 Mean threshold differences from size III with a background of 3 15 asb versus size V with a background of 31.5 asb (test 3 minus test 2) as a function of eccentricity.

mean threshold differences from size III to V test objects were dependent on depth of the visual field defect. In general, selecting a visual field defect of greater depth caused a larger threshold difference between size III and V test objects. Twenty-four percent of points tested exhibited more than two standard deviations of difference from the normal group (Fig. 7A and B).

In the glaucoma patients, 13% of points were blind with both the V-31.5 asb and III-31.5 asb combinations. This increased to 20% by dimming the background and retaining test size III.

The bomb clusters were evaluated in the glaucoma group by obtaining the difference in thresholds between the spot size V and the best seen of 19 loci in the bomb cluster (Fig. 8). These were grouped according to a difference of 2 dB or less (recruitment), 3 to 9 dB (summation), and 20 dB or greater (pathologic summation). In the glaucoma group, 22% of clusters had a 2 dB or less change, 51% fell between 3 and 9 dB, and 27% showed a difference of 10 dB or more. Among normal subjects, the maximal difference between thresholds to size V and the best of the bomb cluster's 19 size III thresholds in the same area was one finding of 9 dB.

Discussion

Spatial summation implies the addition of visual information from adjacent retinal areas through the use of larger test targets[8]. In the normal eye, spatial

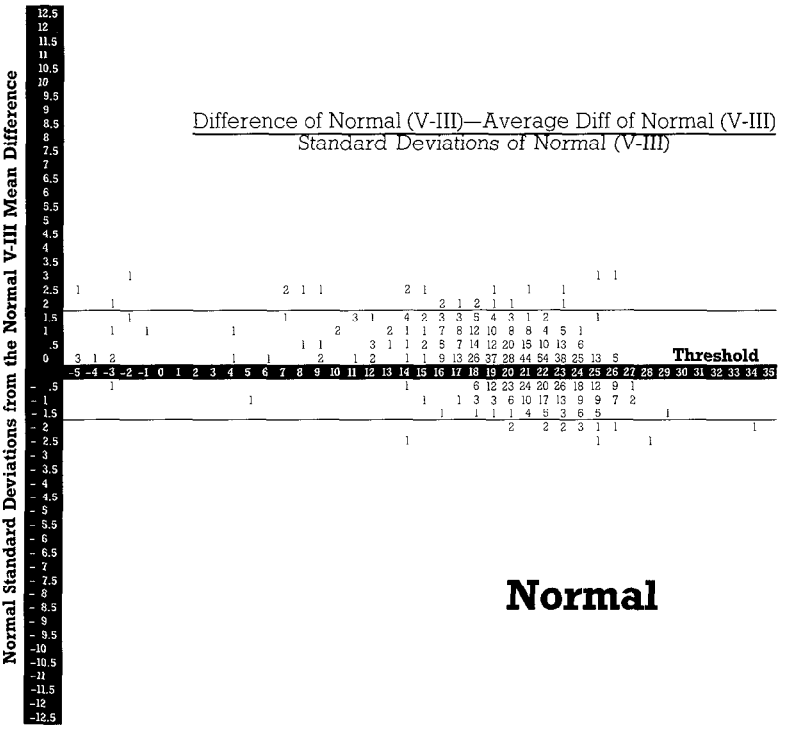

Fig 7A Number of normal standard deviations from the normal V-III mean difference as related to threshold (III) - the Normal Group The mean differences between sizes III and V thresholds in 15 normal subjects at each of the 55 test loci were calculated with their standard deviations The individual differences were subtracted from the group's mean for each point. These differences between group mean and individual change were divided by the group's standard deviation of mean difference so the individual changes could be evaluated as to their likelihood of chance occurrence. Thus, the values were plotted in terms of the number of standard deviations they lie from the normal mean difference and as a function of threshold (III).

summation plays a more significant role with smaller test objects than with the larger ones studied here. As stimuli are presented at progressively eccentric locations in normal fields, threshold increases (sensitivity decreases) and spatial summation becomes more nearly complete[2-6]. The larger receptive fields in the retinal periphery may account for this phenomenon.

Louise Sloan thought it was "surprising that a disease process could improve the capacity for summation"[9]. *Subsequent investigators concurred that spatial summation was altered in impaired visual fields and, the greater the threshold defect, the more nearly complete was spatial summation[11]. Hallett determined that there

*This is similar to the concept of photometric dysharmony characterized by a significantly greater increase in threshold for small than for large test objects introduced by Dubois-Poulsen[10].

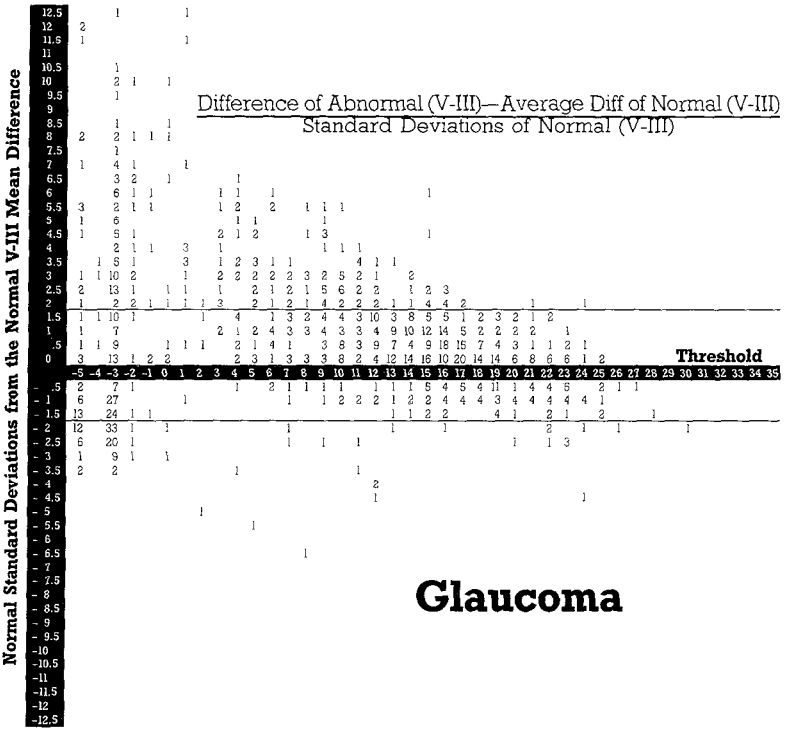

Fig 7B Number of normal standard deviations from the normal V-III mean difference as related to threshold (III) - the Glaucoma Group. Among the 19 eyes of 18 patients who were studied, most were classified as advanced glaucoma Calculations for the individual differences in this group's plot still used means and standard deviations from the normals. Values which lie just outside the lines at two standard deviations have a 95% chance of being abnormal and those which are well away from the line are obviously pathological.

is normally a large variation in spatial summation and that human spatial summation depends on the activity of more than one overlapping retinal ganglion cell[12].

According to Goldmann, a 1.0 log unit increase in sensitivity can be expected from a 1.2 log unit increase in test object size during kinetic testing of normals[2]. With the same increase in size, a 0.49 log unit (4.9 dB) increase in sensitivity was found in our normals. Smaller receptive fields located in central retinal areas and static testing may explain this deficiency in expected summation.

In glaucoma patients, areal summation brought the average improvement in threshold up to 6.4 decibels, even with 13% of points testing blind to both test objects. This improvement in summation was marked for some loci, with 24% of thresholds exhibiting more improvement than two standard deviations of normal variance at the same loci. Bomb cluster analysis revealed at least three possible mechanisms for this phenomenon (Fig. 8): *1* recruitment of nearby undisturbed vision (21.6%) ,*2* classic spatial summation (51.4%),*3* pathologic summation (27%). Seventy-three percent of the time the results of the bomb cluster analysis could be explained by the first two mechanisms. However, the remaining 27% of bomb clusters were blind to a test size III over a large portion of the spot size V area. These mainly blind portions of the visual fields still exhibited an average of 14.5 decibel improvement in threshold when tested with larger test objects. This is

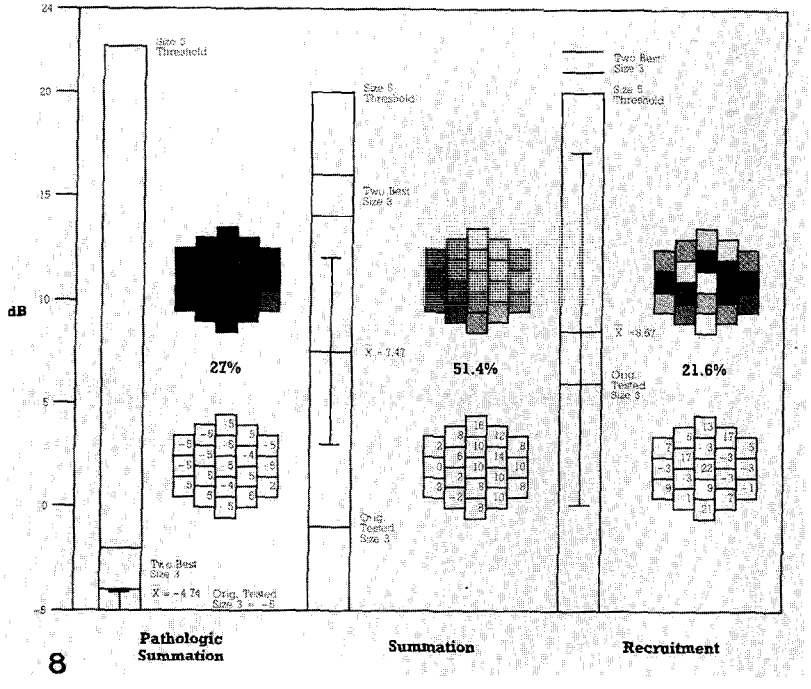

Fig 8 Bomb cluster analysis. On the bar graphs showing decibels, the lowest zone extends from the maximal available test intensity to the mean of the 19 size III test. One standard deviation to each side of the mean is shown traditionally. The intermediate bar zone shows the range from mean to the best seen size III threshold. The top zone, which actually reflects downward in many cases of recruitment, shows the difference between size III best seen and the size V threshold

Three different patterns of bomb cluster help account for the erratic behavior of defective zones in glaucomatous visual fields When any one of the size III thresholds is within 2 dB of the size V threshold, that sensitive zone can account for the size V result by recruitment. When a number of size III stimuli are seen within 3 to 9 dB of the V threshold, these can be accumulated as in the classical summation model. The absence of any size III threshold within 10 dB of the size V threshold implies a different type of summation which requires destruction of sensitivity to size III test, uncovering a system which summates from an area much larger than is normally utilized (pathological summation).

unexplained by the first two mechanisms. We believe that pathologic summation may account for this phenomenon by the unmasking of larger, less sensitive receptive fields.

We were unable to correlate the incidence or magnitude of large differences between thresholds to sizes III and V with slope as determined by vertical and horizontal nearest neighbor thresholds on the 6° grid. Also frustrating were our attempts to correlate the actual thresholds to size III and the slope-projected thresholds at the same locations versus the III-V threshold differences. The traditional measure of variance, RMS, also showed little, if any, correlation with the differences between thresholds for test sizes III and V.

The mechanism for this marked improvement in threshold probably does not relate to the classic summation theories previously described. Okamoto used a fundus perimeter to examine spatial properties in humans and found that the diameter of Y-cell receptive fields was three times that of the X-cell[13]. The diameter of these receptive fields increases with retinal eccentricities from the fovea. The size of these fields may be 30 minutes of arc at the fovea, and up to 216

minutes of arc at 20° eccentricity[14]. These large peripheral receptive fields may accommodate a spot size V (104 to 120 minutes of arc). Loss of smaller, more sensitive receptive fields may facilitate summation over a much broader region mediated by larger, less sensitive receptive fields. Although theoretical, the unmasking of these larger, less sensitive receptive fields may explain why increasing the test object size is effective in uncovering previously blind areas of the visual field.

Conclusions

1. Enlarging test object size is more helpful than extra contrast in uncovering and following remaining useful vision in severely damaged glaucomatous eyes. Increasing the contrast helps normals more than enlarging test object size.
2. The capacity for spatial summation is greater in the glaucoma group; it gradually increases with increasing distance from the fovea, and increases even more in areas of the visual field which are 'blind' to the size III test object.
3. Recruitment of nearby areas of nearly normal sensitivity, and classic summation, account for most (73%) of the large differences between thresholds of sizes III and V, 27% defy analysis.
4. The apparent loss of optic nerve axons without visual field loss is probably the result of widespread hidden microscotomas without large areas of confluence, as is well illustrated by bomb cluster analysis. These widespread tiny defects may also account for high RMS numbers and other evidence of excess fluctuation during static visual field testing. They may also be responsible for concentric contraction and photometric dysharmony in kinetic perimetry.
5. Loss of smaller more sensitive receptive fields may facilitate summation over a much broader region mediated by larger, less sensitive receptive fields. The unmasking of these larger less sensitive receptive fields may explain why increasing test object size is effective in uncovering previously blind areas of the visual field.

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CHOROIDAL ANGIOGRAPHY FINDINGS IN PATIENTS WITH GLAUCOMA-LIKE VISUAL FIELD DEFECTS

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An example of a patient with a visual field defect typical for glaucoma, but with no other signs of glaucoma, is shown This patient had normal intraocular pressures and a physiological optic disc, but had a history of frequent cold hands and feet and migraine headaches In capillary microscopy of the nailfold, a tendency for vasospasms was found. Using a new method of choroidal angiography, the arterial and capillary filling time, the arterio-venous passage time in the choroid and the amount of capillary perfusion of the choriocapillaris were determined Reduced filling and passage times and a rarefaction of the perfused choriocapillaris were found.

Under treatment with Nifedipine, a normalization of the visual field occurred Capillary microscopy of the nailfold and parameters of choroidal bloodflow returned to normal values.

The authors conclude that in cases where the visual field appears glaucomatous, but no other glaucoma symptoms are present, a vasospastic syndrome may be suspected, which may respond to Nifedipine treatment.

Introduction

In 1985 Phelps and Corbett[1] found that 47% of their patients with low-tension glaucoma suffered from migraine. This suggested for the first time that vasospastic events might play a role in the pathogenesis of low-tension glaucoma. In 1986 Gasser and associates[2] described an ocular vasospastic syndrome in which patients with unexplained scotomas producing visual loss had abnormal capillaroscopic responses to cold in the nailfold of the finger. These patients had a history of frequent cold hands and feet and migraine headaches. In 1987 Flammer and Guthauser[3] found a significant improvement of visual fields during treatment with Nifedipine in patients with vasospastic syndromes. They suggested that the visual field defects which showed an improvement during treatment with a calcium antagonist were caused by choroidal vasospasm. This is supported by the facts that the scotomas are not homonymous, which means that they are not of cortical origin, in retinal vessels of these areas no changes could be observed, and choroidal vessels, similar to capillaries of the nailfold, have a sympathetic innervation[4]

We present a patient in whom it was possible to verify choroidal vasospasm as an origin of glaucoma-like visual field defect, using a new method for quantification of choroidal bloodflow.

Methods

For quantification of choroidal perfusion, we used a new method of Indocyanine green video-fluorescence angiography and statistical picture analysis, as described by Prünte and Niesel in 1988[5,6]. Using this method, it is possible to determine the following useful parameters:

1. The coefficient of variance of gray values at the peak of capillary filling (CVGB), which is correlated to the amount of perfused capillaries. Normal values range from 8 to 13. Higher values indicate a rarefaction of the perfused capillaries.

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2. The mean arterial filling time (AFT).
3. The mean capillary filling time (CFT).
4. The mean arterio-venous passage time (AVP).

These parameters were determined for a round area with a diameter of 4 degrees in the macula.

The visual field examinations were made on an Octopus automatic perimeter using program G1. For quantification of the visual field defects, we used the visual field indices MD and CLV[7,8].

The ICG angiogram and the visual field examination were performed before any treatment and two weeks after treatment with 20 mg Nifedipine twice a day.

Patient and results

The patient demonstrated was a 52-year-old male who suffered from verified open-angle glaucoma in his left eye. For one year he had noticed increasing loss of visual acuity and increasing visual field defect in the right eye. The highest intraocular pressure ever measured was 20 mm Hg. The optic disc of the right eye appeared normal and did not fit in with the visual field damage with an MD of 12.0 and a CLV of 32.0 (Octopus program G1). He had a history of frequent cold hands and feet and migraine headaches. The capillary microscopy of the nailfold of the finger showed a tendency for vasospasm with a normalization of capillary bloodflow 20 minutes after oral administration of 20 mg Nifedipine. The amount of perfused capillaries in the choroid was reduced, indicated by the CVGB value of 15.2. AFT was 2.0 sec, CFT 2.5 sec and AVP 4.0 sec.

After these examinations, we started therapy with 20 mg Nifedipine twice daily. Eighteen days later these examinations were repeated. The visual field showed normalization. The value for MD was 1.8 and for CLV 3.5. We also found normalization in ICG angiography. CVGB was 12.9, which indicated a normal amount of perfused capillaries in the choroid. The filling and passage times increased under treatment with Nifedipine. AFT became 2.5 sec, CFT 3.5 sec and AVP 5.5 sec. There was no change in visual acuity (8/10) after 18 days' treatment with Nifedipine.

Discussion

These results show a correlation between reduced capillary perfusion in the choroid and visual field defects in a patient with a vasospastic syndrome. This patient showed normalization of the visual field and choroidal bloodflow parameters during treatment with 20 mg Nifedipine twice daily.

It is very interesting to note that filling and passage times in the choroidal network were reduced under vasospastic conditions. We assume that this is caused by an increased bloodflow through arteriovenous shunts in the choroid, if the overall capillary diameter is reduced as found under vasospastic conditions. We found these results confirmed in other patients with vasospastic syndromes.

Furthermore, the results shown here demonstrate the possibility of successful treatment of choroidal vasospasms by calcium antagonists.

We conclude that in cases where the visual field appears glaucomatous, but no other glaucoma symptoms are present, a vasospastic syndrome may be suspected, which may respond to Nifedipine treatment.

Acknowledgement

This work was carried out at the University Eye Hospital, Bern, Switzerland

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NEWER NON-STANDARD TECHNIQUES

NOISE-FIELD CAMPIMETRY
A new perimetric method (snow campimetry)

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Patients with circumscribed scotomata are able to perceive these when they look at a field of small black and white random dots flickering at high frequency (noise-field), similar to the flicker ('snow') of a television screen after the end of transmission This subjective perception of scotomata can be used as a screening method, to be followed by manual or automated grid perimetry on the same monitor, which can be restricted to the damaged visual field area The results of noise-field campimetry and traditional test point perimetry are compared in 250 patients with pathological visual field defects. Homonymous hemianopias due to supragenicular damage occupy a special position, since they are either not perceived at all in the noise-field, or to a much smaller spatial extent The blind spot and some congenital field defects are also not perceived as scotomata in the noise-field. All acquired circumscribed scotomata due to lesions of the first, second or third neuron, on the other hand, are clearly perceived in the noise-field, if the patient is capable of steady fixation.

Introduction

When patients with circumscribed scotomata within the central 30 of the visual field, such as Bjerrum scotomata, look at a homogeneous bright or dark field, they usually do not perceive their scotomata, at least not as a circumscribed area contrasting with the background. The scotomata are noticed only indirectly by the invisibility of objects within the region of the visual field defect. Against a homogeneous background, such scotomata thus have the same appearance as the blind spot in healthy observers. This, too, is noticeable only by the invisibility of objects within its limits.

The pathological scotomata can be clearly perceived, however, when instead of a homogeneous field, the patients view a field of small black-and-white random dots flickering randomly at a high temporal frequency (white noise). This resembles the flicker of a television screen after the end of transmission ('snow'). When the patient fixates a clearly visible spot in the center of the screen, the scotoma is perceived as a region with less or no flicker, and of a different brightness from that of the surround. The observer can precisely 'draw' the borders of the scotoma onto the screen with his finger. Patients usually do this spontaneously, without being asked, since the image of the sharply delineated 'cloud' in the noise-field is very impressive. All circumscribed scotomata caused by damage to the retina, the optic nerve, the chiasm, or the optic tract, can be delineated by the patients in the same way as glaucomatous field defects.

The only exceptions are the physiological blind spot and congenital field defects like nerve fiber bundle defects caused by congenital pits of the optic disc. In addition, homonymous hemianopias due to lesions in the optic radiation or the visual cortex are only perceived in the noise-field when they are of relatively recent onset. If such supragenicular hemianopias are older than two years, usually no defect is seen in the noise-field.

The description of the subjective perception of the scotoma in the noise-field can

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easily be combined with a quantitative perimetric examination on the screen of the same monitor. In this case, the description of the scotoma in the noise-field serves as a rapid screening method telling the ophthalmologist whether and where there are field defects within the central 30 degrees. This is followed by manual kinetic perimetry or automated grid perimetry in the region of the scotoma, using the monitor as test field. The advantage of this combined method is that traditional quantitative perimetry needs only to be carried out in regions with visual field defect, saving a considerable amount of time.

Methods

The noise-field is generated on the screen of a black-and-white computer monitor by means of a program which allows variation of the temporal frequency, luminance, and size of the light and dark stimulus elements. Pilot experiments showed that scotomata are most clearly perceived with a high flicker frequency, high contrast, and small dot size. Most of the examinations described below were therefore carried out under the following conditions: a flicker frequency of 50 Hz, luminance of 60 cd/m^2 and 0.8 cd/m^2 of the light and dark dots, respectively, with either 50% or 70% of the dots being dark, and square dots of 15 min arc.

Drum and co-workers[1] reported a perimetric procedure using a similar flickering field. However, this was used as a background for traditional perimetry in which a single stimulus is used to sample the test field. In contrast, the method described here does not use an isolated stimulus. Instead, the test field itself, with its high contrast, continuously moving elements of only a few minutes of arc, provides simultaneous stimulation of each point of the 30 degree visual field.

The patients sit at a distance of 30 cm from the monitor, with the head placed in a chin rest (Fig. 1). The test field of the monitor is a rectangle 38 cm long and 25 cm high, subtending a visual field of approximately 35 in the horizontal and 24 in the vertical direction. A figure of polar coordinates within the same field, containing circles at 5 distance from each other, can be displayed on the screen at any time by pressing a key. The distance between the circles is corrected for the flat projection of the display, *i e* , it increases with increasing eccentricity. Apart from

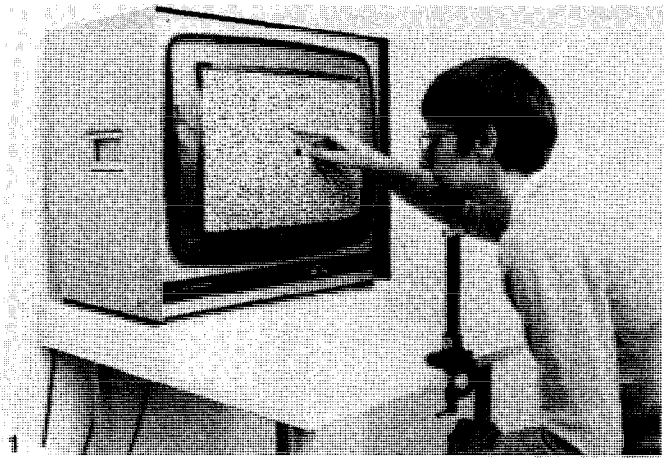

Fig 1 The examination set-up: the patient looks at the noise-field and 'draws' the outline of the scotoma with her finger, which in this case is perceived above the fixation point on the monitor.

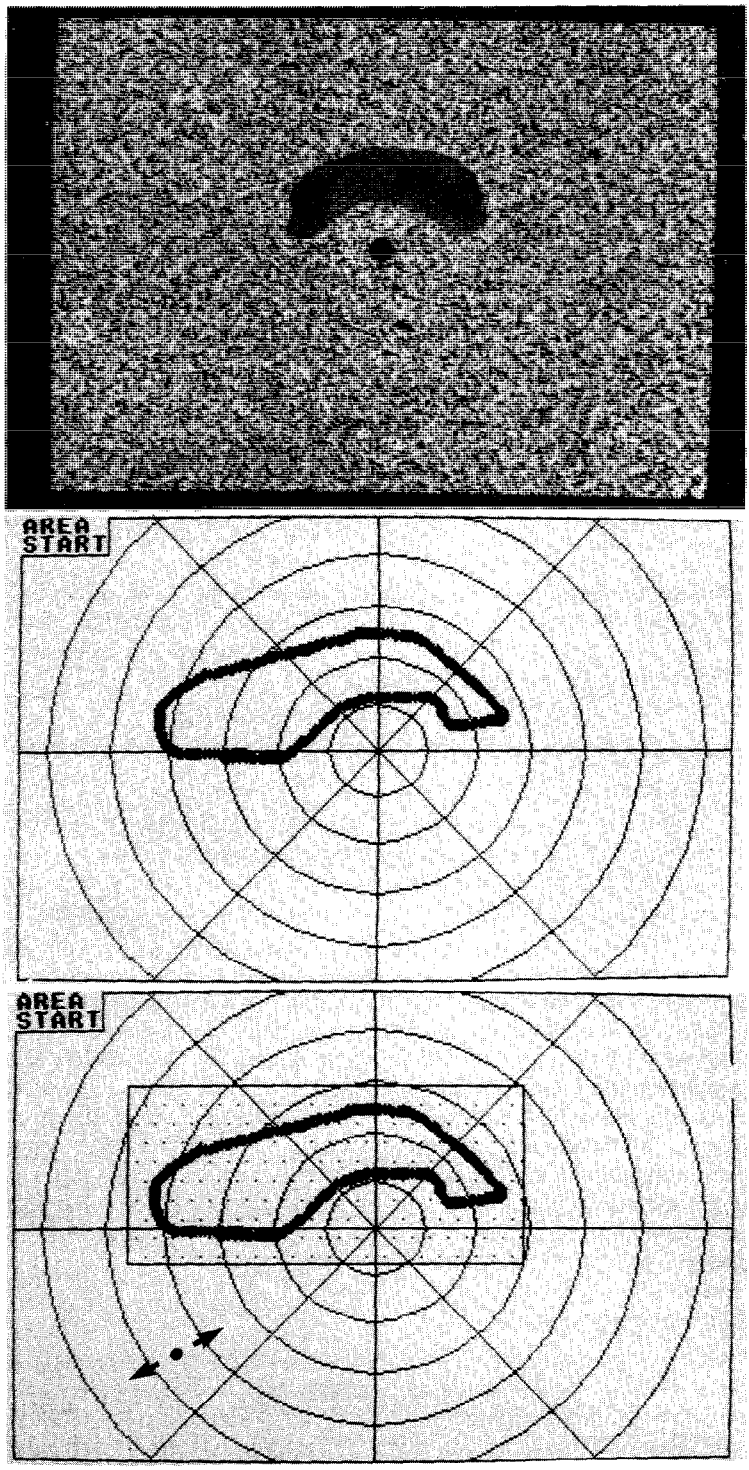

Fig 2 Examination procedure: a The patient perceives a scotoma and marks it as in Fig 1 The examiner draws the marked borders with the mouse b. The polar coordinates of the visual field are displayed on the screen. The examination area for grid perimetry is chosen, in which the test points are presented consecutively in random positions with a chosen density c. In this case, approximately 100 test points were presented one at a time in the critical area The patient indicates the test points perceived by pressing a key. After the examination, all points which were not seen appear on the screen as a scotoma. The 'mouse' can also be used for manual perimetry with a moving test point, which is indicated schematically at the bottom of the figure

the noise-field and polar coordinates, a homogeneous field can be displayed for traditional quantitative perimetry. The luminance of this field can be varied between 60 and 0.8 cd/m (Fig. 2a-c).

The routine examination begins with the presentation of the noise-field (Fig. 2a). The ophthalmologist can draw the scotomata reported by the patient onto the screen by means of a 'mouse', *i.e.*, a small displacement-measuring device connected to the computer. If the mouse is moved manually across a plane surface, a marker visible on the screen is displaced accordingly. The scotoma thus sketched and displayed on the polar coordinates then forms the basis for further examination (Fig. 2b). The region of the field defect can be examined with traditional static or kinetic perimetry. The results of the current examination, as well as those of later visits, are stored on polar coordinate plots.

During a kinetic perimetric examination, the ophthalmologist moves the test point freely across the screen by means of the mouse; borders of the scotoma are marked by a key press (Fig. 2c). Grid perimetry can be done automatically, *i.e.*, test points are presented randomly within the region of the field chosen by the examiner. The desired grid density is chosen before the examination (for example, in Fig. 2c, the test points are separated by 2 in the vertical and horizontal direction). The patient indicates the perception of a test point by pressing a key. We have found that occasional presentations of test points at random positions across the entire monitor reduce the patient's tendency to abandon fixation and look at the test field. The visual field plot, together with all the findings of the examination, can be printed out at the end.

Results

Fig. 3 shows the results of noise-field perimetry in 250 patients with visual field defects due to lesions at various locations along the optic pathway, as indicated in the schematic drawing. All 250 patients also had a thorough field examination with traditional perimetry, using a manual or an automated Tübinger perimeter. The agreement or differences between the results of traditional and noise-field perimetry can be seen in Fig. 3.

The number of patients in this comparative study of the two perimetric methods was originally 258. Results from eight patients were not included because they could not be induced to fixate steadily during the noise-field examination. This tendency for unreliable fixation is greater with the noise-field than with traditional perimetry because the patients perceive their scotoma and are tempted to 'look at it'. This, of course, moves the scotoma, and the patient then makes contradictory reports on its location. The examiner, however, will notice poor fixation by observation of the patient's eye movements, and can remind him to fixate properly. In the case of the eight patients excluded, even repeated insistence could not induce steady fixation.

Discussion

As can be seen in Fig. 3, homonymous hemianopias caused by supragenicular lesions are not perceived in the noise-field if they have existed for some time. Only very recent defects are perceived with a shape identical to the field loss measured with traditional perimetry. In all cases of old supragenicular lesions, the patients very clearly perceive the flickering noise throughout the perimetrically blind region, in the same way as it is seen in the rest of the visual field.

The exceptional findings of noise-field perimetry with supragenicular

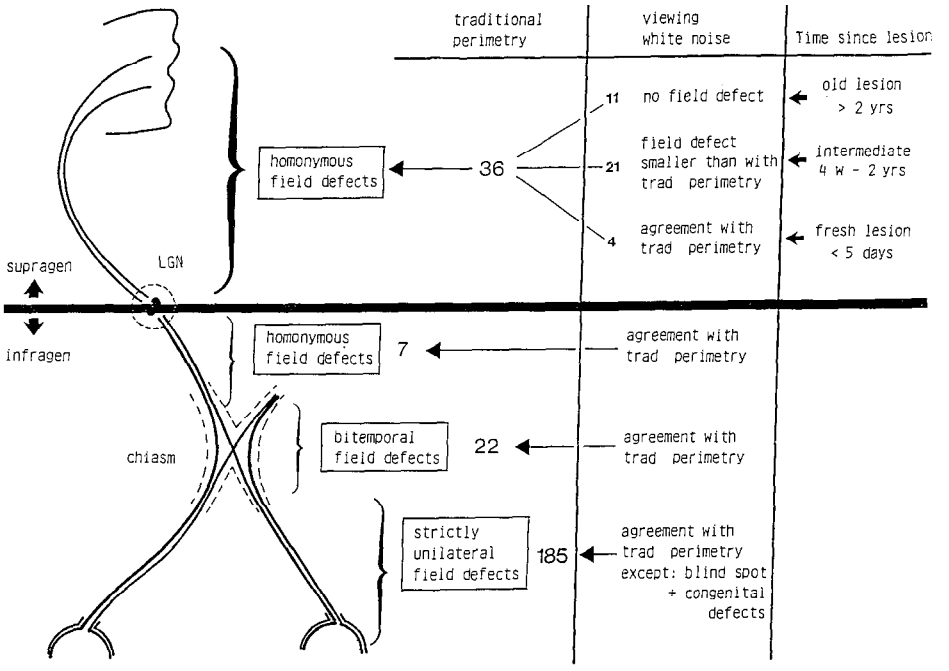

Fig 3 The results of a comparative study with noise-field perimetry and traditional test point perimetry in 250 patients

homonymous hemianopias as compared to infragenicular defects are reminiscent of similar results described in the literature as 'blindsight' or 'Riddoch's phenomenon'[2-9]. The lack or only partial perception of supragenicular hemianopias in the noise-field awaits further detailed study. Already at this point, however, it seems likely that noise-field perimetry in combination with traditional perimetry will give an indication of the supra- or infragenicular location of the underlying lesion in the optic pathway. This makes noise-field perimetry particularly important for neuro-ophthalmological differential diagnoses.

The subjective perception of visual field defects in the noise-field has another considerable advantage, the significance of which will only become clear in the future. This is that attentive patients can observe their own scotomata at home, with the television screen. They only need to be instructed to observe a constant distance from the screen (approximately 30 cm), cover one eye, and steadily fixate a fixation point. A possible enlargement of the absolute scotomata or the appearance of new scotomata can then be detected by the patients themselves, provided they are reliable observers. Any change in perceived scotomata should lead to another visit to the ophthalmologist.

In conclusion, the new method of noise-field perimetry described has three important advantages:

1. It can be used for an extremely rapid screening prior to traditional perimetry so that subsequent perimetry only needs to be carried out in the region of the visual field in which no flicker was perceived. This obviates time consuming examinations of intact parts of the visual field, and considerably shortens the whole perimetric examination. For practical reasons, it is useful to carry out both noise-field and test point perimetry with the same monitor.

2. Noise-field perimetry, in combination with traditional perimetry, can given an unequivocal topodiagnostic indication of the supra- or infragenicular location of the lesion.
3. The subjective perception of scotomata in the noise-field can be used by patients to observe their own field defects. This is particularly important for glaucoma patients. They can detect a possible enlargement of existing scotomata, or the appearance of new scotomata on their own television screen, provided they keep the observation conditions constant.

Despite its great practical advantages, the method has two disadvantages which, however, only rarely play a significant role:

1. The perimetric examination on a flat screen (campimetry) only allows measurements within an area of approximately 30 eccentricity (60 diameter). Field defects outside this area have to be examined with a hemispherical perimeter.
2. .The tendency for unreliable fixation is greater with noise-field perimetry than with traditional test point perimetry, but most patients who initially do not fixate steadily can easily be induced to do so.

Noise-field perimetry on its own cannot replace traditional test point perimetry. In combination with traditional perimetry, however, the new method provides an important enrichment of the perimetric examination process.

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A NEW PERIMETRY BASED ON EYE MOVEMENT

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Abstract

Due to the difficulty of maintaining eye fixation during the assessment of visual fields, the authors have developed a new perimetry utilizing eye movements to the target. A test target is displayed on a screen by a computer and the subject's eye movements are monitored through measurement of the corneal reflex. When an eye movement towards the target occurs, the computer recognizes it as a positive response and displays a new target

Introduction

It is very difficult to measure the visual fields of children and subjects whose fixation is not good. When we display a new target to such subjects in conventional perimetry, they look at the target itself and their fixation is no longer stable. For this reason, Enoch *et al.* tried to measure visual fields using a kinetic approach[1]. Oculokinetic perimetry was also developed by Damato[2]. Although Damato's approach is simple, it also needs fixation. Jernigan developed a new technique using eye movements to measure the visual field[3]. It has many different test point patterns but the central target had to be projected before measuring each point.

We devised a new type of perimetry based on eye movements. Eye movements are used to confirm the perception of the target. Targets are displayed one by one, and the subject is told to move his or her eye towards the target every time a stimulus is seen. We do not want to use a central fixation target every time before measuring each point. This approach requires immediate eye position recognition and judgment to decide on the next target position. We use an Eye Mark Recorder and two computer units to solve this problem. This system works well and can indicate up to ten targets per second and recognize the eye position 30 times per second. There is no need to display a central target between each stimulus because this new perimeter recognizes the eye position immediately and sets that position as the axis of fixation.

The new perimetry is fully computer controlled, so improvements are easy by just changing the computer program. Many new approaches may be possible using this unit.

Instrument

A block diagram is shown in Fig. 1. The Eye Mark Recorder recognizes the eye position through the corneal reflex. A small LED illuminates the cornea and a video camera catches the corneal reflex in the Eye Mark Recorder (Fig. 2). The output signal from the video camera is sent to the first computer. This is called the Eye Position Detector and has a video RAM to store the video signal from the Eye Mark Recorder which is A/D converted. The frame memory is immediately scanned and the corneal position is determined every 1/30 seconds through the Eye Position

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Detector. These eye position data are sent to the control computer.

We used a 16-bit MS-DOS based PC as the control computer. The control computer recognizes the eye position and judges whether the subject sees the target or not. Then a new position is calculated and displayed on the target screen.

A liquid crystal display is used as target screen, and is attached just in front of the Eye Mark Recorder. Therefore the relative position of the target screen and the subject's eye is always stable and not influenced by the subject's head position. The Eye Mark Recorder and the liquid crystal display are mounted on a headset unit (Fig. 3).

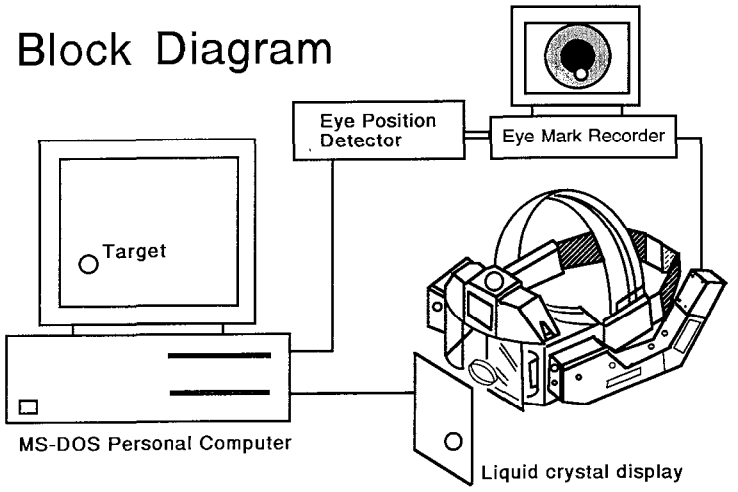

Fig 1 Block diagram of the new perimeter

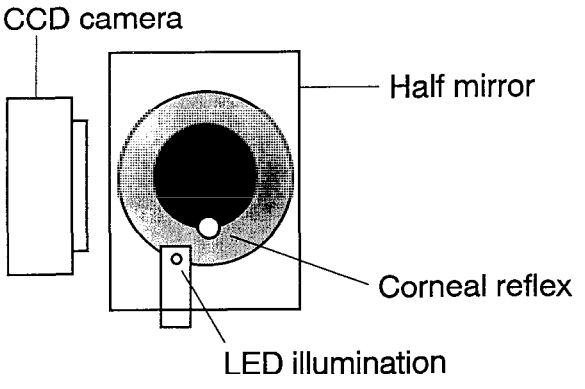

Fig 2 A small LED illuminates the cornea and a video camera catches the corneal reflex in the Eye Mark Recorder

Fig 3 The Eye Mark Recorder and the liquid crystal display are mounted on a headset unit

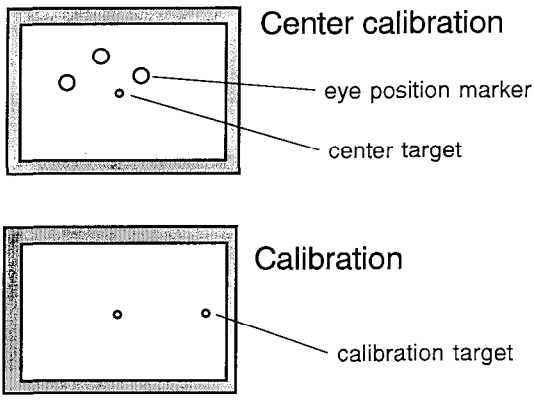

Fig 4 Measuring method (1) center calibration and calibration

Measuring method

1. *Center calibration* A central target is displayed. The subject looks at the target and the corneal reflex is adjusted to the center (Fig. 4).

2. *Calibration.* A calibration target is displayed 10 degrees from the center. The subject is asked to look at the target and the control computer calculates calibration automatically (Fig. 4).

3. *Measurement.* Targets are displayed one by one and the subject is instructed to look at the target every time he or she can see it. The control computer recognizes the subject's eye position, and displays a new target according to it. A stimulus is regarded as perceived when the Eye Mark Recorder indicates that the patient has

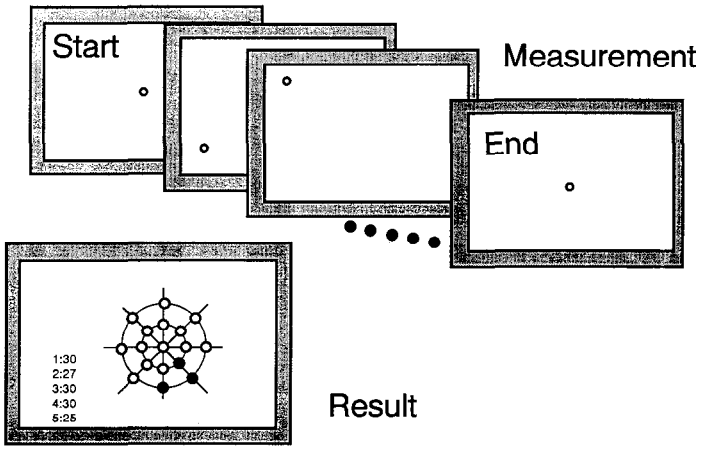

Fig 5. Measuring method (2) measurement and result display

moved his eyes to the vicinity of the target. Test target interval, number of targets and target positions are all changeable. Perceived stimuli and eye position are recorded and calculated after the measurement (Fig. 5).

4. Display result. The results are displayed on the computer screen (Fig. 5).

Conclusions

We have developed a new perimeter based on eye movements. Stable fixation is not necessary during assessment since the patient is instructed to move his or her eye to the target. This new perimeter continuously monitors a subject's eye position, recognizing whether he sees the target or not. Targets are displayed one by one at very short intervals. This method may be useful for examining the visual fields of young children and patients who cannot get up from bed, etc. It can also be used for eye movement research.

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PATTERN DISCRIMINATION AND LIGHT DETECTION TEST DIFFERENT TYPES OF GLAUCOMATOUS DAMAGE

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We tested glaucoma patients, glaucoma suspects and control subjects with a new type of perimetry based on pattern discrimination instead of light detection. Patients were asked to detect a patch of non-random dots embedded in a surrounding field of dynamic random dots The stimulus had the same fraction of black and white dots as the surround, so there were no luminance cues to detection We varied the regularity, or 'coherence' of the stimulus dots to find the 50% detection threshold The fully coherent target was a static, 1 sec duration, 20x20-dot checkerboard. Coherence was reduced by switching randomly selected black-white dot pairs A new set of dots was switched with each background frame Patient groups were based on intraocular pressure and conventional perimetry (Humphrey program 30-2 or Octopus program 32) Pattern discrimination thresholds were measured with a brief staircase procedure at a subset of the Humphrey 30-2 test positions. We tested two locations at a time, diametrically opposite the fixation point This minimized uncertainty about the target location while still avoiding fixation bias

Using a new criterion-free ROC analysis derived from signal detection theory, we estimated the separation of the normal data distribution from the suspect and glaucoma distributions for both the pattern discrimination and conventional tests. The pattern discrimination test produced greater separations than conventional perimetry for the suspect group and equivalent separation for the glaucoma group However, details of field defects for the two tests were poorly correlated, and mean pattern discrimination and conventional defects for the same patient often differed by several standard deviations. These results suggest that pattern discrimination and light detection are mediated by different mechanisms that can be differentially damaged in glaucoma.

Introduction

During the last several years, we have been developing a new type of visual field test that is based on pattern discrimination rather than light detection[1-3]. The patient's task is to detect a patch of non-random black and white dots embedded in a surrounding field of dynamic random dots. We have argued that, in theory, this test should be more sensitive to early glaucomatous optic nerve damage than light detection perimetry because pattern detection requires cooperating responses from a number of neighboring ganglion cells, whereas light detection can be mediated by single ganglion cells.

In this report, we compare glaucomatous visual field loss measured with pattern discrimination perimetry (PDP) and conventional automated visual fields (CVF) using the Humphrey and Octopus perimeters. The results suggest that the PDP and CVF tests may measure different aspects of visual function that can be differentially affected in glaucoma.

Apparatus

The pattern discrimination perimeter is a computer-controlled video display with additional hardware for maintaining subject alignment, monitoring fixation and recording responses. For the prototype unit, a 40" diagonal Mitsubishi rear-projec-

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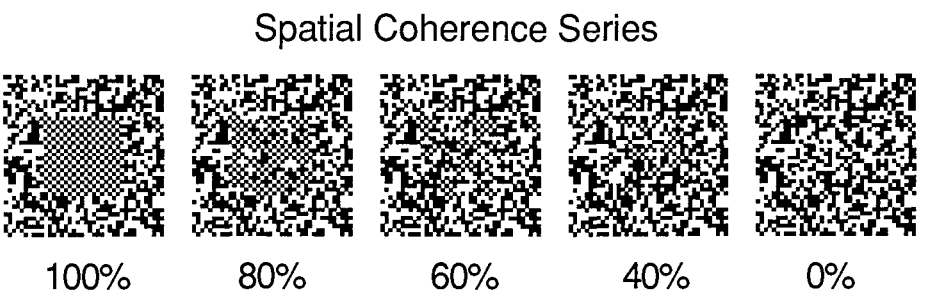

Fig 1. Series of pattern stimuli with spatial coherence decreasing from left to right

tion television is controlled by a North Star Horizon computer. To monitor fixation, the experimenter views a magnified image of the subject's eye produced with a small CCD television camera and video screen. The subject's responses are fed directly to the computer via a pushbutton.

Stimuli

The stimulus display is a field of 256x256 random dots, half black and half white, which is refreshed at a frequency of 15 Hz. The subject is located so that the display screen subtends an angle of 49° vertically by 62.5° horizontally, and each pixel subtends about 15′ of arc. The stimulus is a patch of non-random dots whose size, duration, position and dot arrangement are under computer control. The stimulus has the same fraction of black and white dots as the surround, so there are no luminance cues to detection.

Stimulus visibility is manipulated by varying the degree of regularity, or 'coherence' of the stimulus dots to find the coherence threshold, *i.e.*, the coherence at which the target is detectable 50% of the time. Coherence can be defined in both the spatial and the temporal domains. Spatial coherence is defined as the degree to which the state of all the dots in the pattern can be predicted from knowledge of the state of a single dot. Fig. 1 shows an example of pure spatial coherence in which the fully coherent target is a checkerboard pattern. Temporal coherence is defined as the degree to which future patterns can be predicted from the current pattern. An example of pure temporal coherence is a spatially random pattern for which none of the dots changes over time. In the present study, we measured coherence thresholds for static checkerboard stimuli that are coherent in both space and time. Coherence is reduced by reversing the contrast of randomly selected black-white pairs of dots. A new independent set of dot pairs is reversed with each background frame.

Subjects

Open-angle glaucoma patients, glaucoma suspects and normal control subjects were categorized on the basis of a complete ophthalmological examination, including central visual fields with either the Humphrey or Octopus perimeter. Glaucoma patients had histories of intraocular pressure (IOP) $\geq$ 21 mm Hg and sensitivity losses $>$ 4 dB for at least three contiguous test positions on the Humphrey 30-2 or Octopus 32 protocol compared to the age-corrected normal means supplied with

the instruments. Glaucoma suspects had IOP≥ 21 mm Hg, but no apparent visual field loss. Control subjects had IOP≤ 18 mm Hg, no family history of glaucoma and no visual field loss. All patients and control subjects were free of non-glaucomatous eye disease. Table 1 shows numbers and age information for the three subject categories.

Table 1 Patient sample

Diagnosis	Number	Median age	Age range
Normal	30	55 5	20-79
Suspected glaucoma	18	58 5	30-75
Glaucoma	27	64 0	25-80

Procedures

All subjects were tested with the static checkerboard coherence test at the central 36 test positions used for the Humphrey program 30-2 and the Octopus program 32. The locations were arranged in a 6x6 square array with 6° of visual angle between nearest neighbors, and were offset 3° from the horizontal and vertical meridians. The targets were 20x20-dot squares (as in Fig. 1) and were presented for a 1 sec duration. Coherence was specified in terms of the percentage of black-white dot pairs reversed per stimulus frame, ranging from 100% coherence with no dot pairs reversed to 0% coherence with half of the dot pairs reversed.

Coherence thresholds were measured with a brief staircase procedure, starting with coherence steps of 20%, followed by 10% steps after the first reversal and 4% steps after the second reversal. The sequence ended after the second negative reversal at the 4% step size, and the coherence threshold was defined as the weighted average of the last three reversals. Randomly interleaved staircases were run simultaneously for pairs of locations symmetrically arranged around the fixation point. This minimized the subject's uncertainty about where the next target would appear while still avoiding the tendency to fixate the target.

In addition to pattern discrimination perimetry, we obtained a conventional visual field from each subject using either the Humphrey (30-2 protocol) or the Octopus (program 32) perimeter. Since the stimulus conditions are not equivalent for the two perimeters, we attempted to make the data comparable by adding to the Octopus data the point-by-point mean differences between Humphrey and Octopus fields from 15 age-matched pairs of normal subjects from another study.

ROC analysis

We used a new criterion-free technique derived from signal detection theory to estimate the separation of the suspect and glaucoma data distributions from the normal distribution for both the pattern discrimination and conventional visual field tests. The technique is described in detail elsewhere[3-5]. Briefly, it is an ROC (relative operating characteristic) analysis that treats the normal data set as a noise distribution and the patient data set as a signal+noise distribution. An ROC curve is defined as the cumulative signal+noise distribution plotted against the cumulative noise distribution. The area under the ROC curve (P_c) is a general index of the difference between the two distributions. Since $P_c = 0.5$ for identical distributions,

the actual discrimination probability, Pd, is given by

$$P_d = 2\,(P_c - 0.5).$$

For the present study, we determined the discriminability of the two distributions by estimating the empirical ROC curve areas from the data using a simulated forced-choice procedure. This is a non-parametric procedure that makes no assumptions about the form of the data distributions. We computed P_d values for glaucoma data vs normal data and for glaucoma suspect data vs normal data for each point in the visual field, both for pattern discrimination perimetry (PDP) and for the conventional visual fields (CVF).

Results and discussion

Fig. 2 shows results of the ROC analysis: Fig. 2A compares the discrimination indices of the PDP and CVF tests for each test position, and Fig. 2B shows the means for all positions in histogram form. Whereas the two tests appear to be roughly equal in their ability to distinguish between the glaucoma and normal distributions, the PDP is substantially better at distinguishing between the glaucoma suspect and normal distributions.

In view of their similar overall sensitivity to glaucomatous defects, it is somewhat surprising to find (see Fig. 2A) that the performance of the two tests at individual positions is completely uncorrelated. This could indicate either that the tests are measuring independently variable visual mechanisms or that noise is obscuring an underlying relationship. To investigate these possibilities, we computed the amount of defect relative to age-corrected norms for each patient threshold measurement, and constructed PDP vs CVF scatterplots for individual patients. Age-corrected normal threshold estimates were obtained for both tests by computing threshold vs age regressions through the normal data for each test position.

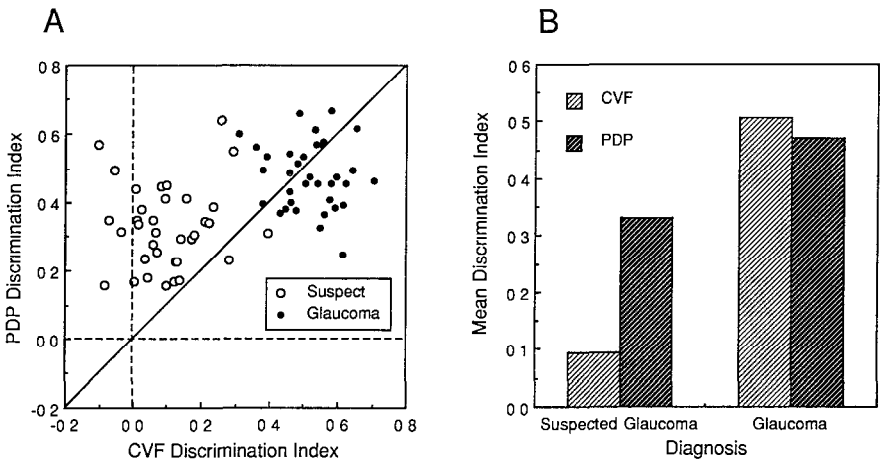

Fig 2 (A) Scatterplot of PDP vs CVF discrimination index (P_d) for glaucoma suspects (open symbols) and glaucoma patients (filled symbols). Each data point indicates the index value for one patient group at one of the 35 test positions (the blind spot position is not plotted) Points above the diagonal line indicate that the PDP defects are more discriminable from normal than the CVF defects. Correlation coefficients are $r = 0.07$ for glaucoma suspects and $r = 0.12$ for glaucoma patients (B) Histogram of the discrimination indices in A, averaged over test position

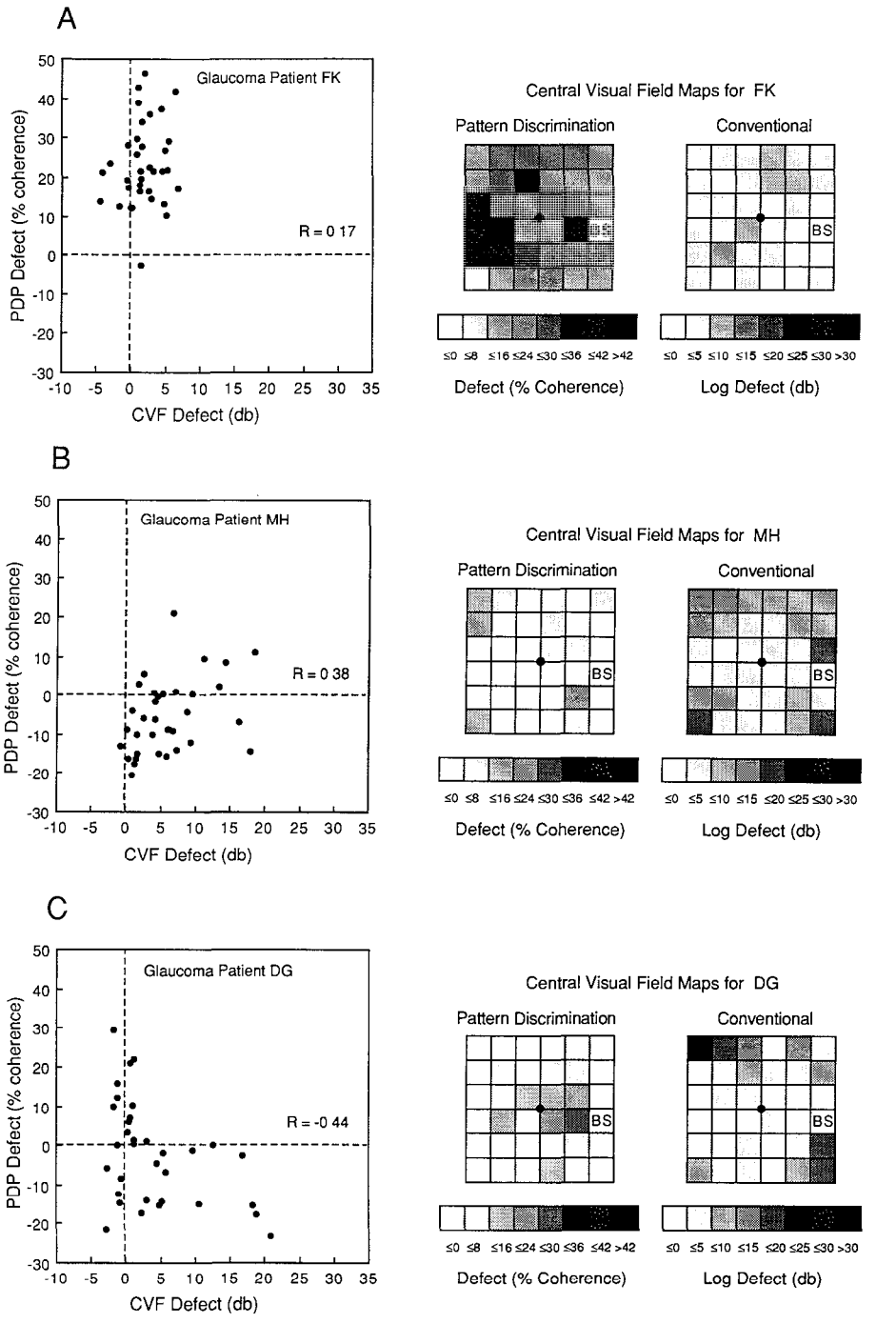

Fig 3 Scatterplots of PDP vs CVF defects (left) and corresponding gray scale visual field maps (right) for glaucoma patients with selective PDP defects (A), selective CVF defects (B) and both types of selective defect in different parts of the field (C). Each square of the gray scale maps is 6 of visual angle per side, and represents the defect for one test position The small central circle indicates fixation, and the blind spot position is labeled BS All visual field maps are converted to right eye format for ease of comparison

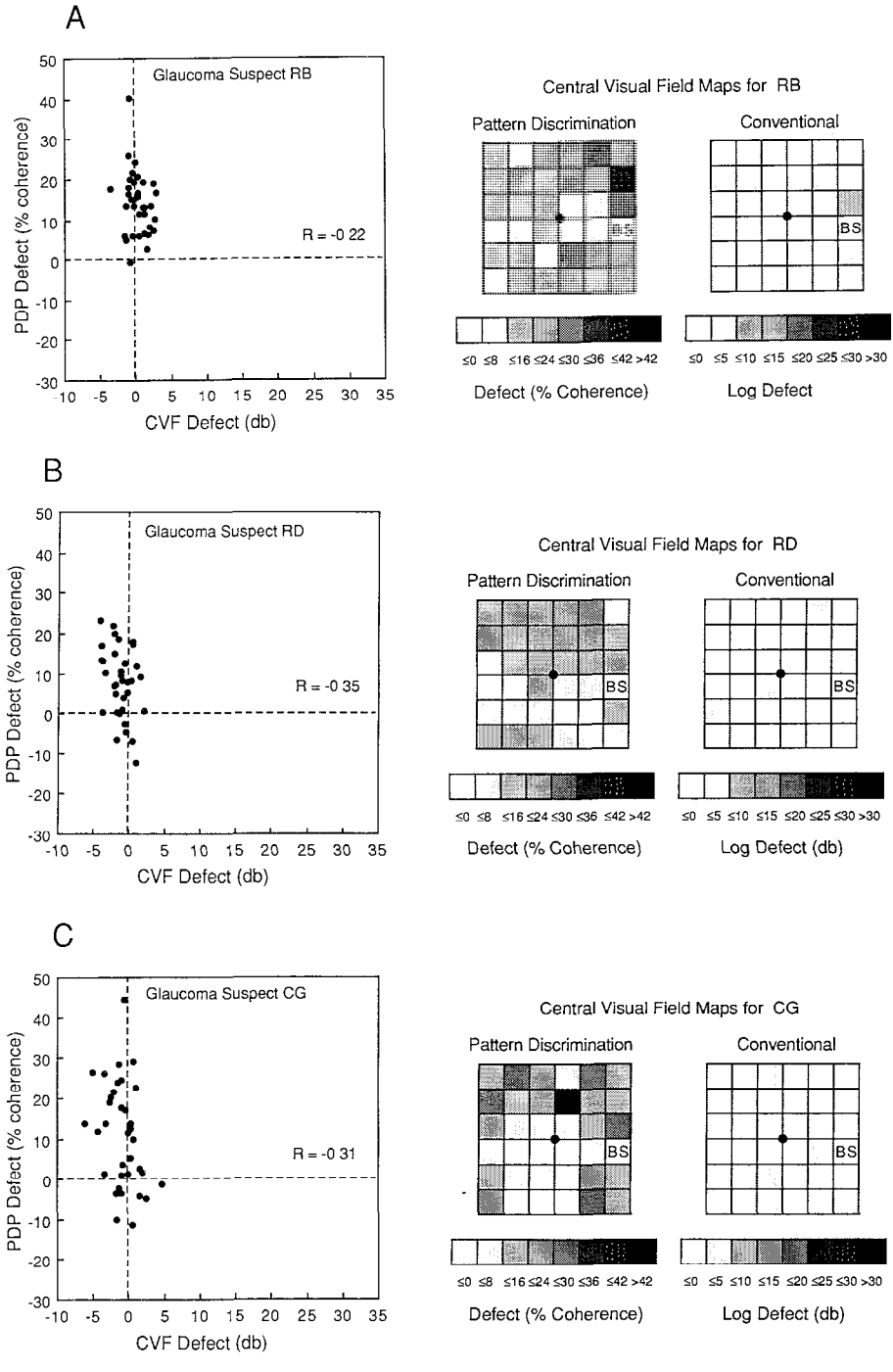

Fig 4 Scatterplots of PDP vs CVF defects (left) and corresponding gray scale visual field maps (right) for three glaucoma suspects with substantial PDP defects but no detectable conventional visual field loss Other details are the same as for Fig 3

Figs. 3 and 4 show representative examples of the resulting scatterplots. Gray scale maps are shown to the right of each scatterplot to indicate the locations of the field defects for each patient. The glaucoma patients in Fig. 3 range from a strongly selective PDP defect (A) to a strongly selective CVF defect (B) to non-overlapping PDP and CVF defects in the same field (C). The strongest correlation of the three is a negative one (-0.44) from the patient with separate PDP and CVF defects. When either defect is considered in isolation, however, the correlation drops to near zero.

Glaucoma suspects are not expected to show selective CVF defects because they are defined to have normal CVF fields. However, seven of our 18 suspects showed pronounced selective PDP defects like those in Fig. 4, and four of these had negative correlations with CVF defects. It will be interesting to follow these and similar suspects over time to determine whether selective PDP defects are indicators of future conversion to overt glaucomatous damage.

In conclusion, the PDP test appears to be as good as the CVF tests at discriminating between groups of glaucoma patients and normal subjects, and better than CVF tests at discriminating between groups of glaucoma suspects and normal subjects. However, the correlation between the two tests for individual patients is very poor, both in terms of the location and the overall degree of sensitivity loss. It remains to be seen whether isolated PDP defects are associated with (or predictive of) glaucomatous optic nerve damage. If they are, the present results suggest that pattern discrimination and light detection tests assess different aspects of optic nerve function that can be differentially affected by glaucoma. Pattern discrimination testing therefore may prove to be a valuable diagnostic tool for the early detection of glaucoma.

Acknowledgements

Supported in part by NEI SBIR grant No EY05136 to LKC Systems, Inc (Now LKC Technologies, Inc) The pattern discrimination perimeter is protected by US Patent No 4634243 LKC Technologies, Inc and authors Drum, Massof and Breton have a proprietary interest in the pattern discrimination perimeter

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MULTI-FLASH CAMPIMETRY AND OPTIC NERVE STRUCTURE IN EARLY CHRONIC OPEN ANGLE GLAUCOMA

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Abstract

The authors have demonstrated previously that temporal resolution visual fields as measured by the multi-flash campimetry (MFC) technique are frequently abnormal in early glaucoma in the presence of normal static automated visual fields and other psychophysical tests. It is not known whether this loss of temporal resolving power represents actual optic neuropathy as opposed to a pressure induced dysfunction. Twenty-five eyes of 25 observers consisting of eight early glaucoma patients, ten glaucoma suspects, and seven controls, were used in this study The MFC thresholds and the neuro-retinal rim areas corrected for magnification induced by the refractive components of the eye (cNRA) were measured for each observer and compared Results showed a significant difference of temporal resolving power and cNRA measurements between groups. Significant correlations were found between the cNRA and the mean MFC sensitivity of the entire visual field. The cNRA is most strongly related to MFC measurements obtained in the classic arcuate area. These results suggest that temporal resolving power as measured by MFC may be a more sensitive and accurate index of glaucoma induced damage than other visual field measurement techniques.

Introduction

We have previously demonstrated using the MFC paradigm that temporal sensitivity visual fields are affected in the early stages of chronic open angle glaucoma[1,2]. MFC fields can be abnormal in the absence of static automated visual field loss as measured by the Octopus G1 program. This is exemplified by the two- and three-dimensional maps in Figs. 1 to 3 which represent MFC visual fields of a normal observer, a glaucoma suspect, and an early glaucoma patient, respectively. The darker gray areas of the two-dimensional maps and the peaks of the three-dimensional maps represent worse temporal resolving power. The glaucoma suspect observer shown in Fig. 2 has normal G1 visual fields but clearly has abnormal MFC visual fields, which are comparable to the MFC fields of a glaucoma patient of the same age group shown in Fig. 3.

Balazsi *et al.* have shown that cNRA measurements are reduced in glaucoma and correlate with visual functions such as Octopus perimetry and spatial contrast sensitivity[3]. In the present study, we compare cNRA and MFC measurements in an attempt to determine whether loss of MFC sensitivity in glaucoma represents actual optic nerve damage as opposed to a pressure induced dysfunction. We also assess whether the relationship between cNRA and MFC is dependent on location in the visual field.

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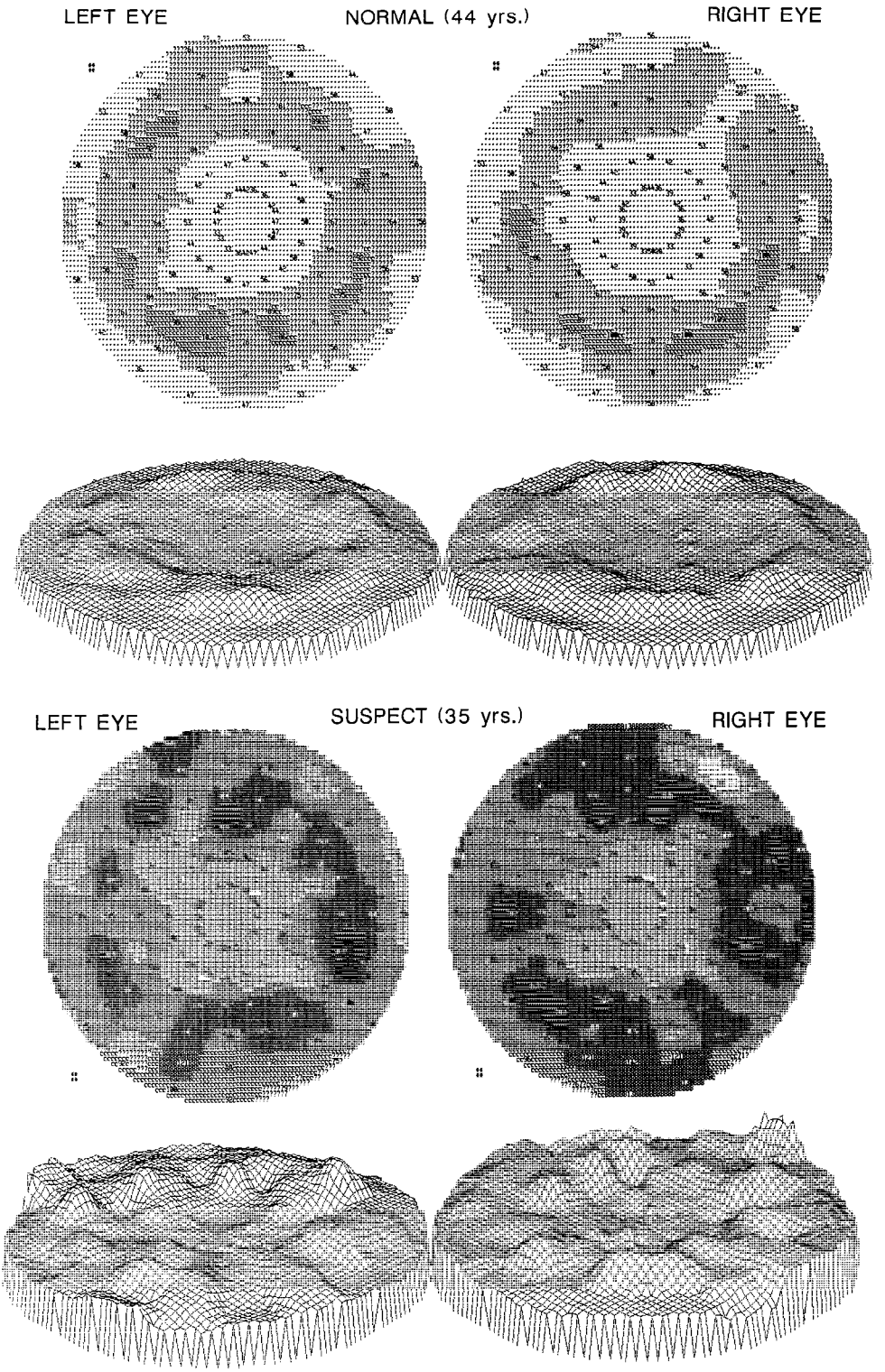
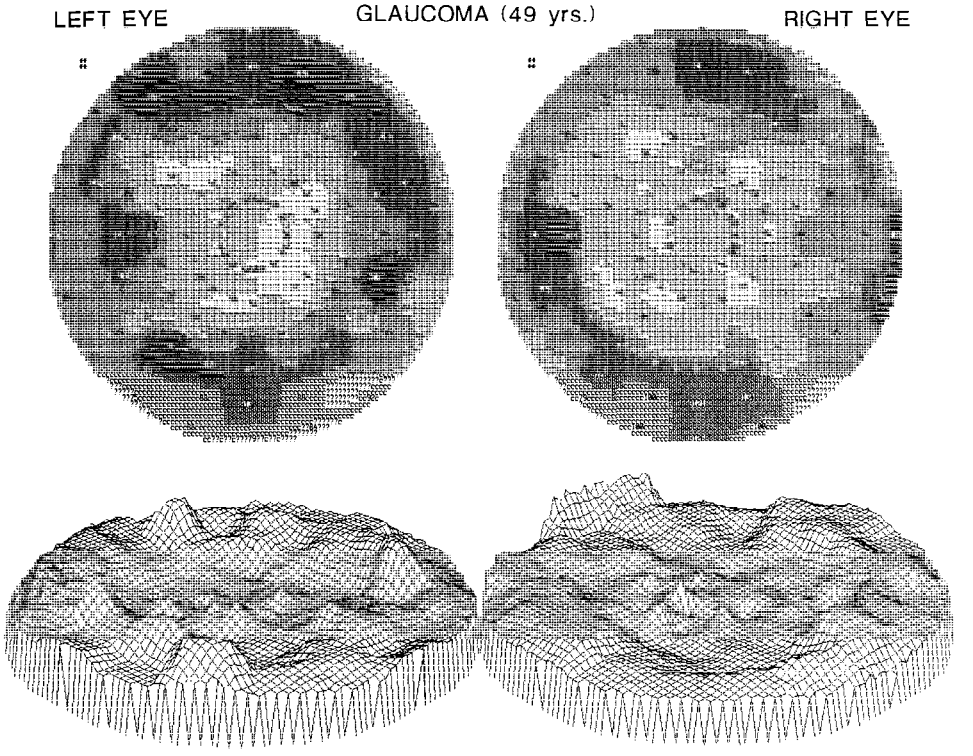

LEFT EYE
NORMAL (44 yrs.)
RIGHT EYE
LEFT EYE
SUSPECT (35 yrs.)
RIGHT EYE



Figs 1 to 3 Two dimensional (2D) and three dimensional (3D) MFC visual fields of a 44-year-old normal observer, a 33-year-old glaucoma suspect, and a 49-year-old glaucoma patient Darker shading and higher mountains reflect poorer temporal resolving power The four stars by the 2D maps indicate the front view of the corresponding 3D fields Each MFC map shows a 40 degree visual field with distance plotted on an octave scale (*i e* , equal distances reflect a doubling of visual field eccentricity)

Methods

Subjects: Twenty-five eyes of 25 observers were used in this study. All participants had 6/7.5 (20/25) or better corrected visual acuity, normal pupils of at least 2.5 mm, open angles, and absence of media opacity or other ocular disease. The observers were separated into three groups consisting of eight early glaucoma patients, ten glaucoma suspects, and seven control observers. The glaucoma eyes had minimum intraocular pressures of 22 mm Hg in addition to early glaucomatous visual field defects as measured by the G1 program of the Octopus perimeter. The glaucoma suspect eyes had minimum intraocular pressures of 22 mm Hg and normal G1 fields. An attempt was made to stratify the age of the study groups in decades. The mean ages for the glaucoma, suspect and control groups are demonstrated in Fig. 4 along with a two-standard error range. No significant differences in age were found between the three groups.

Apparatus. A detailed description of the apparatus and procedures used for MFC has been reported previously[4]. Multi-flash campimetry was implemented on a PDP11/10 computer interfaced with a large screen cathode ray tube (Hewlett Packard 1310A equipped with a P15 phosphor).

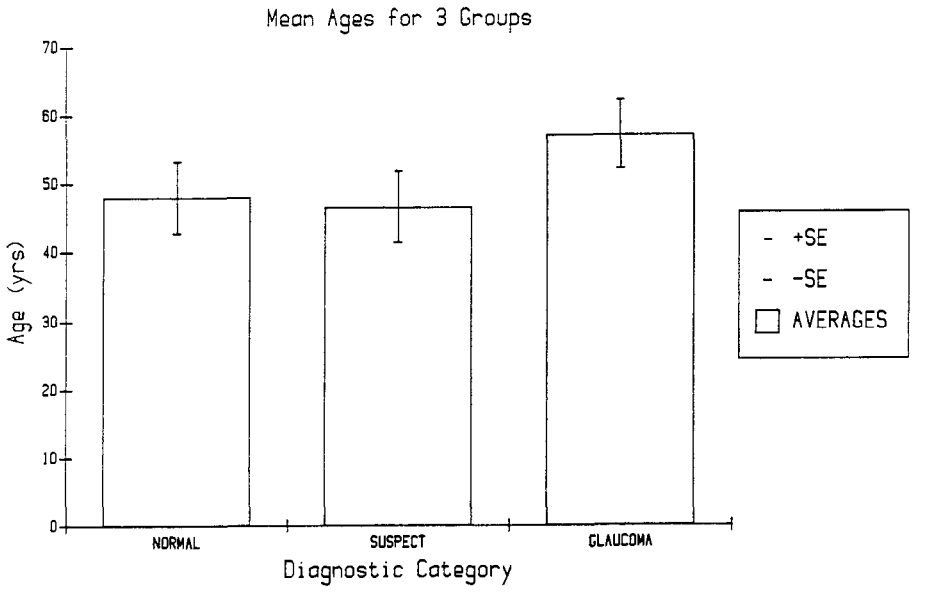


Fig 4 Bar graph representing the mean ages, with a two-standard error range, for the control, glaucoma suspect, and glaucoma groups

Procedure: Multi-flash campimetry tests temporal resolving power in 120 points of a 40 degree visual field. The display was divided into four randomly presented quadrants. Within each quadrant, all the target points were constantly illuminated and one of the points was randomly chosen to assess the off-period necessary to perceive a 5 Hz flicker. This was accomplished by systematically decreasing the duty cycle in steps of 1.4% (*i.e.*, decreasing the on-period and increasing the off-period in steps of 2.8 msec) until the observer detects flicker and depresses a response key. The average luminance level of the entire 200 msec cycle was kept constant by increasing the intensity of the light in proportion with the decrease in the duty cycle. Each point on the screen subtends six minutes of visual angle. In this study, the display consisted of six concentric circles each containing 20 points. The retinal eccentricities of the radii of the circles subtended 0.625, 1.25, 2.5, 5.0, 10.0, and 20.0 degrees, respectively.The cNRA was measured using a previously described technique[3]. The neuro-retinal rim was observed on a stereophotograph pair, and its outline traced from a third photograph projected onto paper at a known magnification. The area of this outline was then measured with the Zeiss IBAS1 image analysis system. The result was then corrected for the magnification induced by the optic components of the eye according to the Littmann method[5], thus yielding the corrected neuro-retinal rim area (cNRA).

Results

A 3 x 6 split-plot analysis of variance (ANOVA) using the three diagnostic categories as the between factor and the mean sensitivity at each visual field eccentricity as the within factor, was performed on the MFC data. A significant difference in MFC thresholds was found between groups, $F(2,22) = 7.48, p < 0.004$. Further, a significant difference was found across the visual field eccentricities, $f(5,100) = 23.81, p < 0.0001$, showing decreased sensitivities for more peripheral

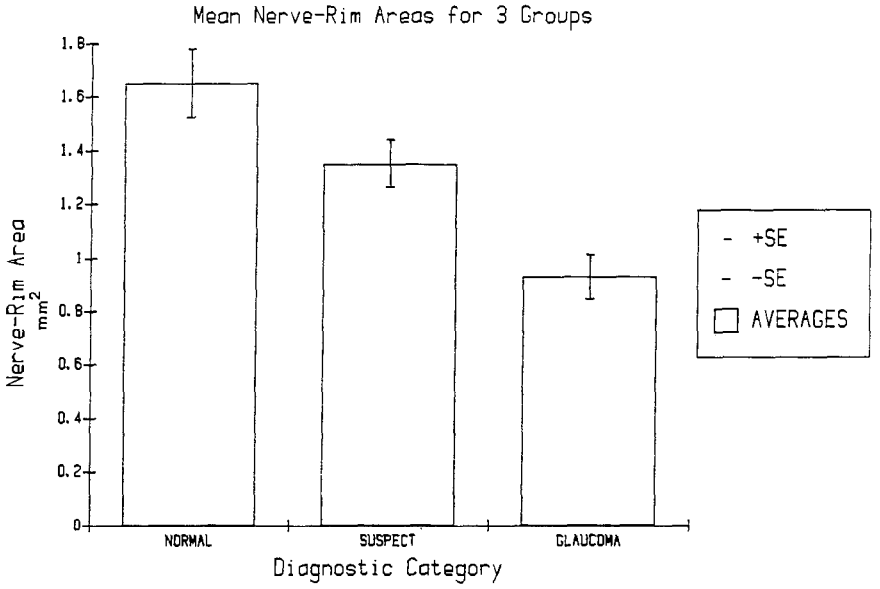


Fig 5 Bar graph representing the mean cNRA measurements in mm^2, with a two-standard error range, for the normal control, glaucoma suspect, and glaucoma groups

eccentricities. This trend is true for all groups as demonstrated by a lack of significant interaction between diagnostic category and visual field eccentricity. These results confirm our previous studies[1,2].

An ANOVA performed on the cNRA measurements shows a significant difference between groups, $F(2,22) = 12.24$, $p < 0.0004$. Post Hoc Sheffé tests demonstrate that both the glaucoma and glaucoma suspect groups are significantly different from the controls but are not significantly different from each other. Group means for the cNRA measurements and a two standard error range are demonstrated in Fig. 5.

Bivariate correlations for the 25 observers were performed showing significant relationships between the cNRA and the mean MFC sensitivity of the entire visual field, and between cNRA and the mean sensitivity of the three most peripheral eccentricities used in the MFC paradigm (5, 10 & 20 degrees). The strongest relationship is between cNRA and the 20 degree eccentricity ($r = -0.61$). A negative correlation is expected because a smaller cNRA represents greater nerve fiber loss and higher MFC values represent a decrease in temporal resolution. Fig. 6 is a scatter-plot diagram showing the relationship between the mean MFC threshold over the entire field and the cNRA. Figs. 7 to 12 are similar scatter-plots of the cNRA and the mean MFC thresholds, obtained at the six different visual field eccentricities.

The vertical axes represent the cNRA in mm^2, and the horizontal axes the respective mean MFC sensitivities for the given visual field eccentricity. An increasing relationship between MFC sensitivity and cNRA can be observed with increasing eccentricity of visual field.

Analysis of the individual diagnostic groups reveals that the strongest correlations are obtained between the cNRA and the three most peripheral eccentricities in the glaucoma group. These coefficients are -0.60, -0.66, and -0.70, respectively, and are statistically significant. Finally, as Fig. 13 demonstrates, no correlation is found between age and the cNRA measurements.

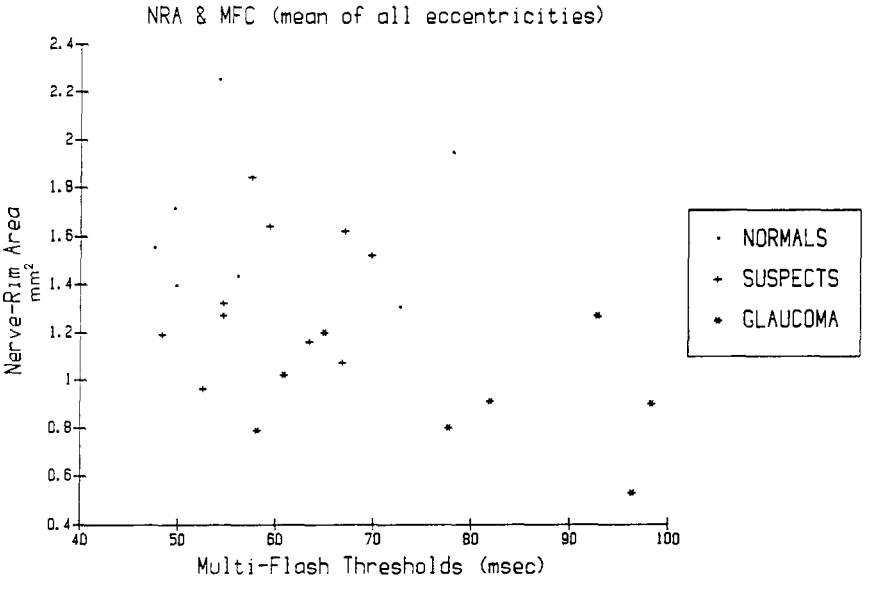
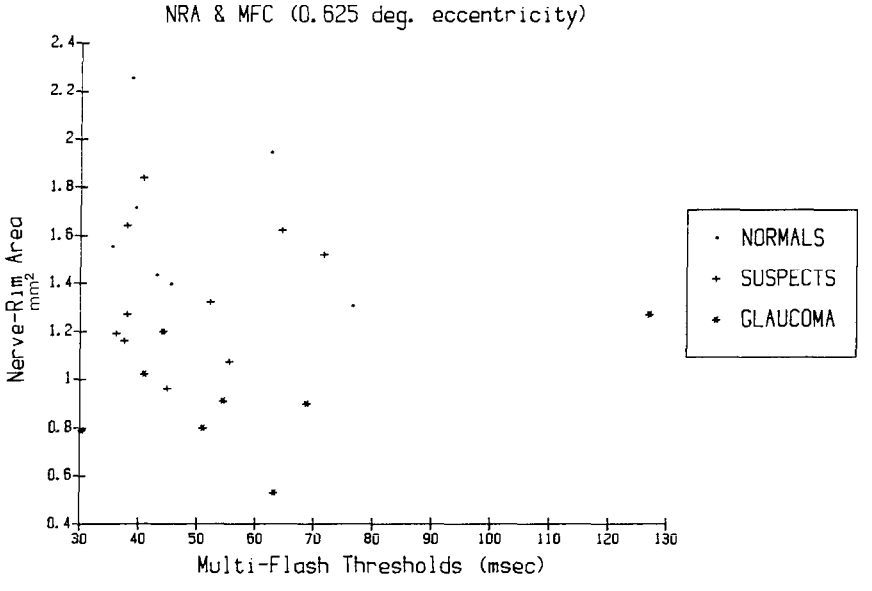


Fig 6 Scatter-plot diagram comparing the cNRA measurements, in mm^2, for the control, glaucoma suspect, and glaucoma groups with their respective mean MFC sensitivity across the entire visual field.



Figs 7 to 12 Scatter-plots comparing the cNRA measurements, in mm^2, for the control, glaucoma suspect, and glaucoma groups with their respective MFC mean sensitivities at the following eccentricities: 0 625, 1 25, 2.5, 5.0, 10.0, 20 0 degrees

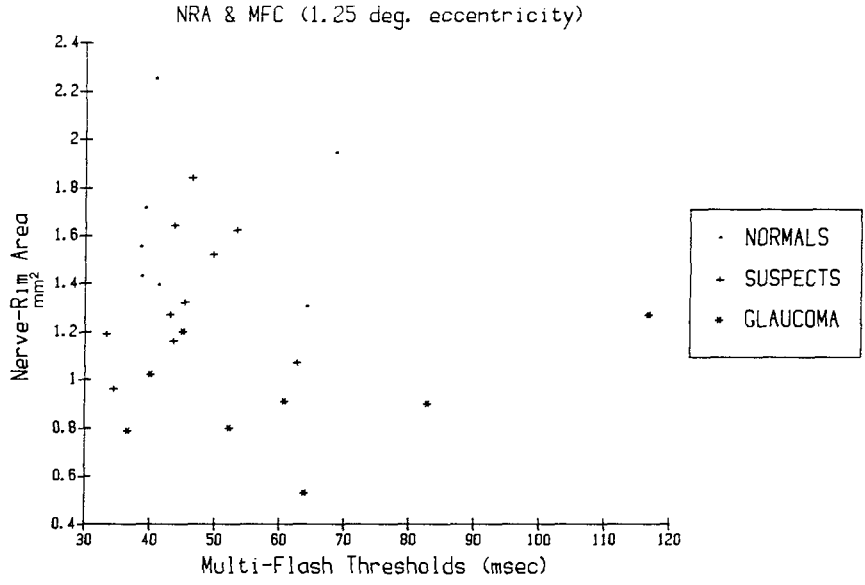

NRA & MFC (1.25 deg. eccentricity)
Nerve-Rim Area mm²
2.4
2.2
2
1.8
1.6
1.4
1.2
1
0.8
0.6
0.4
30
40
50
60
70
80
90
100
110
120
Multi-Flash Thresholds (msec)
NORMALS
SUSPECTS
GLAUCOMA

Fig 8

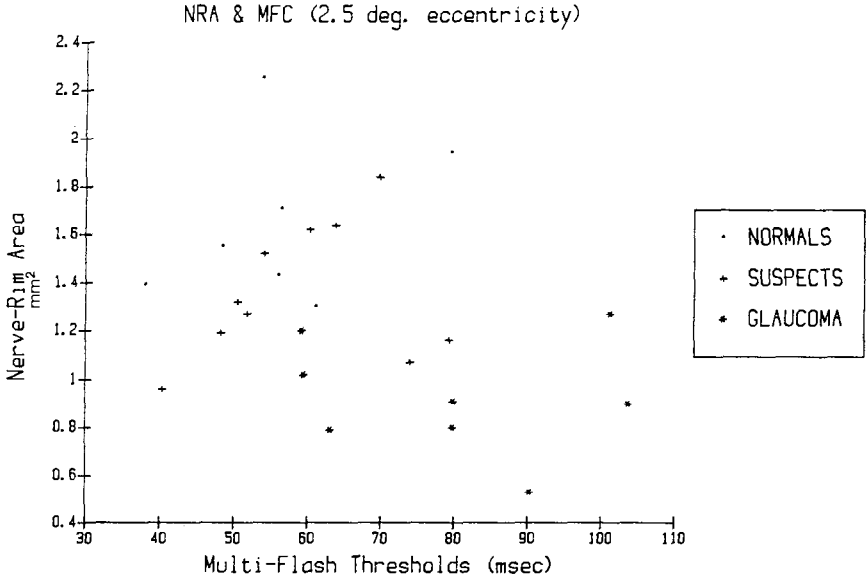

NRA & MFC (2.5 deg. eccentricity)
Nerve-Rim Area mm²
2.4
2.2
2
1.8
1.6
1.4
1.2
1
0.8
0.6
0.4
30
40
50
60
70
80
90
100
110
Multi-Flash Thresholds (msec)
NORMALS
SUSPECTS
GLAUCOMA

Fig 9

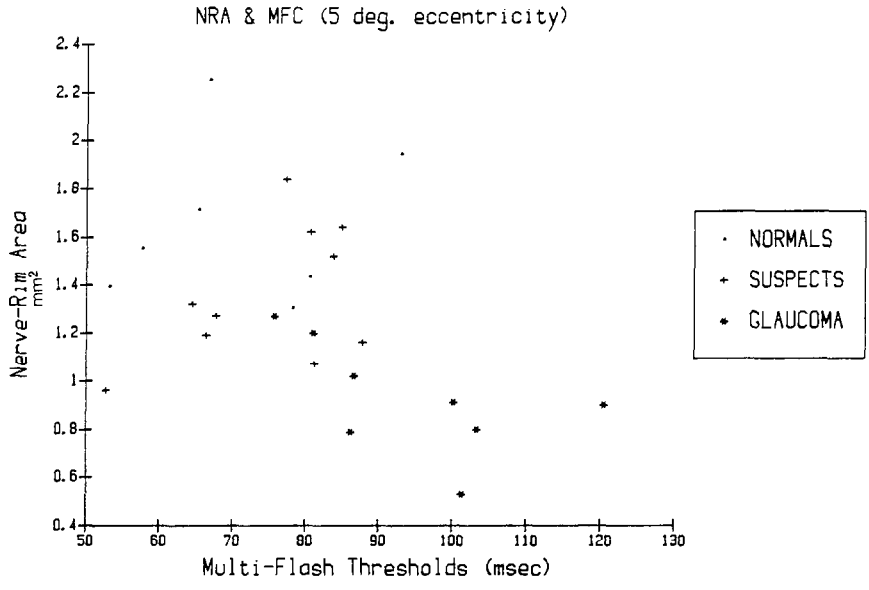

NRA & MFC (5 deg. eccentricity)
Nerve-Rim Area mm²
2.4
2.2
2
1.8
1.6
1.4
1.2
1
0.8
0.6
0.4
50
60
70
80
90
100
110
120
130
Multi-Flash Thresholds (msec)
NORMALS
SUSPECTS
GLAUCOMA

Fig 10

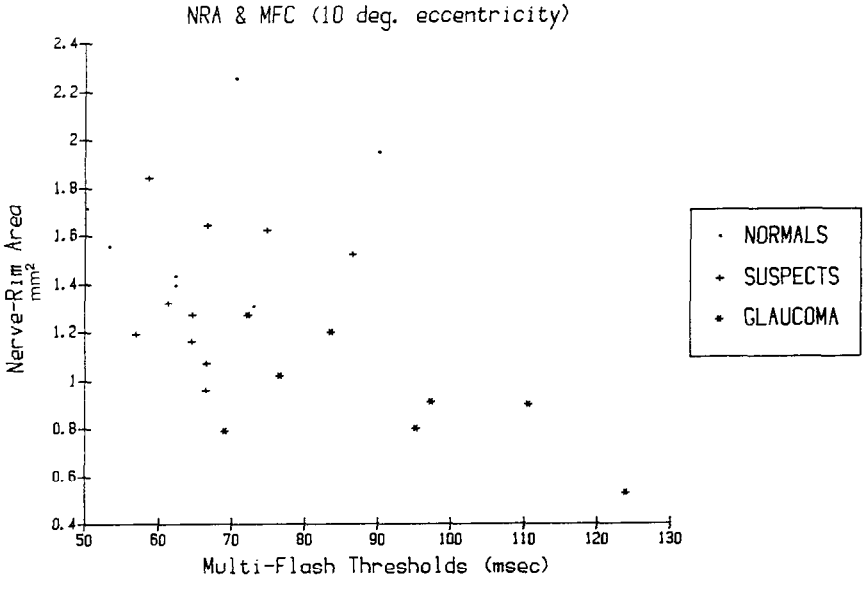

NRA & MFC (10 deg. eccentricity)
Nerve-Rim Area mm²
2.4
2.2
2
1.8
1.6
1.4
1.2
1
0.8
0.6
0.4
50
60
70
80
90
100
110
120
130
Multi-Flash Thresholds (msec)
NORMALS
SUSPECTS
GLAUCOMA

Fig 11

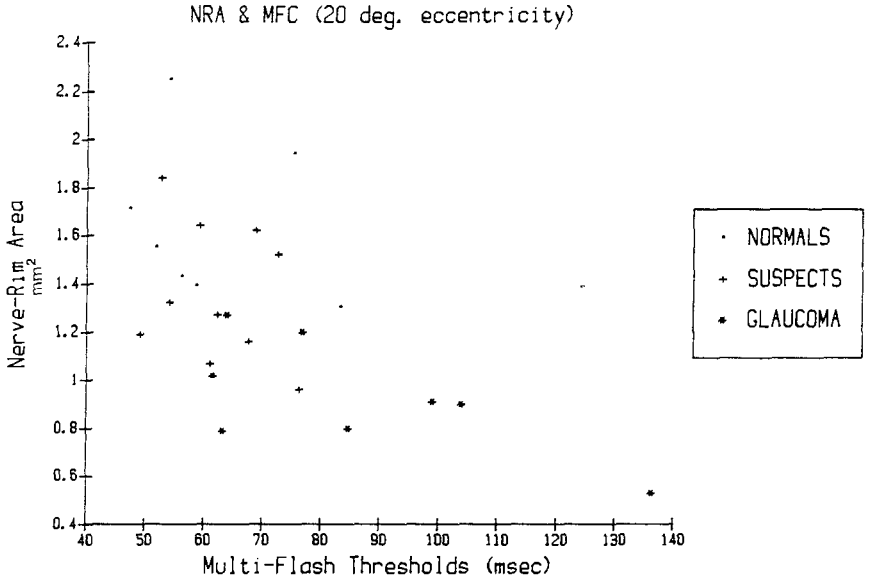


Fig 12

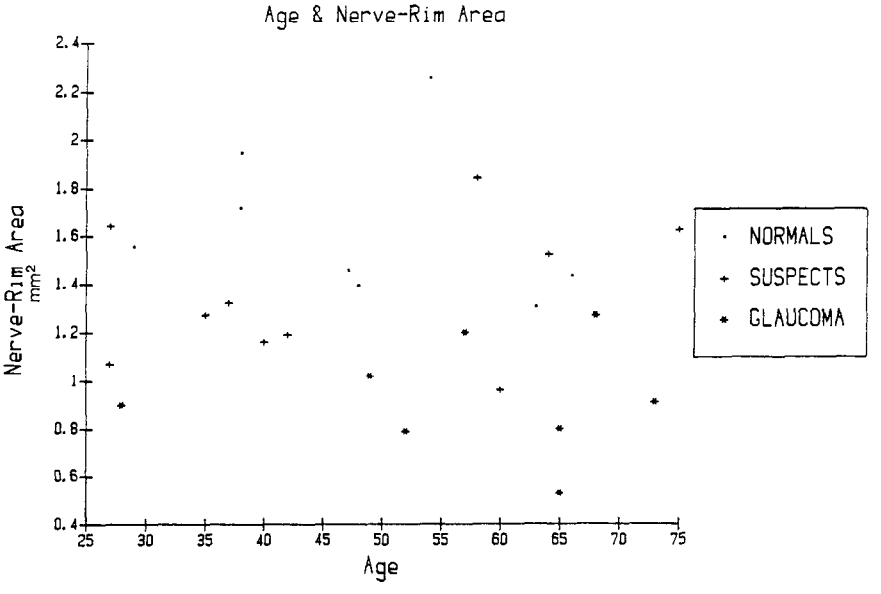


Fig 13 Scatter-plot comparing the cNRA measurements, in mm^2, for the control, glaucoma suspect, and glaucoma groups with age

Discussion

This study assessed whether temporal sensitivity loss across the visual field as measured by the MFC technique is due to acquired optic neuropathy as opposed to a pressure induced dysfunction. This was done by comparing the MFC results with the respective cNRA measurements for glaucoma, glaucoma suspect, and normal observers. The results demonstrate both a loss of MFC sensitivity across the visual field, and a reduction of cNRA measurements due to glaucoma. A significant relationship was found between MFC sensitivity and cNRA measurements which suggests that the MFC sensitivity loss is due to nerve fiber loss. Furthermore, it was shown that this relationship strengthens with increasing visual field eccentricity and is strongest in the classic arcuate area.

The present results extend our previous findings and demonstrate that temporal resolving power as measured by MFC may be a more sensitive and accurate measure of glaucoma induced optic neuropathy than standard automated perimetry. We believe that testing the differential light threshold alone is not sufficient to assess visual function in glaucoma and that testing for temporal resolving power should be considered for future perimetric techniques.

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AUTOMATED FLICKER PERIMETRY VERSUS QUANTITATIVE STATIC PERIMETRY IN EARLY GLAUCOMA

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Abstract

An automated flicker perimeter was constructed to measure Critical Flicker Fusion Frequency (CFF) over the central 40 degrees of the visual field with a centrally condensed test point pattern of high resolution. A quantitative bracketing procedure in combination with a fast strategy was used Stimulus presentation is randomized, the patient's responses are registered and processed by a computer. The results obtained from 54 eyes with ocular hypertension (OH, n = 31) and primary open angle glaucoma (POAG, n = 23) with the standard program (89 test points, 81 up to 30 deg) are presented and compared to age-corrected normal values. As a reference, all eyes were subjected to quantitative static perimetry using program G1 of the Octopus 201. 64% of eyes with OH with a normal or practically normal static visual field already showed pronounced to advanced defects in flicker perimetry, 13% showed moderate defects, and only 23% had no or negligible defects. In cases of POAG, 52% of patients revealed more defects with flicker perimetry than with light sense perimetry. In 35% of cases, the defects were approximately equal in distribution and in only 13% of cases did flicker perimetry indicate less defects than static perimetry Flicker perimetry for measuring temporal resolution of the central visual field seems to be more sensitive to glaucomatous damage than quantitative light-sense perimetry. The Y-ganglion cells, being the physiological correlate to the temporal transfer properties, are obviously affected early and selectively by glaucomatous damage in the course of the disease.

Introduction and aim

Impairment of temporal and spatio-temporal transfer properties has been described as an early indicator of glaucomatous damage. The numerous investigations dealing with this question may be divided into two groups:

1. Analysis of the temporal or spatio-temporal transfer properties at the fovea only or at a few isolated locations in the central visual field[1-12].
2. Perimetric examination of the central or entire visual field using a temporal or spatio-temporal threshold criterion[13-30].

Flicker perimetry in terms of Critical Flicker Fusion Frequency (CFF) is the classical psychophysical technique in this field[13-25], the greater part of investigations in the older literature being of restricted value, however, because of methodical deficiencies, inadequate light-sense perimetry used as a reference, or insufficient and inaccurate clinical selection criteria. During the last years promising new perimetric techniques have been developed ('grating perimeter'[26,27], 'multi-flash campimetry'[28-30]).

Adequate information concerning both diffuse and localized glaucomatous damage[31,32] may only be obtained by the second type of approach: a perimetric examination of the central or entire visual field with a sufficiently high spatial resolution is essential. The use of a temporal threshold criterion seemed to be especially promising. Thus we tried to develop a perimetric technique adequately

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characterizing the temporal transfer properties of the central visual field on the following conditions: The parameter tested should be clearly defined and represent an essential feature of temporal transfer. The method should allow a sufficiently high spatial resolution appropriate to detect both diffuse and localized glaucomatous damage. The threshold criterion should be simple and unequivocal. The examination should be fully automated, providing a reasonable duration of measurement and permitting statistical evaluation of the data obtained. Taking into consideration all these demands, we resorted to CFF as threshold criterion and developed a fully automated flicker perimeter.

The aim of the present study is to test the clinical applicability of our type of automated flicker perimetry for the detection of functional changes induced by glaucoma, in comparison to conventional quantitative static light-sense perimetry. Of special interest is the question of whether or not it is possible to find defects in flicker perimetry in case of normal outcome of light-sense perimetry (in ocular hypertension).

Method

The flicker perimeter (Fig. 1) consists of a hemisphere of radius 30 cm with 149 Light Emitting Diodes (LEDs) installed in such a way that they are prevented from direct illumination by the light source of the surroundings (peak wavelength 590 nm, diameter 1 deg, time-average luminance = luminance of the surroundings = 50 cd/m^2). A typical time course of a stimulus is shown in Fig. 1. As the time-average luminance of the stimulus is constant and equals the luminance of the surroundings, the patient has to press his key only when he notices flickering anywhere in his visual field. An electronic interface controlled by a computer provides the stimulus generation. The sequence of stimulus presentation is randomized for location. Fixation is controlled according to the method of Heijl and Krakau[33]. Catch trials testing for false-positive and false-negative answers allow control of the patient's

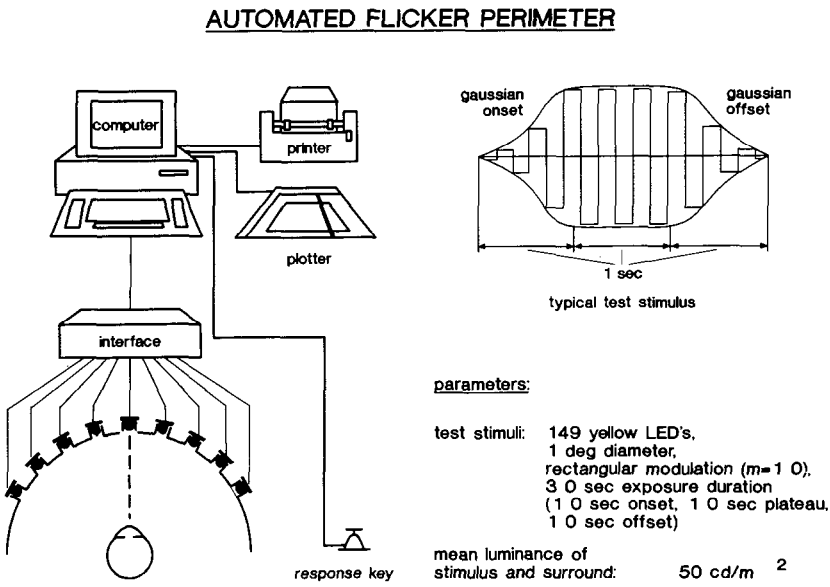

Fig 1 Automated flicker perimeter, at left schematic diagram of the apparatus, at upper right a typical test stimulus.

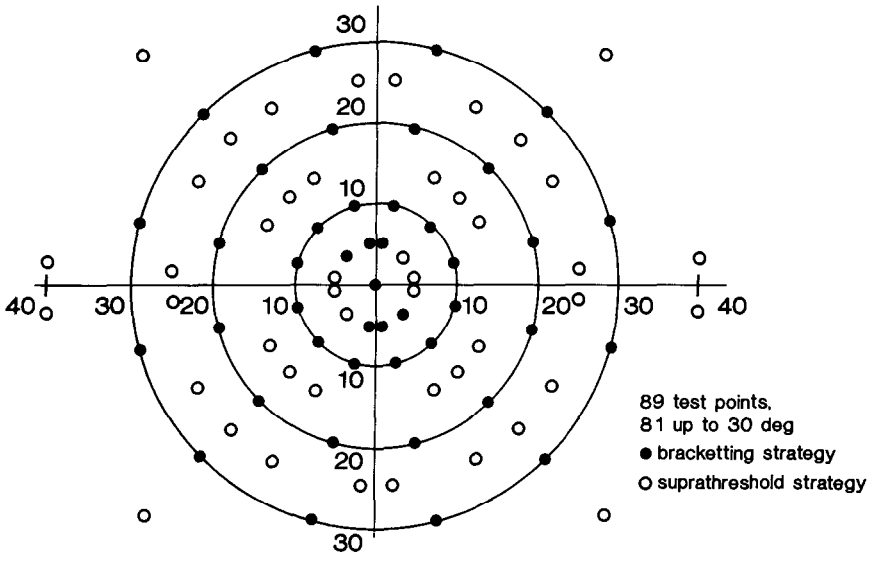

Fig 2 . Standard test point pattern (89 test points, 81 up to 30 deg): 43 points are measured by a bracketing strategy (filled circles), 46 points are tested by a suprathreshold fast strategy (open symbols).

cooperation. Results may be plotted as absolute values or relative to age-corrected standards numerically (in Hz) or with symbols (in steps of 5 Hz). The standard test point pattern consists of 89 stimuli up to 40 deg of visual angle, 81 up to 30 degrees (Fig. 2): at first, about one half of the stimuli is measured by means of a full bracketing strategy (43 points, full symbols), then the rest is tested by means of a suprathreshold fast strategy entering the bracketing procedure only if the 'suprathreshold' stimulus presented is not perceived (46 points, open symbols). Age-corrected normal values were calculated in steps of ten years from 38 normal individuals of 24 to 76 years of age using the full bracketing strategy for all 89 test points of the standard pattern. A simple statistical program allows the calculation of global parameters for the central 30 deg of the visual field (or parts of it): Mean CFF per test location (MF; average of measured CFF values), Mean Frequency Defect per test location (FD; average of difference between measured CFF–values and age-corrected normal values) and Defect Volume (DV; addition over all test locations of the differences between the measured CFF values and age-corrected reference values (reference value = mean normal value - one standard deviation of the mean)). It should be noted that both the relative defect values in the graphical representation of the results (see Figs. 3,4 and 5) and the Defect Volume DV refer to these reduced reference values and not to the mean values. This is very important for the interpretation of the results and the evaluation of a defect indicated in a CFF field. For more details concerning method and strategies, we refer to[34].

In addition, all eyes included in the study were subjected to quantitative static perimetry using program G1 of the Octopus 201 system. G1 measures 59 test locations up to 26 deg, testing each point twice[35].

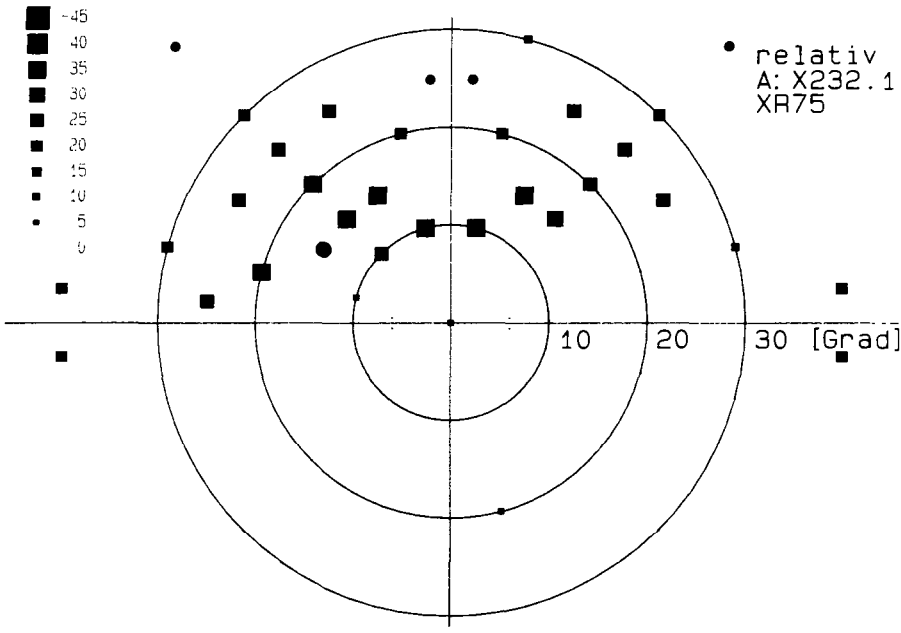

Fig 3 CFF field of eye No. 232, 71 years, right eye, OH; the corresponding G1 field shows entirely normal light difference sensitivity (program G1: MD=-0.3 dB; CFF field: DV = 603 Hz). Test points measured by full bracketing strategy are indicated by squares, test points measured by suprathreshold fast strategy are indicated by circles; the greater the symbol the deeper the defect (see scale at upper left).

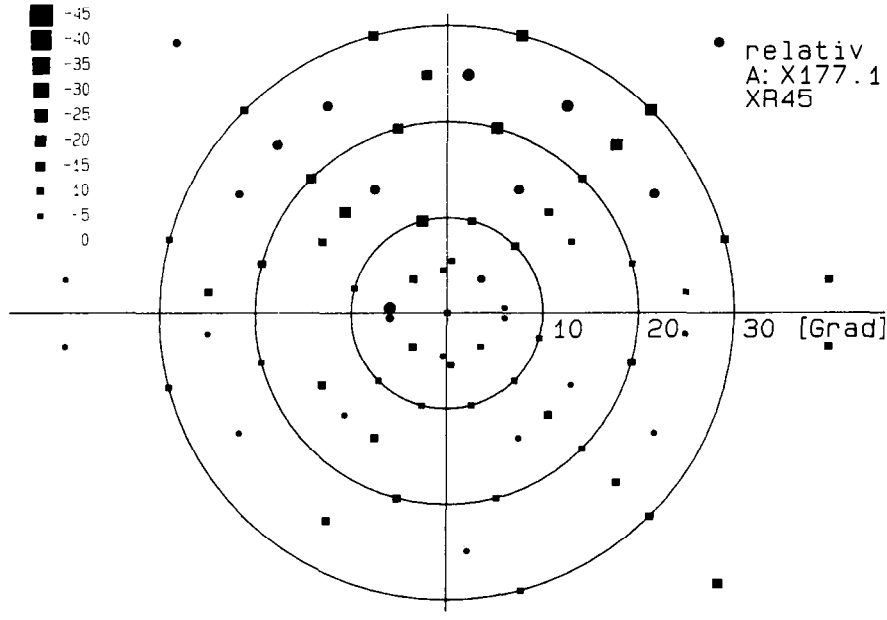

Fig 4 CFF field of eye No 177, 43 years, left eye, OH; as in Fig. 3 the corresponding static field is completely normal (program G1: MD = 0.1 dB; CFF field: DV = 516 Hz) For explanation of the symbols, see legend to Fig 3

Results

Up to now, more than 80 eyes of patients with different types of high-tension glaucoma, ocular hypertension and low-tension glaucoma have been examined with the standard program of our automated flicker perimeter. In the following, the results of two subgroups are specified: ocular hypertension (OH; n = 31) and primary open angle glaucoma (POAG; n =23). The inclusion criteria are as follows:

-intraocular pressure without therapy 22 mm Hg or more, measured on at least two different clinical examinations
-best corrected visual acuity of 0.6 or more
-refractive error less than ±5 dpt spherical
less than 2 dpt cylindrical
-no opacities of the refractive media detectable on slit-lamp examination
-no abnormal degenerative alterations of the macula
-no other relevant ocular pathology

Classification as OH or POAG was done according to the results of Octopus program G1: 31 eyes were classified as OH, 22 of them showing an entirely normal central visual field, nine having some minor disturbances (*i e.*, up to three relative defects ≤8 dB, only two of them being in direct neighborhood). Twenty-three eyes already showing moderate to pronounced defects in light-sense perimetry were classified as POAG.

Figs. 3 and 4 show the CFF fields of two eyes with OH: In the first case (Fig. 3) the CFF field shows a deep localized scotoma with a steep slope at the central border in the upper hemifield approaching the center up to 10 deg of visual angle. The second case (Fig. 4) is an example of a CFF field with rather uniformly distributed diffuse damage with relative defects of up to about 20 Hz. The cor-

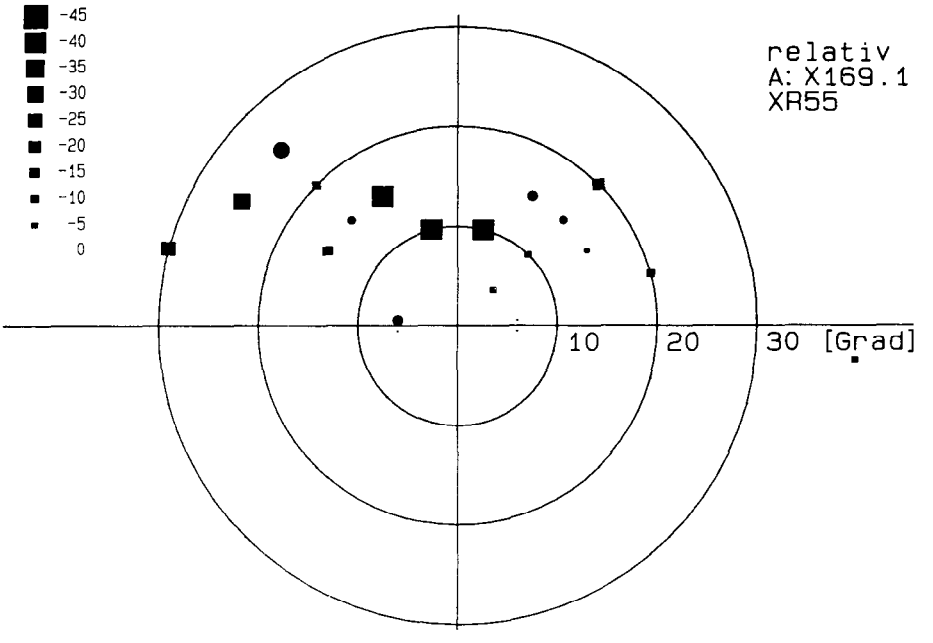

Fig 5 CFF field of eye No. 169, 57 years, left eye, POAG: DV = 271 Hz. The corresponding static field is shown in Fig 6 For explanation of the symbols, see legend to Fig 3

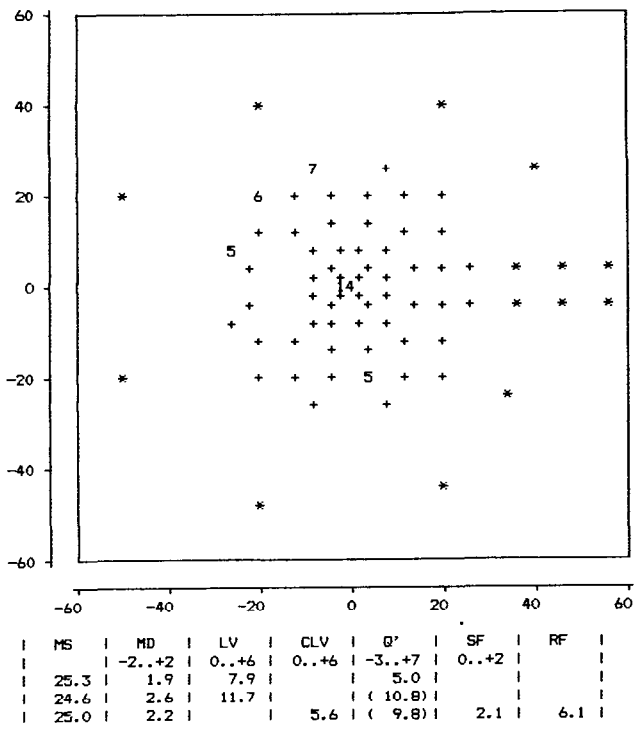

Fig 6 Static field of eye No 169 (program G1): MD = 2.2 dB. The corresponding CFF field is shown in Fig 5.

responding fields of program G1 are entirely normal in the central part up to 26 deg. Fig. 5 shows the CFF field of an eye with POAG: there is a deep, almost absolute, punched-out scotoma paracentrally in the upper hemifield, large parts of the area of the scotoma in the CFF field show normal light difference sensitivity (Fig. 6).

Tables 1 and 2 summarize the results of all eyes with OH and POAG: 64% of eyes with OH with a normal or practically normal static visual field already show pronounced to advanced defects in flicker perimetry, 13% show moderate defects (*i.e.*, only relative defects ≤15 Hz, DV ≤50 Hz) and only 23% have no or negligible defects in their CFF fields (*i.e.*, up to three defects ≤10 Hz, DV ≤15 Hz; Table 1). In 52% of the cases of POAG, flicker perimetry indicates more defects than light sense perimetry, in 35% of the cases the defects are approximately equal in distribution and in only 13% of the cases does flicker perimetry indicate less defects than static perimetry (Table 2).

Discussion

The most striking observation arising from the present study is the fact that about 2/3 of the eyes with OH (64%) show pronounced to advanced defects in automated flicker perimetry with an entirely or practically entirely normal light difference sensitivity in quantitative static perimetry. Similarly, in cases of POAG, about half of the eyes examined (52%) present more defects in flicker perimetry than in light-sense perimetry. The fact that visual field damage, indicated by flicker perimetry

Table 1 Automated flicker perimetry vs quantitative static perimetry in ocular hypertension (OH; $n = 31$).

a.	No or negligible defects in flicker perimetry (up to three defects ≤10 Hz, defect volume ≤15 Hz)	7/31	23%
b.	Moderate defects in flicker perimetry (only relative defects ≤15 Hz, defect volume ≤50 Hz)	4/31	13%
c.	Pronounced to advanced defects in flicker perimetry (all other visual fields)	20/31	64%
			100%

Table 2 Automated flicker perimetry vs quantitative static perimetry in primary open angle glaucoma (POAG; $n = 23$)

a	Defects are approximately equal in flicker perimetry and light sense perimetry	8/23	35%
b	Flicker perimetry indicates less defects than light sense perimetry	3/23	13%
c.	Flicker perimetry indicates more defects than light sense perimetry	12/23	52%
			100%

and light–sense perimetry, differs in location and extent, is not surprising because we have to bear in mind that both perimetric techniques test completely different psychophysical qualities. On the one hand there is CFF as a parameter of temporal high-frequency transfer, and on the other hand there is light difference sensitivity as a parameter of spatial low-frequency transfer. Surprising, however, is the fact that temporal transfer indicates defects in such a high percentage even with still normal static light difference sensitivity (in cases of OH), or is impaired more than light sense perimetry (in cases of POAG).

In automated flicker perimetry, a localized and diffuse type of damage may be distinguished such as in quantitative static perimetry[31,32]. Figs. 3 and 5 show examples of a more localized damage with deep scotomas of steep slope. Fig. 4 shows an example of a more diffuse type of damage. Taking all eyes with OH together, there is an accumulation of defects in CFF fields in the upper hemifield, especially in the nasal upper quadrant. Considering the eyes with POAG, the type of visual field damage has to be taken into account: eyes with a more diffuse type of field damage in static light-sense perimetry also show an accumulation of defects in the corresponding CFF fields in the nasal upper quadrant; eyes with a more localized type of field damage in static light-sense perimetry, however, show an accumulation of defects in the CFF fields in the nasal lower quadrant.

There is a highly significant positive correlation between the Mean Defect MD in program G1 and the Defect Volume DV in the CFF fields (Fig. 7): $r = 0.826$

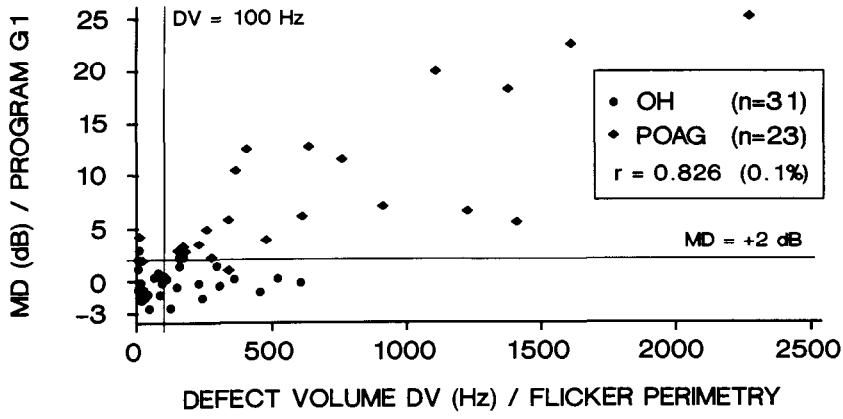

Fig 7 Correlation between the Mean Defect MD in program G1 and the Defect Volume DV in the CFF fields (circles: OH, rhombs: POAG). The values of MD = +2 dB and DV = 100 Hz indicate approximate empirical limits between 'normal' and 'pathologic'

(significant at the 0.1% level, *t*-test). An increase in overall damage in light–sense perimetry (characterized by the value MD) is obviously rather strongly correlated with an increase of overall damage in flicker perimetry (characterized by the value DV). It has to be considered, however, that there are quite a number of eyes (especially in the group of OH (filled circles)) with markedly pathological CFF fields (elevated DV value) and still normal static fields (normal MD value).

We may conclude that automated flicker perimetry measuring temporal resolution in the central visual field seems to be more sensitive to glaucomatous damage than is quantitative static light–sense perimetry. This idea is supported by the results of recent histopathological studies[36] showing that glaucomatous damage selectively affects large optic nerve fibers and, thus, especially the fibers of the Y-ganglion cells. The Y-ganglion cells, however, should be considered as the physiological correlate of the (excellent) temporal transfer properties of the paracentral retina as measured with automated flicker perimetry. The most urgent question arising from our study is whether or not eyes with defects in automated flicker perimetry and still normal light difference sensitivity (*e.g.*, the majority of eyes with OH) will develop defects in quantitative static perimetry in the future. In order to answer this question, a long-term follow-up study has been started which is trying to control the development of glaucomatous visual field damage during the next several years. From a clinical point of view, it is unclear at the moment whether or not a patient with a defect in the CFF field and normal static field has to be classified as OH or POAG, *i.e* , whether or not therapy should be started.

Acknowledgements

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HIGH-PASS RESOLUTION PERIMETRY
Recent developments

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Introduction

High-pass spatial frequency filtered resolution targets offer several advantages over classical perimetric targets, including a more distinctive appearance at threshold, a much narrower threshold zone, and, perhaps most important, a more direct insight into structural properties of the visual system. Test results are intuitively comprehensible even to naive test subjects, indicating a more direct bearing on vision of daily life.

This mini review briefly summarizes recent developments in high-pass resolution perimetry (HRP). Clinical experience has been reported by other investigators[1]; see also other reports in this volume.

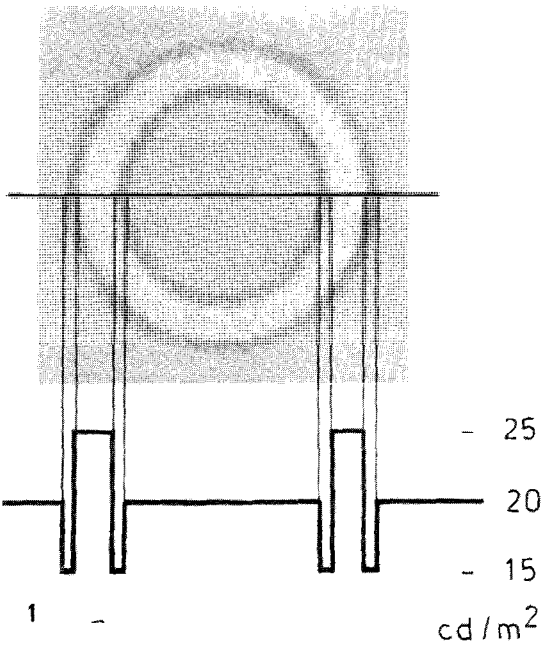

Fig 1 Construction of HRP test target. View figure at different distances to see how the ring melts into the background when visual angle falls below resolution limit Inset: luminance levels on video monitor. Contrasts are not exactly identical to those of video display due to limitations in reproduction process

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Nature of the test

HRP uses ring-shaped targets of different sizes at constant contrast (Fig. 1). The targets are filtered in the spatial frequency domain to suppress low frequencies. This affects perception in a peculiar way: the targets are either resolvable or completely invisible, depending on their size. The close coincidence of detection and resolution thresholds makes for a very simple test task and makes acuity perimetry clinically practicable. Paradoxically, the same property works against use of high-pass or 'vanishing' targets in central vision testing[2]. However, special display formats seem to allow a unified approach to central and peripheral acuity measurements (in preparation).

Because the test task is identical to that of classical perimetry (the subject is asked to respond whenever a target is seen), it may be difficult to recognize that the threshold actually reflects resolution rather than detection. This can be surmised already from the construction of the target: if neither the bright core nor the dark borders can be discerned, the target melts imperceptibly into the background (Fig. 1). More direct support that the task concerns resolution comes from the good correlation with results using standard resolution targets, the linear relationship of results to receptive field separations, and the similar degree of binocular summation[3,4]; see also below. Classical perimetry differs in all these regards. Further dissimilarities are encountered occasionally in pathological conditions: Fig. 2 shows one example.

HRP has been implemented in computer graphics as a visual field screener. Briefly, a personal computer generates on a test monitor targets of different sizes (scale factor 0.1 $\log_{10}$ units - 1 dB) against a 20 cd/sq m background. Contrast is 0.25. Presentation time is 165 ms. Thresholds are obtained in 50 locations within 30 degrees of eccentricity (Fig. 2). Results are given in both decibels and minimum angles of resolution (MAR), with the smallest target (stroke width 11.6′) defined as 0 dB. A more detailed technical description of the 'Ring Visual Field Screener' is available in the Ophthimus System Manual*. The target properties and numerous feedback devices make for a very easy test, with an average duration of 5.5 minutes[5,6].

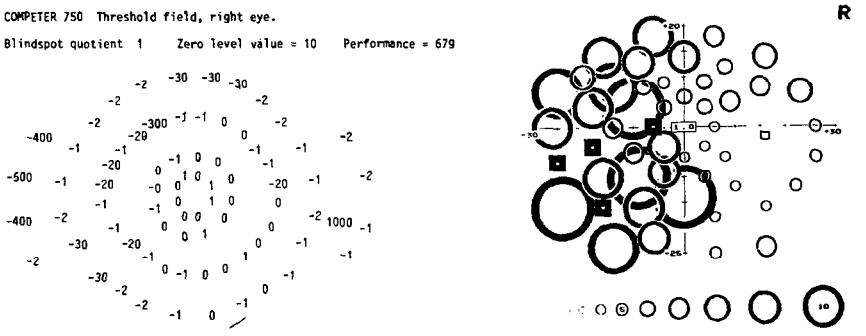

Fig 2 Example of dissociation of results in conventional perimetry (left) and HRP. The latter represents results by plotting threshold targets to scale at each test location. Small squares represent locations where largest target was not seen. Case of right occipital glioma. Left eye results were similar (not shown) Kinetic perimetry was normal.

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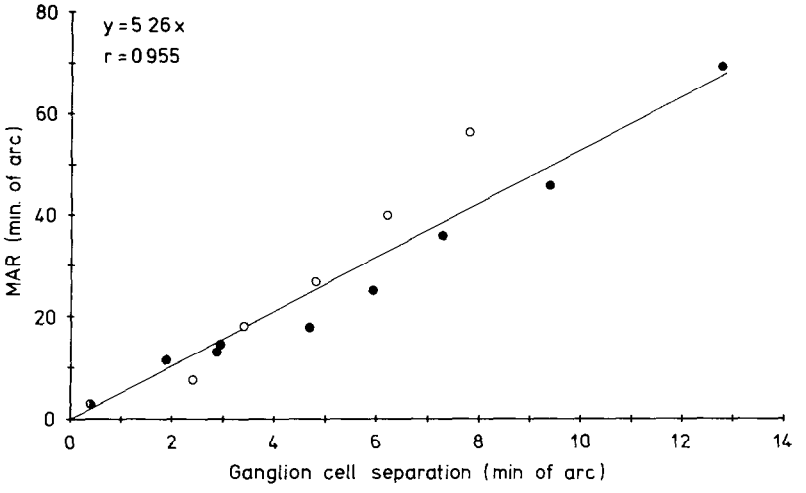

Fig 3 Relationship between ganglion cell separations at 10 degree intervals along horizontal meridian and HRP thresholds in corresponding loci, in a normal subject. Open and closed circles represent nasal and temporal meridians, respectively. Inset: least squares regression through origin and correlation coefficient

Neuroanatomical relationships

It is known that peripheral MARs for conventional resolution targets vary as a function of the separation of retinal receptive field centers (the ganglion cells). The relationship is linear through the origin, *i.e.*, MAR is exactly proportional, except for stochastic deviations, to local ganglion cell separations[7-9]. The proportionality factor (the regression coefficient) will be designated F in the following. The same relationship has been shown to apply to HRP targets (Fig. 3). In contrast, the relationship between ganglion cell separations and differential light sensitivity is non-linear and excludes the origin[3].

The proportionality is also applicable in reverse: MAR measurements allow estimation of the separation between functional ganglion cells, *i.e.*, an actual count of working retino-cortical neural channels. A neural channel is defined here with reference to a retinal ganglion cell and includes its retinal input elements (the receptive field), its output axon, and the axon's suprageniculate extension to the visual cortex.

Estimating retino-cortical neural channels

Each MAR result can be directly converted into an estimate of the local ganglion cell separation. The relationship has the simple form

$$S = \text{MAR} / F$$

where S is the ganglion cell spacing in minutes of arc. Hence, the number N of ganglion cells per degree of visual angle equals $1/(60 \times S)$, and $N \times N$ estimates the number of cells per square degree. F can easily be determined from the visual field scores and published data on S. F averages 8.95 ± 2.09 (SD)[10].

Note that these results apply only to HRP under the conditions described above,

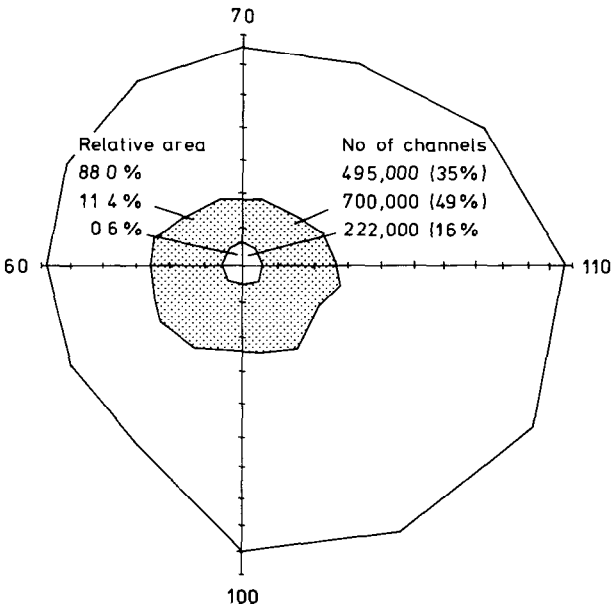

Fig 4 Relative surface areas and estimated numbers of neural channels in different subdivisions of visual field, *in right eye format Lambert's area-true projection* Tick intervals represent 10 degrees of polar distance. Stippled area is tested by Ring Visual Field Screener. Numbers in parentheses are percentages of total number of channels Average from 30 normal subjects (mean age 41 years)

and under careful control of all extraneous variables that may exert influence on acuity. The precision of the estimates is naturally critically dependent on the qualities of the cell counts used in establishing F. Regrettably, very few counts are available, and only Oppel's[11] data from the horizontal meridian of five eyes illuminate normal variability. Fortunately, anatomical variability appears to be much smaller than the psychological counterpart. Part of the structural variability appears to be attributable to age, although the number of observations is again small[12]. The limitations of the anatomical data caution against absolute estimates but should not interfere with relative comparisons within or between subjects.

An estimate of the total number of ganglion cells normally contained within the tested area can be obtained by interpolating over test locations (Fig. 4). The results are compatible with previous estimates from direct cell and axon counts. The same computational model can be used to illuminate pathological conditions, *e.g.*, a uniform threshold evaluation. On average, a 1 dB elevation of test scores corresponds to a 39% reduction in ganglion cells, 2 dB to 62%, and 3 dB to 78%13. Note that these estimates do not apply to ordinary perimetry.

An important question is what bearing ganglion cell estimates have on different types of disorders of the visual system. While this requires additional study, it is argued that the ganglion cells are in a key position to reflect many forms of retinal and neural lesions. This is because these cells are the output units of the retina. Preganglionic damage can be envisaged to deprive a larger or smaller proportion of ganglion cells from their normal inputs, attenuating or cancelling their outputs. While these ganglion cells presumably remain normal, they should appear muted or silent to higher visual centers, effectively depriving these of spatial detail in relation to the degree of injury. Postganglionic visual pathway damage can effectively be viewed as a disconnection of ganglion cells. Hence, even if the primary

damage does not involve the ganglion cells themselves, it seems feasible to express different degrees of visual system damage, irrespective of actual mechanisms and actual locations, in terms of *functionally equivalent* damage to ganglion cells. A more detailed discussion of these concepts of 'pathophysical analysis' has been presented elsewhere[14].

Estimates of the number of functional channels offers improved assessment of severity of disease and improved staging schemes. Amplification does not seem necessary.

Estimating criterion levels

While the proportionality factor F appears to be relatively constant for each individual, there is considerable variation between individuals (SD 2.09). This is presumably at least in part attributable to variations in psychological factors, *e.g.*, criterion setting or the individual judgment of what defines a meaningful stimulus. Because F can be estimated from the individual visual field record, it is possible to compensate for this source of variation. The effect amounts to a 57% reduction in the width of normal limits. The same procedure can be used to compensate for training effects. Unfortunately, it cannot as yet be applied to abnormal visual fields[16].

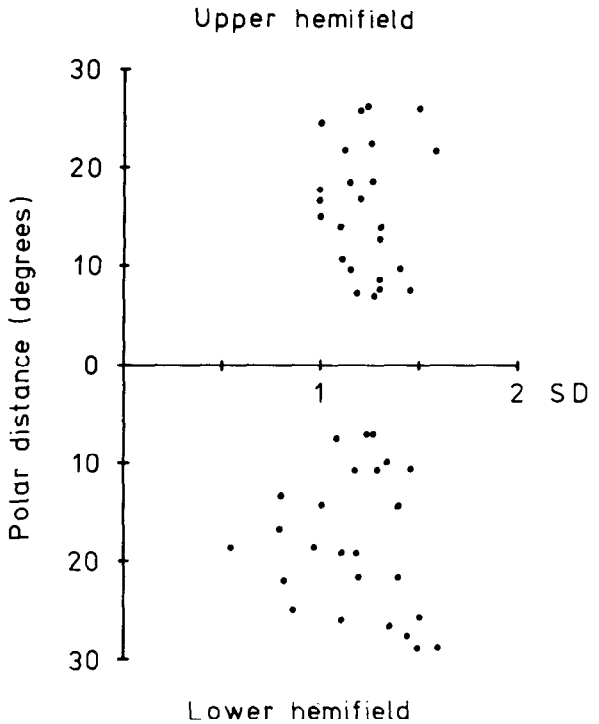

Fig 5 Standard deviations for each test location for 30 normal subjects versus angular distance from fixation axis

Statistics

A remarkable property of HRP is the small width of the threshold zone. Frequency-of-seeing curves indicate that optimum step size is 0.5 dB or less[3]. Classical perimetry uses 1-4 dB steps, although both tests produce similar gradients (in dB/degree) of the normal threshold surface. Another interesting difference applies to variability with eccentricity: this is negligible with HRP (Fig. 5) (*cf.* reference 15).

An analytical program has been developed to aid evaluation of test results in Ring perimetry. In addition to descriptive results and reliability statistics, the program analyzes the shape of the threshold surface by means of a correlative procedure that depends on an extended isopter concept. The resulting 'Form Index' has been shown to have a good sensitivity for low-degree optic neuropathy and a specificity of 97%[16] The program also estimates the functional fraction of neural channels and, whenever possible, the criterion level. The channel fraction is adjusted for age and for criterion level.

Practical considerations

The fairly limited range of target sizes prevents application of HRP in subjects with severe loss of vision. However, such subjects can be examined with a raised contrast level. The use of spatially extensive targets naturally works against exact definitions of defect borders, and also works against precise delineation of depth for circumscribed defects. The blind spot, for instance, can never be shown to be an absolute defect. While theoretically objectionable, practical experience indicates that these are minor disadvantages, which are easily offset by the superior patient acceptance and the short examination time. Interestingly, measuring the blind spot may be quite problematic in ordinary perimetry. Sometimes it cannot be found at all[17].

The physical size of liminal targets has important effects on the optimum placing of test locations. For instance, there is little point in respecting the vertical meridians. It appears better to adapt the pattern to common varieties of field defects that are more difficult to detect than quadrant-related defects, namely nerve fiber bundle defects. These considerations motivate the somewhat unorthodox test pattern (Fig. 2). The standard pattern can be complemented with a user-selectable grid for additional detail.

Technical limitations prevent the Ring Screener from determining thresholds inside 5 degrees of eccentricity in normal eyes. An obvious solution is to test the very central field at a larger eye-to-screen distance. A Ring test variant allowing free selection of test distance is presently under evaluation. This test, which employs 33 symmetrical test locations, offers a unique possibility to prove (or disprove) central vision loss also in so-called hysterical disorders. Incidentally, vanishing acuity targets appear to be well suited to preferential looking acuity tests. Such tests are currently being explored.

Acknowledgement

The author has a proprietary interest in the computer programs described in this report, but not in the design principles

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COMPARISON OF AUTOMATED CONVENTIONAL AND SPATIAL RESOLUTION PERIMETRY IN CHIASMAL LESIONS

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Abstract

The visual fields of 64 eyes of 36 patients with chiasmal lesions were examined both with the Octopus, program 32, and with spatial resolution perimetry using high-pass spatial frequency filtered ring-shaped targets on a TV screen A data reduction of this 'Ring test' facilitates the estimation of functional deficits. The loss of mean sensitivity of the affected quadrant in a percentage of sensitivity of the adjacent unaffected quadrant for each method was correlated For mild to moderate depression of sensitivity, there was no obvious difference between either technique Patients' acceptance of spatial resolution perimetry was excellent due to the short duration and special features of the program

Introduction

Perimetry by means of high-pass spatial frequency filtered test targets on a video screen[1,2] might be more sensitive to functional loss due to nerve fiber damage than conventional perimetry using light difference sensitivity. These two fundamentally different methods cannot be directly correlated. Furthermore, it is impossible to decide which one of them is correct if differences occur. Nevertheless, we tried to compare results from a group of patients with documented lesions of the chiasmal region.

Material and methods

Sixty-four eyes of 36 patients were examined. One patient had an infarction of the posterior cerebral artery, one a traumatic optic tract lesion. All other patients suffered from a tumor near the chiasm or optic tract, which had produced marked hemiopic defects prior to removal of the tumor. On examination one-third of the eyes presented with more or less normal fields.

Conventional perimetry was carried out on an Octopus Computer perimeter using program 32. Mean sensitivity was assessed for each quadrant with program Delta.

Spatial resolution perimetry ('Ring test') was performed in the majority of patients on the same day. Fifty ring-shaped stimuli of varying sizes were automatically presented on a TV screen within 30°in random order. Detection and recognition coincide in this arrangement[1,2].

Field graphs are printed with ring symbols, the size of the rings corresponding to the individual thresholds. A data reduction to mean ring diameters for each quadrant was automatically performed and given in each graph. A transformation into 'sensitivity values' allowed a comparison of both methods in terms of mean loss of sensitivity in percent of sensitivity of the normal or less involved opposite

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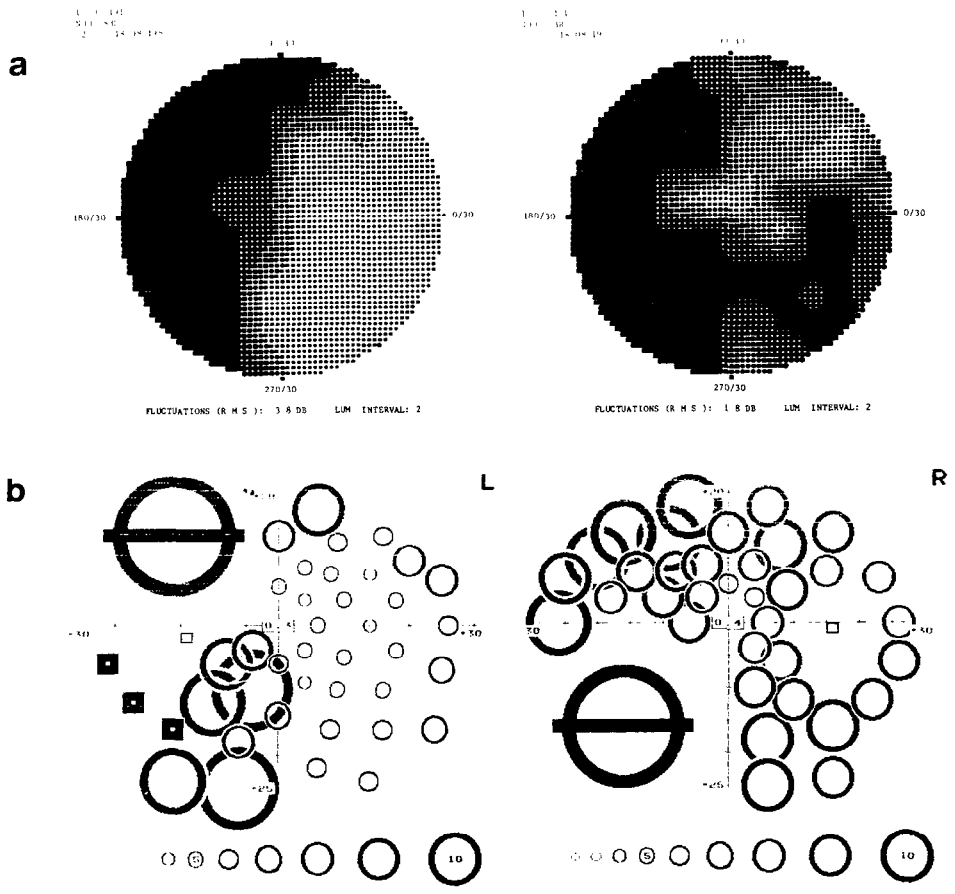

Fig 1 A 69-year-old male (Ni,K), lesion of the optic tract due to craniopharyngeoma, removed 14 years previously a Octopus fields: Nearly absolute homonymous hemiopic defect with faint remnants of sensitivity, and in OD an additional absolute nerve fiber defect in the inferior temporal Bjerrum region together with general depression. b. Ring test: absolute quadranopia in lower nasal field OD and upper temporal field OS General depression in the remaining field OD, deep relative defect in lower temporal field OS

quadrant (Ring sensitivity = (Ring score -14)x-2, maximal score = 14). Other features of the statistical program[3] were not used in this context.

Results

The dynamic range of both methods may be evaluated by comparing quadrants with 'absolute' defects (sensitivity value 0) in either one of the two. In seven of those 25 quadrants, both had coinciding absolute defects (Fig. 1, OD). In 16, only the Ring test had an absolute defect, whereas conventional perimetry showed some remnants of sensitivity (Fig. 1 OS), 4.1 dB at the most (Fig. 2, OS). This was, at least in some cases, due to a precipitate conclusion of the program in the initial test phase. In the temporal quadrants of one eye the Octopus found no sensitivity, the Ring test minimal sensitivity.

The weakest possible stimulus, sensitivity value 28 for the Ring test and 51 dB for the Octopus, was never required in either method. Mean sensitivity of a whole quadrant for a normal population is around 21 for the Ring test, 24-28 dB for the Octopus, depending on age.

A comparison of mean sensitivity between adjacent quadrants was performed by separating the upper and lower hemifields, giving a total of 132 pairs of quadrants for each method. In 11 pairs, the Ring test showed a lower sensitivity in that quadrant in which conventional perimetry resulted in a higher sensitivity. Those conflicting tendencies were only observed in practically normal fields. The differences between the nasal and temporal quadrant exceeded a value of 2.2 dB only in two pairs of quadrants. The maximal difference was 5.5 dB, suggestive of a nasal depression for the Octopus, never observed before, and a normal result in the Ring test (Fig. 3 OS, lower hemifield).

Depression of sensitivity was calculated for the remaining 121 pairs of quadrants in percent of the better quadrant (Fig. 4). The correlation coefficient was 0.9, p = 0.0000, independent regression line is y = 0.96x -5.3.

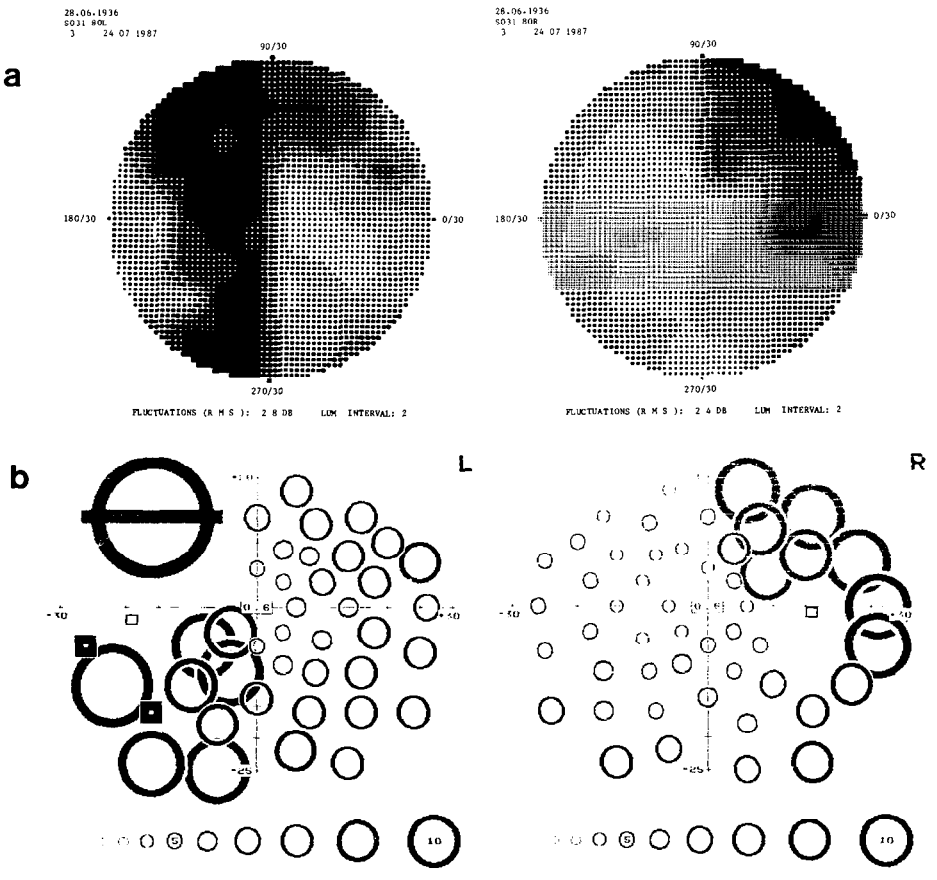

Fig 2 A 51-year-old male (Sa,H), both transnasal and transfrontal removal of pituitary tumor. a Octopus: Partial recovery from bitemporal absolute hemianopia, predominantly in OD. b. Ring test: Coinciding upper temporal deep defect OD. Absolute quadranopia in upper temporal, deep relative defect in lower temporal field OS.

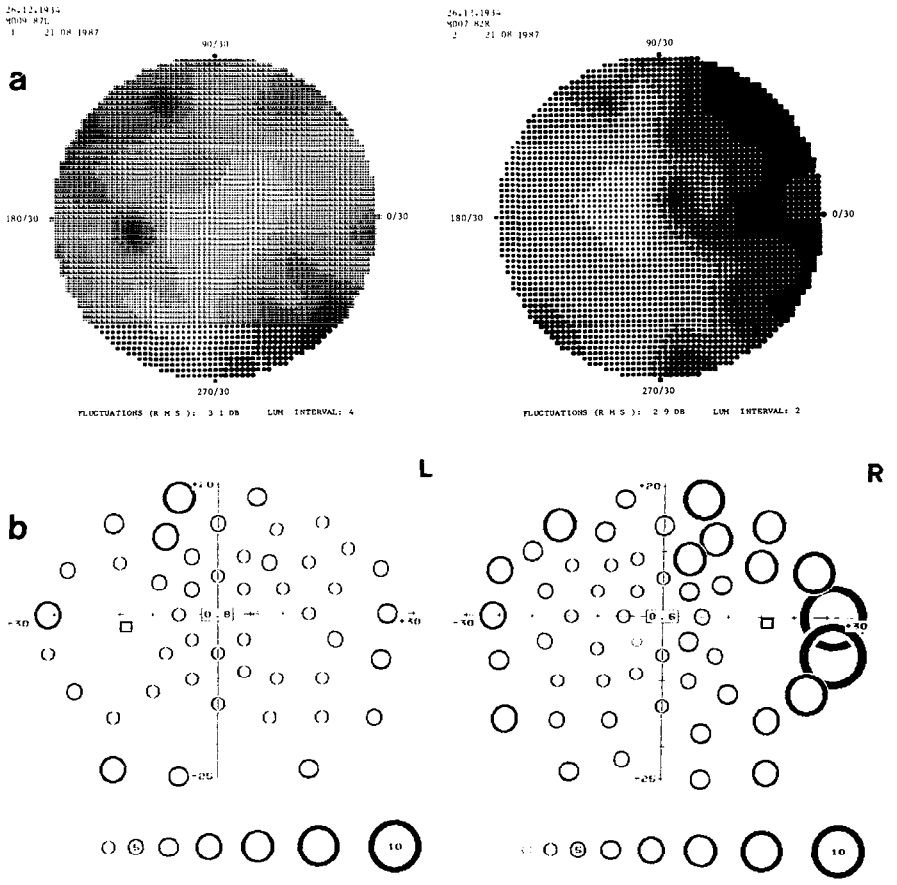

Fig 3 A 50-year-old male (Ma,G), transfrontal removal of pituitary tumor 26 years, transnasal removal of recurrent tumor 14 years, radiation ten years previously, repeatedly improving a bitemporal hemianopia, especially OS a Octopus: Dense relative defect in upper, less dense in lower temporal quadrant OD. Slight depression in upper temporal and lower nasal field OS b Ring test: Corresponding results for OD and upper hemifield of OS Unaffected lower hemifield OS.

The transition from reduced to absent sensitivity revealed a gap for the Ring test compared to the Octopus. A new calculation of the material omitting all quadrants with absolute defects for either one of the two methods, results in a flatter slope of the independent regression line, $y = 0.59x + 2.96$, and a lower correlation coefficient of 0.84 (p still 0.0000).

On the whole there is a tendency for markedly damaged quadrants to reveal more depression in conventional perimetry than in the Ring test, at least for the scaling of sensitivity used in this study. Mean deviation from coincidence of percentual depression was for all pairs $7\% \pm 16.4\%$ in this direction. The most extreme of these deviations (solid arrow) is the upper hemifield of Fig. 2, OD. Earlier conventional fields in this eye had indicated more remaining sensitivity in the upper nasal quadrant, however.

Maximal deviation in the opposite direction (open arrow) was an absolute defect for the Ring test with some preserved light difference sensitivity (Fig. 2, OS). The

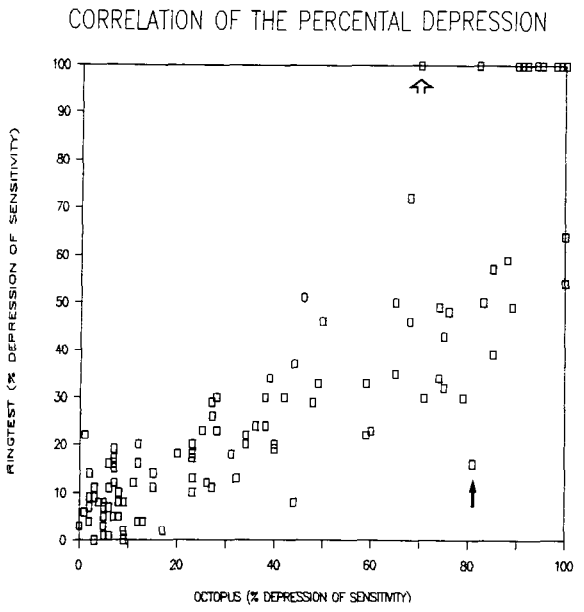

Fig 4 Correlation of depression of sensitivity of an affected quadrant in % of the sensitivity of the less involved adjacent quadrant

transition from defective to normal fields is smooth and well balanced between both methods, neither showing constantly more pathology than the other.

Patients' acceptance was inquired in all cases. The Ring test took only five to six minutes per eye, the Octopus at least twice as long. A number of features of the strategy of the Ring test reinforced very effectively the patients' motivation. Thus, most subjects preferred the Ring test.

Comment

Spatial resolution in this arrangement is supposed to reflect retinal ganglion cell density[4]. Perimetric results of that kind may deviate from those of light difference sensitivity in conventional perimetry, as assumed for glaucoma[5].

The scaling of sensitivity has a considerable influence on the comparison of the results of both methods (Fig. 4). A direct correlation is thus not possible, especially for severely damaged fields. Some of these extended absolute defects were actually due to artifacts in the initial phase of the test, which calls for close supervision of the patients' performance at the beginning.

A correlation in mild defects may shed at least some light on the performance of this new technique. In our preliminary study, we were not able to demonstrate more pronounced involvement of spatial resolution in chiasmal lesions than that of conventional perimetry. Similar results were obtained in glaucoma[6]

It was apparent that the design of this procedure has advantages due to the simple, commercially available computer hardware and an extensive data reduction program[3]. The patients' acceptance was excellent thanks to a number of special feedback features of the program[2] and to the short duration of the test. The longer conventional examination may lead to more data on an individual field, however, including the periphery.

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COMPARISON OF AUTOMATED CONVENTIONAL AND SPATIAL RESOLUTION PERIMETRY IN GLAUCOMA

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Abstract

Spatial resolution perimetry was performed in 116 eyes of 63 subjects with chronic and low tension glaucoma, ocular hypertension and normal ocular findings in comparison with conventional computer perimetry. High-pass filtered ring-shaped stimuli of varying sizes were generated on a TV screen using a personal computer. Conventional fields were assessed with Octopus program G1 A correlation of the glaucomatous loss of mean sensitivity in the whole central field and in quadrants for both methods revealed no obvious discrepancy, especially for moderate field damage. The correlation of form indices of both methods turned out less convincing Patients' acceptance was excellent due to the short duration of the test and a number of features of the program

Introduction

The evaluation of spatial resolution by means of a video screen has recently been advocated as a perimetric procedure[1,2]. A first clinical trial demonstrated its usefulness in glaucoma[3]. It is not possible to directly compare spatial resolution perimetry with conventional perimetry using light difference sensitivity: the scaling of sensitivity cannot be equalized, and differences between the plots of the two methods may be due to the fundamental psychophysical dissimilarities which cannot be expressed in terms of false positive or negative results. We nevertheless tried to correlate those data to get some impression of the reliability of this new perimetry technique in glaucoma.

Material and methods

One hundred and sixteen eyes of 63 subjects with chronic open angle and low tension glaucoma including some glaucoma suspects and normal subjects were examined with the Octopus computer perimeter, program G14, and with high-pass spatial frequency filtered test targets, 50 rings of varying sizes in 13 steps[1,2]. For this 'Ring test' a personal computer and an additional TV monitor was used. Six eyes were examined twice with a few months' interval, calculated as independent eyes. One hundred eyes had defects in the Octopus field, equally distributed over all three classes of the estimated severity.

Mean sensitivity in the whole field and quadrants was calculated for the Octopus in dB, and for the Ring test in units derived from the mean threshold sizes of the stimuli. Scaling of the units was adapted to the scale of conventional perimetry as closely as possible in order to achieve equal values for both absolute defects (value 0) and normal sensitivities (unit = (Ring score -13)X(-2.8), maximal score limited to 13).

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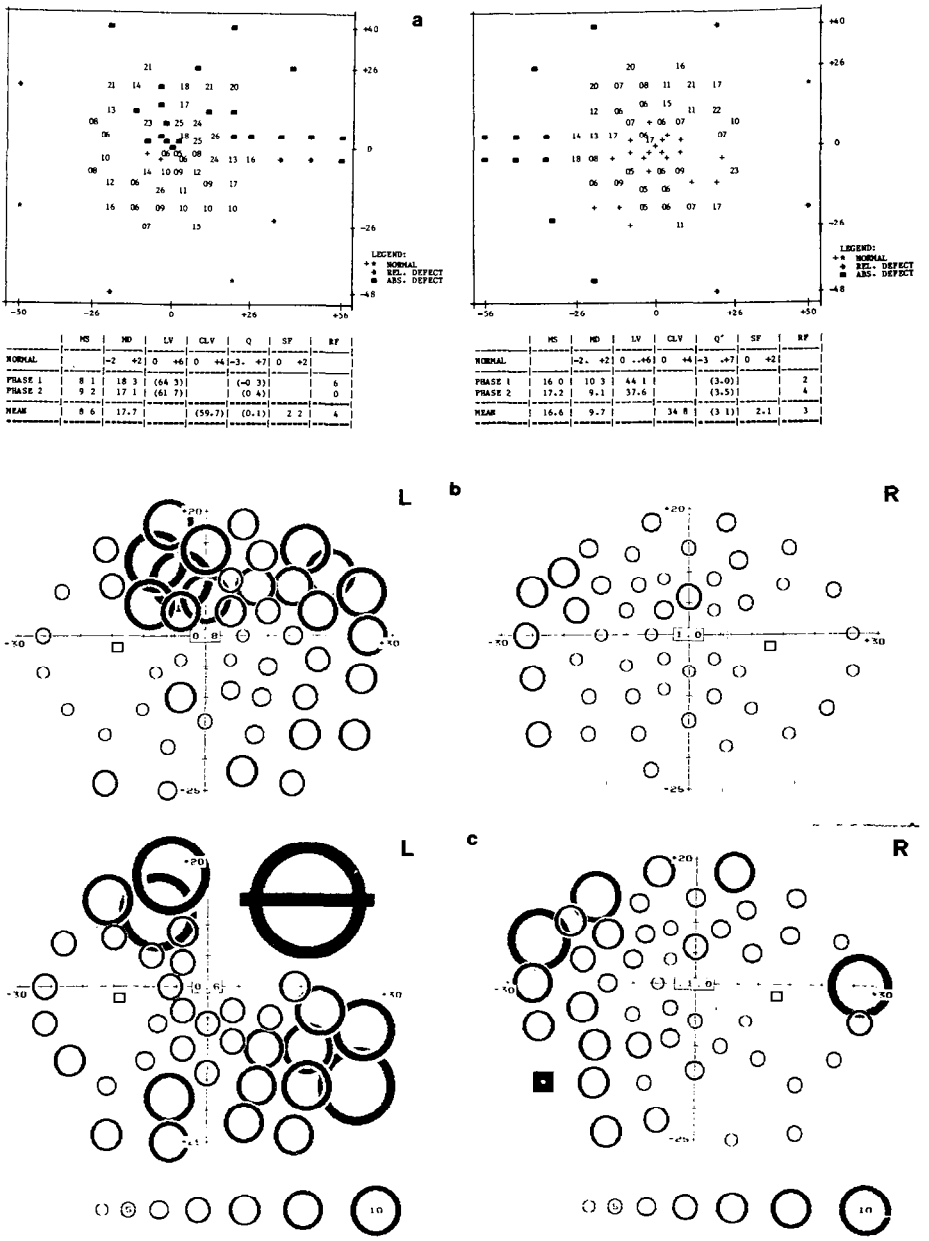
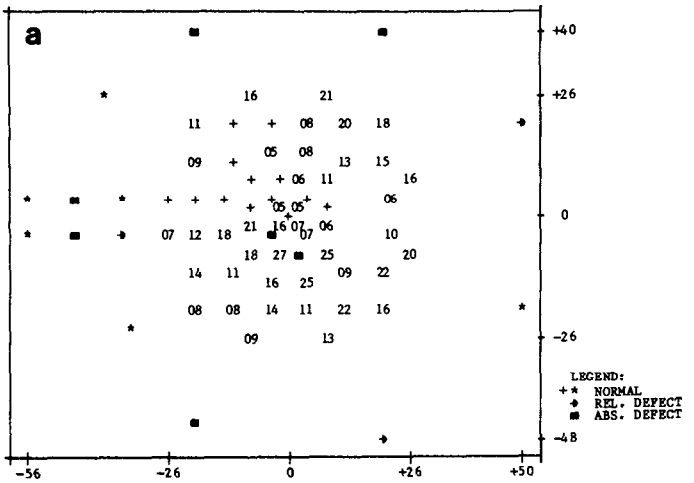
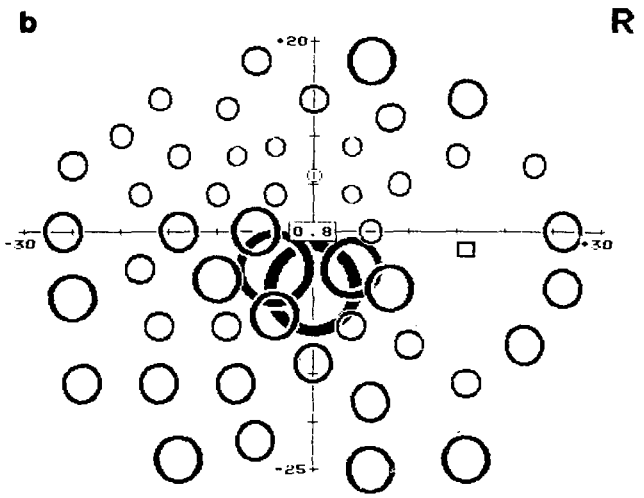


Fig 1 A 71-year-old female (Be,A), total glaucomatous cupping OU a Octopus fields, program G1 OD: General depression and absolute nerve fiber defect in upper hemifield. OS: Isolated relative nerve fiber defects in upper hemifield b Ring test fields: Nerve fiber defects corresponding to Octopus fields, visible as enlargement of dark rings in affected areas. c. Ring test fields four months later. OD: Same arrangement, somewhat more pronounced OS: Absolute defect of upper temporal quadrant, depression of lower hemifield, predominantly nasally, more pronounced than in previous field (b). Octopus fields of second instance exactly corresponding for OD and lower hemifield of OS, but no upper nasal absolute quadranopia (omitted)



	MS	MD	LV	CLV	Q'	SF	RF
NORMAL		-2...+2	0...+6	0...+6	-3...+7	0...+2	
PHASE 1	12.5	14.1	(65.6)		(1.6)		8
PHASE 2	14.3	12.3	54.6		(3.1)		4
MEAN	13.4	13.2		49.3	(2.2)	2.7	6



Mean quadrant scores: 5 2 ± 1 2 5 6 ± 1 3
7 5 ± 1 4 7 2 ± 1 0

Fig 2 A 66-year-old female (Ha,L), total glaucomatous cupping. a. Octopus field: Lower hemifield diffuse depression and tiny paracentral absolute nucleus, upper field some depression mainly temporally b. Ring test field with exactly corresponding defects.

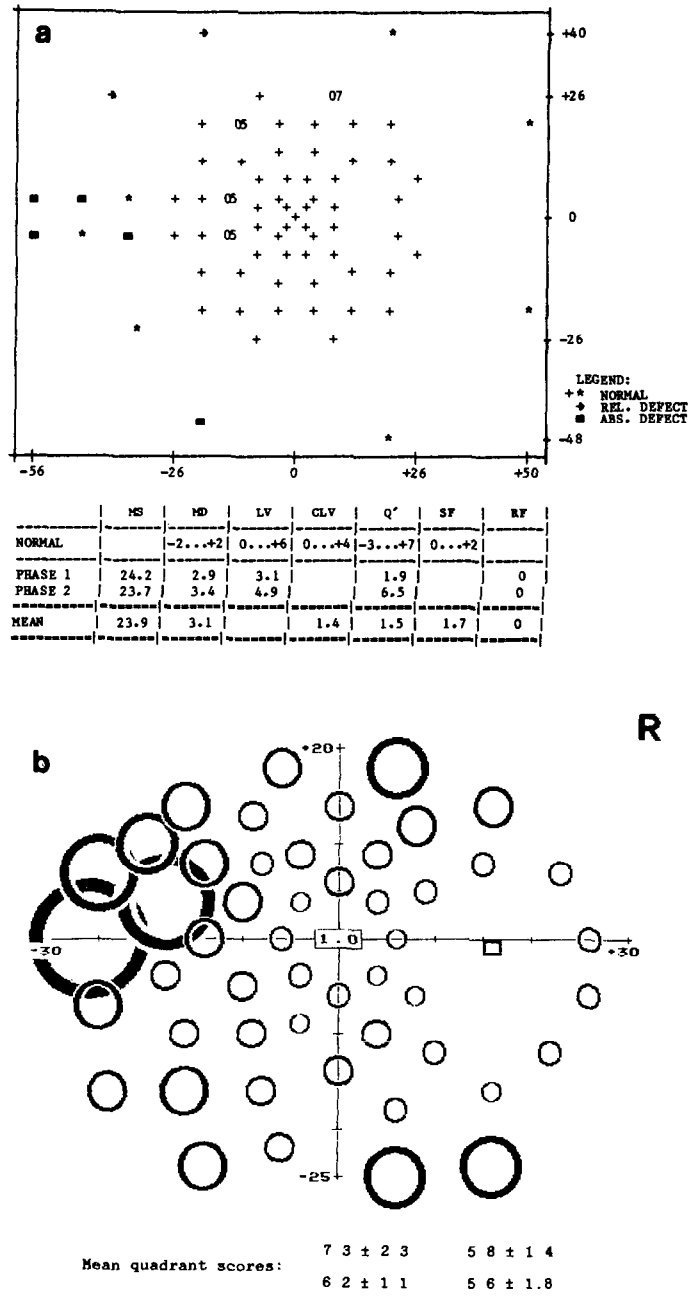
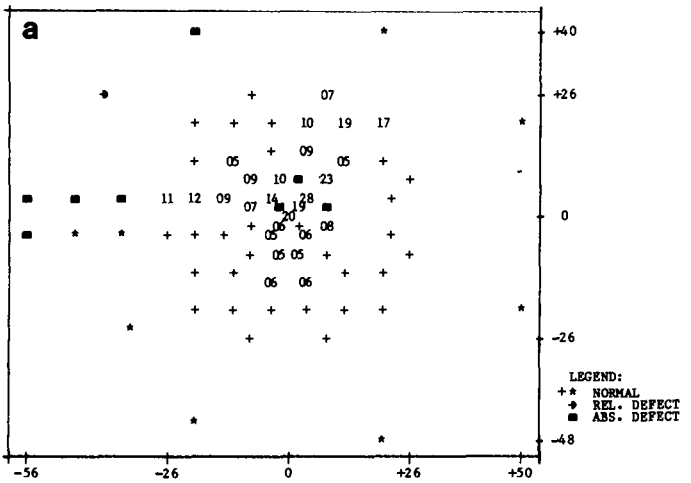


Fig 3. A 60-year-old male (Ma,H), temporal glaucomatous cupping. a. Octopus field: Only mild isolated depressions without nerve fiber appearance b Ring test field: Nerve fiber defect in upper hemifield, most markedly nasally, supported by separate conventional perimetry.



	MS	MD	LV	CLV	Q'	SF	RF
NORMAL		-2...+2	0...+6	0...+4	-3...+7	0...+2	
PHASE 1	18.6	8.7	62.4		(5.8)		2
PHASE 2	19.1	8.2	67.1		(5.5)		10
MEAN	18.8	8.4		61.9	(5.8)	1.8	5

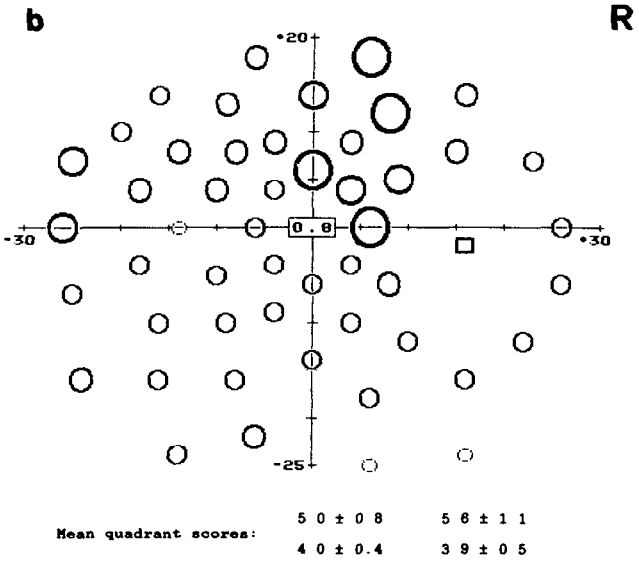
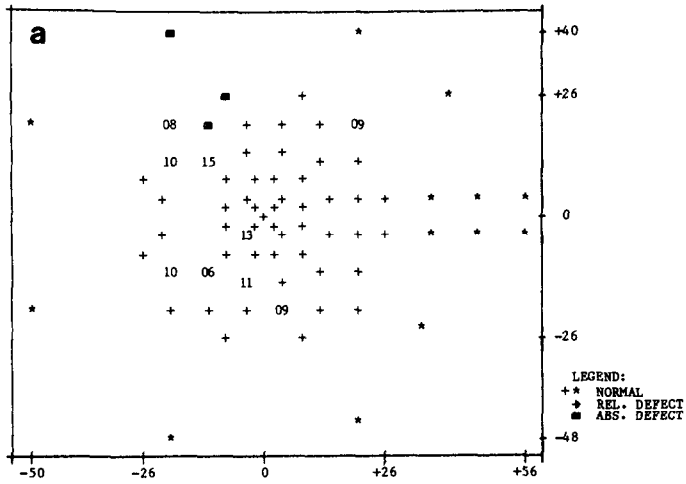


Fig 4 A 56-year-old male (Hi,G), low tension glaucoma, wide cups. a Octopus field: Upper hemifield diffuse depression and absolute nucleus, some paracentral depression inferiorly. Severity of defects verified by additional conventional perimetry b Ring test field: Mild diffuse depression in upper hemifield, prevailing in temporal quadrant.



	MS	MD	LV	CLV	Q'	SF	RF
NORMAL		-2...+2	0...+6	0...+4	-3...+7	0...+2	
PHASE 1	22.0	4.7	30.8		(6.7)		0
PHASE 2	22.4	4.3	30.5		(7.1)		0
MEAN	22.2	4.5		27.8	(7.3)	1.7	0

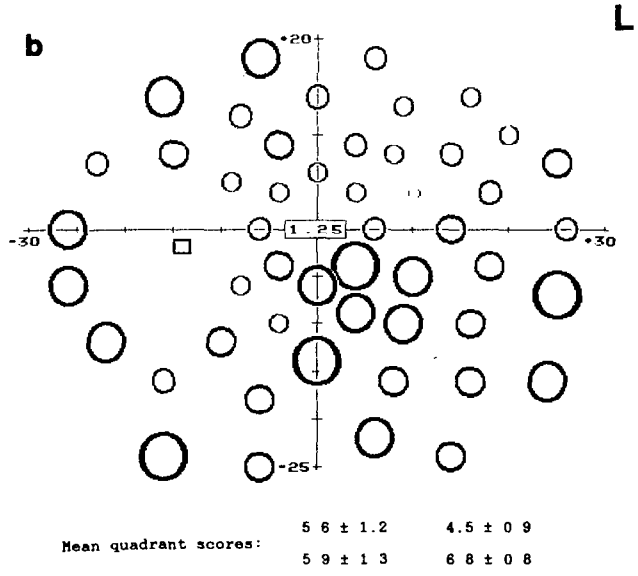


Fig 5 A 65-year-old male (Th,C), glaucomatous cupping a. Octopus field: Scattered relative defects below, relative and absolute defects above blind spot. b. Ring test field: Moderate depression in lower hemifield with accentuation in nasal paracentral region. This pattern supported by separate Octopus field, program 38

Results

Clinical estimation

Eighty-nine of the 100 defective Octopus fields had results comparable to the ones of the Ring test (Figs. 1a,b, 2), 11 revealed deviations in their appearance from the Ring test records. In seven of these, the Ring test had more pathology (Fig. 1c, OS, Fig. 3), in three the Octopus (Fig. 4). One field presented differently distributed defects of equally moderate severity (Fig. 5).

A further analysis taking other clinical data into account disclosed that the more affected plot of the Ring test corresponded in four of the seven fields to an absolute defect of a whole quadrant (Fig. 1c), in which some light difference sensitivity was still present. Such a misleading result, mostly unmasked by a repeated measurement, is printed if the largest target in the initial phase of the test was missed twice. The remaining three Ring test fields had obviously more pathology than the conventional fields, and fitted better to all other available data (Fig. 3).

A deviation in the opposite direction was present in three fields with more damage for conventional perimetry (Fig. 4), supported by repeated field examinations. The arrangement of defects as apparent in the Ring test field of Fig. 5 was confirmed by further perimetric results. The 16 unaffected Octopus fields were also unsuspicious in the Ring test.

Correlation of sensitivity

A statistical analysis revealed a good correlation of mean sensitivity values of both perimetric methods (Fig. 6). Correlation coefficient was for the whole field and each quadrant around 0.9.

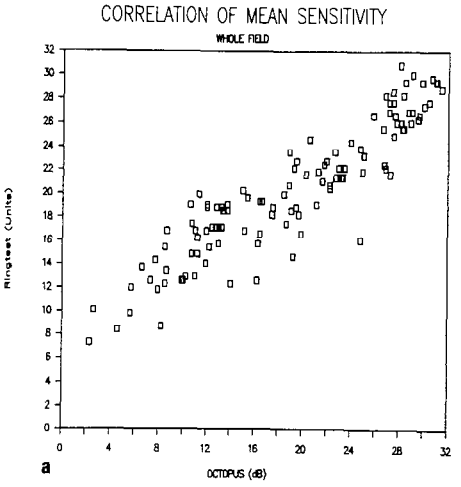
The upper nasal quadrant showed a remarkably high number of absolute defects and an independent regression line very close to perfect coincidence. The largest deviation in this respect occurred in the upper temporal quadrant, where deep depressions of sensitivity were as infrequent as in the lower temporal quadrant. In the upper temporal region, the Ring test disclosed slightly less involvement for severe damage compared to the Octopus.

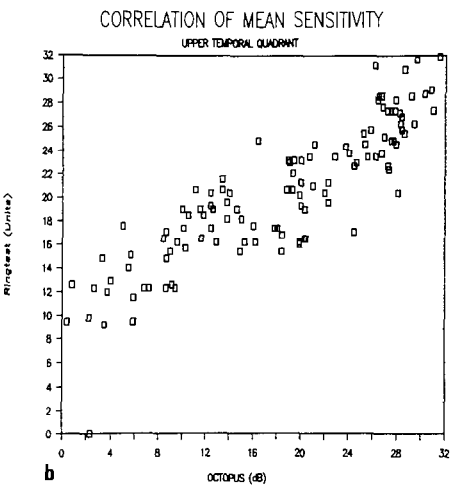
Correlation of form index

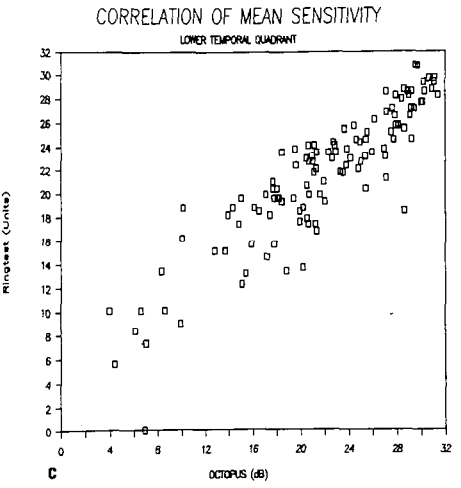
Both methods perform a data reduction not only for mean sensitivity but also for localized deviations from the normal shape of the island of vision. A comparison of the 'Corrected Loss Variance' of the Octopus[4] with 'Form Units' (100-form index x 100) derived from a statistical program of the Ring test[5] yielded a weak but significant correlation ($r = 0.52$, $p = 0.0000$).

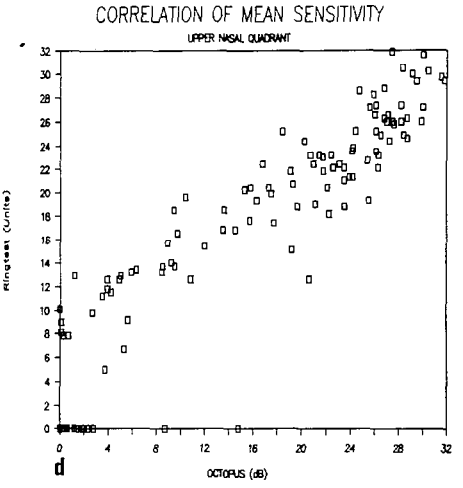
Comment

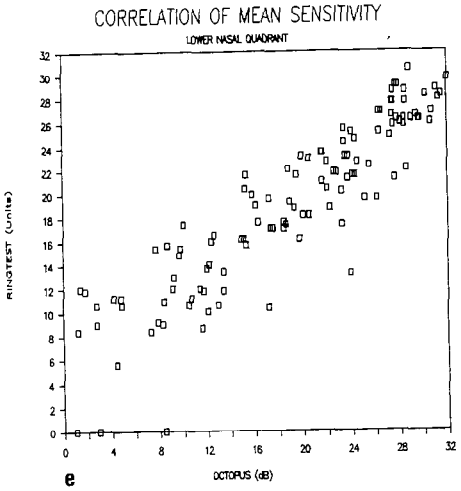
Spatial resolution perimetry presumably reflects ganglion cell density[1] and might therefore be valuable in chronic glaucoma. A comparison with conventional computer perimetric findings is of limited validity since the scaling of sensitivities cannot be equalized. In this material, the adjustment was ob-viously superior to the one used in a separate study in chiasmal lesions[6]. The correlation of mean sensitivities revealed no major dissimilarities between the two methods. On the basis of a clinical comparison[3], one might have expected differences. A close super-


CORRELATION OF MEAN SENSITIVITY
WHOLE FIELD
Ringtest (units)
OCTOPUS (dB)
a


CORRELATION OF MEAN SENSITIVITY
UPPER TEMPORAL QUADRANT
Ringtest (units)
OCTOPUS (dB)
b


CORRELATION OF MEAN SENSITIVITY
LOWER TEMPORAL QUADRANT
Ringtest (units)
OCTOPUS (dB)
c


CORRELATION OF MEAN SENSITIVITY
UPPER NASAL QUADRANT
Ringtest (units)
OCTOPUS (dB)
d


CORRELATION OF MEAN SENSITIVITY
LOWER NASAL QUADRANT
RINGTEST (units)
OCTOPUS (dB)
e

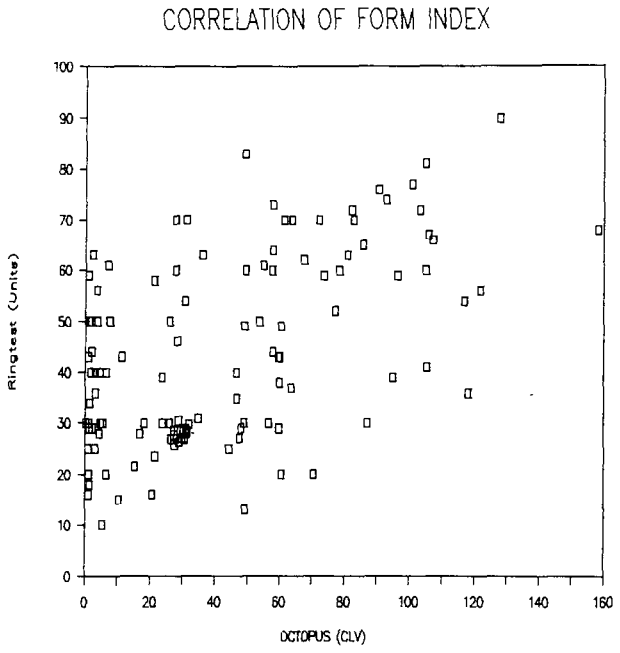


Fig. 7. Correlation of 'Corrected Loss Variance' of Octopus fields and 'Form Units' of Ring test (r = 0 52, p = 0 0000)

vision dur ing the initial phase of the Ring test seems necessary, however, to avoid false positive quadranopic findings[6]

The TV screen covers only the central 30 degrees, whereas the Octopus is also able to examine the periphery. Ring test stimuli exactly on the nasal horizontal meridian were less useful in identifying nasal steps.

The Ring test was well accepted by patients due to the short duration, about five to six minutes per eye, and to a relatively easy and stimulating procedure, including a number of feedback devices[2].

Acknowledgements

Dr Lars Frisén provided us with the Ring test set-up and technical help The software for the analysis of quadrants of the G1 program was made by my son Dominik

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←

Fig. 6. Correlation of mean sensitivity per test location of Octopus fields and Ring test. a Whole field (r = 0 91) b Upper temporal quadrant (r = 0.88) c Lower temporal quadrant (r = 0.9) d Upper nasal quadrant (r = 0.91) p = 0 0000 for each correlation4 Flammer J: The concept of visual field indices Graefes Arch Clin Exp Ophthalmol 224:389-392, 1986

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THE INFLUENCE OF FEEDBACK DEVICES, LEARNING AND CHEATING ON THE RESULTS OF HIGH-PASS RESOLUTION PERIMETRY

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The recently developed computerized acuity perimetry, using high-pass filtered stimuli, was tested in normal subjects with regard to the influence of feedback devices on the examination results and the effect of learning and 'cheating', i.e., active scanning of the screen instead of maintaining steady fixation Eleven normal subjects were examined with and without the feedback devices No difference in the examination results were found. However, all subjects preferred the examination which included feedback routines.

Serial HRP examinations were performed in ten normal subjects. The learning effect was found to be very small.

Five normal subjects with experience and knowledge of perimetric principles were requested to try to deceive the system by not maintaining stable fixation and actively scanning the screen for the stimulus. The examination results deteriorated slightly, but not to pathological levels The fixation control, consisting of periodic presentation of a suprathreshold stimulus in the blind spot, did not reliably detect this 'cheating' strategy.

In the aspects studied, the HRP system seems to be adequate for clinical use.

Introduction

In order to increase the sensitivity and minimize the variability of perimetric results, a great number of computerized visual field tests have been developed during the last decade. Yet some variability remains. The variation may be of a psycho-physiological nature, such as short-term fluctuation[1-3]. Learning effects[4] and long-term fluctuation, *i.e.*, variation in measurement over time when the short-term fluctuation has been compensated for[2,5], also influence the examination results. Some patients perform poorly in computerized perimetry[6,7], presumably due to the lack of feedback during the examination, and prefer manual perimetry[8].

The recently developed high-pass resolution perimetry system (HRP) using high-pass spatial stimuli[9,10] was reported to show rather low variability in the examination results[11]. This may be due to the properties of the stimulus and/or the effect of the various feedback devices included in the HRP system. The feedback routine consists of:

1. Acknowledgement of each legal response by presenting a contrasting square at the location of the latest stimulus presented.
2. Possibility to correct erroneous responses.
3. Annoying beeps when illegal responses are given in addition to an error text at the place of the fixation target.
4. Examination pace continuously adapted to the reaction time.
5. Automatic rest after half the examination time.
6. Possibility for the patient to rest at any chosen time.
7. Fixation target adjusted to make fixation easier and stable and to counteract after-image.
8. Suprathreshold 'catch targets' after four non-seen presentations, and
9. Blind spot checks.

The aim of the present study was to evaluate the influence of the feedback devices

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on examination results and to quantify the effects of learning in HRP. In addition, the influence of 'cheating', *i.e.*, unstable fixation, on the examination results was tested.

Subjects and methods

All subjects in the study, six males and 20 females, were healthy volunteers without any history of ocular disease and with a corrected visual acuity of at least 1.05/5.

High-pass resolution perimetry

The high-pass resolution perimetric system used in this study has been described elsewhere[11]. Briefly, the equipment consisted of an IBM AT personal computer with a second graphics card. The stimulus display monitor was a 17-inch Electrohome with 25 kHz horizontal frequency.

Influence of feedback devices

Eleven healthy subjects, aged 22-57 years (mean 35.2, SD 11.6), all of them new to HRP, were enrolled in the study. Two examinations of each subject's right eye were performed, one using the standard HRP program, the other using a modified program with all feedback routines removed. Six subjects started with the standard, five with the modified program. The subjects were instructed in the usual manner to maintain fixation on the fixation mark and press the button whenever a stimulus was perceived. Before the examination, information about the feedback routines was also given. After completion of the two examinations, each subject was asked which type of examination he or she preferred.

Learning effect (long-term fluctuation)

Ten volunteers aged 24-30 years (mean 26.5, SD 2) were recruited, all new to HRP. Six of the subjects were emmetropic, two were myopic (-2 D and -6 D, respectively) and two were hyperopic (+0.50 D and +1 D). The subject with 6 D myopia wore contact lenses.

Six examinations were made on one eye of each subject on days 1, 3, 6, 14, 21 and 44 at approximately the same time of day and under the same conditions. From the printouts of the six separate tests of each subject, the threshold range for each of the 50 tested locations was determined.

Cheating

Five subjects aged 29-48 years (mean 37, SD 7) took part in the study. All of them had knowledge of perimetric principles and were well experienced with HRP. Two examinations were performed on one eye of each subject. Before the first examination, the subject was instructed in the usual manner to keep stable fixation and before the second examination the subject was instructed to try to deceive the system by actively scanning the screen for the stimulus. The fixation control consisted of periodic presentation of a suprathreshold stimulus in the blind spot.

Table 1 Mean resolution threshold, examination and reaction time (mean SD) and subject preference from examinations with and without feedback routines (11 subjects)

	Feedback	No feedback
Mean resolution threshold	3.8 +0 6	3.8 +0.4
Mean examination time	4.9 +0 7	4 5 +0 4
Mean reaction time	0.5 +0.1	0.5 +0.05
Subject preference	11	0

Results

Influence of feedback devices

Table 1 shows mean resolution threshold, examination time and reaction time from examinations with and without feedback. Examination time was slightly longer when feedback was used; otherwise no difference was observed in these parameters.

All 11 subjects reported, when asked immediately after the second examinations, that they preferred to be examined with the feedback devices included in the method.

Learning effect (long-term fluctuation)

Fig. 1 shows mean and SD of mean resolution threshold and form index from the six examinations. Mean resolution threshold improved slightly between examinations 1 and 2 (0.2 dB) and somewhat more (0.6 dB) between examinations 1 and 6. Regarding form index, a small variation within normal limits was observed.

Fig. 2 shows the distribution of variation for the 50 tested locations in the ten normal subjects (in total 500 locations). A variation of up to 3 dB in one single test location occurred in 85% of the tested locations and may not be regarded as pathologic. A 4 or 5 dB variation in one isolated test location was observed in 4.8%. In one eye only was a variation of 4 dB observed in two adjacent locations.

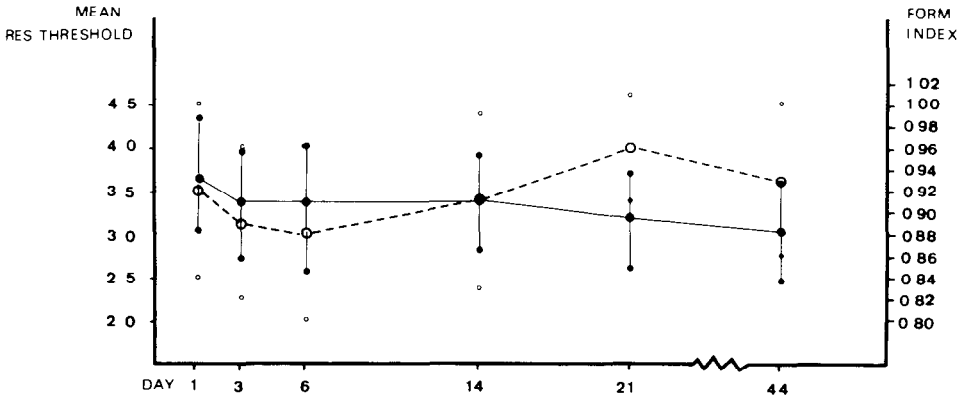

Fig 1 The mean and SD of mean resolution threshold (continuous line) and form index (dotted line) from six examinations of ten subjects.

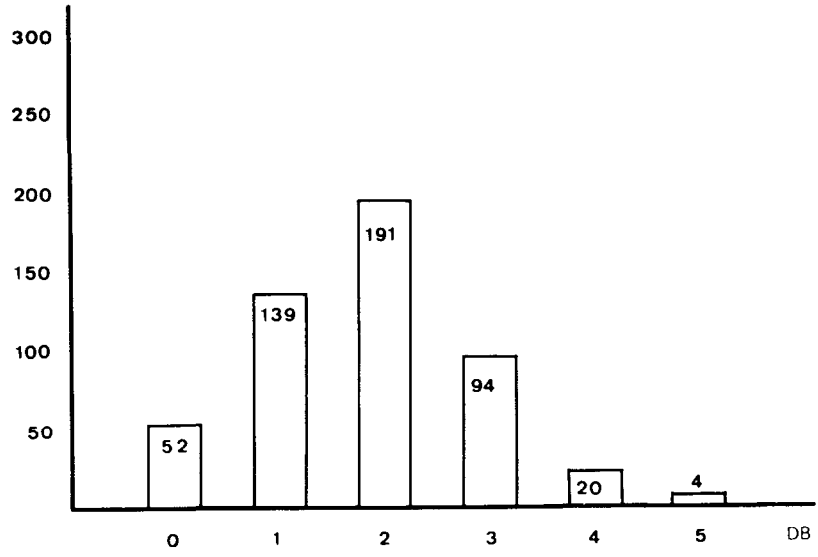

Fig 2 The difference between the highest and lowest threshold measure in each location during the six examinations for the 50 tested locations in the ten normal subjects (= 500 locations)

Fig. 3 shows the distribution in the visual fields of the test locations showing a variation of 4 or 5 dB.

Cheating

Table 2 shows mean resolution threshold from five subjects trying to deceive the system by not maintaining fixation and actively scanning the screen for the stimulus. A slightly higher mean threshold was observed. In the five standard examinations zero to two responses to the seven to 16 blind spot stimulations were observed. During cheating, one to four responses were elicited by the ten to 14 blind spot stimulations. Thus, the fixation control device did not reliably reveal this cheating strategy.

Table 2 The mean resolution threshold (mean SD) from standard examinations with stable fixation and 'cheating' examinations, when the subjects actively scanned the screen for the stimulus

	Standard examination	'Cheating'
Mean resolution threshold	3 24 ±0 15	3.8 ±0 4
Responses/presentations of the blind spot stimulus	0–2 / 7–16	1–4 / 10–14

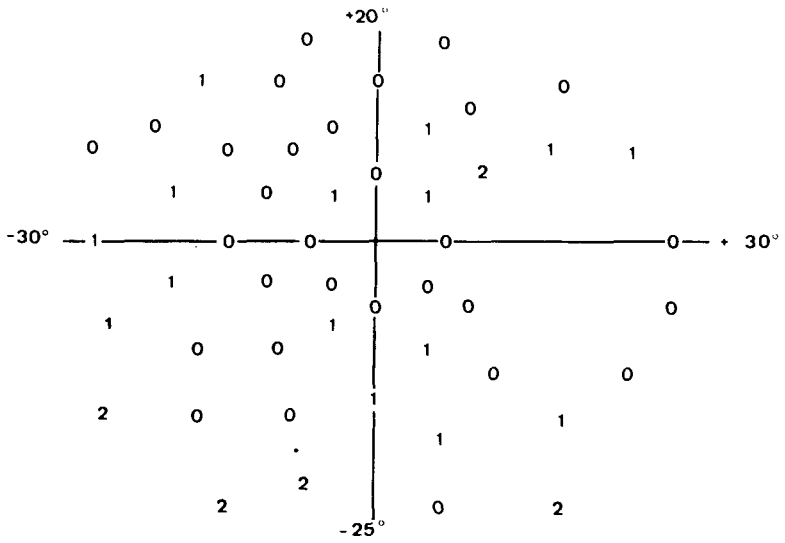

Fig 3 Distribution of test locations showing a variation of 4 or 5 dB during the six consecutive examinations.

Discussion

High-pass resolution perimetry (HRP) has been reported to be of diagnostic value in glaucoma[11] and neurologic disorders[12]. In the current study, the HRP system was evaluated with regard to the influence of the feedback devices, the learning effect and 'cheating', *i.e.*, trying to deceive the system by actively scanning the stimulus screen instead of maintaining steady fixation. All 11 tested subjects preferred the examination which included the feedback devices. No difference in examination results was observed. The effect of learning was very small. The variability of each test location was on average 3 dB and at most 5 dB. The 'cheating' strategy led to a slight deterioration of examination results but not to a pathological level. The fixation control device (suprathreshold stimulation in the blind spot) did not reveal the 'cheating' strategy. The reason for this may be that it was easy for the subjects tested to suppress responses to the blind spot stimulus, especially since they were aware of its function.

In comparison with other instruments (Competer/Digilab 75011, Octopus[1-5,13]), the variability of the HRP system was lower, regarding both the average threshold in the tested field and the thresholds for each location tested. However, the physiologic difference between high-pass resolution and differential light threshold stimuli may make numerical comparisons less relevant.

Removal of the feedback devices did not increase the inter-individual variability. Thus, the stability of the examination results may be related to the stimulation (spatially high-pass filtered ring-shaped optotypes). The short examination time presumably also contributes to this stability.

The HRP system seems to be tolerant for confounding factors related to the examination procedure, yet sensitive for optic nerve damage, and thus suitable for clinical use.

Acknowledgements

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PERIPHERAL DISPLACEMENT THRESHOLDS IN GLAUCOMA AND OCULAR HYPERTENSION

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Abstract

Peripheral displacement thresholds were found to be abnormally elevated in ocular hypertension and glaucoma. This psychophysical measurement of movement sensitivity may provide earlier indications of loss of visual function than conventional perimetry since it may be primarily mediated by large diameter nerve fibers. Sensitivity is little affected by refractive error, pupil size, or neutral density filters. There was little difference between the effects of timolol or pilocarpine on this measure of visual function over the course of a year

Introduction

At the previous IPS meeting we showed that peripheral displacement thresholds (PDT) can be abnormal in glaucoma and ocular hypertension even when Humphrey computer visual fields show normal sensitivity[1]. PDT can be considered a hyperacuity measurement of movement sensitivity. Quigley *et al.'s*[2] recent demonstration that the larger diameter optic nerve fibers are selectively damaged in human glaucoma suggests a mechanism for this abnormal motion sensitivity. We have investigated the use of PDT as a routine diagnostic procedure in a prospective study with over 70 patients followed for more than a year who were randomly allocated to treatment either with timolol or pilocarpine. We found PDT to be robustly immune to pupil size, refractive error, and other factors. There was no significant difference between timolol or pilocarpine in visual function measured by PDT over the course of one year.

Methods

Peripheral displacement thresholds were measured for a 2 minute by 2 degree vertical line generated by computer on a green phosphor video display viewed at 1.24 meters. The stimulus luminance was 7 Cd/sq m and the background (which subtended 8 x 10 degrees) was 27 Cd/sq m. The stimulus was presented at 15 degrees temporal field on the 30 or 330 degree meridian and would move from side to side for a two-second period at the rate of 2.5 Hz at 10 magnitudes of displacement from 0 to 18 minutes of arc where each was presented ten times. The subject was instructed to respond if movement was seen and the fraction of yes responses was recorded. The results were fit by probit analysis and the 50% point used as threshold.

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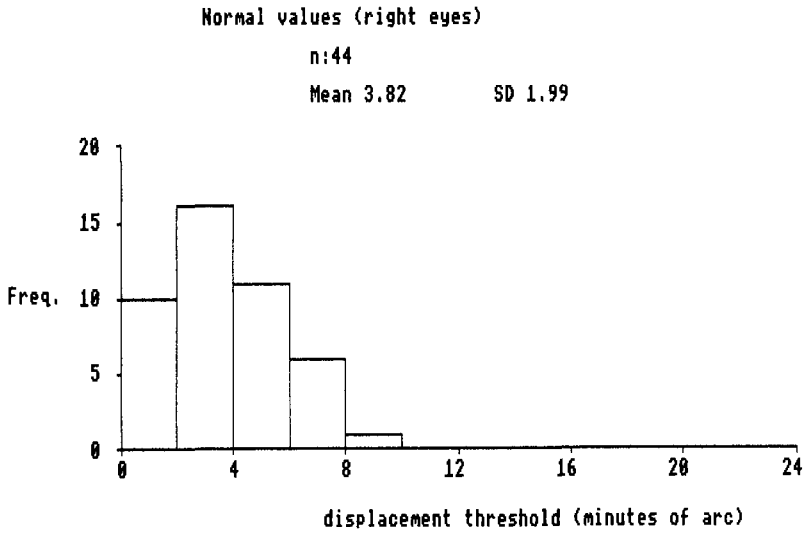

Fig 1 Histogram summary of results of normal PDT for these conditions.

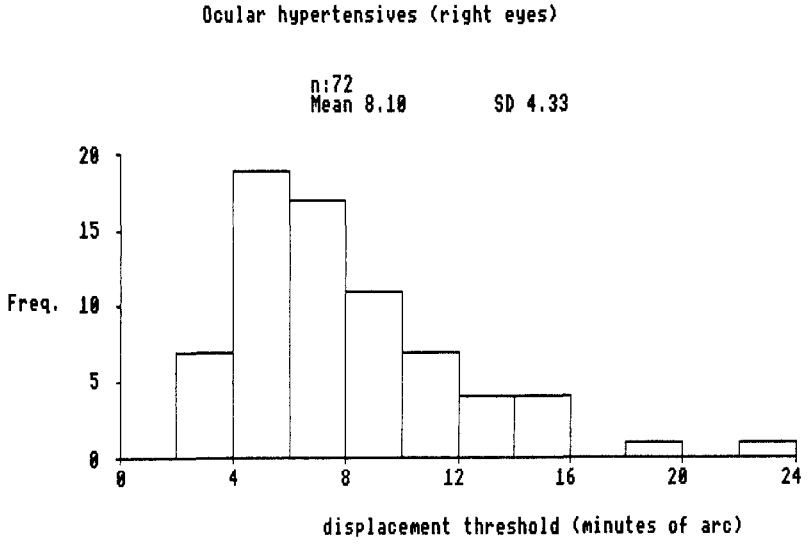

Fig 2 Histogram summary of results for ocular hypertensives.

Results

Fig. 1 shows the results in these conditions in 44 right eyes of normal subjects. These were chosen largely from the spouses of patients and the mean age was 54.1 years with a standard deviation of 13.6. The mean value for the peripheral displacement threshold was 3.82 minutes of arc with a standard deviation of 1.99.

The ocular hypertensive group had a mean age of 58.4 with a standard deviation

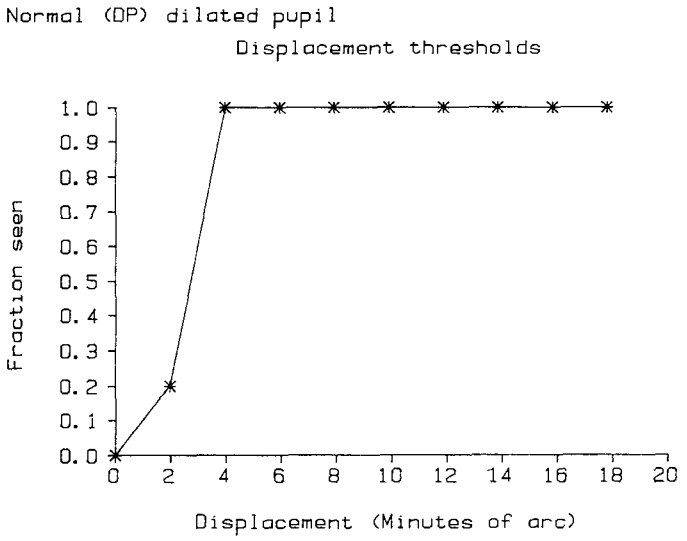

Fig 3 Example of a measurement of peripheral displacement thresholds in a normal with a dilated pupil.

of 12.2 years. One-way analysis of variance showed no significant age difference at the 0.05 level.

In the OH group, the mean PDT was 8.10 minutes of arc with a standard deviation of 4.33. The Newman-Keuls test showed the OH group to be significantly different from the normal at more than the 0.01 level. (Minimum significant difference for $p = 0.01$ is 1.82 while the difference between the means is 4.28.)

To prepare the use of PDT as a routine diagnostic procedure, we investigated how such factors as pupil size, refractive error, or optical media density changes may affect PDT.

Effect of pupil size

The pupil of a normal subject whose PDT was 2.8 minutes of arc was dilated with 1% cyclopentolate to 8 mm and the measurements repeated as shown in Fig. 3, resulting in a PDT of 2.7 minutes of arc. When the measurements were repeated with a 2 mm artificial pupil (Fig. 4), the PDT was 3.0 minutes of arc. In summary, the effects of pupil diameter are seen to be insignificant.

Effect of neutral density filters

The measurements were repeated with the 2 mm artificial pupil and the addition of a 1.0 log unit neutral density filter (NDF) to approximate the effects of an optical media opacity as shown in Fig. 5. The PDT was 4.2 minutes of arc. Even for a 3.0 log unit NDF, the PDT was 4.5 minutes of arc. This range was within the range of the 95% confidence interval of 1.9.

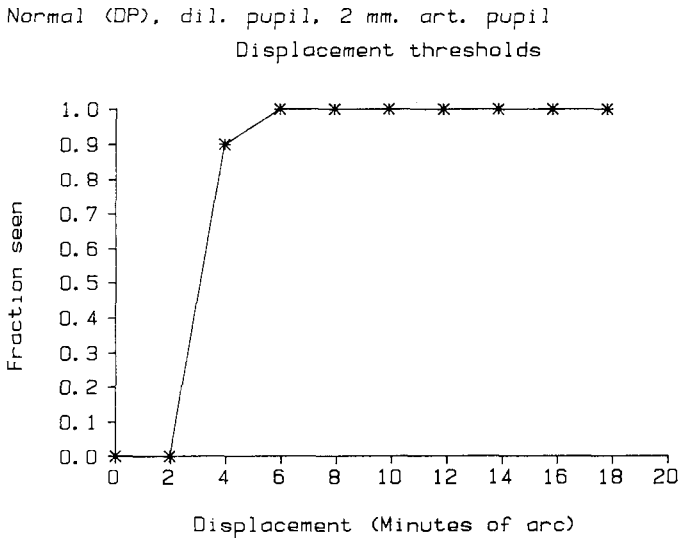

Fig 4. Repeat measurements of Fig. 3. with a dilated pupil and a 2 mm artficial pupil.

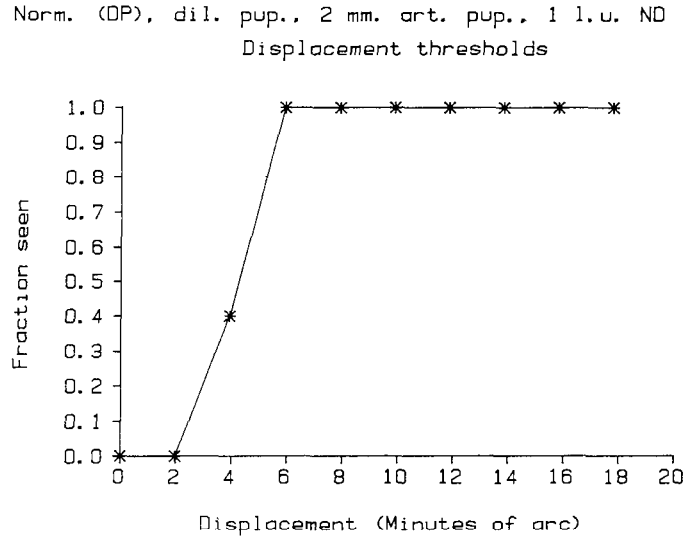

Fig 5 Repeat measurements with a dilated pupil, a 2 mm artificial pupil, and with additional 1 log unit neutral density filter

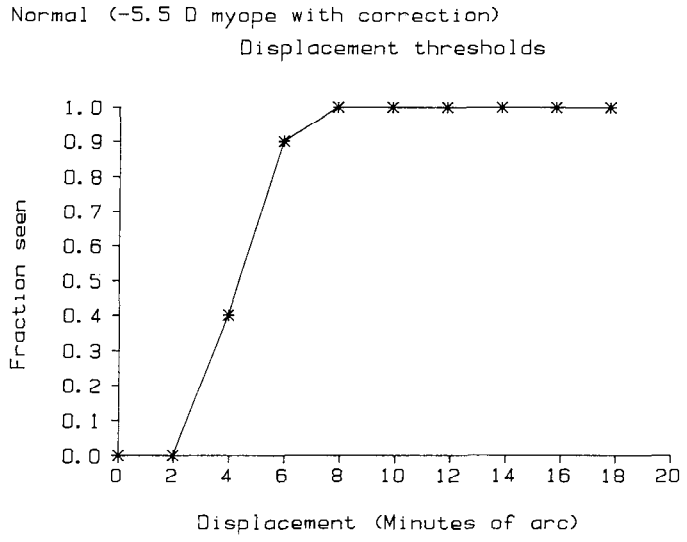

Fig 6 PDT measurements in a normal myope with correction.

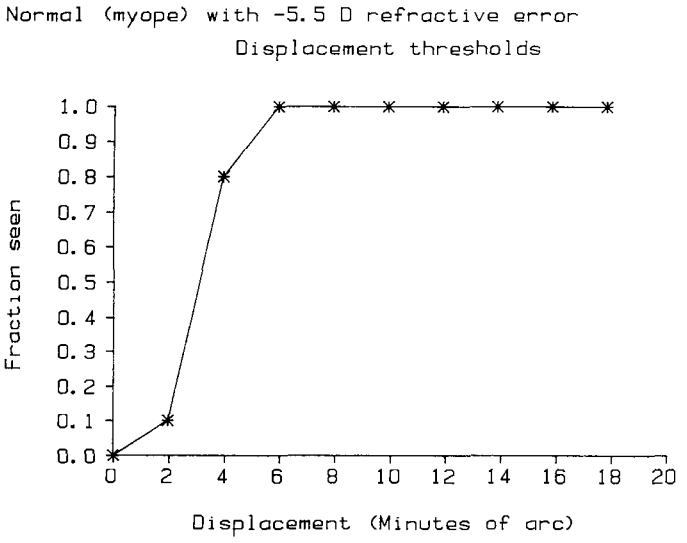

Fig 7. Measurements of PDT in the same myope without correction

Effect of refractive error

The effects of moderate refractive error were also investigated. Measurements of PDT in a normal myope of -5.5 diopters were made with and without correction. Fig. 6 shows the results with correction where the PDT was 4.2 minutes of arc.

Fig. 7 shows the results made without wearing the correction. In this case the PDT was 3.2 minutes of arc, or slightly better.

Discussion

These results show that PDT are relatively unaffected by such factors as pupil size, neutral density changes mimicking optical media opacities, and refractive error, similar to other hyperacuity measures[3,4]. PDT therefore allows a measurement of visual function, relatively immune from artefact, which can detect abnormal function before conventional visual fields. The basis for this may be related to the different ganglion cell types which process visual information in the retina.

In the primate visual system there are different neuron types which have been subdivided into the magnocellular and parvocellular systems. These receive inputs from two major classes of ganglion cells where the magnocellular system receives input from the A cells which have the coarsest axons of any ganglion cell type[5].

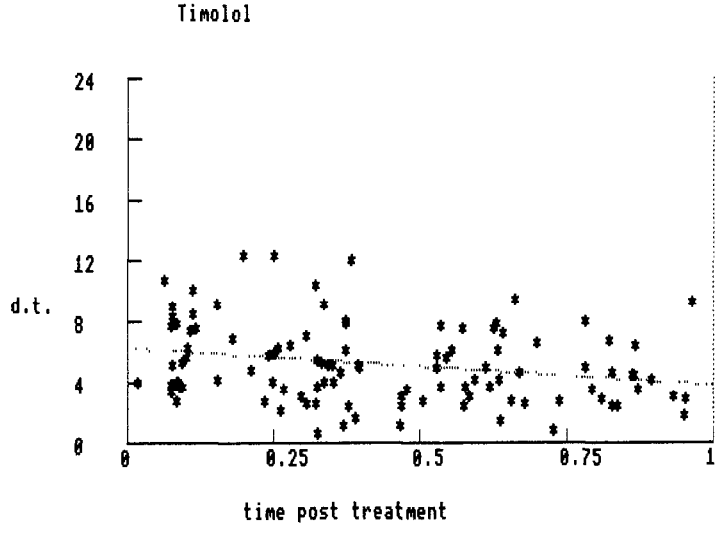

Fig 8a PDT measured over a year in a group of OH treated with timolol

The magnocellular system is thought to be highly sensitive to movement[6]. Therefore larger diameter ganglion cell axons would be expected to subserve movement information. Since the larger diameter optic nerve fibers have been shown to be selectively lost in glaucoma[2], we would expect movement detection to be preferentially affected. Therefore, we emphasize the potential of movement thresholds in investigating these diseases.

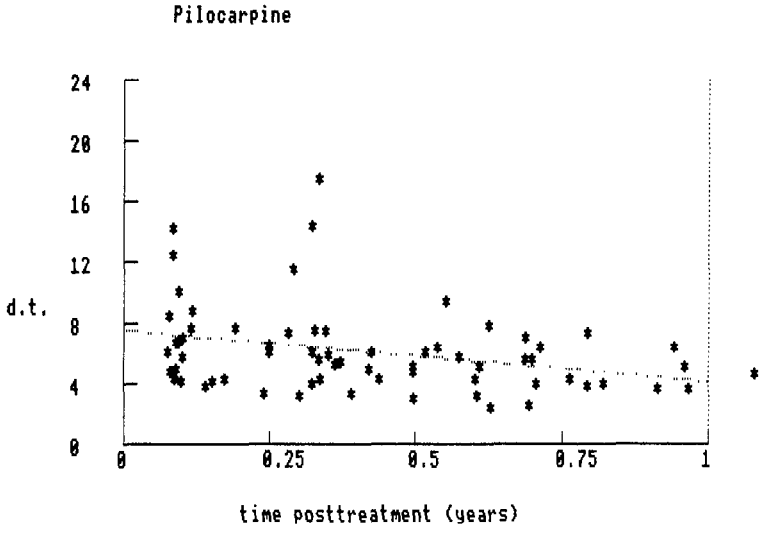

Fig 8b Same for a group treated with pilocarpine.

Comparison of the effects of timolol and pilocarpine

A group of ocular hypertensives were randomly allocated to treatment with either timolol or pilocarpine and investigated over the course of one year at approximately three-month intervals. Both groups showed a small improvement in PDT (Fig. 8a and 8b, slope -2.4 and -3.3, respectively) which may be attributable to learning effects. There was little difference attributable to timolol or pilocarpine in the visual function between the two groups over a one-year period. We plan to continue to follow the visual function of these groups and extend these measurements throughout the visual field in order to be able to detect local areas of abnormality which may correspond to suspicious areas of nerve fiber layer photographs.

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MISCELLANEOUS

PERIPHERAL VS. CENTRAL CONFIRMATORY TESTING

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Additional visual field testing is often required to confirm defects found on central threshold testing We tested 97 patients with a Humphrey 30-2 threshold test in both eyes, using a peripheral screening 68 point test in one randomly assigned eye and a 24-2 threshold test in the other eye as additional tests Criteria were assigned for ten visual field defect types according to two levels of diagnostic confidence and each field chart was graded independently

The 30-2 test revealed a defect in one eye in 80% which was generally confirmed by the Peripheral 68 test 61% of the time. In the other eye, with additional testing by the 24-2 test, the percentages were respectively 89% and 77%. All visual field defect types except focal peripheral depression, generalized nasal depression, hemianopia, and residual island of vision were confirmed more often by repeat central threshold testing (24-2) than by the Peripheral 68 test It is recommended that the choice of peripheral vs. central confirmatory testing should be made on an individual basis after the 30-2 test results have been obtained.

Introduction

A single static threshold visual field test confined to the central 30 degrees may show abnormalities which are not sufficiently pathognomonic to allow a visual field diagnosis to be made with any certainty. Additional visual field testing may need to be done to determine if the abnormality is reproducible, to discover if it extends into areas of the field not tested initially, or to investigate the alignment of the defect along the vertical or horizontal meridian. Two popular options for additional testing are simply to repeat the central field test, perhaps on a more limited scale, or to test the field peripheral to 30 degrees. This study was done to discover which of these two options offers the greatest degree of confirmation of a visual field diagnosis made tentatively on the basis of the result of the initial test.

Material and methods

Ninety-seven patients referred to the visual field service were tested with a Humphrey Field Analyzer using programs 30–2 (central 30 degree threshold grid test with 6 degree spacing between points), 24–2 (omitting the outer ring of test locations except the two nasal ones from the 30–2 pattern) and Peripheral–68 (threshold-related, eccentricity-compensated suprathreshold screening from 30 to 60 degrees eccentricity with 12 degree grid spacing)[1]. On even numbered dates, patients received a 30–2 test followed immediately by a 24–2 test on the right eye, then a 30–2 test followed by a Peripheral–68 test on the left eye. On odd numbered dates, the right eye received a 30–2 test followed immediately by a Peripheral-68 test on the right eye, then a 30–2 test followed by a 24–2 test on the left eye. Fifty-seven of the patients had previous automated perimetry experience. The remainder received a brief preliminary test, the results of which were discarded, prior to beginning the initial 30–2 test on the right eye.

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Table 1. Criteria for grading field defects

	30-2 Test		*24-2 Test*		*Peripheral-68 test*	
	Probable (grade 2)	*Possible (grade 1)*	*Probable (grade 2)*	*Possible (grade 1)*	*Probable (grade 2)*	*Possible (grade 1)*
Generalized depression	*Mean defect and foveal sensitivity both significant* at the 1% level	at the 5% level	*Mean defect and extrapolated foveal threshold both significant* at the 1% level	at the 5% level	*26 dB central reference level (default) and/or 2/3 of the test points missed* both criteria present	only one present
Overall peripheral depression	*In the outer two rows (44 test points of the pattern deviation plot three or more points in three or more quadrants significant* at the 1% level	at the 5% level	*In the outer two rows (34 test points) of the pattern deviation plot three or more points in three or more quadrants significant* at the 1% level	at the 5% level	*Of the points in each of three out of four quadrants* 2/3 points missed	1/3 points missed
Focal peripheral depression	*In the outer two rows of the pattern deviation plot in two* or fewer *quadrants significance reached by* >5 adjacent points at 1% >3 adjacent points at 5%		*In the outer two rows of the pattern deviation plot in two* or fewer *quadrants significance reached by* >5 adjacent points at 1% >3 adjacent points at 5%		*In only one or two quadrants were there* 2/3 points missed	1/3 points missed
Nasal depression	*Considering the ten peripheral nasal (PN) and temporal (P) points on the pattern deviation plot significant PN minus significant PT points* >2 at the 1% level	>2 at the 5% level	*Considering the 12 peripheral nasal (PN) and temporal (PT) points on the pattern deviation plot significant PN minus significant PT points* >2 at the 1% level	>2 at the 5% level	*Considering the 12 peripheral nasal (PN) and temporal (PT) points, missed PN minus missed PT points is greater than* seven points missed	three points missed
Nasal step	*Consider points corresponding to others on the opposite side of the horizontal meridian* more than one point at least 6 dB less sensitive	one point at least 6 dB less sensitive, or more than one point >2 dB less sensitive	*Consider points corresponding to others on the opposite site of the horizontal meridian* more than one point at least 6 dB less sensitive	one point at least 6 dB less sensitive, or more than one point >2 dB less sensitive	*Subtract the number of missed points on one side of the horizontal meridian from those on the other side* two or more points	one point

Table 1. Cont.

	30-2 Test		*24-2 Test*		*Peripheral-68 test*	
	Probable (grade 2)	*Possible (grade 1)*	*Probable (grade 2)*	*Possible (grade 1)*	*Probable (grade 2)*	*Possible (grade 1)*
Hemianopic step	*Consider three or more adjacent points corresponding to others on the opposite side of the vertical meridian* each at least 6 dB less sensitive	each at least 3 dB less sensitive	*Consider three or more adjacent points corresponding to others on the opposite side of the vertical meridian* each at least 6 dB less sensitive	each at least 3 dB less sensitive	*Subtract the number of missed points on one side of the vertical meridian from those on the other side* two or more points	one point
Remaining island of vision	*Any cluster of adjacent seeing points surrounded by 0 dB* more than two points	only one or two points	*Any cluster of adjacent seeing points surrounded by 0 dB* more than two points	only one or two points	*Any cluster of adjacent seeing points* more than two points	only one or two points
Arcuate scotoma	*Depression of adjacent points contiguous with and above or below the physiologic blind spot with sparing of points central to them (total deviation plot)* six or more at 1% level	four or more at 5% level	*Depression of adjacent points contiguous with and above or below the physiologic blind spot with sparing of points central to them (total deviation plot)* six or more at 1% level	four or more at 5% level	*Cannot be confirmed by peripheral test*	
Central scotoma	*Depression of foveal sensitivity and at least one parafoveal point (total deviation plot)* to the 1% level	to the 5% level	*Depression of foveal sensitivity and at least one parafoveal point (total deviation plot)* to the 1% level	to the 5% level	*Cannot be confirmed by peripheral test*	
Isolated paracentral	*Two or more adjacent depression paracentral points surrounded by norm. points (pattern deviation plot)* to the 1% level	to the 5% level	*Two or more adjacent depressed paracentral points surrounded by norm. points (pattern deviation plot)* to the 1% level	to the 5% level	*Cannot be confirmed by peripheral test*	

Visual field charts were printed using the single field analysis option of the Statpac™ statistical analysis package. Criteria for diagnosis of ten types of visual field defect were developed (Table 1). We tried to assign sufficiently rigorous standards for probable (Grade 2) defects so that only those which would present no difficulty in interpretation to the practitioner would be so assigned. On the other hand, the standards for possible (Grade 1) defects were relaxed so that fields with questionable abnormalities would be included. Only those which clearly showed no defect of the type were assigned Grade 0. The criteria were designed arbitrarily on the basis of prior clinical experience and modified as necessary to avoid assignment of excessive numbers of fields into abnormal diagnostic categories. To avoid errors in scoring, each author independently graded each field; discrepancies were identified and corrected according to the criteria. An individual field could receive Grade 1 or 2 scores in more than one type of defect; the categories were not intended to be exclusionary.

No attempt was made to determine whether the visual field was normal or abnormal by reference to a previous field or other clinical data, only whether any defects found by the 30–2 test were confirmed by the second test. Similarly, when the initial test showed no defect of a given type (Grade 0), no analysis was done to determine if the second test confirmed the absence of a defect, since neither second test was as thorough as the 30–2 test.

Subjective analysis was performed as a way of comparing the overall clinical impression of the field charts. First, the defects present on the 30–2 test were listed. Then the companion test, either Peripheral 68 or 24–2, was reviewed to see if defects confirming the 30–2 result were present. Lack of confirmation was scored if the companion test showed no defects, or if the defects were not consonant with those on the 20–2 test.

Despite the fact that Statpac™ normative data is based on reliable subjects, we included patients with false negatives and fixation losses over 33% as long as they could complete the testing sequence satisfactorily. In this situation, Statpac™ was not being used to indicate normality or abnormality, where inclusion of unreliable patients invalidates the statistical analysis. The effect of poor reliability applied equally to both 24–2 and Peripheral 68 tests, which were being compared. Only patients with false positive responses over 33% on any of the tests were excluded.

Results

The ages of the 97 study patients ranged from 26 to 94, with a mean of 58; there were 56 men and 41 women. The indication for visual field testing was glaucoma or suspect glaucoma in 78%, the remainder of the patients had neurologic or retinal disease (Table 2). Ninety-two patients successfully completed the protocol; five were withdrawn from the study due to fatigue during testing, inability to perform the tests properly, or inadequate clinical data.

Among the 92 eyes receiving the 30–2 and Peripheral 68 tests, 74 (80%) showed a probable or possible defect (Table 3). The Peripheral 68 test showed defects consonant with those on the 30–2 test in 45 of those 74 cases (61%). In four instances (5%), the peripheral result caused the initial diagnostic impression based on the 30-2 test to be changed. The remaining 26 eyes (34%) showed no confirmation of the 30-2 by the Peripheral 68 test.

Among the 92 fellow eyes receiving the 30–2 and 24–2 tests, 82 (89%) showed a field defect. The 24–2 test showed defects consonant with those on the 30–2 test in 63/82 (77%), defects which caused the provisional diagnosis to be altered in two eyes (2%), and no confirmation in 17 eyes (21%).

Analysis of confirmation rates for each of the ten types of visual field defect was

Table 2 Indication for visual field testing

Glaucoma	33	(34%)
COAG	25	
Pigmentary	4	
Low tension	4	
Glaucoma suspect	43	(44%)
IOP over 21	26	
Suspicious discs	17	
Neurologic disease	16	(17%)
Optic neuropathy	7	
Stroke	5	
Chiasm pathology	3	
Amblyopia	1	
Retinal disease	5	(5%)

Table 3 Confirmation of 30-2 test result by Peripheral 68 or 24-2 test

Test run	One eye 30-2 and P-68	Other eye 30-2 and 24-4
No VF defect	18/92 (20%)	10/92 (11%)
VF defect	74/92 (80%)	82/92 (89%)
Confirmed	45/74 (61%)	63/82 (77%)
Redefined	4/74 (5%)	2/82 (2%)
Not confirmed	26/74 (34%)	17/82 (21%)

performed using the scores from each field (criteria listed in Table 1). The rate at which probable defects (Grade 2) on the 30–2 test were confirmed at either grade level on the Peripheral 68 or 24–2 test was determined first. While the numbers of each defect are small (Fig. 1), the 24–2 test had superior confirmation rates for generalized depression, overall peripheral depression, and nasal step. In addition, the 24–2 test was able to confirm arcuate, central, and isolated paracentral scotomas, which the Peripheral 68 could not because it did not test centrally. The Peripheral 68 had better confirmation rates for focal peripheral depression, nasal depression, hemianopic step, and remaining island of vision.

The rate at which either probable or possible defects (Grade 1 or 2) on the 30–2 test were confirmed at either grade level on the companion test was also calculated. The 24–2 test was superior to the Peripheral-68 test in confirming generalized depression, overall peripheral depression, and nasal step defects. As previously mentioned, arcuate, central, and isolated paracentral scotomas can be confirmed only by the 24–2 test. The Peripheral-68 had higher confirmation rates for focal peripheral depression, nasal depression, hemianopic steps, and the few cases of remaining island of vision.

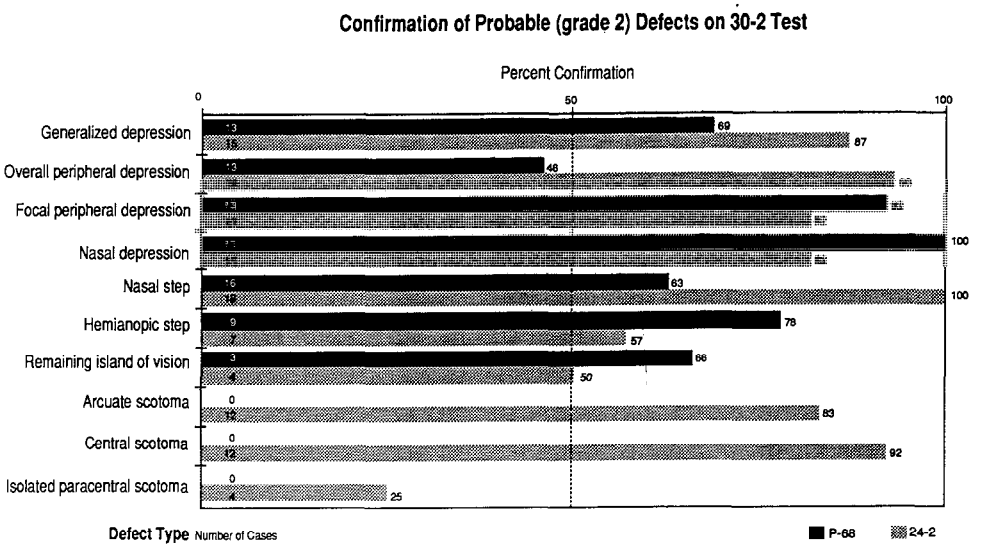

Fig 1 Percent confirmation of probable (Grade 2) defects on 30-1 test by Peripheral-68 test (hatched bars) and 24-2 test (dotted bars) The number at the base of each bar indicates the number of 30-1 field charts which contained a field defect of that type.

Discussion

The subjective analysis of the field charts to obtain an overall clinical impression showed that the 24–2 had defects consonant with the 30–2 test in 77% of the eyes with defects, while the Peripheral–68 showed consonant defects only in 61%. Subjective analysis is fraught with potential for bias, but there was no objective way to evaluate overall confirmation ability. The single field analysis printouts for the 30–2 and 24–2 tests look quite similar, while the Peripheral–68 printout has no gray scale but only a notation of seen and missed points. This fact, together with the inability of a peripheral test to confirm strictly central defects, could easily explain the different overall subjective confirmation rates.

Mills found confirmation of defects found in a central suprathreshold screening test by peripheral suprathreshold testing in 62% of cases[2]. Stewart *et al.* found that supplementation of a central suprathreshold test with kinetic peripheral testing provided subjective confirmation of a central defect in 43% of eyes[3]. Their kinetic isopter tested only the far periphery, and might have missed confirming defects in the mid-periphery, accounting for a lower confirmation rate than in the peripheral suprathreshold studies.

Confirmation rates were also determined using grading criteria for ten types of field defect. While the criteria were arbitrary and not intended to be a standard for use in other clinical circumstances, they did allow a more objective analysis of the relative performance of the 24–2 and Peripheral-68 tests in confirming 30–2 results.

First considering only probable (Grade 2) defects on the 30–2 tests, confirmation rates were determined. While the clinician is less likely to require confirmation of a probable defect than a possible defect, a second field should be able to confirm the probable defect a large percentage of the time. Either the 24–2 or the Peripheral-68 did so at least 78% of the time in 8/10 defect types. Lower rates were observed in the few patients with isolated paracentral scotomas and remaining islands of vision.

The real clinical usefulness of a second test is to obtain confirmation of *possible*

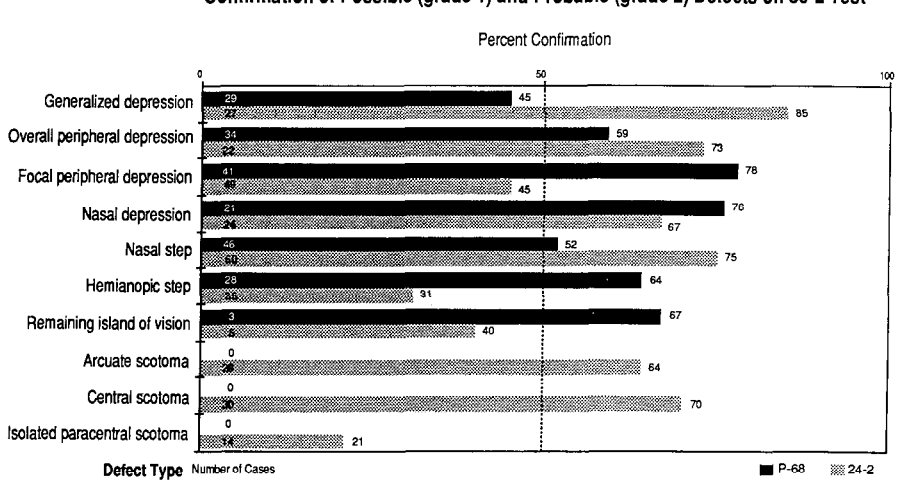

Fig 2. Percent confirmation of possible and probable (Grades 1 and 2) defects on 30-1 test by Peripheral-68 test (hatched bars) and 24-2 test (dotted bars) The number at the base of each bar indicates the number of 30-1 field charts which contained a field defect of that type

field defects appearing on the initial 30–2 test. Consequently, confirmation rates of all defects (Grades 1 and 2) were calculated. As expected, the numbers of cases of each defect type are larger, and rates are somewhat lower than for probable defect alone. However, the same relative performance of the 24–2 and Peripheral 68 tests for each of the ten defect types was observed as during analysis of probable defects alone.

The 24–2 test performed better than the Peripheral–68 in confirming generalized depression, probably because foveal threshold extrapolated from the 'primary points' is more accurate using paracentral rather than peripheral threshold determinations. The higher confirmation rate of the central 24–2 test on fields with overall peripheral depression is somewhat more surprising. The problem may be semantic, since the 'peripheral depression' referred to on the 30–2 test affects the region peripheral to 20 degrees but inside 30 degrees eccentricity, while the Peripheral–68 tests only outside that area. The 24–2 test was also superior in confirming nasal steps, apparently because most of them extended sufficiently central to be detected as a threshold step. Most of the Peripheral–68 tests which failed to confirm a nasal step had missed suprathreshold points on both sides of the nasal horizontal meridian.

As expected, the Peripheral–68 test was superior in confirming focal peripheral depressions and nasal depressions which on the printout could be seen to extend into the periphery from the limit of central testing. On the 24–2 test, the elimination of the outer ring of test points often made the defect undiscoverable. The clear superiority of the Peripheral-68 test in confirming hemianopias is more difficult to explain. We were surprised at the frequency of hemianopic steps fulfilling the criterion of three adjacent points at least 3 dB less sensitive than corresponding points on the opposite side of the vertical meridian. In all but eight of the patients, there was no clinical reason to suspect chiasmal or posterior visual pathway involvement. However, the Peripheral -68 tended to confirm these steps more often than the 24-2 test. In this situation, the 'better' confirmation rate actually may be

clinically disadvantageous.

The centrally located defects (arcuate, central, and isolated paracentral scotomas) were confirmed only by the 24–2 central test. Why so few of the 14 paracentral scotomas were confirmed is not clear. The confirmation rates for the two tests were not compared statistically because it was difficult to select a test with sufficient power to be applicable to the circumstance in which a 30–2 and a Peripheral–68 were run on one eye, and a 30–2 and a 24–2 on the fellow eye (not the same eye).

It is important to note that this study did not address the issue of the usefulness of peripheral testing in various clinical circumstances. For example, peripheral testing might have uncovered scotomas which were missed on central testing. Those events would have been ignored by the analysis used in this study, since only eyes with central field defects were considered. Consideration of eyes with normal 30–2 tests would have required a reference (gold standard) against which to validate abnormalities found on the confirmatory tests.

Nor does it address the issue of whether a confirmation by a second test run in the same test session is a definite indication of abnormality. Recent evidence indicates that normal fields may have clusters of depressed points[4] and that these 'abnormalities' in normal fields can be found on a second test from the same test session[5].

The results of this study indicate that the 24–2 on average may be a better second test to run than the Peripheral-68 to confirm 30–2 results, even though it takes nearly twice as long to perform. However, it would be more sensible to choose the confirmatory test based on the type of defect discovered on the 30–2 test. In this study, for focal peripheral depression, nasal depression, and remaining island of vision, the Peripheral-68 would be a good choice. However, for generalized depression, overall depression of the periphery of the central test, nasal step, and arcuate, central, and paracentral scotomas, the 24–2 was a better confirmatory test.

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AUTOMATED STATIC PERIMETRY IN CHLOROQUINE AND HYDROXYCHLOROQUINE THERAPY

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We examined retrospectively the charts and visual field examinations of 135 patients followed approximately every six months while on chloroquine or hydroxychloroquine therapy for rheumatoid arthritis or systemic lupus erythematosus The purpose of this study was to determine whether there were any trends in the behavior of the visual fields of the group as a whole as measured by automated static perimetry

At each visit the visual field was tested using Octopus program 11 The drug taken, its average daily dose, the total duration of therapy and the cumulative dose at the time of the visit, were determined There were 666 examinations (left and right eyes inclusive) of patients on chloroquine and 186 examinations of patients on hydroxychloroquine Of these, 494 and 164 examinations, respectively, had complete drug information available

Indices were calculated for each examination and were correlated with drug type, average daily dose and cumulative dose No significant correlation existed between mean sensitivity, mean defect, corrected loss variance or short-term fluctuation and the drug type, average daily dose or cumulative dose for either chloroquine or hydroxychloroquine

Introduction

The antimalarials chloroquine and hydroxychloroquine have been used in the treatment of rheumatoid arthritis and systemic lupus erythematosus since the early 1950s. Ophthalmologic manifestations of these drugs have been described since the late 1950s. Some, such as corneal deposits, have proven to be reversible and are not felt to be of major significance[1,2]. However, a typical pattern of retinal toxicity associated with antimalarial therapy has been much more worrisome and has received substantial attention in the literature. There have been several reviews which provide a useful perspective on the population at risk for retinal toxicity[1-3]. Factors which have been implicated in the development of this toxicity are: specific drug taken, duration of therapy, daily dose, cumulative dose of drug taken and age of the patient. A consensus seems to be emerging that there is a maximum daily dose for each drug, expressed in mg/kg lean body weight/day, which, if respected, minimizes the potential for development of retinal toxicity[2-5]. Mackenzie[4] suggested guidelines of up to 3.5-4.0 mg/kg/day of chloroquine and up to 6.0-6.5 mg/kg/day of hydroxychloroquine. These roughly correlate, for a person of 60 kg lean body weight, to dosages of 250 mg/day or 400 mg/day of chloroquine or hydroxychloroquine, respectively.

A number of studies attempted to identify a sensitive method of detecting the earliest stages of retinal toxicity[6-10]. In most reports populations of patients on antimalarial therapy were studied to identify those patients who showed evidence of retinal toxicity (either on ophthalmoscopy or on testing of retinal function). Attempts were then made to define the characteristics of those who developed toxicity. Tests of retinal threshold sensitivity in patients with toxicity often showed disturbances in the central and pericentral areas.

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There has been relatively little investigative effort to date to detect and define signs of decline in retinal function as defined by repeated quantitative testing in large groups of patients on chloroquine or hydroxychloroquine therapy. Current theories of pathophysiology of the retinal damage suggest a gradual toxic effect on the retinal pigment epithelial cells and photoreceptors[1], thus it might be expected that sufficiently sensitive methods of quantitative threshold testing in the foveal and parafoveal regions might reveal a subtle yet measurable change in retinal sensitivity in all patients on therapy. Consistent with this, Carr[6] showed that there was a close relationship between the total dose of chloroquine and retinal thresholds for red light, after dark adaptation, at the fovea and 5 degrees from the fovea. Friedmann[11] reported reversible increases in threshold to white and red test targets which were related to cumulative dose of chloroquine. These changes were found in the absence of observable macular changes.

The development of visual field indices as applied to automated static perimetry data has provided quantitative descriptions of threshold retinal sensitivities and thus allowed detailed quantitative comparison of the behavior of the visual field over time[12]. Although the visual field indices were developed in order to aid in the detection and follow-up of glaucomatous change, they may also prove to be of value in detecting and following other conditions which gradually show progressive visual field changes.

The purpose of this study is to:

1. determine whether there are measurable changes in central and pericentral retinal threshold sensitivities to white light in patients on chloroquine or hydroxychloroquine therapy; and
2. to delineate any correlation to drug type, cumulative dose or average daily dose.

Methods

We examined retrospectively the complete visual field records of a series of patients referred to the Nova Scotia Eye Centre for ophthalmologic assessment related to chloroquine or hydroxychloroquine therapy. Our practice has been to carry out a complete ophthalmologic examination on such patients before the start of therapy, and then follow-up examinations at approximately six-month intervals thereafter. One hundred and thirty-five patients were selected who had had a baseline visual field examination using Program 11 on the Octopus 201 perimeter and at least one repeat examination centered on the fovea, in which sensitivity is measured three times at each point (Fig. 1). There were 666 and 186 visual field examinations of patients on chloroquine and hydroxychloroquine, respectively. The visual field examination raw data was first transferred to a microcomputer using the Octosoft software package, and then to a mainframe computer for further analysis. The visual field indices mean sensitivity (MS), mean defect (MD), short-term fluctuation (SF), and corrected loss variance (CLV) were calculated for each visual field examination using formulae published by Flammer[12].

Clinic charts of these patients were reviewed, and for the date of each visual field examination an attempt was made to identify the specific drug taken, its daily dose, the total duration of therapy and cumulative dose to date. The average daily dose of the drug was then calculated by dividing the cumulative dose by the duration of therapy.

This drug information was paired with the visual field data. After excluding examinations for which complete drug data were not available, there were 494 and 164 examinations of patients on chloroquine and hydroxychloroquine, respectively. Each patient's first examination was his or her baseline for statistical comparison. Subsequent visual field examinations were then grouped for analysis according to

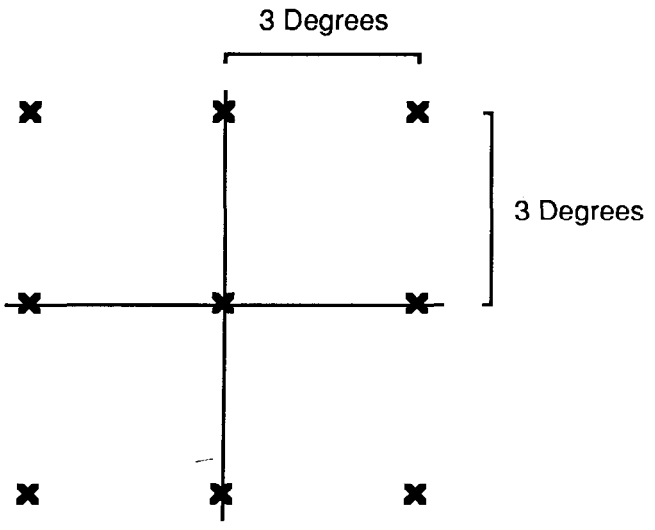

Fig 1 Program 11 Nine point grid with three determinations at each point

drug taken and cumulative dose to date. In order to examine the effect of average daily dose, these groups were then also further subdivided (Table 1). Statistical analysis was performed using the SPSS/X software package.

Results

The mean and standard deviations of each of the visual field indices for each drug and cumulative dose group are presented in Table 2. For each index both paired *t*-tests and Wilcoxon paired rank tests were used to compare the examinations in each group with their own baseline examinations. The level of significance used throughout was 1% (*i e.*, alpha = 0.01).

There was, in general, excellent agreement of results of parametric and non-parametric tests. Mean sensitivity (MS) and mean defect (MD) were the only indices which showed any significant comparisons. When compared to baseline, cumulative dose groups 1, 3 and 4 in the chloroquine group showed significant improvement in mean defect (*i.e.*, the mean defect became less positive), and similarly cumulative dose groups 1 and 3 showed significant improvement in mean sensitivity. It would appear that most of this represents a learning effect from the first examination to the subsequent ones. When the analysis was repeated using each patient's second examination as baseline, only the mean defect of cumulative

Table 1 Grouping criteria

Drug groups	Cumulative dose	Average daily dose groups
1 Chloroquine	1 1– 99 g	1 ≤250 mg/day chloroquine or
2. Hydroxychloroquine	2. 100–199 g	≤400 mg/day hydroxychloroquine
	3 200–299 g	2. >250 mg/day chloroquine or
	4. 300–599 g	>400 mg/day hydroxychloroquine

Table 2 Visual field indices (mean ± standard deviation) by drug group and cumulative dose group

		Baseline	Cumulative dose group 1	2	3	4	5
	n	155	150	92	58	32	3
Drug group 1	MS	29 9±4 3	30.8±4.0	31.2±3 0	30.9±4.7	31 6±2 0	30.6±0 4
	MD	0 4±4.0	−0 3±3 7	−0 4±2 7	−0 4±4 4	−0.3±1.9	−1.0±2.5
	SF	2.7±1.0	2.4±1 0	2 5±1 9	2 4±1.2	2.0±0.5	2 7±0.5
	CLV	−1 4±9.7	−0 6±2 6	−0 6±2 0	−0 8±2 5	−0.4±0 9	−0.8±0.6
	n	53	31	35	19	18	6
Drug group 2	MS	31 5±2 0	30 9±3.3	31.6±2.0	32 5±2 4	30 7±2 9	28 9±1 5
	MD	−0 3±2 1	−1.0±2.9	−0.5±1 9	−1 2±1 7	0.1±1 9	0 3±2 0
	SF	2 6±2 2	2 5±1 0	2 2±0 7	2.4±0.7	2 3±0 6	2.5±0.6
	CLV	−0 3±3 2	1 3±12	−0.7±1.0	−1.0±0 7	−0 5±0 9	−1 0±1 4

dose group 4 continued to show significant change. Testing of the subgroups as divided by average dose revealed no new significant relationships.

An analysis of variance was performed for each of the visual field indices with drug group, cumulative dose group, and average dose group as factors, while allowing for age as a covariate. This also failed to show any consistent relationships between the indices and drug factors. There was, as expected, a significant relationship between sensitivity and age ($p < 0.001$) and a somewhat less expected one between short-term fluctuation and age ($p < 0.001$).

Conclusions

Quantitative description of a multiple phase visual field examination using visual field indices allows for sensitive statistical comparisons of visual fields followed over time. This may be useful in detecting and following conditions other than glaucoma which are characterized by progressive visual field changes. In this study, we were unable to demonstrate any measurable trend in the central retinal sensitivity to white light as tested with quantitative Octopus perimetry in patients on chloroquine or hydroxychloroquine. There may, in fact, be no change in retinal function in the majority of patients on antimalarial therapy, but only in the few patients who go on to develop the typically described 'premaculopathy' or 'maculopathy'. It is also possible that there are changes undetected by testing with white stimuli which would be detected by quantitative testing with red stimuli. Lastly, it is possible that no such changes take place at, or within 3 degrees of, the fovea, though may be measurable in other areas of the visual field.

Further studies addressing these possibilities would help to define the changes in retinal function which take place in patients on antimalarial therapy.

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SPATIAL ADAPTIVE VISUAL FIELD SCREENING
A clinical study

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The authors tested the central 30 degrees field of 161 eyes of 157 persons, 63 of whom were normal and 94 abnormal, with a spatially adaptive screening program and a full threshold program (30-2) on the Humphrey perimeter. The screening test, a special version of the ADT program, was threshold-related and eccentricity compensated, and the locations of its 76 primary points were identical to those of the standard threshold program. In the screening test, resolution was increased from 6 degrees between points to 3 degrees in areas around missed primary points. This was achieved by adding a cluster of secondary points around each missed primary point.

Surprisingly, this spatial enhancement strategy did not improve either the sensitivity or the specificity of the screening test beyond that achieved by considering only primary test points. Eyes in which points had been missed during the screening test often showed depressed differential light sensitivity, defined as a measured threshold level 6 or more dB below the age-corrected normal reference value, in the same area also in the threshold field. This was true not only in abnormal but also in normal eyes. In many instances these areas of low sensitivity were located in the midperiphery where they might have been caused by ptosis or lens-induced artifacts, but they also frequently occurred paracentrally where they could not be explained by such disturbing factors. The number of missed points was usually quite low in normal fields, supporting the conclusion that the observed spatial concordance was not due to chance. Instead, the finding implies that these allegedly normal subjects had persistent shallow depressions in their visual fields. This seems to indicate that not all normal subjects have the same regular and smooth slope of differential light sensitivity, but that even the normal hill of vision may be allowed to show true differences among individuals.

This finding has disturbing implications for the importance of shallow 'confirmed defects' in the diagnosis of disease.

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THE SIGNIFICANCE OF PERIPHERAL SUPRATHRESHOLD MEASUREMENTS IN THE OCTOPUS PROGRAM G1**

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Abstract

The G1 program has become the most frequently used program on the Octopus automated perimeter In a recent study on the peripheral visual field in early glaucoma, we found that 12% of the patients had an abnormal peripheral visual field but a normal central field. Since the G1 program measures 14 peripheral points semiquantitatively, we wanted to know the significance of defects reported at these locations We compared the results of semiquantitatively measured peripheral points in the G1 program with the results of quantitatively measured points at similar locations in a Sargon program (PH). We created a new index NDG1 based on the semiquantitative measurements of the G1 program 77% of the subjects with an abnormal mean defect as measured with the PH program had a normal NDG1 These results show that it is important to measure the peripheral visual field quantitatively in doubtful cases.

Introduction

Program G1[1] has become the most frequently used program on the Octopus automated perimeter. Originally developed for glaucoma, it is now used for a wide range of ophthalmological and neurological diseases.

Program G1 measures 58 test locations within the central 26 degrees quantitatively and 14 test points in the periphery with a two-level test. The strategy of the two-level test is the following: First, a suprathreshold stimulus 6 dB above the age corrected normal value is presented. If this stimulus is seen, this test location is considered as normal. If it is not seen, a stimulus with maximal light intensity (1000 asb) is presented. If this is seen, a relative scotoma is recorded for that location; if it is not seen, an absolute scotoma is recorded.

Due to the nature of this fast strategy, it is very difficult to decide whether a relative or absolute scotoma in the periphery of the G1 is significant or not. This decision is becoming more and more important: first, because program G1 is used for an increasingly wider variety of ophthalmological diseases; and second, because the peripheral visual field seems to be important in detecting early visual field defects in glaucoma. In a recent study of the peripheral visual field in early glaucoma[2], we found that 12% of the glaucoma patients tested had an abnormal peripheral visual field, as measured with quantitative perimetry, and a normal G1 program.

On the other hand, only 1% had an abnormal G1 and a normal periphery. This implies that it is necessary to test the peripheral visual field quantitatively in suspicious patients having ocular hypertension with a normal G1.

Since an additional quantitative program for the peripheral visual field is time consuming and tiring for our patients, some decision criteria for when to order such

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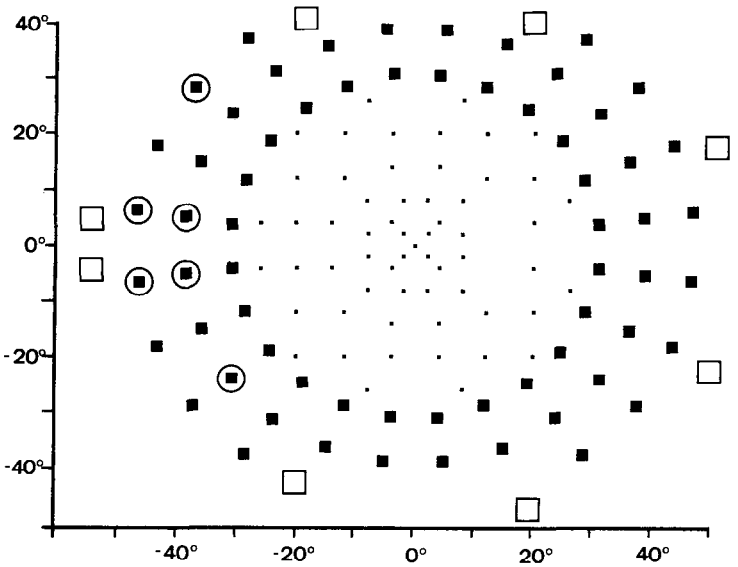
a test must be found. Given that we have 14 semiquantitatively tested peripheral locations in program G1, we would like to know how significant one or more absolute or relative defects are at these locations. With this knowledge, we hope to avoid too many visual field tests.

Material and methods

Sixty normals and 77 patients with either glaucoma or ocular hypertension were tested with program G1[1] and a Sargon program designed for the quantitative testing of the peripheral visual field (PH). All subjects underwent a complete ocular history and ophthalmic assessment including visual acuity (>20/40 to be included), biomicroscopy, measurements of the IOP (<21 mm Hg for normals), and fundoscopic assessment. The glaucoma patients had an early visual field loss as measured with program G1 (MD<10 dB). All tests were carried out in one session using the Octopus 201 automated perimeter.

The peripheral visual field was tested quantitatively with the Sargon program PH. This program consists of 64 points in an even grid distribution from 30-50° horizontally and from 30-40° vertically. Each point is tested twice. With these 64 points we calculated the mean defect (MD_{PH}). In program G1, 14 points in the peripheral visual field are tested semiquantitatively (Fig. 1). We matched six peripheral points of program G1 with six points of program PH at similar locations (Fig. 1). For eight test locations of the G1 program, there was no corresponding



· = quantitatively tested locations of the G1 program.

□ = semiquantitatively tested locations of the G1 program.

■ = quantitatively tested locations of the SARGON program PH.

◉ = test locations which are examined both, semiquantitatively by theG1 program and quantitatively with the PH program.

Fig 1 Distribution of the test locations of the G1 program and the Sargon program PH Test locations are also shown which are examined both semiquantitatively by the G1 program and quantitatively with the PH program.

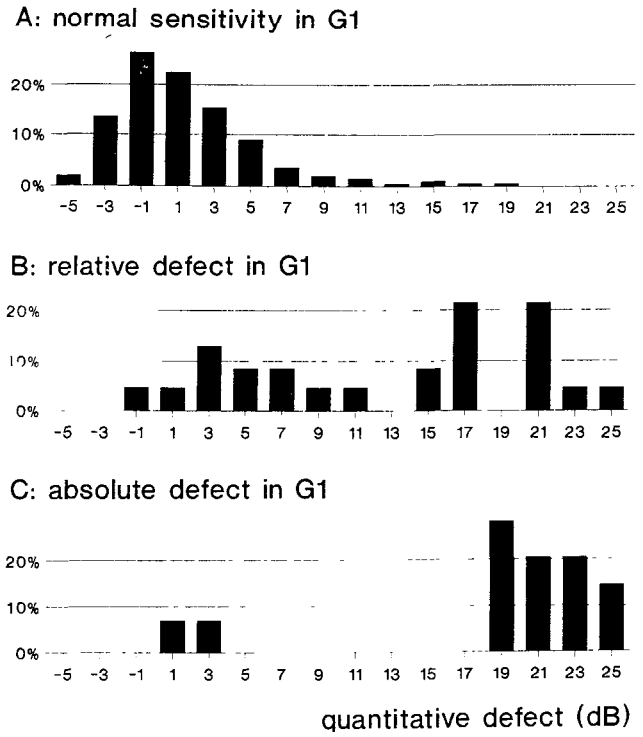


Fig 2 Distribution of quantitative test results (measured with a Sargon program PH) in single test locations for the three possible results (normal, relative defect, absolute defect) in the G1 periphery. There is a better conformity with the results in PH if the result in G1 is normal than if it is relatively or absolutely defect.

location available with program PH, which is why these were not used for comparing the two examination methods.

To be able to compare overall results of programs G1 and PH for the periphery, we created a new simple index (ND_{G1}) by counting the peripheral test locations of G1 with a relative or absolute defect. ND_{G1} = number of peripheral points with a relative defect + twice the number of points with an absolute defect. Since 14 peripheral test points are examined in the G1 program, this index has a possible range of 0 to 28.

Results

The differential light sensitivity of single peripheral test locations has been measured with both program G1 (semiquantitative measurements) and a Sargon program PH (quantitative measurements). The relationships between the semiquantitative and quantitative results are shown in Table 1. Of the 113 tested locations with a defect of 6 dB or more, as found by program PH, only 23% are found to be abnormal in program G1. With the peripheral locations of G1 considered as being normal (785 test points for all patients), 89% of the locations show a defect of less than 6 dB with PH. If there is a relative or absolute defect (37 test locations with program G1), there is a defect of 6 dB or more in 76% of the PH test locations. Those test locations with a relative defect in G1 do not differ from those with an

Table 1 Quantitative and suprathreshold perimetry of peripheral test points

Quantitative	Number of test points	Suprathreshold		
		normal	relative defect	absolute defect
Normal	709	98.7%	1.0%	0.3%
Defect 6-12 dB	61	93.4%	6.6%	–
Defect 12 dB	52	53.8%	23.1%	23.1%

Suprathreshold	Number of test points	Quantitative		
		normal	defect 6-12 dB	defect >12 dB
Normal	785	89 2%	7 3%	3 6%
Relative defect	23	30.4%	14.4%	52.2%
Absolute defect	14	14 3%	–	85.7%

absolute one when examined quantitatively with program PH (*t*-test, $p>10\%$).

Fig. 2 shows the distribution of quantitative test results (measured with PH) for the three possible results in the G1 periphery. There is a better conformity with the PH results if the G1 results are normal than if they are relatively or absolutely defective.

Semiquantitative measurements of program G1 were used to create a new index: ND_{G1} = number of peripheral points with a relative defect + twice the number of points with an absolute defect. There is a good correlation ($r = 0.63$) of ND_{G1} with the mean defect of program PH (MD_{PH} = mean defect of 64 test locations measured quantitatively with Sargon program PH) (Fig.3). From our results of 60 normal subjects, we calculated a 95% percentile of 4 for ND_{G1} and of 1.99 for MD_{PH} (Table 2). 77% of the subjects with an abnormal MD_{PH} (larger than the 95% percentile) had a normal ND_{G1}. Five percent of those with a normal MD_{PH} had an abnormal ND_{G1}, whereas in 71% of all subjects tested, both indices showed the same result (Table 3).

Fig. 4 shows the percentage of subjects with abnormal MD_{PH} for the possible results of ND_{G1}. If one peripheral test location in program G1 is abnormal, 50% of the subjects had an abnormal MD_{PH}. If four peripheral test locations in G1 are abnormal, 80% of the subjects had an abnormal MD_{PH}.

Table 2. Normal values for MD_{PH} and ND_{G1}

	n	Mean	SD	95% percentile
MD_{PH}	60	0 00	1 19	1.99
ND_{G1}	60	0.65	1.47	4.00

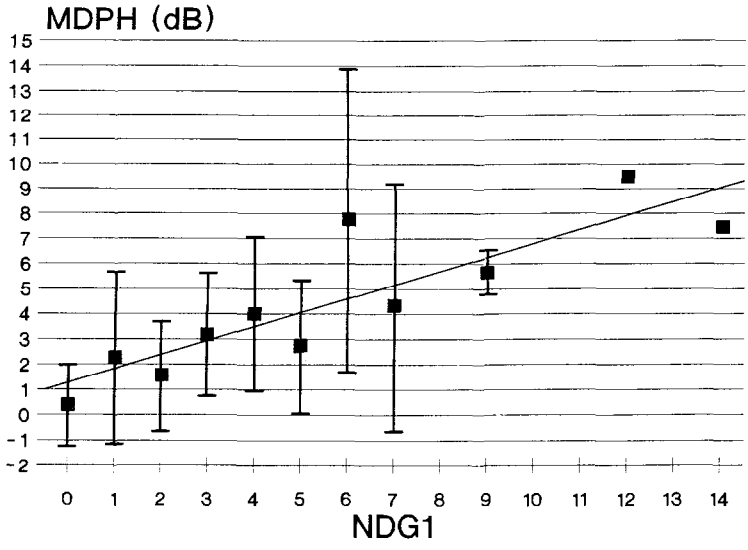


Fig 3 Semiquantitative measurements of program G1 were used to create a new index: ND_{G1} = number of peripheral points with a relative defect + twice the number of points with an absolute defect There is a good correlation of ND_{G1} with the mean defect of program PH (including 64 test locations measured quantitatively). The mean defect ± the standard deviation is plotted as a function of ND_{G1} There was only one patient each with ND_{G1}s of 12 and 14

Table 3. ND_{G1} in subjects with normal and pathological MD_{PH}

	n	Percent of subjects with ND_{G1}=									
		0	1	2	3	4	5	6	7	8	9
Normal MD_{PH}	92	72%	8%	11%	3%	1%	3%	1%	1%	–	–
$MD_{PH\ 2,0-3,9dB}$	19	53%	16%	11%	16%	5%	–	–	–	–	–
MD_{PH}>4 dB	26	8%	15%	12%	15%	12%	8%	12%	4%	–	8%

Discussion

Suprathreshold measurements with the G1 program are valuable in excluding possible damage of the peripheral visual field. Without any defects reported in the G1 periphery, the probability for a normal periphery is greater than 85%. It is difficult, however, to conclude from the suprathreshold measurements that the patient's periphery is abnormal. Patients with an ND_{G1} of between 1 and 7 often have a normal MD_{PH}, but there is also a substantial group among these subjects with a pathological MD_{PH}. Only an ND_{G1} of 7 reliably indicates an abnormal MD_{PH}. We suggest, therefore, that in the clinical use of the G1 program, any defects found in the periphery should be considered as a sign of a possible abnormal sensitivity. Patients with peripheral defects, especially ocular hypertensives and doubtful cases, should undergo an additional quantitative test of the peripheral visual field.

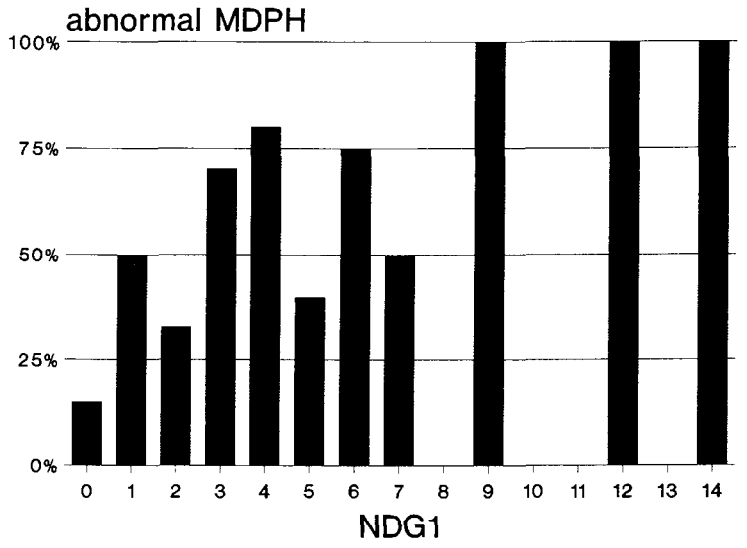


Fig 4 Percentage of subjects with an abnormal MD_{PH} = mean defect of Sargon program PH (quantitative testing) for the possible results of ND_{G1} (= number of peripheral points with a relative defect + twice the number of points with an absolute defect) If one peripheral test location in program G1 is abnormal, 50% of the subjects have an abnormal MD_{PH}

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KRAKEN
A computer simulation procedure for static, kinetic, suprathreshold static and heuristic perimetry**

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Abstract

KRAKEN is a computer simulation model of visual field testing designed to evaluate perimetric test strategies, patient response characteristics and their interactions. It is written in Turbo Pascal for operation on an IBM PC/AT-compatible system with an EGA monitor and Summagraphics digitizing tablet KRAKEN consists of a 'patient' module and a 'perimeter' module The 'patient' is a stochastic system that includes a high resolution visual field sensitivity surface (selected from a database of more than 1000 visual fields of normal individuals and patients with glaucoma, neuro-op disorders or retinal disease) and a variety of response characteristics (reaction time, fluctuation, fatigue, errors, etc.) The 'perimeter' module includes a collection of device characteristics (target presentation pattern, test strategy, decision rules, etc.) that can be adjusted to emulate existing automated visual field procedures, or to provide new custom-designed perimeters and test strategies Manual kinetic and suprathreshold static perimetry can also be performed on the 'patient' by means of the digitizing graphics tablet. The 'patient' and 'perimeter' modules communicate through a software interface designed to emulate the visual field testing process, and a multi-window color graphics display provides on-line information about test parameters, visual field characteristics and sequential progress of the test procedure KRAKEN has been used to evaluate the accuracy, efficiency and reliability of existing test strategies, interactions among test parameters and patient response characteristics, and related topics It is now being used as a development tool for the generation of heuristic test procedures and 'expert systems' for perimetry.

Introduction

Perimetric test procedures, especially those that have been developed for automated visual field testing, have undergone tremendous advances within the past 15 years[1-6]. Although these new test procedures have improved the diagnostic efficacy of automated perimetry, many clinical problems (*e.g*, test time, fatigue, false alarms, misses, fluctuation, fixation losses) still remain. Interpretation of test results, even with the assistance of statistical analysis packages, becomes difficult when the patient's responses depend on many other factors besides the underlying visual field sensitivity.

Clinically, there is no direct method for analyzing all of the factors that contribute to visual field determinations. A patient's 'true' visual field is not known *a priori*, but rather is estimated by the visual field test procedure employed. These procedures are considerably less rigorous than standard psychophysical methods, and are

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therefore especially susceptible to patient errors, variability and related factors. To evaluate the performance characteristics of automated perimetric test strategies, investigators have typically conducted clinical comparison studies, whereby a new procedure and a known standard visual field methodology are evaluated in a selected patient population and a group of normal observers. These types of investigations involve a large amount of time and patient resources, with results often being published after extensive changes have been made to the device or it has been discontinued. In addition, control and specification of many aspects of visual field testing are hard to achieve in a clinical environment. In order to provide a more systematic study of the many components of visual field testing and their interactions, computer simulation provides a viable option to define strengths and weaknesses of various approaches and narrows the scope of eventual clinical studies.

Computer simulation has been a useful tool for studying complex processes. With computer simulation, it is possible to construct a model of a complicated, interactive system, specify the input data, define a set of test conditions, and evaluate the output data and the behavior of the system. Several previous investigations of automated perimetry have successfully used simulation techniques to define optimal parameters for specific devices and test procedures[4-9]. The present study extends this work to provide a broader evaluation of test strategies, patient response characteristics and their interactions through KRAKEN, our perimetry simulation model.

With KRAKEN it is possible to trace the interaction of many test strategies and decision criteria with various visual field properties and patient response attributes. The accuracy, efficiency and other aspects of the perimetry test process can thereby be determined under a variety of clinically relevant test conditions. This paper provides an overview of KRAKEN's features and how they interact.

KRAKEN consists of four major components:(1) the patient module, (2) the perimeter module, (3) the interface module and (4) the report generation module. These components are described in greater detail below.

The patient module

The patient module of KRAKEN includes more than 1000 digitized visual fields of normal observers (350 eyes, 50 in each age group of 5-20, 21-30, 31-40, 41-50, 51-60, 61-70 and over 70), and patients with glaucoma (400 eyes), optic nerve disease (150 eyes), retinal disease (70 eyes) and chiasmal and post-chiasmal disorders (80 eyes). To be included in the database, normal observers were required to have a best-corrected visual acuity of 20/20 OU (20/40 or better for the over 70 age group), IOP of less than 30 mm Hg OU, no history of ocular or neurologic disease or surgery, a normal eye examination, and no medications being taken that are known to affect visual field sensitivity. Patients were included if they had a well-established diagnosis of a single disease entity, no history of other systemic, ocular or neurologic disease, and were not taking medications that are known to significantly affect visual field sensitivity.

In order to have information available for the full peripheral visual field, manual kinetic perimetry test results from the Goldmann perimeter were used to establish the visual field database. Each kinetic visual field examination consisted of at least five isopters, with multiple target luminances used to map out scotomatous areas. Details of our standard kinetic perimetry test procedures have been described elsewhere[10]. The Goldmann visual field plots are then digitized by tracing each isopter and scotoma on a Summagraphics Summasketch Plus (MM1201) graphics tablet attached to an IBM PC/AT-compatible system, where the coordinates are

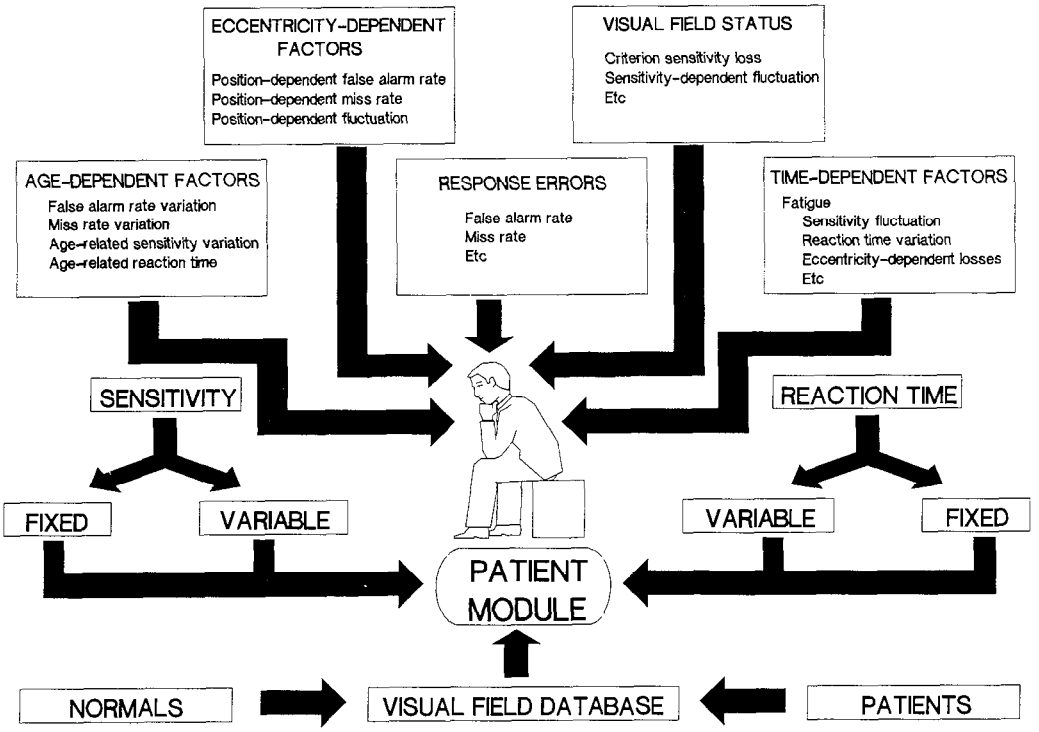

Fig 1 Schematic diagram of the patient module of the KRAKEN simulation program

stored along with relevant patient information. A similar earlier version of this procedure has been described elsewhere[8].

Since the manual kinetic visual fields obtained with the Goldmann perimeter were obtained with various target size-luminance combinations, all data was converted to sensitivity values (in dB). The V/4e target was defined as the stimulus corresponding to 0 dB of sensitivity, and Goldmann's target size-luminance equivalency equation (0.6 log unit change in target area equals a 0.5 log unit change in luminance) was used to convert all data to a common sensitivity metric. A high resolution visual field sensitivity surface was then generated by performing a linear interpolation along radii and meridia in a polar coordinate system. A minor amount of smoothing was performed to minimize digitization artifacts. The final result is a visual field sensitivity surface consisting of 32,400 values, one for each degree of radius and meridian of the visual field out to 90 degrees eccentricity.

These visual fields serve as a baseline for testing by the simulated perimeter. If no other patient response characteristics are specified, similar response patterns will occur each time the test is performed, with minimal differences (within the resolution of the test strategy) between input and output. However, KRAKEN can modify the sensitivity of the patient's visual field and the accompanying response patterns that occur. Erroneous and unexpected results can then be obtained for various test locations, as well as different findings for repeated tests. KRAKEN has a variety of methods by which these patient response variations may occur.

The sensitivity of each point can be made to fluctuate by a specified amount. The distribution of possible values is defined as a gaussian (normal) distribution with

the mean defined by the sensitivity value from a specific test location (provided by the high resolution visual field sensitivity surface) and a predetermined standard deviation (*e.g.*, 2 dB). Since it is possible to test the same visual field locations using a variety of fluctuation values, we can evaluate how the simulated patient's response variation interacts with particular test strategies and decision criteria. The amount of fluctuation can also be varied as a function of the patient's age, visual field eccentricity, and for areas of visual field loss, since previous studies have demonstrated that these factors may influence the magnitude of variation in visual field sensitivity[11-14]. It is also possible to alter the patient's response fluctuation as the test progresses to simulate the effects of fatigue and attention loss[15]. After all of these adjustments have been made to the patient's sensitivity value, it is then compared to the stimulus luminance to generate a yes ('seen') or no ('not seen') response.

Three additional factors which may affect response behavior of the simulated patient are reaction time, false alarms and misses. Many automated perimetry test strategies have a time period within which a valid response will be accepted. Unlike traditional psychophysical test procedures, yes ('seen') responses are determined by the patient, but no ('not seen') can be determined by either the patient or the test procedure (*i.e.*, a yes response occurred too short or too long after the stimulus presentation). The patient's reaction time can thus be an important factor in the stimulus/response relationship. The simulated patient's reaction time can be set to a fixed value or can fluctuate about an average value in a manner similar to that described for sensitivity fluctuation (*i.e.*, sampling from a Poisson distribution). Adjustments for age, stimulus eccentricity, visual field loss and fatigue can be applied to the reaction time value for individual target locations during the test procedure.

Three response outcomes, based on reaction time characteristics, can thus occur for each stimulus presentation: (a) if the patient's reaction time is within the acceptable response limits of the test strategy, a yes or no response will be generated on the basis of the patient's sensitivity and the target luminance; (b) if the patient's reaction is too short or too long, a no response will be generated, irrespective of the patient's sensitivity and the target luminance; (c) if the reaction time is very long, a no response will be generated for the present stimulus, along with a yes response for the next stimulus.

In KRAKEN, false alarms and misses are defined as errors on the part of the simulated patient (inadvertently pressing the response button, forgetting to press the response button, etc.). For this simulation, such errors are considered separately from the frequency of seeing curve; they are discrete events that are not directly related to sensitivity or stimulus intensity. The percentage of trials in which false alarms and misses occur is specified, and a yes (false alarm) or no (miss) response is 'forced' for the proportion of stimulus trials indicated (regardless of stimulus luminance and visual field sensitivity comparisons), according to a random selection process.

The perimeter module

For static and suprathreshold static test procedures, the simulated perimeter can test a predetermined presentation pattern of up to 500 visual field locations selected from 32,400 potential sites (90 degrees of radius by 360 degrees of meridional angle). Kinetic and heuristic test procedures are able to access all 32,000 visual field locations at any time. Several general test procedures (static, suprathreshold static, automated kinetic, manual kinetic, heuristic) are available within the perimeter module of KRAKEN. Various operational parameters of the simulated

perimeter (*e.g.*, initial stimulus luminance values) can also be specified or adjusted.

Testing for most procedures can be performed according to a predefined pattern or a random presentation sequence. The test procedure continues until all target locations have satisfied the test strategy criteria for defining a final response value. Specific criteria vary from one test strategy to another. Special features of particular automated perimeters or techniques (*e.g.*, RMS deviation, checks for false positives and false negatives, repeated testing, etc.) are also included in the simulations of specific devices.

In addition to interacting with the simulated patient, the perimeter module manages a pseudo-clock (for simulated test time). The pseudo-clock is updated as each stimulus presentation is completed, taking into account the duration and interstimulus interval of the targets displayed, the reaction time of the simulated patient, and the response criteria for the simulated perimeter. This not only provides an indication of elapsed time for the test procedure, but also serves as a basis for updating time-dependent variables that are altered by fatigue.

Test strategies

Four major test strategies (static, suprathreshold static, kinetic and heuristic) are available for the simulated perimeter. Static perimetry can be performed using an ascending method of limits or a staircase procedure (the technique used by most of the current automated devices). The staircase procedure has a number of variables that can be individually altered, including initial step size, final step size, number of reversals, starting position of the staircase (start from previous results, start from normal population averages, start from fixed values, etc.). Criteria and procedures that are specific to a particular device (*e.g.*, rechecking 'suspicious' values, multiple testing of points) can also be incorporated.

Suprathreshold static test routines have been divided into three main categories, consisting of a fixed luminance for all test locations ('plateau' profile), a series of steps or zones of test luminances that vary with visual field eccentricity ('terrace' profile), and a continuous linear gradient of luminance that varies with visual field eccentricity ('slope' profile). Each of these options can in turn incorporate rechecking of selected target locations, can incorporate a multi-luminance follow-up test for points that were not initially detected, can check 'suspicious' points, and can perform preliminary threshold determinations at a small sample of points to estimate the slope of the visual field profile for suprathreshold testing.

The kinetic test portion of KRAKEN includes a provision for manual testing (using the Summagraphics digitizing pad) as well as an automated kinetic visual field test procedure. The manual kinetic option allows the operator to use manual kinetic visual field techniques on any of the simulated patients in the visual field database with any preselected values for patient response attributes (fluctuation, reaction time, false alarm rates, etc.). This feature of KRAKEN has value as an instructional tool as well as providing a mechanism for quantitatively studying the test strategies and criteria used by expert perimetrists.

At the present time, automated kinetic test procedures are directed towards the development of optimal test procedures and strategies for rapid evaluation of the peripheral visual field, as described in previous studies[16,17]. Both manual and automated kinetic routines relay heavily on the use of the pseudo-clock, since target position varies as a function of time. Here, the simulation departs slightly from clinical test conditions, since the kinetic test procedure is modeled by a series of very short interval discrete detection events (approximately every 25 milliseconds) rather than as a continuous function. Our preliminary evaluations indicate that this departure of the simulation model produces negligible influences on manual and

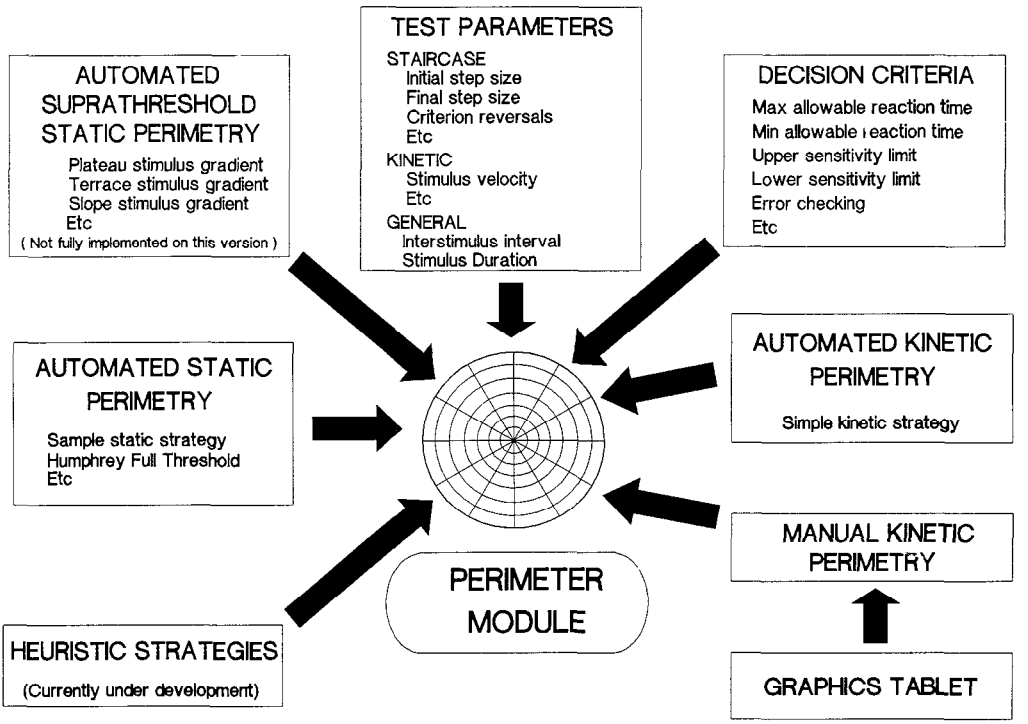

Fig 2 Schematic diagram of the perimeter module of the KRAKEN simulation program

automated kinetic test procedures.

A series of heuristic test procedures for automated perimetry are currently under development using KRAKEN. These strategies incorporate artificial intelligence and expert systems approaches to perimetric testing, and incorporate several key features such as 'real-time' utilization of patient response information as the test is being performed, hypothesis testing about the presence and nature of local visual field characteristics and patient response properties and adaptive test strategies.

Visual display

KRAKEN takes advantage of the IBM-PC EGA graphics capabilities to provide an on-line display of various aspects of the ongoing test process. These include: initial visual field sensitivity levels for target locations to be tested (from the visual field sensitivity database), a dynamic display of tested target locations, final estimated sensitivity values for individual visual field locations, and dynamic parameters for simulated patients (fatigue weightings, etc.) and simulated perimeters (staircase decision rules, etc.).

At any point during the simulated test session, it is possible to step through the procedure one presentation at a time or allow the procedure to continue unabated. The single-stepping is especially useful for studying the dynamics of various heuristic procedures and qualitatively evaluating the interrelationships among various patient response properties and test procedures.

Report generation

The result of each simulated visual field test, as with an actual perimetric examination, consists of estimated threshold sensitivity values for each test location. Since the initial visual field sensitivity values are known for the simulated patient, it is possible to compare actual and estimated values to determine the magnitude and frequency of errors. The number of presentations for each test location and the simulated test time can also be examined. Thus, the accuracy, stability, reproducibility and efficiency of various test strategy-patient characteristic combinations can be quantitatively assessed. The report generation section of KRAKEN provides individual and cumulative test results and related information in a manner that can be efficiently stored, retrieved and analyzed by statistical packages (currently, we are using SYSTAT for the IBM PC).

Discussion

While KRAKEN is not intended as a replacement for clinical trials or psychophysical evaluations of automated perimetry, it can complement such research in several ways. First, the visual field sensitivities and response properties of 'patients' can be specified prior to testing, and can be systematically varied during the test procedure. In clinical trials of perimetry in patient populations, these values can only be assumed or estimated. The efficacy of the clinical evaluation thus depends on the validity of initial assumptions and the accuracy and precision of estimates of response parameters. This factor, combined with the multivariate interactive properties of visual field testing, makes it extremely difficult to determine the influence of a specific patient response variable on a particular test strategy, or to determine how various components of perimetric testing interact with one another in a clinical testing environment. With simulation, the influence of one or more patient response characteristics on one or more test strategy components can be systematically studied.

Another advantage of simulation is that a large variety of test strategy parameters, patient response characteristics and visual field properties can be examined very quickly. A typical clinical evaluation of an automated perimetric test strategy in 150 to 200 eyes requires six to 12 months to complete patient recruitment, clinical testing and analysis of data. These studies are usually performed to define the clinical performance characteristics of the procedure or to determine optimal parameters for routine examinations. By the time this information has been obtained, the manufacturer of the device has often modified the procedure, discontinued the product or gone out of business, making the research findings obsolete. Simulation can help to provide a quick preliminary comparison of the utility of a new procedure in comparison with more traditional approaches. In a previous version of KRAKEN[18], 36 combinations of different patient response characteristics and test procedures were evaluated for 350 normal visual fields (a total of 12,600 visual fields), were tested and analyzed in less than one day. Although computer simulation is not a replacement for clinical trials, it makes it possible to rapidly determine which procedures are least susceptible to patient variability and errors, which are most efficient, and where the flaws exist in specific test strategies. This can provide a more directive, efficient approach to clinical validation studies.

A third advantage of simulation is that it allows more global aspects of perimetry to be addressed. Rather than examining specific attributes of one device, or comparing one device with another, a variety of options and conditions can be extensively explored. One is not bound by the constraints of a particular device. In addition, simulation provides a viable approach to evaluate various theoretical

models upon which automated perimetry test procedures are based. In this manner, the validity and appropriateness of various components of the model can be evaluated, and the significance of violations or deviations of the assumptions of the model can be assessed. This provides a useful method for refining the underlying theoretical development upon which perimetric test strategies and procedures are based.

Computer simulation also makes it possible to evaluate new test strategies and procedures without extensive hardware and software development and implementation. This not only saves a large amount of time and expense, but it also makes it possible to examine several alternative approaches before final decisions about hardware and software designs impose limits on the types of tests that can be performed.

Finally, the manual testing option available in KRAKEN now provides a means of studying the strategies and criteria employed by expert and novice perimetrists. The information derived from these evaluations will help to direct the development of heuristic test procedures that improve the accuracy and efficiency of automated perimetric tests.

KRAKEN will be a valuable tool for distinguishing among various test strategies and developing algorithms that deal more effectively with variability, inconsistency and errors on the part of the patient. Promising approaches can be readily delineated from those which do not appear to be of additional value. This should permit more informative and efficient approaches to the development of automated perimetric test strategies and their subsequent validation through clinical trials.

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INFLUENCE OF ANTIHISTAMINES ON CENTRAL VISUAL FIELD ASSESSMENT

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The study investigated single doses of 10 mg triprolidine (a classical antihistamine) and 10 and 20 mg loratadine (a non-centrally acting antihistamine) on the outcome of clinical perimetry. The sample comprised eight age-matched subjects highly trained in automated perimetry and who also conformed to other rigid inclusion criteria The right eye was investigated with the Humphrey Field Analyser 630 (program 30-2) on four occasions each separated by a wash-out period of at least one week. The global short-term fluctuation was higher than placebo for loratadine 10 mg ($p< 0.05$) and loratadine 20 mg ($p < 0.05$) Alcohol, administered in a weight related amount to produce a blood alcohol concentration of 50-70 mg% one hour after ingestion, and placebo were then investigated to verify the sensitivity of the experimental procedures as a measure for detecting changes in CNS function. Alcohol produced a decrease in sensitivity ($p< 0.01$), increased pattern ($p< 0\ 01$) and corrected pattern standard deviations ($p< 0.05$) and an increased number of stimulus presentations ($p< 0.05$). Finally a single dosage dose response investigation was carried out with terfenadine 60 mg and 120 mg (a non-centrally acting antihistamine). No significant differences compared to placebo were found for any of the indices or reliability parameters.

Introduction

The interpretation of perimetric abnormality depends not only upon the magnitude of the measured sensitivity, but also upon that of the short-term and the long-term fluctuation and that of the catch trials.

Several studies have implicated alcohol in the outcome of automated visual field investigation[1,2]. In contrast, short-term treatment with 5 and 10 mg diazepam has little effect on the differential light threshold recorded with automated perimetry, the short-term fluctuations or the catch trials[3].

The clinical profile of the classical antihistamines demonstrates undesirable central nervous system effects, such as daytime drowsiness and depression, and anticholinergic effects, such as dry mouth. Their influence on clinical perimetry is unknown.

The purpose of the study was to investigate the effect of an antihistamine with known CNS depressant action on the outcome of clinical perimetry and to compare the results with those of a non-centrally acting antihistamine.

Material and methods

Three drugs were chosen for the study: triprolidine - a moderately potent and sedative antihistamine[4], loratadine - a non-sedative antihistamine, and terfenadine - a non-sedative antihistamine[4]. All drugs were H_1-receptor blockers. In addition, alcohol was used as a further control to verify the sensitivity of the experimental procedures in detecting CNS depressant function.

The subjects were high-quality observers selected from a group of volunteers from an undergraduate population following routine clinical examination which additionally included an ECG and blood tests for routine haematology and biochemistry. History of allergy including hay fever was excluded and all medica-

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tion except oral contraception was contraindicated. The final sample comprised eight age-matched females (mean age 20.52 years, SD 0.86 years). Seven of the subjects were emmetropes and the eighth within a maximum power meridian of −2.00 D; all had a visual acuity of equal to or better than 6/5 in each eye, and intraocular pressures of less than 22 mm Hg. Informed consent was obtained from each subject prior to the start of the study.

The experimental procedures were divided into three separate parts. The first comprised a double-blind four-armed treatment involving placebo, loratadine 10 mg and 20 mg, and triprolidine 10 mg administered via a balanced order design. Two-and-a-half hours prior to visual field assessment the subjects ingested the test medication with 100 ml of water, starving after a light breakfast in the morning. On each occasion, the subjects took two capsules containing either 10 mg of loratadine and placebo triprolidine, 20 mg of loratadine and placebo triprolidine, placebo loratadine and 10 mg of triprolidine or placebo loratadine and placebo triprolidine. Each treatment was separated by a wash-out period of at least one week. Each subject underwent visual field assessment at the same time of day during each session.

The second part comprised a simple cross-over design involving placebo and alcohol administered in a weight-related amount to produce a blood alcohol concentration of 50-70 mg% one hour after ingestion. Following both overnight starvation and abstinence from alcohol, subjects ingested within a ten-minute period a dose of either vodka and orange juice or an orange juice diluted with water to the same volume and with vodka wiped around the rim of the glass. Each assessment was separated by a wash-out period of one week. Blood alcohols were measured at 45 minutes and at 90 minutes. Visual field assessment was undertaken on average 75 minutes after ingestion.

The third part comprised a double-blind three-armed treatment dose response study involving placebo, terfenadine 60 mg and terfenadine 120 mg. On each occasion, the subjects took two capsules each comprising either placebo, placebo and terfenadine 60 mg, or terfenadine 60 mg. The remaining methodology was as that for the first two parts of the study.

Central visual field assessment on each occasion was undertaken for the right eye with the Humphrey Field Analyser 630 and Statpac software using Program 30-2 (stimulus size III). Pupil size was measured several times during each perimetric examination with the video monitor of the perimeter and amplitude of accommodation by standard clinical techniques at the end of each session. Operator involvement during each examination was kept to a minimum: subjects were realigned when necessary. Prior to commencement of the study, each subject underwent between three and five training sessions with Program 30-2, each of which were conducted on separate occasions. The data was analyzed in terms of the visual field indices: mean deviation, pattern and corrected pattern standard deviation and short-term fluctuation and in terms of the number of stimulus presentations, false-positive and false-negative responses.

The study was undertaken in conjunction with several other tests of visual and psychomotor performance, including critical flicker fusion and reaction time, which were always administered prior to visual field assessment and with suitable inter-test rest periods; the methods and results of these will be reported elsewhere.

Results

Triprolidine, loratadine 10 and 20 mg and placebo

All treatments produced a reduced mean deviation, *i.e.*, a lowering of sensitivity;

the results, however, did not reach statistical significance with a one-factor repeated measurement ANOVA (Table 1).

The short-term fluctuation was higher than placebo for both loratadine 10 and 20 mg. A one factor repeated measurement ANOVA showed the treatment to be statistically significant ($F = 3.23$; $p < 0.05$); the differences between loratadine and placebo using two-tailed t tests were each significant at the $p < 0.05$ level (Table 1). The short term fluctuation was higher than placebo for triprolidine although this difference was just outside statistical significance.

The pattern standard deviation was higher than placebo for triprolidine and of a similar magnitude to placebo for both concentrations of loratadine. Using a one-factor repeated measurement ANOVA, the results did not reach statistical significance. The corrected pattern standard deviation was lower than placebo for triprolidine, lower for loratadine 10 mg than triprolidine and lower for loratadine 20 mg than loratadine 10 mg. This trend reflects the influence of the short-term fluctuation on the corrected pattern standard deviation: as the magnitude of the short-term fluctuation increases, that of the corrected pattern standard deviation decreases[5] The results did not reach statistical significance, however, using a one factor repeated measurement ANOVA.

Table 1 Group mean visual field indices and reliability parameters as a function of drug One standard error of the mean is given in parenthesis (*indicates a probability of $p<0$ 05)

Visual field index	Treatment			
	Placebo	Triprolidine	Loratadine 10 mg	Loratadine 20 mg
Mean deviation (dB)	−1 87 (0 43)	−2 11 (0.27)	−1 89 (0 48)	−1 79 (0 42)
Short-term fluctuation (dB)	1.07 (0.01)	1 44 (0 18)	1 54 (0.13)*	1 47 (0 14)*
Pattern standard deviation (dB)	2.01 (0.22)	2 23 (0 02)	2 07 (0.21)	1 92 (0.14)
Corrected pattern standard deviation (dB)	1 52 (0.27)	1 26 (0 39)	1.09 (0.38)	0 87 (0.27)
Stimulus presentations	441 6 (9.9)	466.1 (10.3)	454 0 (9 62)	450 0 (10 2)
False-positive responses (%)	3.91 (3 91)	4 13 (2 74)	1 67 (1 13)	2 44 (1 81)
False-negative responses (%)	2 99 (1.52)	4 75 (1 45)	6 41 (2.63)	3 57 (3.57)

The number of stimulus presentations was higher for triprolidine (mean 466.1; SEM 10.4) than placebo (mean 441.6; SEM 9.9) and higher for loratadine 10 mg (mean 454.0; SEM 9.6) and for loratadine 20 mg (mean 450.0; SEM 10.2) than placebo although all results failed to reach statistical significance.

Alcohol and placebo

The group mean blood alcohol concentration at the end of the visual field examination was 66.9 mg% (one standard error of the mean 3.53). Three subjects exhibited a decreasing blood alcohol level compared to the initial measurement at

45 minutes, three an increasing level and two an identical level.

Alcohol produced a greater reduction in the mean deviation, *i.e.*, a lowering of sensitivity, than placebo (two-tailed *t* test $p< 0.01$), an increased pattern standard deviation (two-tailed *t* test $p< 0.01$) and an increased corrected pattern standard deviation (two-tailed *t* test $p< 0.05$). The number of stimulus presentations was also increased by alcohol (two-tailed t test $p< 0.05$). The short-term fluctuation, the rate of false positives, of false negative responses and of fixation losses were all unaffected (Table 2).

Table 2 Group mean visual field indices and reliability parameters as a function of placebo and alcohol One standard error of the mean is given in parenthesis (* indicates a probability of $p < 0.05$ and ** of $p < 0.01$)

Visual field index	Treatment	
	Placebo	Alcohol
Mean deviation (dB)	−1.62 (0.46)	−2 75 (0.56)**
Short-term fluctuation (dB)	1.53 (0 19)	1 52 (0.23)
Pattern standard deviation (dB)	2.09 (0.26)	3.01 (0.47)**
Corrected pattern standard deviation (dB)	1 19 (0 43)	2.31 (0.53)*
Stimulus presentations	454 5 (7 60)	491.4 (15.04)*
False-positive responses (%)	1 13 (1 14)	3.38 (2.42)
False-negative responses (%)	2 35 (1 57)	6.98 (2.58)

Terfenadine 60 mg and 120 mg and placebo

All three treatments produced a reduced mean deviation, *i.e.*, a lowering of sensitivity. Nevertheless, the results for each visual field index and for each reliability parameter (Table 3) all failed to reach statistical significance using one factor repeated measures ANOVA.

Discussion

The data demonstrates that the mean deviation, the short-term fluctuation, the pattern and corrected pattern standard deviations and the number of stimulus presentations can each be influenced by particular drugs. It must be stressed, however, that these findings apply only to the short-term application of the drugs in question and only in relation to young and healthy subjects highly experienced in perimetric observation. Within the limits of the measurement techniques employed, no significant differences were found between either pupil size or amplitude of accommodation.

Surprisingly, the use of an antihistamine with a known CNS depressant action had little effect on the results of clinical perimetry. The mean proportionate increase in the magnitude of the short-term fluctuation was 48.8% for loratadine 10 mg and 34.1% for loratadine 20 mg. The mechanism for these increases is not known.

The mean proportionate decrease in the magnitude of the mean deviation statistic as a result of alcohol was approximately double (94.5%) although there was a large inter-subject variation (SEM 29.18) whilst that for the pattern standard deviation was 41.3% (SEM 9.62). The inter-subject variability in sensitivity increased with

Table 3. Group mean visual field indices and reliability parameters as a function of drug. One standard error of the mean is given in parenthesis

Visual field index	Treatment		
	Placebo	Terfenadine 60 mg	Terfenadine 120 mg
Mean deviation (dB)	−1.36 (0 52)	−1 06 (0.44)	−1.10 (0.67)
Short-term fluctuation (dB)	1.26 (0.09)	1 33 (0 10)	1.09 (0.16)
Pattern standard deviation (dB)	2 10 (0 20)	1.91 (0.15)	1 80 (0 10)
Corrected pattern standard deviation (dB)	1.40 (0 31)	0.97 (0.29)	1.17 (0.22)
Stimulus presentations	446.6 (10.00)	437.7 (9.58)	436 6 (8 27)
False-positive responses (%)	2.08 (2 08)	3.39 (2.53)	5 70 (3 05)
False-negative responses (%)	1.63 (1.07)	1 28 (0 84)	0.78 (0 78)

increase in eccentricity and was greater for alcohol than for placebo. Sensitivity tended to decrease with increase in eccentricity to a greater extent for alcohol than for placebo; *i.e.*, a steepening of the hill of vision as a result of alcohol. The steepening effect was of a similar magnitude for the nasal and temporal meridians but the superior meridian exhibited a greater reduction in sensitivity than the inferior meridian which amounted to a difference of 4 dB at 27° eccentricity (Table 4). The mechanism for this eccentricity effect is unclear. The association of upper lid action with the steepening effect in the periphery of the superior field cannot, however, be ignored. Blood alcohol concentration measured at the end of the visual field examination correlated poorly with both absolute and proportionate index values. The mean proportionate number of stimulus presentations increased by 8.1% (SEM 2.86).

The effect of alcohol on the outcome of the visual field examination in general is equivocal. A decrease in sensitivity with increase in eccentricity from 60° to 90° temporally has been reported[1] using Program 51 of the Octopus perimeter at an increasing BAC of 100 mg/l; statistically significant increases were also found in the number of false-positive and false-negative responses and in the short-term fluctuation. In contrast, a reduction in sensitivity out to an eccentricity of 25° was not found with Program Jo of the Octopus perimeter at a BAC of approximately 0.08%[2]. A statistically significant higher number of false-positive responses was, however, found together with a tendency towards an increase in the number of false-negative responses, the number of stimulus presentations and the short-term fluctuation. The results of the present study may in part be explained by the BAC, by the eccentricities under examination and by the use of trained observers: with alcohol the catch trials and short-term fluctuation remain unaffected indicating good observer reliability thus permitting delineation of the true effect, namely an eccentricity-dependent reduction in sensitivity.

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Table 4. Sensitivity (dB) as a function of eccentricity for alcohol and placebo for the superior and inferior meridians (top) and nasal and temporal meridians (bottom). One standard error of the mean is given in parenthesis. Sensitivity at each eccentricity is represented as the mean of the two immediate stimulus locations 3° either side of the vertical and horizontal, respectively

Treatment	*Eccentricity (°)*									
	Superior								*Inferior*	
	27	*21*	*15*	*9*	*3*	*3*	*9*	*15*	*21*	*27*
Alcohol	18.2 (3.26)	25.1 (0.80)	28.1 (0.62)	30.6 (0.03)	32.7 (0.42)	33.0 (0.63)	30.7 (0.49)	30.0 (0.38)	28.1 (1.01)	25.3 (0.90)
Placebo	22.5 (1.51)	27.9 (0.64)	29.7 (0.53)	31.6 (0.40)	33.2 (0.41)	33.6 (0.33)	31.9 (0.50)	30.4 (0.64)	29.4 (0.75)	27.5 (0.78)
Difference	4.3	2.8	1.6	1.0	0.5	0.6	1.2	0.4	1.3	2.2
Treatment	*Eccentricity (°)*									
	Nasal								*Temporal*	
	27	*21*	*15*	*9*	*3*	*3*	*9*	*15*	*21*	*27*
Alcohol	25.06 (1.13)	28.6 (0.92)	30.9 (0.50)	31.7 (0.53)	32.9 (0.54)	32.9 (0.67)	31.1 (0.56)	–	29.6 (0.85)	29.1 (0.99)
Placebo	26.5 (0.65)	29.6 (0.58)	31.1 (0.62)	32.5 (0.53)	33.1 (0.36)	33.8 (0.35)	32.2 (0.59)	– –	30.2 (0.87)	30.2 (0.72)
Difference	1 4	1.0	0.2	0.8	0.2	0.9	1.1	–	0.6	1.1

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GRAY SCALE DISPLAY OF PERIMETRIC RESULTS
The influence of different interpolation procedures

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The study describes three mathematical ways for the interpolation of perimetric data: linear interpolation, a 'four points' interpolation and a mixed interpolation Using these procedures, the authors tested the gray scale display of various visual fields and found marked differences between the procedures: The 'four points' interpolation gives a smooth but inexact outlining The mixed interpolation is the most exact method and is recommended for scientific use. Linear interpolation is less exact but gives a smoother outlining of scotoma borders. Therefore, it more resembles our knowledge of the morphology of visual fields and is thus the best compromise for clinical use

Introduction

Although interpolated gray scale displays of automated perimetric fields are controversial[1,4], many users look at them first when reading a visual field. There are two main reasons: firstly, the gray scale resembles most the isopter charts of kinetic perimetry; secondly, the gray scale display gives information at first sight.

Nevertheless, the gray scale display is already a form of interpretation. The same field may look very different if it is displayed by different computer perimeters, even if test point pattern and values are nearly the same (Fig. 1). There are four factors which influence the gray scale outlook: (1) printing/display symbols; (2) size and scale of the chart; (3) interpolation procedure; (4) interpolated resolution.

This study intends to examine one of these factors, the interpolation procedure. Since the introduction of interpolation to static perimetry by Fankhauser *et al.*[3], there have been two descriptions of principles: linear interpolation in a rectangular grid[5] and linear interpolation in an irregular grid[2]. We have limited our study to rectangular grids, but tested three different interpolation procedures: linear interpolation, 'four points' interpolation and mixed interpolation.

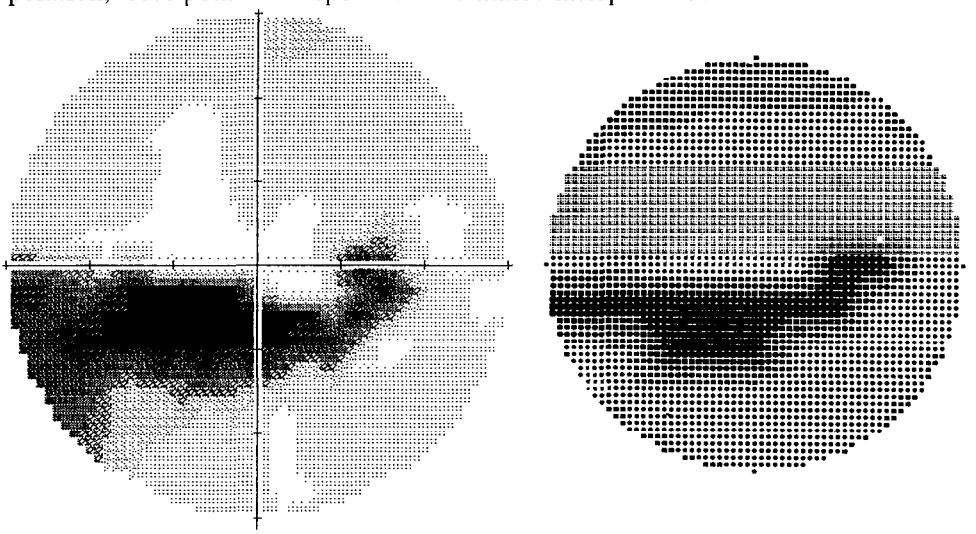

Fig 1 The same visual field recorded and displayed in a gray scale by two different automated perimeters.

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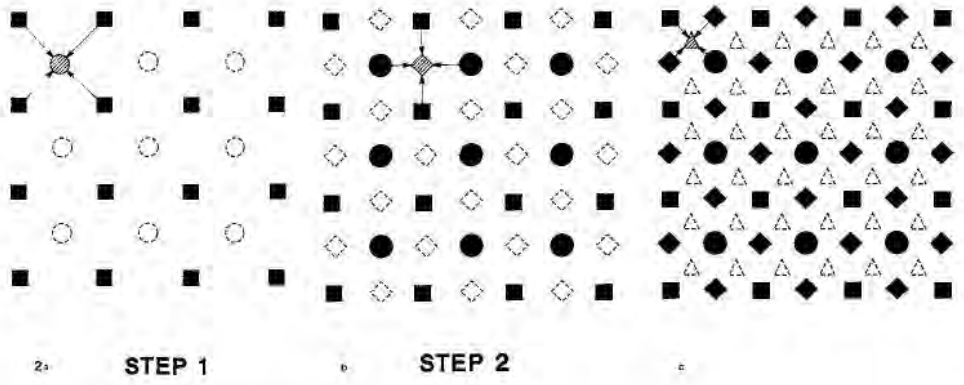


Fig 2 'Four points' interpolation procedure (see text)

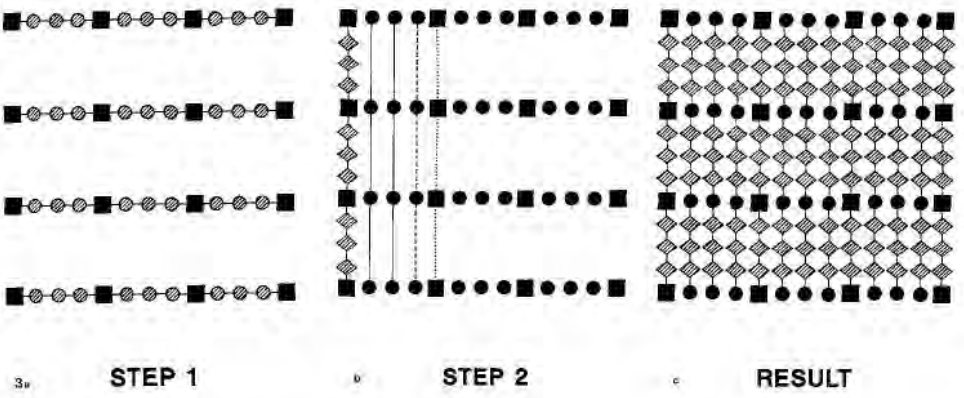


Fig 3 Linear interpolation procedure (see text)

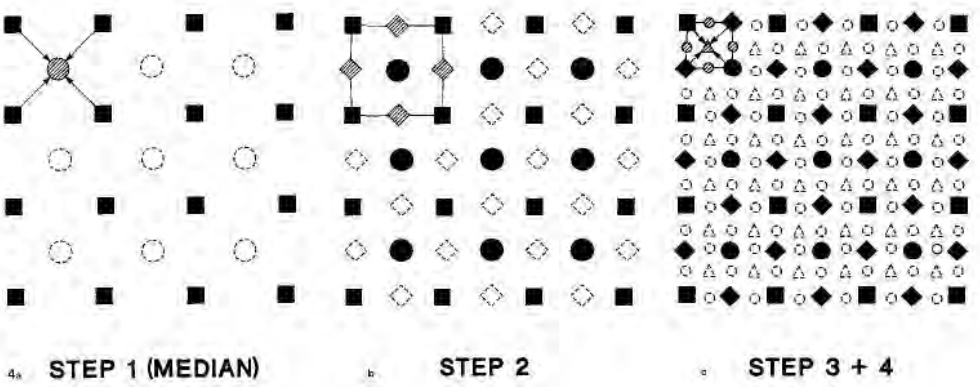


Fig 4 Mixed interpolation procedure (see text)

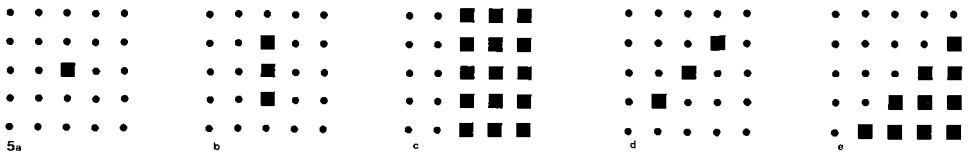
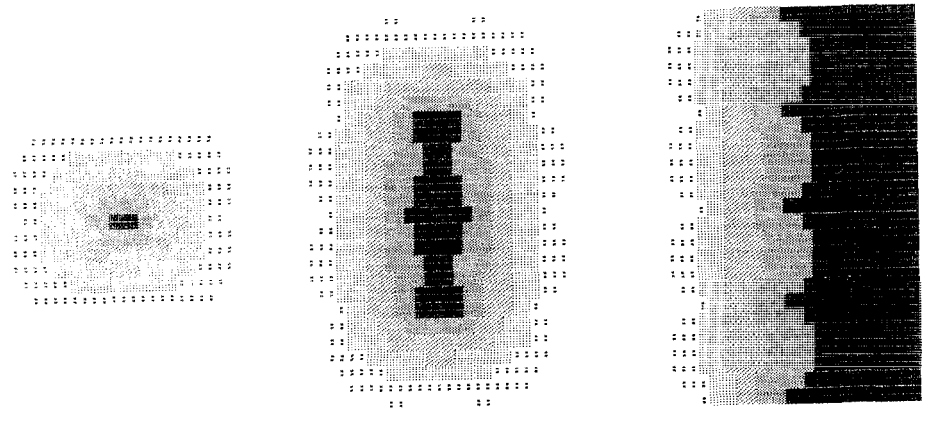


Fig 5 The five artificial visual fields used for the test: a single point; b. vertical line; c vertical border; d. diagonal line; e diagonal border



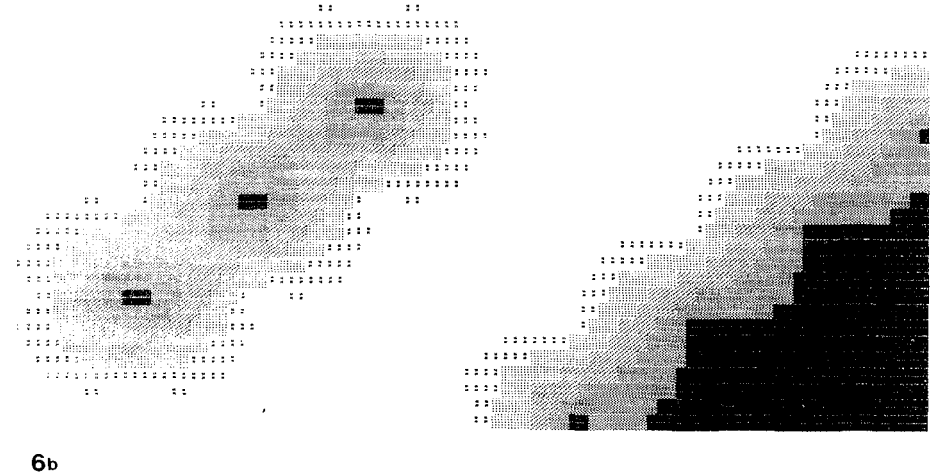


Fig 6 Gray scale results of the five field types using 'four points' interpolation.

Procedures

'Four points' interpolation procedure (Fig. 2): In each square of four measured points, a new center point is interpolated as the mean decibel value of the four corner points. In the following steps, the same is repeated for the smaller squares of measured and interpolated points that result from previous steps.

Linear interpolation procedure (Fig. 3): From each measured point to the next, a mathematical linear interpolation is performed. The values of interpolated points depend on their distance from existing points. In the first step, this procedure is performed in the x-axis direction, in the second step in the y-axis direction. Detailed formulas are given by Weber *et al.*[5].

Mixed interpolation procedure (Fig. 4) In the first step, a 'four points' interpolation takes place, but with a difference: not the mean, but the median of the four points is taken. So, a very high or low value of one point does not influence the result. In the second step, a linear interpolation in both directions is done, but only one point is interpolated. So, at the end of the second step, the grid is again rectangular and the same steps are repeated: step 3 corresponds with step 1, step 4 corresponds with step 2, and so on.

Methods

First, each of the procedures was tested with artificial fields that represented the typical geometric elements of visual field alteration. Five field types were chosen (Fig. 5). Horizontal lines and borders were not added as their interpolation results are similar to vertical lines and borders. The field had a 5x5 point pattern, and the interpolated resolution was eight times higher than the original test pattern (*e.g.*, 1°, if a spacing of 8° would have been assumed). The interpolation and graphic display was made by a computer program specially designed for this purpose.

Second, we implemented the interpolation procedures into a standard perimetric data program to test them on real fields. We used the PERIDAT by Ralph Geiger, a program that transfers visual fields from the Humphrey Field Analyzer to a personal computer, stores them in a database and displays them in various ways. The gray scale results with each of the interpolation methods was compared for several fields.

Results

Testing artificial fields, the 'four points' interpolation (Fig. 6) gives a naturally round shaped single point display. A vertical line is not exactly linear, but the dark area is broader at the measured point and smaller in between. A vertical border is irregular, too. A diagonal line appears like three overlapping single points. A diagonal border is undulated heavily.

The linear interpolation (Fig. 7) also creates a single round point. Vertical line and the vertical border are exactly linear, as they should be. A diagonal line and a diagonal border are not linear, as with the 'four points' interpolation.

The mixed interpolation (Fig. 8) results in a peculiar but mathematically exact rhomboid single point. A vertical line is exactly linear with triangular edges. A vertical border is exactly linear. A diagonal line has linear gray scale borders, but with more intensive gray zones at the measured points. A diagonal border is correctly linear.

The *in vivo* test with real fields showed visible differences in all cases. If the value slope was gentle, the differences were small and not of clinical importance

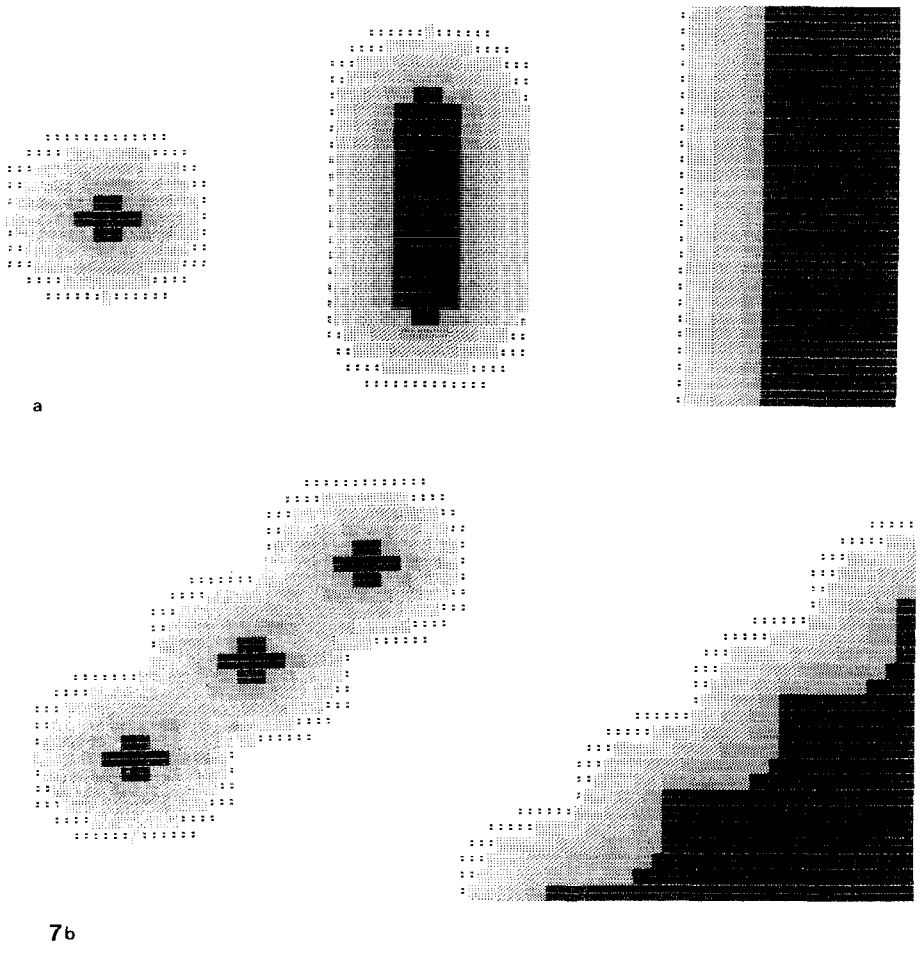


Fig 7 Gray scale results of the five field types using linear interpolation.

(Fig. 9). If the field had small scotomas with steep slopes and even diagonal connections as from the blind spot to a paracentral scotoma (Fig. 10), the differences were striking and may have influenced interpretation. (The different outlining is related to the procedures, because we did not extrapolate and cut the gray field as is usual in standard perimetric programs.)

Discussion

This is the first study comparing three different interpolation procedures. Some additional procedures were tested, but not reported because their display was not satisfactory. The four points interpolation gives a smooth outline of field alterations. The linear interpolation moreover produces realistic linear borders in the x-axis and y-axis direction, but not in diagonal directions. It is the quickest algorithm of all three, with regard to calculation time on the computer. Mixed interpolation is the most realistic procedure, taking the pure information given by the measured points into account. The peculiar outlook of single points, as the blind

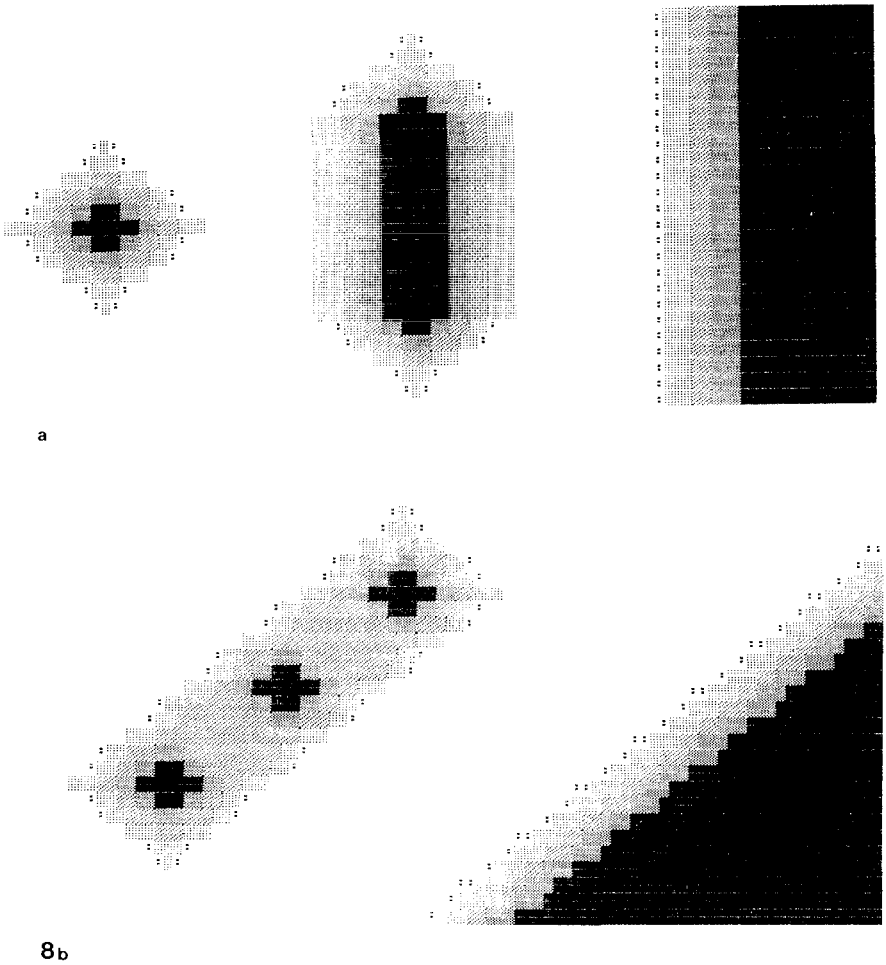


Fig 8 Gray scale results of the five field types using mixed interpolation

spot, is mathematically exact. Nevertheless, rounded shapes are more suited to our knowledge of the morphology of scotomata. Therefore, linear interpolation seems to be the best compromise of exactness and acceptance by the user. If isopters are needed for scientific studies, mixed interpolation is superior.

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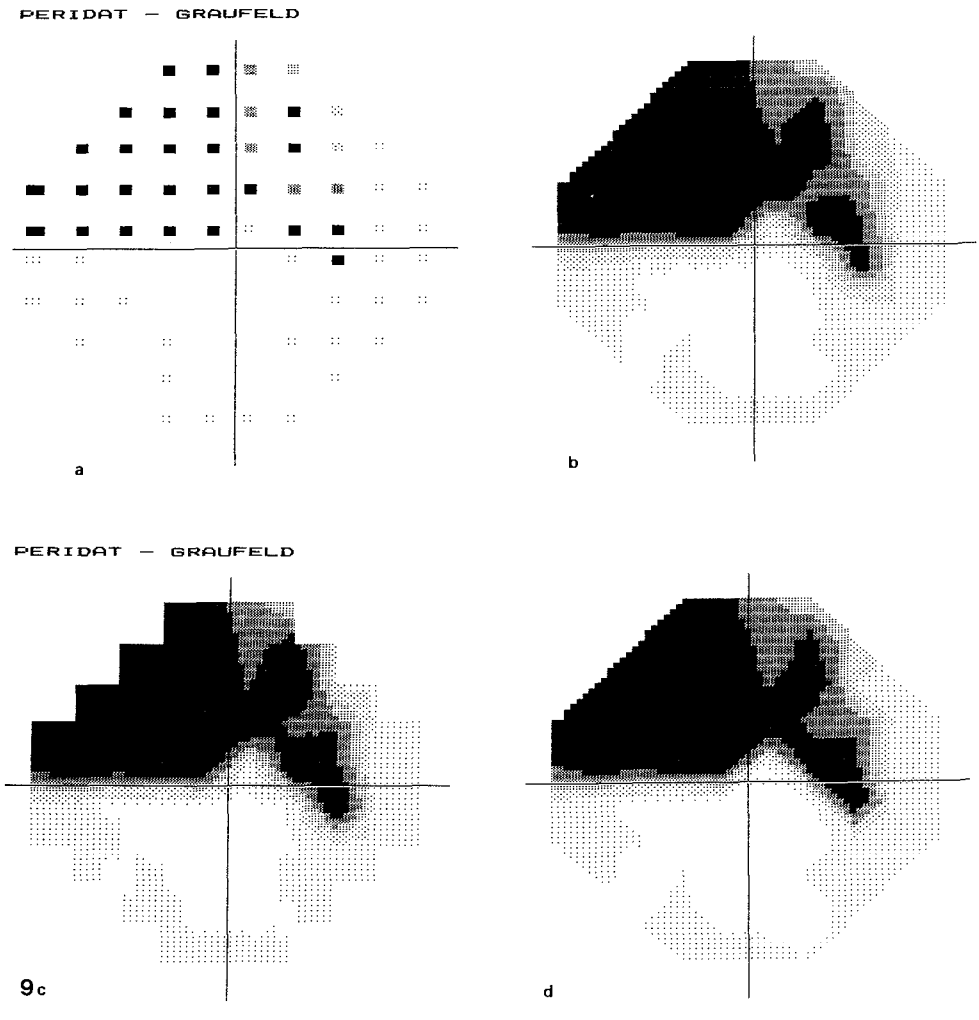

Fig 9 Gray scale example of a field with moderate slopes: a not interpolated; b 'four points' interpolation; c. linear interpolation; d mixed interpolation

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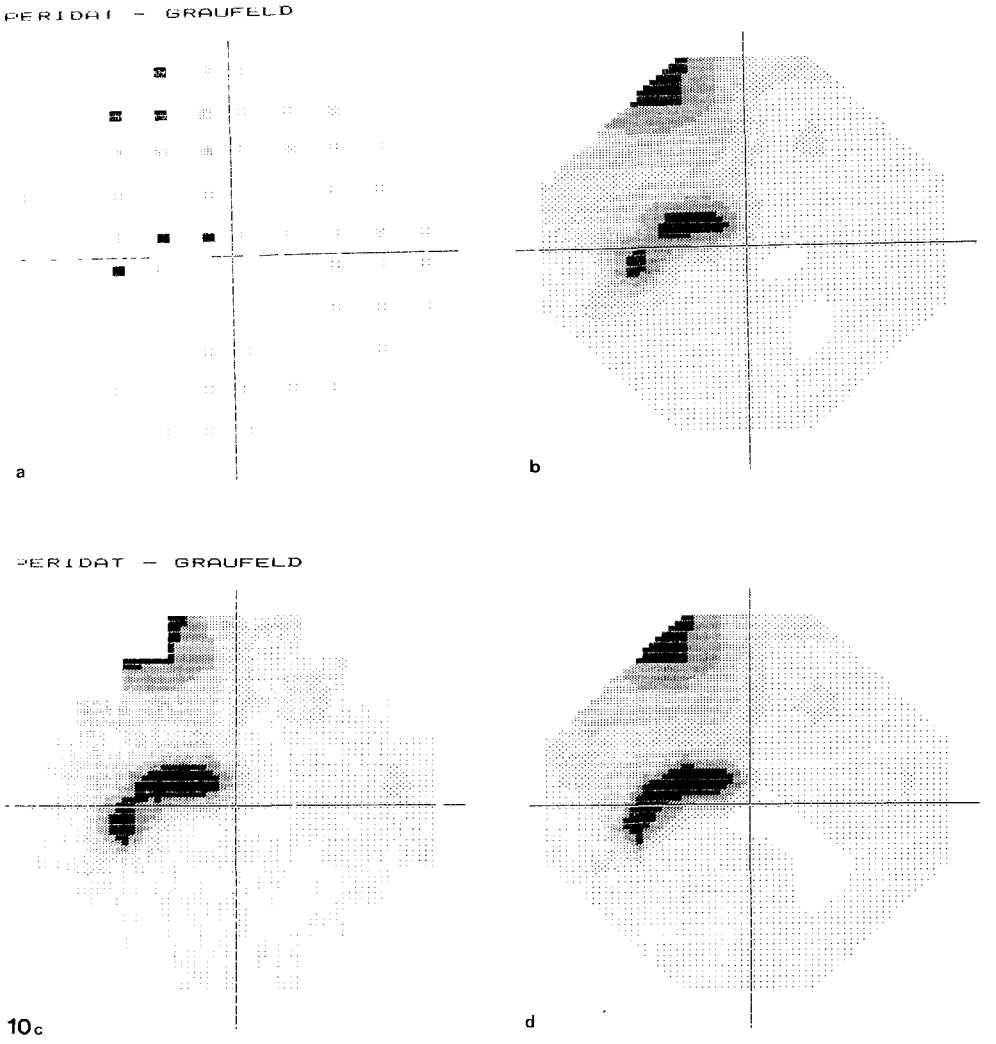

Fig 10 Gray scale example of a field with steep slopes: a not interpolated; b 'four points' interpolation; c linear interpolation; d mixed interpolation

THE RELATIONSHIP BETWEEN THE LENS OPACITY METER 701 READINGS AND THE VISUAL FIELD

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Basel, Switzerland

The patients for this study were selected from inpatients who were awaiting cataract surgery The cataract density was measured in each patient prior to surgery with the Lens Opacity Meter 701, which gave a numerical quantification of the opacity of the lens The visual field of these patients was measured before and after the cataract surgery with the computerized perimeter Octopus 201 using the profile program F_2 along the horizontal axis

The correlation between the Lens Opacity meter 701 readings and the improvement in the postoperative field was significantly high for nuclear and cortical cataracts; posterior subcapsular cataracts did not show a good correlation

Introduction

The influence of the opacity of optic media on the visual field has been studied by many research workers[1-3]. Different methods have been used, either to stimulate a cataract or to quantify the real lens opacity[1,2,5] and to correlate this opacity with the impairment of the visual field.

Quantification of the opacity of the human lens has been performed with different techniques. The stray light scattered back from the cataractous lens has been measured using the Scheimpflug principle integrated with a digital densitometer[5]. More recently, the back light scatter of the normal human lens has been measured and numerically quantified using the Lens Opacity Meter 701[6]. Opacity of optic media as well as glaucoma can induce diffuse visual field defects[8], which is the reason why it is important to identify how much is due to lens opacity and how much to glaucoma[3].

It is our intention to study the influence of cataract on the visual field; for this purpose, we investigate the visual field changes in cataractous patients before and after lens extraction in order to correlate the amount of opacity measured with the OLM 701 and the improvement of the postoperative visual field.

Material and methods

For this study we examined 113 cataractous patients who were awaiting cataract surgery; their ages ranged from 52 to 88 years with a mean of 67±14 years.

The lens opacity was checked one day before surgery, the visual field was checked twice, one day before surgery and six weeks later. Some patients did not return regularly after surgery, so we were able to study 39 cataractous eyes in total.

The lens opacity was quantified with the Opacity Lens Meter 701, which measures the scattered back light of a dark red beam running along the optic axis of the lens.

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The visual field was examined with the profile program F_2 on the Octopus 201 computerized perimeter. The differential light sensitivity profile along the horizontal axis was measured with a double determination in 11 test points, distributed in a range of 20° of eccentricity.

Results

The comparison of the visual field before and after surgery showed that there was a marked influence of the cataract on the mean sensitivity. The pre-operative mean sensitivity in all 39 eyes was 16 dB on average and the postoperative mean sensitivity was 24 dB; we could therefore observe a postoperative mean sensitivity improvement of 8 dB on average. At first the delta mean sensitivity, before and after surgery, did not correlate well with the cataract density, determined with the Opacity Lens Meter 701. The relationship between improvement of the postoperative mean sensitivity and OLM readings did not reveal a definite trend. We therefore selected our cases according to the different types of cataract, *e.g.*, nuclear and cortical and posterior subcapsular cataract. We had 15 nuclear and cortical cataracts and 24 posterior subcapsular cataracts. When considering the posterior subcapsular cataract only, we did not notice a definite correlation between amount of opacity and postoperative sensitivity ($r = 0.28$, $p = 0.1868$). However, in the nuclear and cortical cataract cases, we observed a good correlation between postoperative mean sensitivity and pre-operative Opacity Lens Meter 701 readings ($r = 0.88$, $p = 0.0001$).

Discussion

The Opacity Lens Meter 701 which was used to examine lens opacity gives a quantitative measurement with a numerical scale. The visual field examination before and after surgery showed a considerable influence due to the cataract.

The central 20° horizontal axis of the visual field was explored by using the program F_2 of the Octopus computerized perimeter. The lens opacity value, determined with the OLM 701, did not correlate with the mean sensitivity improvement after surgery in posterior subcapsular cataract cases; at the moment we do not know the reason for this.

However, patients who had a nuclear and cortical cataract showed a strong correlation between opacity values and improvement of sensitivity.

Our study suggests that the Lens Opacity Meter 701 readings can provide a good prediction of the influence of cataract on the visual field in cases of nuclear and cortical cataract.

We are looking forward to correlating the OLM 701 readings with other visual field indices using the G_1 program.

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PERIMETRIC FOLLOW-UP OF SECONDARY CATARACT

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Abstract

The main complication of extracapsular cataract surgery is posterior capsule opacification (secondary cataract) Within two years, in 25% of patients operated on by the extracapsular technique, a posterior capsule discission is necessary Patient follow-up is normally based on periodic examination of the visual acuity In our opinion, this procedure must be associated with more accurate functional tests, with a precise evaluation of the central and paracentral sensitivity A group of 78 patients was examined by automated perimetry every six months for a period of three years after surgery We used the program 30-I of the Humphrey 630 perimeter and a static profile program with the automated Goldmann perimeter 'Perikon', along the horizontal meridian. Eighteen subjects (23%) showed a sensitivity loss after 12 months, and 28 (36%) after three years Twenty-one of these subjects underwent YAG laser capsulotomy, followed in many cases by a restoration of the threshold values. Compared with the visual acuity assessment, perimetry permitted an earlier detection of the presence of a secondary cataract and a more precise identification of cases in which deterioration of the visual function arose from optic nerve or retinal alterations. These results were obtained analyzing the shape of the static profiles and taking into account the behavior of some perimetric indices

Introduction

At present, extracapsular cataract extraction (ECCE), with or without intraocular lens implantation, is by far the most frequent cataract surgery technique. The advantages it offers over traditional intracapsular cataract extraction (ICCE) are well known[1-3], as is its main complication, *i.e.*, secondary cataract formation.

Posterior capsule opacification has been reported to affect nearly 25% of eyes operated on using ECCE. Younger patients are more affected and the frequency of this complication increases with the time elapsed from surgery[1-3].

Clinically, visual acuity determination is the most frequently used method for monitoring the presence and evolution of a secondary cataract. Precise evaluation of central and paracentral retinal sensitivity could offer additional information for quantifying the visual impairment produced by the secondary cataract and the real necessity of laser treatment. In our opinion, perimetry helps to determine whether such visual deterioration is due only to the secondary cataract, or to an associated retinal or optic nerve disorder.

Material and methods

Seventy-eight eyes selected at random from a pool of eyes operated on by the same surgeon, an expert in ECCE, utilizing a mechanically-aided irrigation-aspiration technique followed by a Kratz modified J loop IOL implantation in the ciliary sulcus, were studied.

The average age of the patients (32 males and 46 females) was 67 years (range:

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58-74). No patient showed any other ocular pathology besides cataract. All subjects underwent a complete ophthalmological evaluation, including indirect illumination photography of the posterior capsule and perimetry, every six months for at least three years after surgery.

After a subjective visual acuity measurement, a computerized static perimetric examination was performed by means of the 30-1 threshold program of the Allergan-Humphrey 630 perimeter. Statistical analysis of the results was carried out by means of the STATPAC program, which helps to evaluate visual field normality on the basis of certain perimetric indices (MD: mean deviation; SF: short-term threshold fluctuation; PSD: pattern standard deviation; CPSD: corrected pattern standard deviation)[4]. A second perimetric test was performed using the automatic Goldmann perimeter Perikon[5,6]: *i e.*, a static profile along the horizontal meridian, with threshold determinations every 2 degrees. The program utilized was the *Selected Static Perimetry* performed with target I (0.25 mm^2). The evaluation of the normality of this static profile was made according to the following criteria: absence of localized sensitivity losses greater than 8 dB; mean threshold value in the tested points with a difference, compared to normal data, not exceeding 5 dB.

The eyes suffering from secondary cataract were divided into two groups on the basis of their perimetric damage. The first group included eyes with only damage of a global type: *i.e.*, high MD and normal PSD, SF and CPSD (STATPAC analysis) or global profile depression without localized defects (Perikon).

The second group included eyes in which two or more visual field indices were altered (STATPAC analysis) or in which the static paracentral profile showed localized sensitivity losses greater than 8 dB (Perikon).

The first group was considered as having a 'good functional prognosis', because on the basis of the perimetric results it was predicted that the loss of function was the consequence of the secondary cataract only.

The subjects of the second group were considered as having an 'uncertain function prognosis', because of the high possibility of the presence of retinal or optic nerve pathology.

When a clinically significant secondary cataract was present together with a noticeable visual impairment, a YAG laser capsulotomy was performed and, 30-45 days later, a perimetric examination was done in order to evaluate the functional recovery.

Results

Fifty eyes (64%) showed no significant modification of the perimetric results during the three years of follow-up. None of these eyes showed a clinically significant secondary cataract.

Twenty-eight (36%) had a worsening of the perimetric results which had a high statistical significance according to the STATPAC. In this group, only 21 eyes (27%) showed a clinically significant secondary cataract requiring YAG laser capsulotomy.

The last seven eyes (9%) showed a worsening of the perimetric results in the absence of secondary posterior capsule opacification. In these eyes, the loss of sensitivity was due to cystoid macular edema and/or vascular optic neuropathy.

Among the 21 eyes showing perimetric deterioration and secondary cataract, 15 were included in the group with good functional prognosis.

The final examination, performed four to six weeks after YAG laser capsulotomy, showed a good functional recovery in many eyes ($n = 14$).

The perimetric criteria adopted in order to predict the visual recovery showed good reliability; in fact, 12 eyes included in the group with good functional

Table 1 Results obtained at follow-up

Total no of eyes (= 78)	1st test (6m)	2nd test (12m)	3rd test (18m)	4th test (24m)	5th test (30m)	6th test (36m)	7th test (after YAG-laser capsulotomy)
Eyes without secondary cataract	73	65	63	61	58	57	//
Eyes with secondary cataract	5	13	15	17	20	21	//
Eyes without cataract, with visual field alterations	4	5 •	6	7	7	7	//
Eyes with cataract and visual field global damage (increase of MD alone) = good prognosis	2	9	10	12	14	15	//
Eyes with cataract and visual field irregular damage (SF and/or PSD increased) = poor prognosis	3	4	5	5	6	6	//
Eyes with good recovery after YAG capsulotomy	/	/	/	/	/	/	12 among the eyes with good prognosis and 2 among those with poor prognosis
Eyes with poor recovery after YAG capsulotomy	/	/	/	/	/	/	4 among the eyes with poor prognosis and 3 among those with good prognosis

This table illustrates the frequency of the secondary cataract and of the visual field alterations during follow-up. At the end of follow-up, 21 eyes underwent YAG laser capsulotomy. Visual functio recovery was in good agreement with the prognosis based on perimetric results.

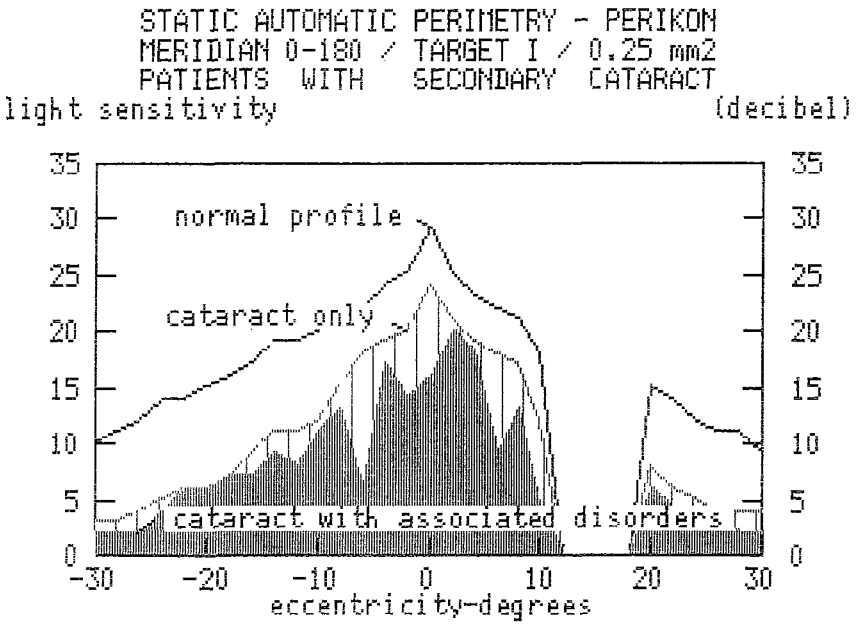

Fig 1 Static profiles of patients with secondary cataract alone and with secondary cataract associated with other pathologies, compared to the normal profile.

prognosis had a complete restoration of visual acuity.

Among the six eyes classified as having a poor prognosis on the basis of perimetric criteria, four showed only slight recovery after laser capsulotomy (visual acuity <0.5).

Table 1 summarizes all results obtained.

Discussion

The advantage of maintaining an anatomical separation between the anterior and posterior segments is the basis for choosing the ECCE technique. The incidence of vitreo-retinal changes has been reported to be lower after ECCE than with ICCE, while it increases to reach the ICCE rate when an early surgical or laser capsulotomy is performed[7-10].

The influence of mild secondary opacification of the posterior capsule on visual acuity is not always easy to quantify. A small fibrous opacity located at the nodal point of the eye is clinically difficult to assess and can be very bothersome to the patient.

Better evaluation of visual function will help discriminate among the different causes of visual loss after ECCE and to improve the rationale for treatment.

MD increase in the absence of significant variations of the other visual field indices was a consistent sign that the visual impairment was the result of the secondary cataract alone and that the YAG laser capsulotomy could restore a good visual function.

Static Goldmann automatic perimetry also showed good sensibility in the assessment of the functional prognosis of eyes affected by secondary cataract.

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RETINAL SENSITIVITY OF THE MACULA WITHIN 6 DEGREES FROM THE FOVEA IN DIABETIC RETINOPATHY

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Abstract

The authors measured quantitative static visual fields from the fovea to an eccentricity of 6° in normal subjects and in patients with diabetic retinopathy, using a fundus photo-perimeter. Patients with diabetic retinopathy had significantly lower sensitivities than the group of normal controls

Introduction

This paper describes the results of an experiment to investigate the distribution of macular retinal sensitivity within 6° of the center in diabetic retinopathy by means of a fundus photo-perimeter[2,3].

Material and method

There were two groups of subjects: (1) Controls, consisting of ten eyes of normal persons (age 50 – 64) with a corrected visual acuity of more than 1.0. (2) Fourteen eyes of patients (age 44 – 63) with stage Ia diabetic retinopathy according to Scott's classification (Group I), and six eyes of patients (age 37 – 59) in stages IIa and IIIa of Scott's classification (Group II).

In Group I, microaneurysms were observed in the periphery of the macula by fluorescein angiography (example in Fig. 1). In Group II, both remarkably increased permeability and occlusion of the retinal vessels were observed (example in Fig. 2). All the cases in Groups I and II were selected from patients with corrected visual acuities of more than 1.0, without intermedial opacities.

The visual field testing was performed with 6.5′ white stimuli at a duration of 0.2 sec and a background of 10 asb, respectively.

Quantitative static perimetry was performed at 25 points, as shown in Table 1.

Results

Fig. 3 shows the average and SD values of the ten eyes of normal control subjects aged 54-60.

When the changes in the retinal sensitivity of the vertical and horizontal visual fields according to the above results were assessed using Student's *t*-test, a significant difference ($p<0.001$) was observed in the circumferences at 4° and 6°. There was no difference in the vertical visual field on the circumference at 2°, nor was any horizontal difference observed at any circumference. A significant difference $p< 0.001$) was seen between retinal sensitivity at the fovea and at 2° around the entire fovea (Table 2).

Table 3 shows the results of comparison of the sensitivity at the various points

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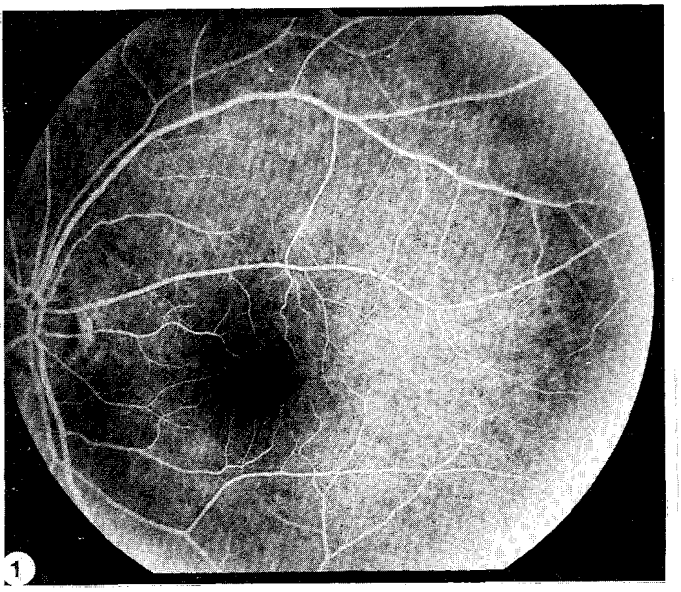

Fig 1 Fluorescein angiography from an eye in Group I

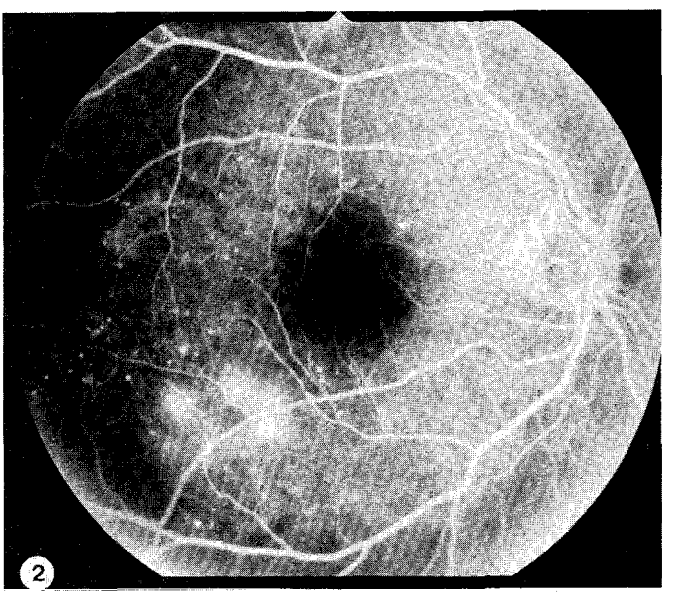

Fig 2 Fluorescein angiography from an eye in Group II

Table 1 Examination condition

1 Target	: White, 6 5 min Maximum luminance 1000 asb
2. Duration	: 0 2 sec
3. Background luminance	: 10 asb
4 Points measured by static perimetry	:

Fovea

2° from the fovea at 45°, 90°, 135°, 225°, 270°, 315° meridians

.4° from the fovea at 15°, 45°, 90°, 135°, 165°, 195°, 225°, 270°, 315°, 345° meridians

6° from the fovea at 15°, 45°, 135°, 165°, 195°, 225°, 315°, 345° meridians

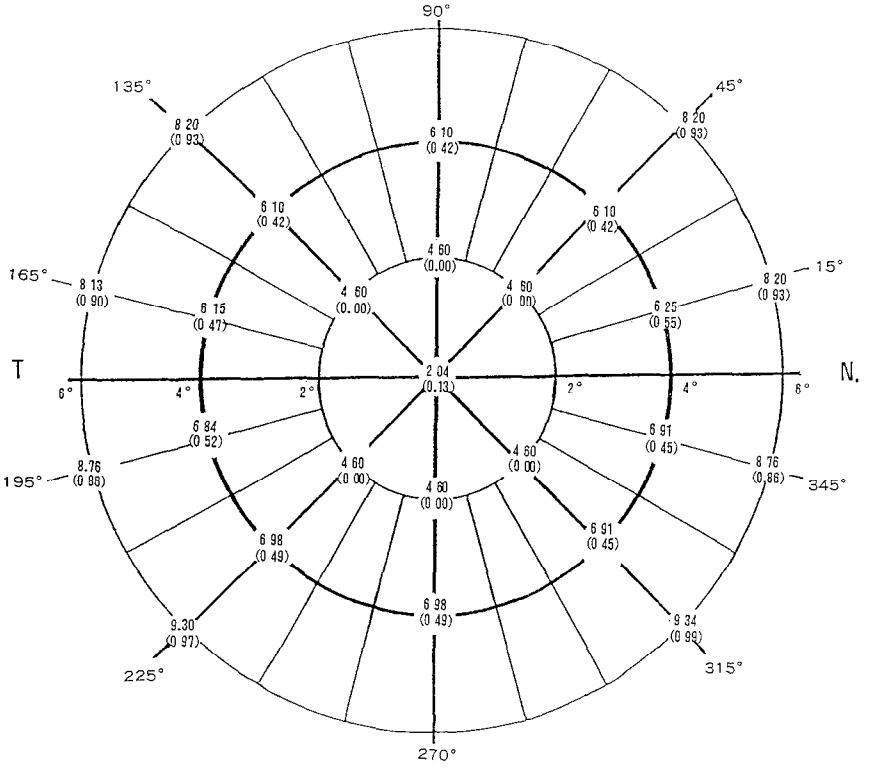

Fig 3 Averages of ten eyes of normal control subjects (SDs in parenthesis)

Table 2 Results of *t*-test, normal subjects, aged 50-64

	$\bar{x}$	SD	$\bar{x}$	SD	P
Fovea and 2°× 360°	2.04	0.13	4.60	0.00	P<0.001
Upper 2° and lower 2°	4.60	0.00	4.60	0.00	N.S.
Upper 4° and lower 4°	6.14	0.45	6.92	0.46	P<0.001
Upper 6° and lower 6°	8.18	0.89	9.04	0.93	P<0.001
Upper 2°+4°+6°and lower 2°+4°+6°	6.45	1.50	7.05	1.80	P<0.001
Right 2° and left 2°	4.60	0.00	4.60	0.00	N.S.
Right 4° and left 4°	6.54	0.59	6.52	0.61	N.S.
Right 6° and left 6°	8.63	1.01	8.60	1.00	N.S.

Table 3 Results of *t*-test comparison in diabetic Group I, Group II and normal 50-64 year-old subject

Diabetic Group I, Group II and normal subjects	Group I		Group II		Normal		Group I vs Normal	Group II vs Normal	Group I vs Group II
	$\bar{x}$	SD	$\bar{x}$	SD	$\bar{x}$	SD	P	P	P
Fovea	3.55	1.31	7.90	3.93	2.04	0.13	P<0.01	P<0.001	P<0.01
2°× 360°	5.82	1.81	15.93	9.49	4.60	0.00	P<0.001	P<0.001	P<0.001
4°× 360°	8.99	4.26	24.97	11.07	6.53	0.60	P<0.001	P<0.001	P<0.001
6°× 360°	12.50	6.30	43.06	16.95	8.61	1.00	P<0.001	P<0.001	P<0.001
Upper 2°	5.75	1.85	15.31	10.97	4.60	0.00	P<0.01	P<0.001	P<0.001
Lower 2°	5.89	1.80	16.54	8.02	4.60	0.00	P<0.001	P<0.001	P<0.001
Right 2°	5.95	1.91	14.64	8.33	4.60	0.00	P<0.01	P<0.001	P<0.001
Left 2°	5.75	1.69	15.83	9.24	4.60	0.00	P<0.01	P<0.001	P<0.001
Upper 4°	8.07	3.24	22.30	9.53	6.14	0.45	P<0.001	P<0.001	P<0.001
Lower 4°	9.91	4.94	27.64	11.99	6.92	0.46	P<0.001	P<0.001	P<0.001
Right 4°	8.91	4.05	24.33	10.62	6.54	0.59	P<0.001	P<0.001	P<0.001
Left 4°	9.13	4.74	25.33	12.04	6.52	0.61	P<0.001	P<0.001	P<0.001
Upper 6°	11.61	5.46	39.96	17.95	8.18	0.89	P<0.001	P<0.001	P<0.001
Lower 6°	13.39	6.97	46.17	15.64	9.04	0.93	P<0.001	P<0.001	P<0.001
Right 6°	12.50	6.18	43.33	18.53	8.63	1.01	P<0.001	P<0.001	P<0.001
Left 6°	12.49	6.47	42.79	15.60	8.60	1.00	P<0.001	P<0.001	P<0.001

in Groups I and II of diabetic retinopathy and in the normal subjects. At all points, there was a statistically significant difference between the values for each group.

Discussion

A statistically significant decrease in sensitivity was observed in Group I points, as compared with normal subjects.

Furthermore, a remarkable decrease in sensitivity was observed in the Group II diabetic retinopathy eyes, not only in comparison with normal eyes but also in

comparison with Group I eyes.

The significant difference between Group I and normal control eyes may be related to the fact that diabetic retinopathy causes hypertrophy of the basal membrane of the retinal blood vessels and metabolic disturbance in the glial cells in its periphery[1].

In conclusion, static perimetric investigation of the macular retinal sensitivity to an eccentricity of 6° in diabetic retinopathy using a fundus photo-perimeter, clearly demonstrated progressive decrease in macular retinal sensitivity due to diabetic retinopathy.

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READING SENTENCES WITH ARTIFICIALLY NARROWED VISUAL FIELDS
Clinical applications

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Abstract

It is qualitatively known that when visual fields become narrow, visual function deteriorates for various tasks such as reading sentences and perceiving patterns It is therefore important to quantitatively assess these abilities in patients with narrowed visual fields

In the first part of the present study, deterioration was quantitatively investigated in a task in which normal subjects read a Japanese sentence with their visual fields artificially narrowed The text was preceded by an illustration whose content was correlated with the sentence The picture was used to facilitate reading of the text A relationship between the size of the artificial visual field and reading speed was obtained

In the second part of the study, reading speed for the same stimuli was measured for patients shown to have narrowed visual fields Reading speed was transformed into functional visual field size using the relationship established for the normal subjects A method to estimate functional field size from the Goldmann perimeter charts was also developed A correlation coefficient of 0 5 was obtained between the two measures

1. Introduction

It has been shown that the ability to read sentences, and to perceive pictures, deteriorates in normal subjects when their visual fields are artificially narrowed. Reading speed of sentences, and the time required for understanding pictures, becomes much longer[1,2]. It has also been shown that in glaucoma patients, whose visual fields are narrowed, a similar deterioration takes place. The importance of assessing visual fields in terms of their capacity to affect the ability to read sentences has been pointed out[3-5]. The term, functional visual field, is introduced to characterize this ability.

In previous research[4,5], stimuli presented to patients were large hiragana letters. Patients were asked to read only one such letter at a time. Reading speed was determined and transformed into a measure of the functional visual field size.

If we are to assess patients' ability in their daily work, it is more realistic to use stimuli made up of sentences rather than stimuli composed of just one letter. In the present study, we employ stimuli in the form of entire sentences. We measure the speed of perceiving this stimulus and transform it into the functional visual field size by using reading speed and the functional visual field size relationship established in normal subjects whose visual fields have been artificially narrowed.

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2. Experiment I: Reading speed in normal subjects with artificially narrowed visual fields

2 1 Principle and apparatus

The method used to artificially narrow the visual field of normals is shown in Fig. 1. A picture on a TV monitor is masked so that only the part of it inside a square can be seen by the subject. When the subject's eyes move over the screen, the movements are detected by a position sensor placed in front of the left eye. The position of the square is controlled so that its center precisely coincides with the visual axis of the subject. In this way the visual field is effectively narrowed down to the size of a square whose side is S in length (see Fig. 1).

The stimuli presented to the subject consist of two parts: picture and text. The latter describes the former. For example, if the picture is the one shown in Fig. 1, the text will be 'a mountain with a vent through which lava, steam, ashes, etc., are expelled either continuously or at irregular intervals'. The text is written in Japanese. In the experiment the picture is presented for only one second and the text follows a dark interval of one second. The subject is asked to read the text silently the moment it appears and when finished, to press a button, which makes the text disappear. Reading time, T, is measured. Stimuli are monocularly observed with the right eye only.

Predictably, reading time will be prolonged under two conditions, firstly when the visual field is narrowed, secondly when there is no picture presented beforehand.

The pictures are drawn in black lines and included in a square of the size 8 x 8 degrees arc of visual angle. The text consists of a single three-line sentence written horizontally. Each line has 13 letters, either of hiragana or kanji characters. The last line may have less than 13 letters, depending upon the content of the sentence.

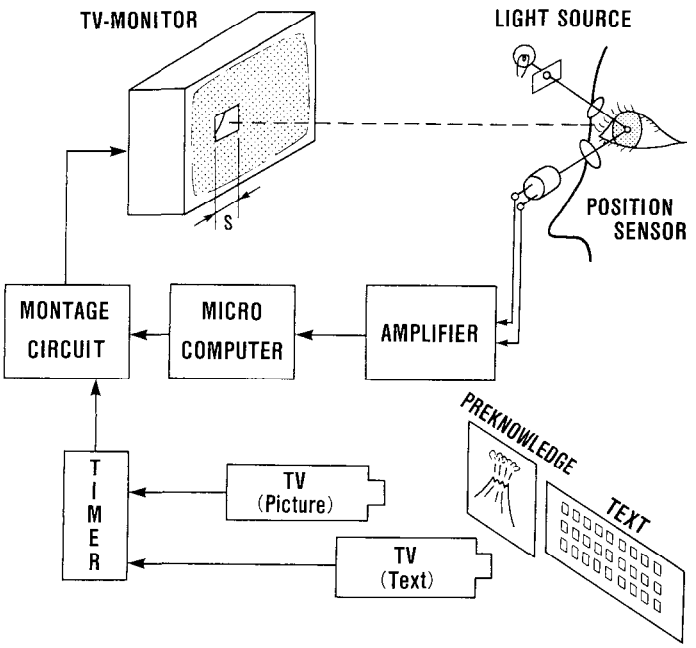

Fig 1 Scheme of apparatus

Each line extends 13 degrees and each letter a little less than one degree. The vertical separation between two lines is approximately one degree. Forty pairs of stimuli were prepared. Each was observed only once by each subject. To measure the effect introduced by pre-exposing the subjects to pictures, stimuli that consisted only of text were also prepared and presented. For the latter only one TV camera was used to present text.

Four male students served as subjects. At the beginning of every experimental session, the subject's eye was precisely positioned so that his eye and the mask on the TV monitor moved synchronously. The subject used a dental impression to fix his head position.

2.2. Results

The reading speed (1/T) is plotted as a function of visual field size S in Fig. 2. Each point represents an average of 40 observations from each of the four subjects. The closed circles are for text reading only (without the pre-exposure to the pictures). When visual field size is plotted in logarithmic units, it is quite clear that reading speed increases linearly with visual field size. This result confirms our previous work[4,5]. When a content-related picture is presented to the subject for one second, reading speed increases (open circles). Subjects can therefore read text faster when given some hints about the text's content by viewing related pictures. The effect of this pre-knowledge on the reading speed becomes greater as the visual field size increases. This was to be expected from our previous work. Thus the effect of visual field size upon reading speed is enhanced by introduction of pre-knowledge. This enhancement is indicated by the difference between the two vertical arrows.

The solid curve of Fig. 2 is the visual field size vs reading speed function. It will be used to evaluate the functional visual field size of patients whose visual field is narrowed.

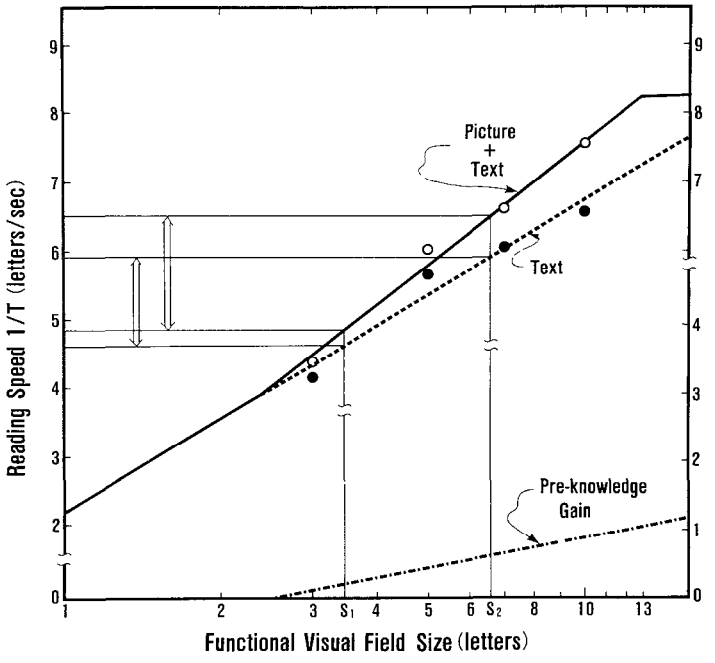

Fig 2 Reading speed of text alone (closed circles) and text with picture (open circles) plotted as a function of the visual field size (artificially narrowed in normal subjects)

3. Experiment II: Reading speed of patients and their visual fields

3.1. Principle and apparatus

It is expected that the reading speed of text will be slower in patients with narrowed visual field, and that when reading speed is measured, we can transform it into the functional visual field by using the visual field size and the reading speed function obtained above.

An apparatus with two slide projectors was set up at a clinic to measure patients' reading speed. Forty stimuli were prepared, each composed of two parts, *i.e.*, a picture and corresponding text. These were the same as those used for the normal subjects in Experiment I. One projector imaged a picture on a rear-screen for one second. The other imaged the text on the same screen after a one-second dark interval. For binocular patients a randomized schedule of test eye changes of 5, 8, 10 or 20 times per session was requested by the investigator. The patient was free to move his or her head, but only in a lateral direction.

The size of the pictures presented was about 60 cm in width and that of the text was 104 cm along one horizontal line. Patients observed the stimuli at a distance of 1 m, seated in a chair. Therefore, the pictures were about 35 degrees arc of visual angle and the text about 55 degrees. The patient was provided with a button that he or she pressed when the text reading was completed. Reading time was measured with a digital timer.

3.2. Patients

Twenty-four patients, 18 males and six females, with ages ranging from 18 to 62, participated in the experiment. Nineteen patients (36 eyes) were diagnosed glaucoma; one patient (two eyes) was diagnosed pigmentary retinal dystrophy; four patients (five eyes) were diagnosed otherwise. All eyes tested had some visual field defect. Sixteen normal subjects also participated in the study. Visual acuity varied from 0.2 to 1.5, but patients had no difficulty in reading the stimulus letters when they observed these from a distance of 1 m. The visual fields of patients were measured with a Goldmann projection perimeter after the text reading test was completed.

3 3 Results

Reading speed varied greatly among patients, covering a range of 1.2 letters/sec to 12.4 letters/sec. Normal subjects showed a range of 6.8 to 17.2 letters/sec with an average of 10.5 letters/sec. Some patients reported that the text was easier to read with the pre-presented pictures, and harder to read when no pictures were presented beforehand.

Reading speeds were transformed into functional visual field size using the solid curve given in Fig. 2. These are plotted as the independent variable along the abscissa of Fig. 3. (Only a total of 43 points are plotted since it was possible to measure reading speed for only one eye of five patients.) When expressed as the number of letters, the functional visual field size varied, as seen in Fig. 3, from 0.6 to 13. A width limit of 13 letters was set in spite of obtained reading speeds greater than 8.2 letters/sec. This caused data points to condense at the functional visual field size of 13 letters. The large variation of estimated functional visual field sizes suggests the validity of the present method used to assess the reading ability of patients with narrowed visual fields.

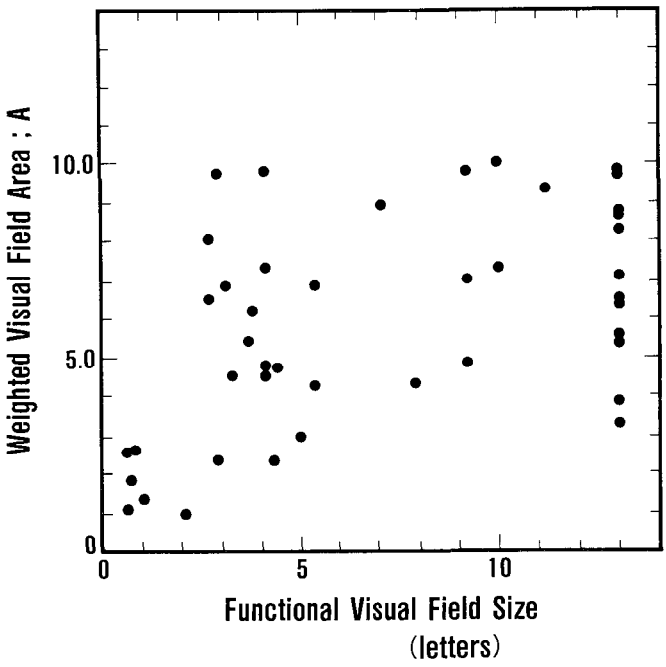

Fig 3 Weighted visual field area based on Goldmann's perimetric measurement plotted against the functional visual field size obtained from the reading speed of text Based on results from 24 patients

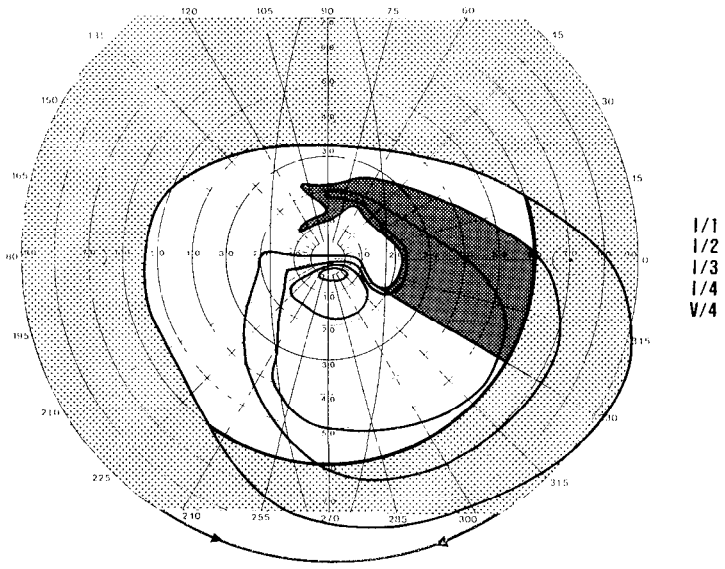

Fig 4 Scheme showing calculation of the weighted visual field area

4. Discussion

Although the patients' capacity to read sentences can be assessed by the above technique, it would be more useful if we could estimate functional visual field size from visual fields obtained with the Goldmann perimeter. The latter is a routine test used in Japan on patients with glaucoma. Accordingly, we measured the areas of visual fields of V/4, I/4, I/3, I/2, and I/1 from the patients' Goldmann charts and calculated the correlation coefficient between our estimates of functional visual field size from the Goldmann charts and the visual field size determined by the method described below.

In measuring the area, a cut-off method was utilized as proposed in our previous paper[5]. We had shown in that paper that if a part of the visual field is separated from the fovea by a scotoma it does not contribute to the perception of patterns, such as sentences and pictures. We proposed that the part may be disregarded for the purposes of assessing the capacity of the visual field for the work of pattern perception. The scheme is shown in Fig. 4 where the part disregarded is indicated by a shaded area. In the present analysis, a similar cut-off operation was also employed for the visual field segments outside of 60 degrees in radius. This region is also considered not to contribute to pattern perception.

A significant correlation was not obtained when each area was independently related to the functional visual field size. We, therefore, sought a function in which all five areas were included. Each area was modified by dividing it into five sections according to the eccentricities 5, 10, 20, 30, and 60 degrees from the fovea. These sections were then weighted by constants l_i, i denoting eccentricities, before being summed up to derive the modified area. The area beyond 60 degrees is disregarded because we can assume that it too does not contribute significantly to sentence reading. The modified areas are further weighted by constants k_j, where j varies from 1 to 5 and denotes V/4, I/4, and so on. The final form of the function is written as

$$A = \sum_{j}\sum_{i} k_j l_i A_{ij}$$

where A^{23}, for example, represents the area covering from 5 degrees to 10 degrees, in the area obtained from the I/3 condition. Constants were sought to get the highest correlation coefficients and the weighted area A was calculated for each patient. The result is plotted in Fig. 3.

The graph indicates that the increase of the weighted visual field area A is correlated to some extent with the increase of the functional visual field size.

While the results indicate the possibility that the functional visual field size can be derived from Goldmann perimetric measurement, the correlation coefficient 0.50 indicates a risk that some patients having good reading ability might be assessed as poor readers if we evaluate them solely from their Goldmann measurement. These patients are those indicated by data points located in the lower right section of Fig. 3.

Acknowledgement

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